2. podiplomski seminar

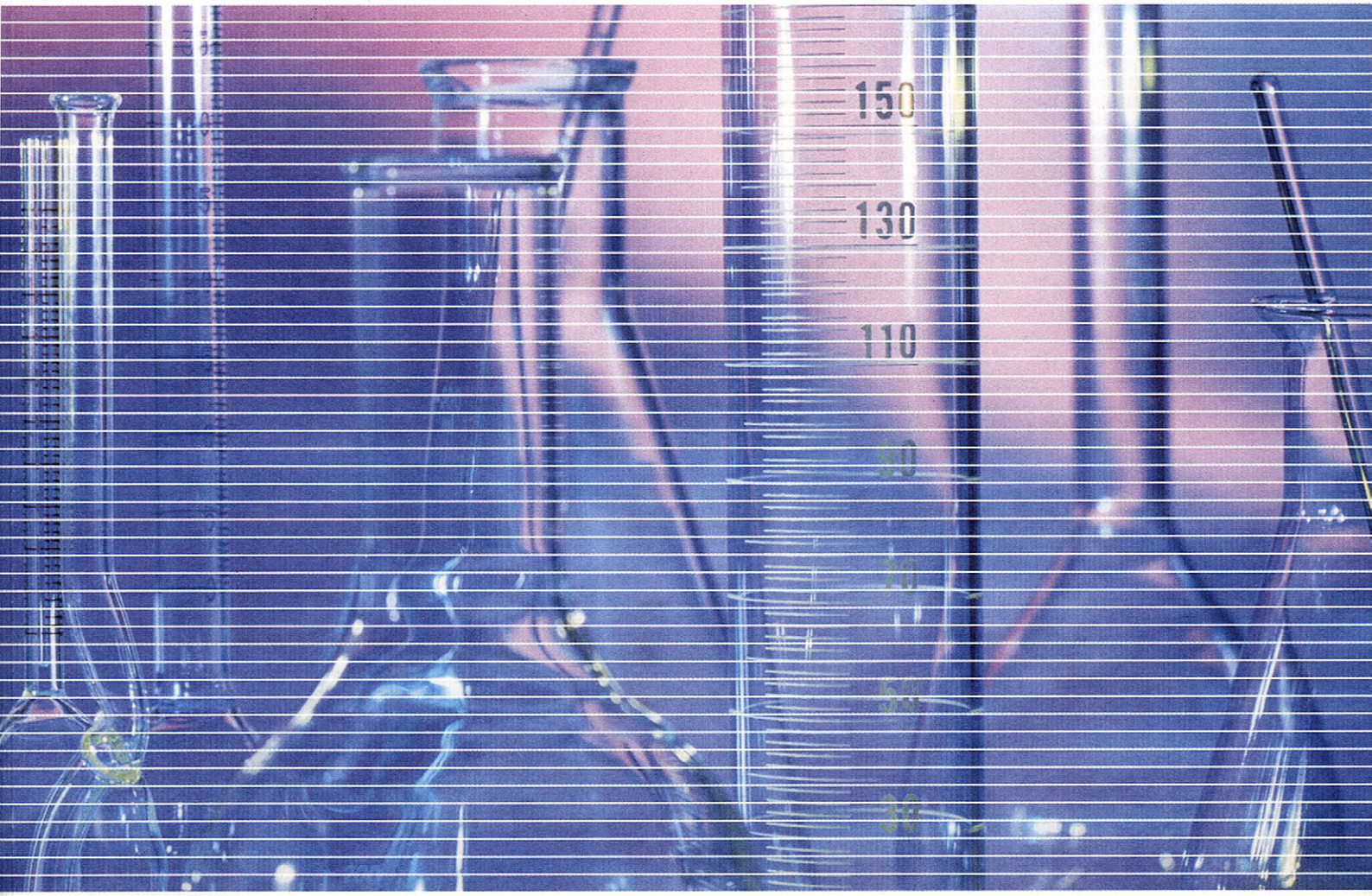
zdravljenje s krvjo v kirurgiji

avtotransfuzija

2nd postgraduate course

blood therapy in surgery

autotransfusion



Portorož, Slovenija, 09. - 11. December 1999

KLINIČNI CENTER LJUBLJANA - SPS KIRURŠKA KLINIKA
UNIVERSITY MEDICAL CENTER - DEPARTMENT OF SURGERY

ZAVOD RS ZA TRANSFUZIJO KRVI
BLOOD TRANSFUSION CENTER OF SLOVENIA

ZDRAVSTVENI DOM LJUBLJANA
COMMUNITY HEALTH CENTER LJUBLJANA

ESTM - EVROPSKA ŠOLA ZA TRANSFUZIJSKO MEDICINO
EUROPEAN SCHOOL OF TRANSFUSION MEDICINE

Pokrovitelji:

MINISTRSTVO ZA ZDRAVSTVO REPUBLIKE SLOVENIJE

WHO - URAD RS ZA SODELOVANJE S SVETOVNO ZDRAVSTVENO ORGANIZACIJO

Patronage:

MINISTRY OF HEALTH OF THE REPUBLIC OF SLOVENIA

WHO - REGIONAL OFFICE IN SLOVENIA

Soorganizatorji:

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ZDRAVNIŠKA ZBORNICA SLOVENIJE

SLOVENSKO ZDRAVNIŠKO DRUŠTVO

ZBORNICA ZDRAVSTVENE NEGE SLOVENIJE

Coorganizers:

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SLOVENIAN MEDICAL ASSOCIATION

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UMBERTO ROSSI

VANDA BRUBNJAK-JEVTIČ

LJUBIŠA LUKIČ

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JELKA MLAKAR

MAJDA ČERNČIČ

DANICA STRAŽAR

VERONIKA PRETNAR-KUNSTEK

Tajnik / Secretary:

GREGOR CERKVENIK

Koordinatorja / Coordinators:

VANDA BRUBNJAK-JEVTIČ

UMBERTO ROSSI

Organizacijska ekipa / Organizer team:

VANDA BRUBNJAK-JEVTIČ

LJUBIŠA LUKIČ

NATALIJA LAMPREHT

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JEAN FRANCOIS BARON *(F)*

PETER EARNSHAW *(GB)*

GIOVANNI INGHILLERI *(I)*

WOLFGANG MEMPEL *(D)*

FRANCESCO MERCURIALI *(I)*

UMBERTO ROSSI *(I)*

DRAGOSLAV DOMANOVIČ *(SLO)*

VANDA BRUBNJAK-JEVTIČ *(SLO)*

LJUBIŠA LUKIČ *(SLO)*

DARKO PAŠKVAN *(SLO)*

BREDA STARC *(SLO)*

NELI VINTAR *(SLO)*

MARJANA ŠALEHAR *(SLO)*

Četrtek 09. dec. 1999
Thursday Dec 9th 1999

16.00 **Registracija**
Registration

18.00 **Otvoritev in sprejem**
Opening ceremony and welcome reception

Petek 10. dec. 1999
Friday Dec 10th 1999

Transfuzijska medicina v kirurgiji
Transfusion medicine in surgery

Smaragdna dvorana
Moderator:
MERCURIALI FRANCESCO

08.30 ROSSI UMBERTO:
Vloga in pomembnost avtotransfuzije v transfuzijski medicini danes
The role and significance of autotransfusion in transfusion medicine today

LUKIČ LJUBIŠA:
Komponentna terapija
Component therapy

MERCURIALI FRANCESCO:
Preoperativno načrtovanje za transfuzijo - individualni pristop
Preoperative assessment of transfusion requirement in surgery - personalized approach

BARON JEAN FRANCOIS:
Vzroki (sprožilci) za transfuzijo v kirurgiji
Transfusion triggers in surgery

10.30-11.00 Odmor / Coffee Break

Alternative pri uporabi krvi
Blood transfusion alternatives

Moderator:
EARNSHAW PETER

11.00 INGHILLERI GIOVANNI:
Načini zmanjševanja perioperativne izgube krvi
Techniques to reduce perioperative blood loss

MERCURIALI FRANCESCO:
Načini zviševanja tolerance za izgubo krvi
Techniques to increase tolerated blood loss

EARNSHAW PETER:
Alternative v transfuziji - pogled kirurga
Transfusion alternatives - the surgeons view

12.30-14.00 Odmor / Coffee Break

Avtotransfuzija
Autotransfusion

Moderatorja:
LUKIČ LJUBIŠA
BRUBNJAK-JEVTIČ VANDA

14.00 DOMANOVIČ DRAGOSLAV
ŠALEHAR MARJANA:
Obveščenost bolnika in privolitev v avtotransfuzijo
Patient's informed consent for autotransfusion

LUKIČ LJUBIŠA:
Preoperativno zbiranje krvi
Preoperative donation of blood

VINTAR NELI
STARC BREDA:
Akutna normovolemična hemodilucija
Acute normovolemic hemodilution

BRUBNJAK-JEVTIČ VANDA:
Perioperativno zbiranje krvi
Perioperative collection of blood

PAŠKVAN DARKO:
Perioperativno (filtracija) in postoperativno zbiranje krvi
Perioperative (filtration) and postoperative collection of blood

Integrirani avtotransfuzijski program
Integrated autotransfusion program

15.30 MEMPEL WOLFGANG:
Organizacija integriranega avtotransfuzijskega programa
Organization of integrated autotransfusion programme

INGHILLERI GIOVANNI:
Rezultati integriranega programa obstoječih avtotransfuzijskih tehnik
Results of integrated use of current autotransfusion techniques

16.30–17.00 Odmor / Coffee Break

17.00 - 18.30 **Avtotransfuzija - danes in jutri**

OKROGLA MIZA, Smaragdna dvorana

Izhodišče za razpravo: VARNA TRANSFUZIJA KRVI

Predlog zakona o preskrbi s krvjo

MODERATOR:
Božidar Voljč

Vloga institucij pri promociji avtotransfuzije

MODERATOR:
Zoran M. Arnež

SODELUJOČI:

Francesco Mercuriali (I)
Jean Francois Baron (F)
Peter Earnshaw (GB)
Wolfgang Mempel (D)

Breda Kutin (Zveza potrošnikov Slovenije)
Damjan Slabe (Rdeči križ Slovenije)
Franc Košir (Zavod za zdravstveno zavarovanje)
Janez Zajc (Ministrstvo za zdravstvo)
Ljubiša Lukič (Zavod RS za transfuzijo krvi)
Stanislav Čelhar (Zdravstveni dom Ljubljana)
Vesna Kerstin-Petrič (WHO)
Vojko Flis (Zdravniška zbornica)

Okrogla miza bo potekala v slovenskem jeziku.

Sobota, 11. dec. 1999
Saturday, Dec 11st 1999

AVTOTRANSFUZIJSKE TEHNIKE

UČNE DELAVNICE Z VIDEO PREZENTACIJO,
Smaragdna dvorana

Osnova učnih delavnic bo video film, ki prikazuje avtotransfuzijske tehnike pri različnih operativnih posegih. Po ogledu filma in delu v skupinah sledi skupna razprava vseh udeležencev delavnic.

9.00 - 10.30 **DELO V SKUPINAH**

Glede na predvideno število udeležencev smo oblikovali pet skupin, ki jih bodo vodili zdravniki in višje medicinske sestre različnih strok iz Zavoda RS za transfuzijo krvi, Zdravstvenega doma Ljubljana, Kliničnega centra Ljubljana: SPS Kirurške klinike (KO za anesteziologijo, KO za plastično kirurgijo, KO za srčno in žilno kirurgijo), Ortopedske klinike Ljubljana in Ortopedske bolnišnice Valdoltra.

ZDRAVNIKI	VIŠJE MEDICINSKE SESTRE
1. skupina	
Melisa Zukanovič	Damjana Hojak
Mario Ponikvar	Marinka Orehek
2. skupina	
Marjana Šalehar	Tatjana Golja
Dragoslav Domanovič	Lucija Skvarča
3. skupina	
Vanda Brubnjak-Jevtič	Zorica Kardoš
Breda Starc	Sonja Prtenjak
4. skupina	
Neli Vintar	Irena Buček-Hajdarevič
Dario Pogorelec	Tea Jurgec
5. skupina	
Darko Paškvan	Brigita Erbežnik
	Vera Čepon

11.00 - 12.00 SKUPINSKA RAZPRAVA UDELEŽENCEV UČNIH DELAVNIC

MODERATORJI:

Melisa Zukanovič

Marjana Šalehar

Vanda Brubnjak-Jevtič

Neli Vintar

Darko Paškvan

The role and significance of autotransfusion in Transfusion Medicine today

Umberto Rossi
(Director, Dept. of Haematology and Blood Transfusion, Hospital of Legnano, Milano, Italy; ISBT Councillor; ESTM President)

The advantages (and disadvantages, or limitations) of autotransfusion, in its different technical and medical procedures, have been the object of several reports, since its very beginning.

A better understanding of the impact of autotransfusion procedures on the improved medical outcome of carefully selected groups of surgical patients has been reached, through Consensus Conferences [12, 39, 40, 43, 48, 49, 50, 51], and scientific debates in the medical literature [3, 8, 9, 15, 16, 18, 35, 41, 43, 52]. The introduction of erythropoietin into medical treatment has widened the field of application of autotransfusion [12, 32 34] and increased its effectiveness.

The practice of autotransfusion has not attained the same level, and has not been accepted with equal favour in different nations and areas of the world, according to the different cultural, medical and transfusional traditions. Its implementation has been only marginally considered in many national, or international, laws or directives on blood transfusion.

The main biological and clinical advantages of autotransfusion have been initially recognized [4, 5, 19, 25, 26, 28, 31, 39, 40, 41, 47] in the following ones:

1) absence of any risk of transfusion-transmitted infections;
2) absence of any risk of alloimmunization to any blood cell antigen.

Besides the obvious observation that the above advantages can only be considered absolute if *all* the blood transfused to a single patient was autologous, with no integration by the homologous supply, their relevance in today's Transfusion Medicine needs to be re-analysed and re-assessed.

I) Absence of any risk of transfusion-transmitted infections

The exceptional increase in popularity of autotransfusion has certainly been due to the worldwide explosion of the AIDS pandemics, and to the diffusion within the general public of a new critical appreciation of all medical procedures, and of blood transfusion in particular.

The "duty" for the attending physician to be able to offer to the patient the possibility of autotransfusion prior to asking him an informed written consent to perform homologous transfusion, originally conceived as a moral and professional duty only, has been pushed in some cases to the level of a legal duty, posing relevant organizational and social problems. A wave of "criminalization" has sometimes attained some Blood Transfusion Centres which could not customarily offer autotransfusion as a regular alternative to homologous transfusion. It is fair to say that the practice of autotransfusion was born in some cases out of these legal or professional worries, rather than out of a perfectly formed conviction of its intrinsic medical advantages.

The value of this motivation (blood "safety") has been progressively diminished by the spectacular progresses made in the screening of donors' blood for infectious agents.

Thanks to the reinforcement of the practice of purely voluntary, non-remunerated periodic blood donation, and to wide-ranged and perfectioned search for immunological or genomic signs of transmissible viruses in donors' blood, one can surely state that homologous blood has never been as safe as today, and that homologous blood

transfusion is by large one of the safest procedures as compared with many other medical procedures.

This holds true in nearly all Western "developed" countries. But one can not forget that "blood safety" (meaning by that an "acceptable" degree of safety) is still a door yet to be open in many "developing" countries, also in Europe.

2) Absence of any risk of alloimmunization to any blood cell antigen

Whether one considers red cell, or platelet, or white cell antigens, this advantage seems rather obvious, and by itself not affected by any scientific progress in immunology in recent years.

While on one side the motivation of "forbidden alloimmunisation" still holds valid, and so will stay in my opinion for many years to come, one should consider on the other side the current progress made in understanding and elucidating the effects of the "immunomodulation" exerted by homologous blood transfusion: if some positive immunomodulatory effects in the recipient patients should be confirmed in the medical literature, these benefits could overshadow the negative risks of unwanted alloimmunizations, and the delicate balance between homologous and heterologous transfusion could be shifted again in favour of homologous blood.

Other arguments should be considered today, concerning the practice of autotransfusion and its regulatory policy.

Let us consider 2 classical "disadvantages", often quoted in the medical literature [1, 3, 16, 17, 22, 23, 36, 37, 53]:

1) increased possibility of misidentification errors;
2) excessive cost of autotransfusion procedures.

It is my firm conviction that these arguments don't hold true, but only originate by misconceptions due to the lack of adequate regulations and efficient operational policies.

3) Increased possibility of misidentification errors

Autologous blood units are rarely considered and processed with the same meticulous care prescribed (by laws and directives) for donors' blood units.

Specific and detailed regulations for autologous blood are lacking in many countries.

Recent results of national surveys within existing haemovigilance programmes (France, Great Britain) have on the other side confirmed the high frequency of misidentification errors in patients receiving homologous blood, and the absolute need to secure in all cases a safe identification patient/unit through specific technical procedures.

Where similar procedures have already been implemented for autologous blood, no errors have been observed.

4) Excessive cost of autotransfusion procedures

This has been a real argument in many circumstances, when proper measures have not been taken in adequate consideration:

A) a critical number of procedures: the higher the number, the lower the personnel's time, due to experience and self-confidence, with increased efficiency and lower costs;
B) autologous blood doesn't obviously need the laboratory tests for homologous blood to be performed, and their cost can be spared.

Moreover, the disposal of autologous blood units that had not to be transfused should be considered obvious, and not be considered a negative factor in the economical balance.

It is, however, certainly true that the economy of autotransfusion procedures could be drastically improved if the autologous blood, once drawn from a patient, could be indefinitely stored for him as frozen blood. The added cost of freezing equipment and organization should be weighed against the economies in medical and personnel's time in future occasions: not to consider the inherent clinical advantages, for the patient, to have the possibility to be auto-transfused in future emergency occasions, that would not allow him to timely auto-donate again his own blood.

From all the above considerations, the role and significance of autotransfusion seem to emerge still unabated in today's Transfusion Medicine, provided clear clinical criteria for its indications are set [2, 4, 5, 12, 26, 42], and an adequate organization is on place [20, 24, 28, 30, 36].

This seems to be true both in "developed" and "developing" countries, where the "safety" motivation can still exert its important additional influence.

Paradoxally, as a consequence of the madly increased costs met with to increase safety of donors' blood in developed countries, an other strong motivation for autologous transfusion has emerged and needs to be discussed: the relative economic convenience of autologous blood units compared with increasingly costly homologous blood units.

5) Relative economic convenience of autologous blood units compared with increasingly costly homologous blood units

As already stated, autologous blood doesn't need any blood testing for transmissible infections.

Some Blood Transfusion Centres feel otherwise, fearing the unsustainable responsibility of the consequences of a misidentification error, in case the autologous unit should be wrongly transfused (untested, and potentially infectious) to an other patient.

This circumstance having to be by no means avoided through other effective specific measures in all cases, the rational basis for the above excess of precaution seems to be very weak.

On the other side, the cost of homologous blood units (thanks to completely irrational, fear-driven policies of many politicians, dictated by an ill understanding of the "precautionary principle") is steadily increasing in many developed countries, and will soon reach levels that will prove impossible to be sustained by even the wealthiest national health economies.

It is not difficult to foresee, by obvious reaction, a strong revival of the practice of autotransfusion, as soon as hospital and public health administrators will have perceived its reaffirmed economic convenience.

As a conclusion, I want to stress that we must therefore be ready: to practice autotransfusion as a customary part of Transfusion Medicine; to perform it at the highest possible medical and organisational quality level; to expand it further, always according to strict clinical indication, whenever possible, in the field of our clinical activity.

To these aims, the ESTM has given its contribution by organising 2 specific courses [29, 31] and introducing issues on autotransfusion in other 2 courses [11, 13], so that many aspects of the different procedures of autotransfusion [5, 6, 7, 10, 14, 19, 20, 21, 24, 25, 26, 27, 28, 30, 32, 33, 34, 36, 37, 38, 42, 44, 45, 46, 49, 53, 54] could be covered in the last years.

I feel that the present course, beutifully organised by Dr. Vanda Brubnjak-Jevtic, perfectly corresponds to this aims.

The specific competence of the lecturers, and the dedication of our Slovenian hosts, are a sound guarantee of a very good course.

My warmest thanks to Dr. Brubnjak-Jevtic, to the teachers and to all the participants for having allowed me to be with the ESTM in Slovenia for the third time.

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Avtotransfuzija
Komponentna terapija s krvjo

Autotransfusion
Blood Component Therapy

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Key words (Blood, component, therapy, transfusion, autotransfusion)

Abstract

Autotransfuson is the safest way of blood transfusion. The donor and recipient is the same person. With introduction of component in autotransfusion we have the opportunity to give to the recipient the most concentrated, pure and potent componet. It is also the best way how to reach the best efficacy with maximal rational use of blood.

Abstrakt

Avtotransfuzija je najvarnejša transfuzija krvi. Dajalec in prejemnik sta isti osebi. Z uvedbo komponentne terapije v avtotransfuziji imamo možnost dati prejemniku najbolj koncentrirano, prečiščeno in učinkovito komponento. Obenem je to najboljši način za dosego največjega učinka in najbolj racionalne uporabe krvi.

Uvod

Avtotransfuzija je zgodovinsko gledano ena od prvih uspešnih oblik transfuzije že v obdobju, ko niso bile poznane krvne skupine.

Avtotransfuzija je oblika oskrbe s krvjo, ki ima številne prednosti in bi morala postati sestavni del vsakega operativnega protokola.

Vsak pacient mora v procesu zdravljenja s krvjo dobiti najvarnejše in najučinkovitejše zdravilo - komponento krvi, ki jo dejansko potrebuje. Komponenta krvi, pripravljena v postopku avtotransfuzije, v večini primerov izpoljnjuje te pogoje.

Vrste odvzemov krvi in krvnih komponent

Pri pacientih, opravljamo tri vrste odvzemov krvi ali njenih komponent:

A) odvzem polne krvi, ki je lahko osnova za pripravo posameznih komponent krvi;

B) odvzem plazme s pomočjo plazmafereze

C) odvzem posameznih celic krvi s pomočjo citofereze

Načrtovanje odvzema

Pacientu odvzamemo tisto sestavino krvi, ki jo ima v zadostni količini, oziroma jo izgublja med operativnim postopkom ali po operaciji. Sestavine krvi nato ustrezno predelamo in pripravimo komponento, primerno za transfuzijo. Glede na vrsto posega in stanje pacienta določimo potrebno količino za nadomeščanje izgubljene krvi ali sestavine krvi.

Komponente krvi

Sveža polna kri vsebuje eritrocite, trombocite, faktorje strjevanja krvi in plazemske sestavine, razredčene s konzervansom. Največkrat pripravimo polno svežo kri pri odvzemih neposredno pred operativnim posegom – hemodilucija ali kot zadnji načrtovani odvzem v postopku žabjega skoka. Hranimo jo na + 4°C. Po dveh dneh hranjenja pade nivo trombocitov in faktorjev strjevanja pod mejo terapevtske učinkovitosti in sveža polna kri postane konzervirana polna kri.

Konzervirana polna kri je komponenta, ki jo pripravimo pri načrtovanih posegih v postopku predoperativne avtotransfuzije. Učinkovita celična sestavina so eritrociti. Ohranjene so še nekatere termostabilne sestavine plazme - albumin. Polno konzervirano kri lahko hranimo 35 dni od dneva odvzema v CPDA-1 (citrat, fosfat, dekstroza, adenin) konzervansu. Večjo količino konzervirane krvi lahko pripravimo s tehniko žabjega skoka, ko najstarejšo enoto krvi vrnemo pacientu in mu odvzamemo novo svežo polno kri.

Koncentrirani eritrociti. Pripravljamo jih iz polne krvi z ločitvijo celic od plazme. Hranimo jih lahko 35 dni, pomešane s CPDA-1 konzervansom, oziroma 42 dni v posebni ohranitveni raztopini SAGM. Terapevtsko pomembna sestavina so eritrociti. Pripravljamo jih v okviru programa predoperativne avtotransfuzije z namenom pripraviti kakovostnejše komponente, kot so koncentrirani eritrociti v posebni ohranitveni raztopini in sveža zmrznjena plazma.

Koncentrirani eritrociti – oprani. To je komponenta, ki jo dobimo pri zbiranju krvi iz operativnega polja. Vso zbrano kri, ki se ob sesanju ne sme peniti, saj kri pri tem hemolizira, filtriramo, da odstranimo koagule, skupke celic in druge večje delce, ki se nahajajo v operativnem polju. Nato kri operemo s fiziološko raztopino, da odstranimo topne neželene sestavine. Pri postopku priprave dobimo oprane eritrocite, ki vsebujejo kot učinkovino le eritrocite v fiziološki raztopini. Komponenta je pripravljena iz zbrane krvi v odprtem sistemu, zato jo uporabimo takoj ali največ po šestih urah hranjenja.Pri uporabi intraoperativne avtotransfuzije in še posebno pri zbiranju krvi po operaciji dobimo **eritrocite,** ki so ostali po končanem procesu strjevanja krvi in nadaljnjem procesu fibrinolize. S postopkom pranja lahko odstranimo preostale neželene sestavine, v primeru direktne transfuzije eritrocitov zbrane po drenu, pa moramo upoštevati možnost bakterijske onesnaženosti in vsebnost neželenih sestavin, ki so ostale po fibrinolizi.

Koncentrirane trombocite za avtotransfuzijo pripravljamo s pomočjo postopka trombofereze. Najboljše učinke dosežemo, če jih pripravimo do tri dni pred operativnim posegom, saj vsak dan hranjenja zmanjšuje njihovo učinkovitost. Koncentrirani trombociti so koristna komponenta pri skrbno izbranih pacientih s koagulacijskimi motnjami in ob načrtovanju večje izgube krvi.

Sveža zmrznjena plazma Učinkovite sestavine so vse sestavine plazme. Hranimo jo eno leto na temperaturi pod -30°C in tako ohranimo 70% učinkovin.

Fibrinsko lepilo pripravimo iz plazme pacienta po odmrznjenju. Komponenta je uporabna pri posegih na tkivu, kjer pričakujemo drobne krvavitve in je vzdrževanje lokalne hemostaze otežkočeno. Fibrinsko lepilo lahko po pripravi zamrznemo in hranimo do operativnega posega podobno kot plazmo.

Krvotvorne matične celice največkrat pridobimo s pomočjo citofereze iz periferne krvi. Hranimo jih globoko zmrznjene v tekočem dušiku. Njihova uporaba ni vezana direktno na operativni poseg je pa zelo koristna komponenta pri pacientih, kjer s citostatiki ali obsevanjem poškodujemo tudi matične celice kostnega mozga.

Terapija krvavitve s krvjo, krvnimi komponentami in zdravili iz krvi

V primerih avtotransfuzije lahko načrtujemo ali predvidimo izgubo krvi in si pomagamo z zbiranjem krvi bolnika, kar nam v večini primerov omogoča uporabo pacientove krvi ali komponent krvi. V primeru nepričakovanih dodatnih izgub krvi pa še vedno lahko uporabimo komponente krvodajalcev.

1.) Pri terapiji akutne krvavitve do 1 litra krvi ponavadi ne načrtujemo avtotransfuzije, saj moramo kot primarno nadomestiti izgubljeni volumen krvi. Upoštevati moramo tudi izhodne laboratorijske vrednosti oziroma zdravstveno stanje bolnika. Izgubljeni volumen nadomeščamo s kristaloidnimi raztopinami – s fiziološko ali s koloidnimi raztopinami, kot so raztopine dekstrana, želatine ali škroba.

2.) Za nadomeščanje oksiformne kapacitete pri krvavitvi večji od 1 litra vsekakor načrtujemo avtotransfuzijo. Običajno dodajamo toliko eritrocitov, da ostane hematokrit okoli 30 oziroma hemoglobin med 80 in 100 g/liter.

3.) Pri izgubi 2 do 3 litrov krvi je avtotransfuzija sestavni del operativnega protokola. Načrtujemo izgubo eritrocitov in njihovo nadomeščanje, hkrati pa moramo upoštevati izgubo beljakovin in ohranjati nivo celokupnih beljakovin nad 52 gramov na liter ter s tem zadosten onkotski pritisk.

4.) Pri izgubi krvi, ki je blizu volumnu celokupne krvi, moramo že upoštevati pomankanje trombocitov, ki je posledica razredčitve s komponentami brez vsebnosti trombocitov, zato moramo dodati koncentrirane trombocite. To so predvsem primeri uporabe intraoperativnega zbiranja bolnikove krvi, ko vračamo bolniku oprane eritrocite. Pri kirurškem bolniku ohranjamo število trombocitov nad 100 000.

5.) Posledica masovne krvavitve, ki presega enkratni volumen bolnikove krvi v 24 urah, je tudi pomankanje faktorjev strjevanja krvi, ki jih nadomeščamo z uporabo plazme bolnika ob uporabi koncentriranih eritrocitov in trombocitov ali z uporabo sveže krvi, če je dosegljiva.

Zaključek

Z uporabo komponent krvi in načrtovanjem avtotransfuzije lahko dosegamo najboljše možne rezultate pri oskrbi pacienta s krvjo in krvnimi pripravki. V veliki večini primerov se tako izognemo neželenim stranskim učinkom in obenem je učinkovitost nadomestne terapije najboljša. Pri načrtovanju nadomestne trerapije upoštevamo priporočilo, da vrednosti hemoglobina ostanejo po operaciji do 100g/l. Uporaba dodatnih enot krvnih pripravkov, ki jih nismo uspeli zagotoviti z avtotransfuzijo, naj bo po možnosti izjema.

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Preoperative assessment of transfusion requirement in surgery Personalized approach

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Blood donation and transfusion practice have been dramatically effected by recent changes in the medical and public perception of risks and benefits of blood transfusion. Allogeneic transfusion had been traditionally considered as an effective therapeutic intervention, but the fear of contracting blood-borne infectious diseases led to the attitude to regard allogeneic blood transfusion as an out-come to be avoided. Although the current blood supply is safer than ever owing to improved donor screening and testing (1,2), allogeneic blood transfusion still involves the risks of causing immunological modifications (3-7) and it is always likely that disease transmission will occur (8-11).

Moreover the introduction of stricter criteria for blood donor selection decreases the availability of donor blood for transfusion. The subsequent reduction in the number of donors and the limited shelf-life of blood have prompted the adoption of strategies to save this precious, limited and perishable resource and to limit the exposure to the risks of allogeneic blood such as a strict observance of the Maximum Surgical Blood Order Schedule (MSBOS) for the requests (12) and a reassessment of the indication for blood transfusion (13). In addition, the use of donor blood in surgery can be substantially reduced by the introduction of autologous blood (AB) transfusion programs. In many Countries, an increase of the use of AB has been documented (14). Transfusion of AB, when possible, is the preferred form of blood replacement for elective surgery. Techniques used to obtain AB include pre-operative AB donation (15,16), acute normovolemic hemodilution (ANH) (17,18), intra-operative (IOS) and post-operative salvage (POS) (19,20).

All these techniques are an attractive way to obtain AB as their feasibility, safety and efficacy in reducing the use of allogeneic blood has been demonstrated in many large clinical studies. Moreover, recently rHuEPO has been approved for use in surgery as it has been demonstrated that it is effective in increasing a patient's red blood cells (RBCs) production in a short period before the operation (so that the amount of autologous blood that can be collected is increased prior to surgery), in correcting anemia preoperatively (so that also patients with low baseline hematocrit can participate in PABD programs) and, consequently, in reducing blood transfusion requirement (21,22).

In the last few years, however, much has changed. The improvement in the safety of allogeneic blood together with the current pressure on cost-containment have provoked a debate on the utilization of alternatives to allogeneic blood. Consequently, to define the precise role of the alternatives techniques in modern transfusion practice, it is necessary to optimize their efficay and restrict their utilization to the patients that really need them.

Primarily responsible for the higher cost of autologous blood and its variations according to procedure results mainly from the units that are collected in excess of the real need. Thus the use of the alternative techniques before low-transfusion risk elective surgery is inappropriate and should be avoided since it is costly, time consuming and can also involve unnecessary health risks to the patients during the donation procedure.

The first step is to identify procedures associated with low transfusion requirements. A reasonable and practical approach one can adopt would be to base decisions about

the need for PABD on the maximum surgical blood order schedule (MSBOS) (12) for the procedure in the hospital at which surgery is to be performed. When patients are candidate to an operation prior to which a type and screen procedure is usually performed, these might be discouraged from predeposit autologous blood. Autologous blood collection should be limited to surgical procedures in which the need for blood transfusion has already been clearly established. However, also in procedures where PABD is appropriate, collection in excess of transfusion, although considered inevitable to provide sufficient blood to meet the need of most patients should be kept to a minimum. A widely utilized strategy to define the number of autologous blood units to collect for each surgical procedures is the schedule of optimal preoperative collection of autologous blood (SOPCAB), suggested by Axelrod et al (23), that takes into account the number of blood units (autologous and allogeneic) transfused to each patient throughout the entire hospital stay for each surgical procedure. The number of units to be collected is determined by the physical capability of the patients, but ideally is equal to the number of units of autologous blood that would guarantee that at least 80-90% of the patients would avoid completely the exposure to allogeneic blood. In our Institute the use of these strategies has allowed to contain the overall wastage of autologous blood below 15%, with a range from 6% to 15% according to the different surgical procedures .

Although valuable to obtain an appropriate management of blood inventory, MSBOS and SOPCAB give no indication on the appropriateness of transfusion indication and on the transfusion need of a specific patient.

Algorithm to define the patient's transfusion requirement

In order to optimize the utilization of all the alternatives to allogeneic blood transfusion we defined a new and more personalized approach of utilization of all the methods to obtain autologous blood in order to offer to each single patient what is really proven to be effective in reaching the main goal of an autotransfusion program, i.e. avoidance of the use of allogeneic blood (24). This new approach is aimed to personalize the patient's transfusion requirement taking into account the two parameters from which it depends, i.e. the perioperative blood loss and the volume of blood that the specificpatient can tolerate to lose before blood transfusion support is indicated.

The perioperative blood loss can be calculated through a constantly updated analysis of the real blood loss occurred in each patient undergoing a specific surgical operation performed by a specific surgical team. This can be obtained performing a retrospective analysis of the patients operated during the last 6-12 months prospectively. The surgical RBCs loss occurring in each patient is given by the circulating RBCs volume reduction from presurgery to a properly determined postoperative time, plus the volume of RBCs transfused during this period. In our setting we decided to consider as postoperative reference the patient's RBCs mass 5 days after surgery as at that time the patient is normovolemic, postoperative bleeding has stopped and blood transfusions is a rare event.

The patient's circulating RBCs volume can be calculated through appropriate formulas that take into account the patient height, weight and hematocrit. The volume of allogeneic RBCs transfused can be easily defined as each units contains around 200 ml of RBCs; the volume of RBCs present in autologous blood units can be easily calculated knowing the volume of blood collected and donor/patient hematocrit value at the time of collection. Similarly, for perioperative salvaged blood the volume of RBCs transfused can be calculated taking into account the volume of washed RBCs transfused and the average hematocrit of salvaged blood after the washing cycle.

Once determined the total RBCs loss of about 40-50 patients the value to assign the predicted surgical RBCs loss for each procedure, subdivided for each surgical team can

be the mean, median or the appropriately selected percentile value of the distribution. In our setting we decided to consider as expected blood loss the value corresponding to the 80th centile of the distribution.

The formulas to calculate perisurgical RBCs loss and an example of their application are reported in table 1.

Table 1.
Mathematical formulas to define the perioperative RBCs loss and example of their application

Perioperative RBC loss (L of RBCs)	=	Circulating RBC volume (C-RBCs-V) reduction (from presurgery to postoperative day 5) plus the RBC volume transfused;

= C-RBCs-V $_{\text{presurgery}}$ **- C-RBCs-V** $_{\text{day 5 postop.}}$ **+ volume of RBC transfused,**

where:

C-RBC-V (in L of RBC) = Predicted Blood Volume (PBV) x Hct;

PBV = female = 0.3561 x height (m)^3 + 0.0338 x weight (kg) + 0.1833

male = 0.3669 x height (m)^3 + 0.03219 x weight (kg) +0.6041

Consequently :

Predicted RBC loss = PBV (Hctpresurgery - Hctday 5 postop) + liters of RBC transfused

Example

Male, 72Kg, height 1.72m, preoperative Hct = 0.36; Hct value 5 days after surgery = 0.29; transfused with 2 autologous blood units (volume: 400mL; hematocrit 0.40 and 0.38, respectively)

PBV = [0.3669 x (1.72)^3] + [0.03219 x (72)] + 0.6041 = 4.789

Surgical blood loss = 4.789 x (0.36 - 0.29) + (400 x 0.4 + 400 x 0.38)

= 4.789 x 0.07 + (0.160 + 0.152) = 0.335 + 0.312 = 0.647 L di RBC

The volume of blood that the patient can tolerate to lose depends upon the baseline circulating RBCs mass (that in turn depend on baseline Hct and the body mass) and the circulating RBCs mass that gives a value of Hct compatible with the clinical and cardiocirculatory condition of the patients. Patient who are in young age and good general condition can safely tolerate low Hct/Hb value (21-24% of Hct) while those who are elderly or suffer from cardiovascular or respiratory diseases affecting oxygen delivery to the tissues have to be maintained to higher Hct/Hb values (27-30% of Hct). Once determined the patient's baseline hematocrit and the minimal acceptable Hct value for the patient the volume of tolerated RBCs loss can be determined according to the formula reported in table 2

Table 2.
Mathematical formulas to define the volume of tolerated RBCs loss and an example of their application

Tolerated Blood Loss = Volume of RBCs loss to reach an accepted minimal Hct value

Tolerated Blood Loss (L of RBC) = (PBV x $Hct_{baseline}$) - (PBV x $Hct_{min.\ accepted}$)

being :

PBV = Predicted Blood Volume

$Hct_{minimal\ acceptable}$ = minimal Hct value compatible with the clinical condition of the patient.

Example

Female, 41 years old, good general conditions, weight 61Kg, height 1,70m;
preoperative Hct = 0,42;minimal aceptable Hct = 0,27

PBV = [0.3561*(1.7)^3] + [0.03308*61] + 0.1833 = 3.951 L

Tolerated RBCs Loss = 3.951 x (0.42 - 0.27)

= 3.951 x 0.15

= 0.592 L di RBC

The difference between the predicted blood loss and the tolerated blood loss is the transfusion requirement of the patient expressed in mL of pure RBCs (Table 3).

Table 3.
Mathematical formulas to define the expected transfusion need and an example of their application.

Transfusion needs = Total estimated RBC loss - tolerated RBC loss

consequently

= Predicted blood loss - (PBV x $Hct_{baseline}$) - (PBV x $Hct_{min.\ accepted}$)

Example

Female, candidate for THR, 60Kg, Height 1.6m, weight 60kg, Baseline Hct: 0.36, minimal acceptable Hct: 0.27, candidate for total hip replacement with a predicted RBC loss of 800mL of RBC.

PBV = [0.3561x(1.6)^3] + [0.0338 x 60] + 0.1833 = 3.627

Tolerated RBCs loss = (3627 x 0.36) - (3627 x 0.27) = 1306- 980 = 326 mL of RBC

Transfusion needs = 800 - 326 = 474 mL RBCs (=2.6 allogeneic blood units)

When a negative figure is obtained it means that the patient can tolerate to lose a larger volume of blood than it is expected to be induced by the procedure the patient is undergoing. In this case PABD is not indicated and after appropriate information the patient is discouraged from predeposit its own blood. In such cases "Type and screen" procedure will be adopted in order to protect the patient from unexpected high surgical blood loss, perioperative blood salvage with the "stand-by procedure"

is carried out. This procedure consists in mounting the aspiration set and the reservoir at the beginning of the operations and proceed to the washing cycle only when the volume of the blood, collected into the reservoir is considered clinically useful by the anesthesiologist.

When a positive figure is obtained, the figure represents the transfusion need expressed in mL of RBCs. In this case the safest and possibly the most cost-effective transfusion strategy has to be defined to obtain the predicted volume of RBCs necessary to cover the transfusion requirement of the patient. Consequently, beside the use of allogeneic blood, the adoption of the different alternative strategies to reduce allogeneic transfusion requirement in surgical patients have to be taken into account. The currently available alternative strategies can be subdivided into 2 groups according to the mechanism by which they affect transfusion requirement, i.e. by reducing the intraoperative and postoperative RBCs loss or by increasing the volume of RBCs that the patient can tolerate to lose before requiring transfusion support (tab. 4)

Tab 4 Strategies to reduce allogeneic transfusion needs in surgical patients

REDUCTION OF PERIOPERATIVE RBCS LOSS
Correction of coagulation impairment
Less invasive surgical procedures
Optimal anesthesiology techniques
Accurate hemostasis
Use of procoagulant drugs
Use of topical glues
Loss of RBCs-poor blood (ANHD)
Intra and post-operative blood salvage
INCREASE OF TOLERATED BLOOD LOSS
Correct indication of blood transfusion
Lower intra and post-operative transfusion trigger
Expansion of circulating RBCs mass
Preoperative correction of anemia
Preoperative blood donation
rHuEPO stimulation of erythropoiesis
Use of blood substitutes

The choice of the transfusion strategy to be adopted should depend on the type of surgery; the time to surgery, the applicability and efficacy of each specific alternative strategy; the general clinical status of the patient (hematological, cardiopulmonary) and consideration on cost/effectiveness. To help make the choice of the best strategy to be used to fulfill the transfusion need it is necessary to know advantages and limits of each alternative strategy, particularly the net gain, expressed in mL of RBCs, that each strategy can provide in terms of reduction of perioperative RBCs loss or increase of the tolerated RBCs loss. This topic will be discussed in the following paper addressing the characteristics of the different alternative strategies will be

We retrospectively applied the algorithm to 577 patients each of whom predonated 2 or 3 units of autologous blood prior to total hip replacement surgery and subdivided the patients according to the calculated transfusion requirement (tab. 5). It can be observed that in patients with calculated transfusion need higher than 500 mL of RBC (representing less than 5% of total evaluated patients), in spite of the utilization of all the currently available autotransfusion techniques only 68% of the patients avoided the use of allogeneic blood while this figure was more than 95% in the group of patients with calculated transfusion need lower than 200 mL of RBC. In this group of patient with low calculated transfusion requirement an overcollection of autologous blood has been documented as demonstrated by the wastage of about 20% of the autologous units collected.

Tab. 5 Transfusion results in 577 patients operated for total hip replacement subdivided according to the expected transfusion requirement calculated with the algorithm (24)

Transfusion requirement	*< 0*	*0-100*	*100-200*	*200-300*	*300-400*	*400-500*	*>500*
NO of Pts (% of total)	50 (8,7%)	48 (8,3%)	67 (11,6%)	90 (15,6%)	139 (24,1%)	156 (27%)	27 (4,7)
% male	98	93	77	39	6,5	1,3	0
Units predeposited (unit / Pt)	103 (2,0)	109 (2,2)	155 (2,3)	230 (2,5)	355 (2,5)	372 (2,4)	64 (2,4)
Units not transfused	20 (19,4)	21 (19,2%)	29 (18%)	33 (12%)	28 (8%)	19 (5%)	0 (0%)
Pts transfused only auto	98%	98%	95%	85%	82%	80%	68%
Pts with discarded units	16 (32%)	16 (33%)	22 (32%)	26 (28%)	25 (18%)	17 (11%)	0 (0%)
Pts transf. with all AB units with postop Hct<27 %	7 (14%)	9 (18%)	10 (15%)	22 (24%)	51 (37%)	74 (47%)	18 (66%)

If we had applied the algorithm for the choice of the most appropriate blood conservation strategies we would have been avoided unnecessary collection of AB in patients with low transfusion requirement thus saving resources that could have been utilized for a rHuEPO treatment in patients at higher risk to require allogeneic blood transfusion because of low baseline Hct values.

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Transfusion Triggers in Surgical Patients

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The primary reason for blood transfusion should be the maintenance of an oxygen delivery (D02) sufficient to meet tissue oxygen demand. Convective D02 can be determined as the product of the blood flow and the arterial oxygen content. A change in hematocrit induces a proportional change in arterial oxygen content and often an opposite chancre in blood flow (related to alteration in blood viscosity). In the perioperative period, experts have considered a hematocrit of 30% as optimal but their recommendations were based primarily on theoretical calculations of maximal D02 to peripheral organs. Awareness of the risks associated with transfusion has brought this threshold into question. Clinical studies on Jehovah's Witness patients have reported that elective surgery can be done safely in patients with a preoperative hemoglobin level as low as 6 g/dL, if estimated blood loss is kept below 500 mL [1]. Hemoglobin level alone was a significant predictor of outcome only at levels below 3 g/dL, the strongest independent factors influencing outcome being sepsis and active bleeding [2].

The decision to transfuse a given patient should not be taken based only on a hemoglobin level [3]. A better knowledge of the physiologic adjustments occurring during anemia and of the clinical factors which can limit the ability of the body to maintain adequate D02 to the tissues would allow the clinician to determine the minimal hemoglobin level for each patient.

Physiologic Adjustments During Anemia

To maintain adequate tissue oxygenation when hemoglobin is reduced, several mechanisms come into play, at both systemic and microcirculatory levels, provided that circulating blood volume is preserved. An increased cardiac output is commonly observed during acute anemia; its degree depends on the level of hemodilution. This augmented cardiac output is mainly due to an elevated stroke volume as long as normovolemia is maintained [4]. The development of tachycardia during anemia indicates hypovolemia, an insufficient hematocrit or an increased tissue 02 demand. The rise in stroke volume during normovolemic anemia is intimately related to the reduction in blood viscosity, leading to an increased venous return and a decreased ventricular afterload. Several experimental observations tended to indicate that the sympathetic innervation of the heart is required to increase cardiac output to a sufficient level during acute anemia.

Although cardiac output increases as hematocrit is reduced, systemic D02 reaches a peak value of about 110% of pre-anemic D02 for a hematocrit of about 30% indicating an optimal compromise between reduced 02-carrying capacity and increased blood fluidity. As hematocrit declines to a level of 20-25%, D02 begins to decrease, and falls below normoxic pre-anemic levels. Therefore, total D02 varies minimally over a wide range of hematocrit values between 25% and 45%, but decreases above and below this range.

During normovolemic anemia, the compensatory increase in cardiac output is also associated with a redistribution of blood flow to areas of high demand, such as the

myocardium and the brain. Indeed, coronary and cerebral blood flow increase out of proportion to the rise in cardiac output, which can be explained only by a regional vasodilatation in these organs [5,6]. The increase in myocardial blood flow is even more important than the increase in cerebral blood flow as myocardial oxygen demand increases during normovolemic anemia. Coronary vasodilatation becomes maximal when the hematocrit is reduced to 10-12%. Below this value, coronary blood flow can no longer match the increased energy demand of the cardiac pump, myocardial hypoxia develops and cardiac output decreases. This is consistent with the decrease in systemic oxygen consumption (V02) that occurs at hematocrit values of 10% [7].

The excess perfusion of the brain and the heart during anemia occurs at the expense of other organs. Several studies have demonstrated that relative vasoconstriction develops in some tissues during acute anemia, so that hepatic, renal and mesenteric blood flows are proportionately less than the total cardiac response [5,6]. This regional circulatory response during normovolemic anemia does not seem to be altered in the presence of significant beta-adrenergic blockade.

In addition to increased cardiac output and redistribution of blood flow to areas of high demand, other compensatory mechanisms come into play in the microcirculation to maintain adequate tissue oxygenation when hemoglobin level is reduced. First of all, during acute normovolemic anemia, the ratio of the microcirculatory to systemic hematocrit is increased, This phenomenon, associated with an increased capillary blood flow velocity allows the maintenance of the net red blood cell flow until the systemic hematocrit falls to 15% [8]. Second, the decreased viscosity associated with anemia results in a better spatial and temporal distribution of the red blood cells in the capillary network, improving cellular 02 extraction [9,10]. Third, during severe anemia (hematocrit below 15%), a shift to the right of the oxygen dissociation curve, related to a rise in red blood cell 2,3-diphosphoglycerate (2,3 DPG), may decrease hemoglobin affinity for 02 and thereby improve 02 delivery to the cells. Van Woerkens et al. recently reported the case history of a Jehovah's Witness patient with extreme hemodilution and D02-dependent V02 due to excessive blood loss during surgery [11]. In this anesthetized patient, V02 started to decline at a D02 of 184 mL/min (4.9 mL/kg/min), which corresponded to a hemoglobin level of 4 g/dL (hematocrit ± 12%). The authors observed a right shift of the oxyhemoglobin dissociation curve, but only when the hematocrit reached 8%.

In summary, the maintenance of adequate tissue oxygenation despite the decreased 02carrying capacities of the blood results from compensatory mechanisms acting at both the systemic (increase and redistribution of the cardiac output) and the microcirculatory level (increased extraction capabilities). These mechanisms allow V02 to remain constant until hematocrit falls to about 10%, at which point it becomes dependent on D02.

Clinical Limits of Anemia

The efficacy of the mechanisms maintaining adequate tissue D02 when blood 02 content is reduced depends first on the maintenance of normovolemia and on the integrity of myocardial function. Hypovolemia blunts the effects of the decreased blood viscosity on venous return, and a depressed myocardial function, even in the presence of an adequate blood volume, prevents the increase in stroke volume associated with the augmented venous return. Animal studies have demonstrated that anemia is not as well tolerated when cardiac function is decreased, as after myocardial infarction or chemically induced myocardial depression [12].

Coronary artery disease (CAD) can also limit the tolerance of the patient to normovolemic anemia. More than 15 years ago, Geha [13] observed that coronary vascular reserve is significantly compromised during progressive hemodilution, indicat-

ing cardiac vulnerability at this level, especially if coronary artery disease should coexists. The lowest tolerable hematocrit in CAD patients is not known, and experimental data on animals with extrinsically applied coronary stenoses remain conflicting. From a theoretical point of view, it has been recently demonstrated that coronary artery disease patients may tolerate some hemodilution intraoperatively although they will require a higher hematocrit during the early postoperative period to meet the increased tissue, especially cardiac tissue, 02 demand. In 27 coronary artery disease patients, Nelson demonstrated that a postoperative hematocrit below 28% was significantly associated with myocardial ischemia and morbid cardiac events [14]. Although the small sample size and case-control nature of the investigation limited the interpretation of these results, this study shows the need for larger clinical studies to better define the tolerance and thus the appropriate management of anemia in patients with coronary artery disease.

Respiratory insufficiency will also limit the tolerance of patients to anemia. Obviously, patients with chronic respiratory failure develop polycythemia in an attempt to maintain adequate tissue D02. However, there is no available data on optimal hematocrit during respiratory insufficiency.

Anesthesia has dual effects on the patient's tolerance of anemia. On one hand, the use of anesthetic agents can decrease tissue 02 demand, essentially by a decrease in sympathetic activity related to the elimination of pain and stress. Moreover, tissue 02 metabolism is also decreased during anesthesia by the presence of moderate hypothermia and the use of mechanical ventilation, which also allows the maintenance of high inspired fractions of oxygen increasing the amount of 02 carried by the plasma. On the other hand, anesthetic agents could alter the increase in cardiac output commonly observed during normovolemic hemodilution [15]. This effect could be attributed to the sympatholytic properties of these agents and to their effects on venous tone and myocardial contractility. These observations also stress the need for adequate monitoring to avoid the development of tissue hypoxia when hemodilution is performed during anesthesia using agents with potent negative inotropic properties.

Controlled hypotension is frequently used during surgical procedures to decrease intraoperative blood losses. However, the combination of controlled hypotension and normovolemic hemodilution could be associated with a decrease in D02 in some organs such as the kidneys and the splanchnic area, which could occasionally be associated with an impaired tissue oxygenation [16]. These observations strongly suggest the need for extensive clinical monitoring of patients in whom hemodilution and controlled hypotension are combined. Higher degrees of hemodilution cannot be recommended in this setting.

Carson has recently performed a retrospective cohort study to determine the effect of perioperative transfusion on 30- and 90-day postoperative mortality [17]. In 20 US hospitals between 1983 and 1993, a total of 8787 consecutive hip fracture patients, aged 60 years or older, who underwent surgical repair were included in the study. Primary outcome was 30-day postoperative mortality; secondary outcome was 90-day postoperative mortality. The «trigger» hemoglobin level was defined as the lowest hemoglobin level prior to the first transfusion during the time period or, for patients in the nontranfused group, as the lowest hemoglobin level during the time period. Overall 30-day mortality was 4.6% (n=402; 95% confidence interval (CI), 4.1%-5.0%); overall 90-day mortality was 9.0% (n=788; 95% CI, 8.4%-9.6%). A total of 42% of patients (n=3699) received a postoperative transfusion. Among patients with trigger hemoglobin levels between 80 and 100 g/L (8.0 and 10.0 g/dL), 55.6% received a transfusion, while 90.5% of patients with hemoglobin levels less than 80 g/L (8.0 g/dL) received postoperative transfusions. Postoperative transfusion did not influence 30- or 90-day mortality after adjusting for trigger hemoglobin level, cardiovascular disease, and other risk factors for death: for 30-day mortality, the adjusted odds ratio (OR) was

0.96 (95% CI, 0.74-1.26); for 90-day mortality, the adjusted hazard ratio was 1.08 (95% CI, 0.90-1.29). Similarly, 30-day mortality after surgery did not differ between those who received a preoperative transfusion and those who did not (adjusted OR, 1.23; 95% CI, 0.81-1.89). Carson et al. concluded that perioperative transfusion in patients with hemoglobin levels 80 g/L (8.0 g/dL) or higher did not appear to influence the risk of 30- or 90-day mortality in this elderly population. At hemoglobin concentrations of less than 80 g/L (8.0 g/dL), 90.5% of patients received a transfusion, precluding further analysis of the association of transfusion and mortality.

The indications for transfusion have never been evaluated in a prospective adequately sized clinical trial. A pilot study was conducted to plan larger clinical trials [18]. Hip fracture patients undergoing surgical repair who had postoperative hemoglobin levels less than 10 g per dL were randomly assigned to receive 1) symptomatic transfusion: that is, transfusion for symptoms of anemia or for a hemoglobin level that dropped below 8 g per dL or 2) threshold transfusion: that is, patients receive 1 unit of packed RBCs at the time of random assignment and as much blood as necessary to keep the hemoglobin level above 10 g per dL. Outcomes were 60-day mortality, morbidity, functional status, and place of residence. Among 84 eligible patients enrolled, (mean ± SD) prerandomization hemoglobin was 9.1 ± 0.6 g/ dL. The median number of units transfused in the threshold transfusion group was 2 (interquartile range, = 1-2), and that in the symptomatic transfusion group was 0 (6; interquartile range, = 0-2) (p 0.001). Mean hemoglobin levels were approximately 1 g per dL higher in the threshold group than in the symptomatic group: for example, on Day 2, 10.3 ± 0.9 g / dL versus 9.3 ± 1.2 g / dL, respectively (p 0.001). At 60 days, death or inability to walk across the room without assistance occurred in 16 (39.0%) of the symptomatic transfusion group and 19 (45.2%) of the threshold transfusion group. Death occurred by 60 days in 5 (11.9%) of the symptomatic transfusion group and 2 (4.8%) in the threshold transfusion group (relative risk = 2.5; 95% CI, 0.5-12.2). Other outcomes were similar for the two groups. Symptomatic transfusion may be an effective blood-sparing protocol associated with the transfusion of appreciably fewer units of RBCs and lower mean hemoglobin levels than are associated with the threshold transfusion policy. However, it is unknown whether these two clinical strategies have comparable mortality, morbidity, or functional status. A definitive trial is needed.

In the critically ill patient, most of the compensatory mechanisms for anemia are altered by the presence of hypovolemia, hypoxemia, depressed myocardial function and/or altered tissue 02 extraction capabilities. Moreover, the 02 demand of the critically ill patient is often increased simultaneously, due to fever, pain or stress. The current clinical guidelines recommend that in at-risk patients, hemoglobin level be maintained between 7.0 and 10.0 g/dL [16]. In septic patients, there is no current evidence for an optimal hematocrit although the maintenance of an hemoglobin level greater than 10 g/dL has been recently recommended. All authors emphasize the need to justify each unit of blood transfused by clinical judgment using a goal-oriented approach.

To determine whether a restrictive strategy of red-cell transfusion and a liberal strategy produced equivalent results in critically ill patients, Hebert et al compared the rates of death from all causes at 30 days and the severity of organ dysfunction [19]. They enrolled 838 critically ill patients with euvolemia after initial treatment who had hemoglobin concentrations of less than 9.0 g per deciliter within 72 hours after admission to the intensive care unit and randomly assigned 418 patients to a restrictive strategy of transfusion, in which red cells were transfused if the hemoglobin concentration dropped below 7.0 g per deciliter and hemoglobin concentrations were maintained at 7.0 to 9.0 g per deciliter, and 420 patients to a liberal strategy, in which transfusions were given when the hemoglobin concentration fell below 10.0 g per deciliter and hemoglobin concentrations were maintained at 10.0 to 12.0 g per deciliter. Overall, 30-day mortality was similar in the two groups (18.7 percent vs. 23.3 percent, P= 0.11).

However, the rates were significantly lower with the restrictive transfusion strategy among patients who were less acutely ill — those with an Acute Physiology and Chronic Health Evaluation II score of or =20 (8.7 percent in the restrictive-strategy group and 16.1 percent in the liberal-strategy group; P=0.03) — and among patients who were less than 55 years of age (5.7 percent and 13.0 percent, respectively; P=0.02), but not among patients with clinically significant cardiac disease (20.5 percent and 22.9 percent, respectively; P=0.69). The mortality rate during hospitalization was significantly lower in the restrictive-strategy group (22.3 percent vs. 28.1 percent, P=0.05). Hebert et al concluded that a restrictive strategy of red-cell transfusion is at least as effective as and possibly superior to a liberal transfusion strategy in critically ill patients, with the possible exception of patients with acute myocardial infarction and unstable angina.

Monitoring of Tissue Oxygenation During Normovolemic Anemia

The adequacy of any hemoglobin concentration in a given clinical situation depends on whether a sufficient amount of oxygen is carried to the tissues to meet 02 needs. In the absence of good clinical signs of inadequate tissue oxygenation, mixed venous 02 saturation (SV02) is frequently used to detect the development of an imbalance between 02 supply and demand. Trouwborst et al. [20] and Rasanen [21] assessed the potential value of monitoring SV02 as an indicator of tissue oxygenation during progressive acute normovolemic hemodilution in anesthetized pigs. They found a significant correlation between changes in SV02 and02 extraction ratio. They determined that the critical hemoglobin value, i.e. the value of hemoglobin below which V02 starts to decline, was around 4.0 g/dL, which corresponded to a SvO2 of 44% and an02 extraction ratio of 57%. In anesthetized animals with or without limited coronary vascular reserve, significant myocardial lactate production reflecting anaerobic metabolism occurred only when systemic 02 extraction ratio exceeded 50%[22]. In a Jehovah's Witness patient dying from massive bleeding, critical hemoglobin level was found around 4 g/dL corresponding to aSV02of 56% and an02extraction ratio of 44% [11]. These experimental and clinical observations tended to indicate that SV02 and02 extraction ratio could be reliable physiologic guide to transfusion. In eight ASA class I anesthetized patients undergoing idiopathic scoliosis correction, Fontana et al. [23] performed profound intraoperative normovolemic hemodilution using a SvO2 of 60% as a «transfusion trigger". In their patients breathing 100% 02, hemoglobin decreased from 10.0 g/dL to a nadir of 3.0 g/dL, while SV02 decreased from 90.8% to 72%. No patients suffered clinically adverse outcome. Despite the very small number of patients (healthy adolescents) included, this study tended to indicate that profound level of normovolemic hemodilution could be performed in some patients using SV02 as the transfusion trigger, without any adverse outcome. Other studies have now tended to confirm these observations [24].

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Techniques of reducing perioperative blood loss

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Prevention of allogeneic blood utilization in surgical patients has become an important topic in transfusion medicine owing to the lack of absolute safety and, more recently, to the increasing problem of donor blood availability. For these reasons in the last decades a number of different strategies involving transfusion practice at different level have been proposed, evaluated and utilized to reduce allogeneic transfusion surgical patient.

Basically these strategies can be divided into 2 groups according to the mechanism they affect the patient's RBCs transfusion requirement:

a) Strategies reducing the patient's perioperative RBCs loss; or

b) Strategies increasing the amount of RBCs that the patient can tolerate to loss before requiring RBCs transfusion support.

The aim of this paper is to review same of the most utilized or promising strategies to preserve allogeneic transfusion by limiting the total volume of RBC that the patients lose during surgery and in the early postoperative period (Tab I).

Tab. I Strategies to reduce perioperative RBCs loss

Identification and correction of coagulation impairment
Less invasive surgical procedures
Accurate surgical hemostasis
Optimal anesthesiological techniques
Regional anesthetic technique
Hypotensive general anesthetic technique
Topical hemostatic agents
Procoagulant drugs
Desmopressin
Aprotinin
Antifibrinolytics drugs
Loss of RBCs poor blood (acute normovolemic hemodilution)
Intra and postoperative blood salvage

Topical Hemostatic Agents

Enhancement of the hemostasis at the site of the surgical wound represents, since long time, a very attractive way to limit perioperative bleeding and to reduce the need for blood transfusion support. A number of natural or synthetic topical hemostatic agent have been developed through the years, including collagen products (i.e. collagen fleece), absorbable gelatin sponges, oxidized cellulose, and synthetic cyanoacrylate-based glue. Among these product fibrin glue has been advocated by many surgeon as the material that best approaches the ideal operative sealant. Fibrin glue, also called fibrin sealant or fibrin adhesive, is a 2 component sealant composed of a variously obtained fibrinogen concentrate (usually containing also other factors such as aprotinin) and thrombin. At the time of utilization the 2 components are mixed in the presence of calcium chloride, thus reproducing the last step of coagulation cascade: thrombin-induced activation of fibrinogen results in the formation of a fibrin clot that consolidates and adheres to the site of application.

As a naturally occurring and human-derived product the material appear to have no tissue toxicity, promotes a firm seal in seconds to minutes, is reabsorbed in days to week and appear to promote local tissue growth and repair (1).

Different types of fibrin glues are currently in use, these products can be basically subdivided into two categories, the commercially prepared and the home-made prepared fibrin glues, that differ for the methods of preparing fibrinogen concentrate. In the commercially prepared fibrin glues, fibrinogen is obtained from fraction I paste obtained through Cohn's fractionation process (2), while in the home-made products fibrinogen is concentrated through the method of cryoprecipitation of allogeneic or autologous plasma (3). Both types of products utilize commercially prepared human thrombin concentrates. Commercially prepared fibrin glues have optimally high fibrinogen concentration, are safe (virus-inactivated), are easy to use but very costly. Home made products conversely, have lower and high variable fibrinogen content, their preparation is time-consuming, can not undergo virus inactivation process but are cheaper.

Beside the large number of experiences demonstrating the efficacy of fibrin glue as adhesive agents in maxillofacial and plastic surgery, numerous reports can be found concerning the hemostatic efficacy of fibrin glue, particularly in European literature. However studies reviewing experiences in human subjects generally fail to compare fibrin glue-treated group with control group. Altogether, despite considerable variation in experimental design these studies have generally shown fibrin sealant systems to be efficacious in controlling slowly bleeding foci, diffuse oozing bleeding from needle puncture site and diffuse parenchymal organ hemorrhage (4).

For these reason fibrin glue has found its most extensive application in the field of cardiothoragic (5) and vascular surgery (6) where it has been successfully used to seal the foci of microvascular bleeding (form anastomoses and needle puncture sites) and in prosthetic valve implantation. Moreover fibrin sealant have been successfully used to control bleeding at the site of dental extraction or minor surgical procedures in patients who are at increased risk for bleeding because of congenital coagulopathies or the use of anticoagulants (7).

Few experiences and reliable data on efficacy have been collected in the field of major bleeding surgery. Recently the efficacy of fibrin glue obtained from cryoprecipitate of autologous plasma has been evaluated in our Institute in patient's undergoing major orthopedic surgery. In this experiment a recently developed automatic device to produce cryoprecipitate has been utilized. The device (Thermogenesis-Dideco Cryoseal) allows to obtain the production of 7-10 mL of cryo from 250 mL of plasma in 30-40 minutes. Cryo was topically applied into the femour canal before the prosthesis installation through a delivery kit allowing the mixing of cryo with a solution of 100U/mL of human thrombin (Ortho Diagnostics) in a 1:1 ratio. The efficacy of the fibrin glue utilization has been determined by comparing between the 2 groups the perioperative RBCs loss calculated as the reduction of the circulating RBCs mass from presurgery to the 5th postoperative day plus the volume of RBCs transfused during this period. Despite age, body mass, baseline and preoperative Hct were comparable in the 2 groups, patients receiving intraoperative application of fibrin glue had significantly lower perioperative RBCs loss (640 ± 121 mL vs 904 ± 152 mL of RBCs; $p = 0.000$), with a mean saving of 264mL of RBCs per patient. Moreover patients in fibrin glue group had a reduced transfusion requirement (2.2 ± 1 vs 2.9 ± 0.9 units of blood) The difference was not statistically significant due to the limited number of cases. None of the patients had any adverse effect related to the use of the study agent. These results, although preliminary, seem to indicate that fibrin glue may represent an effective further strategy to reduce perioperative blood loss also in major bleeding surgery. However further studies are needed to define the cost-effectiveness of the procedure and the role that fibrin gluing may have in transfusion medicine.

Perioperative salvage

Perioperative salvage refers to the collection and reinfusion of autologous RBCs lost by a patients during surgery (intraoperative salvage) or in the early postoperative period from surgical drains (postoperative salvage).

Two kinds of systems are currently available for these procedures. The basic difference is whether or not cells are washed before they are returned to the patient. In the washing systems, aspirated RBCs are concentrated in a centrifuge and then washed with saline. The end product, the patient's own red cells suspended in saline, is then spun off into a concentrated pack for reinfusion. These systems represent by far the most extensively utilised method for intraoperative salvage. In the systems for transfusion of unwashed RBCs, the collected shed blood, mixed or not with anticoagulant, is returned to the patient through filters. The use of these systems is generally restricted to the postoperative salvage.

When the safety profile is concerned it has been observed that if the shed blood is collected by sterile methods and properly transfused the procedure has few risks. In particular it has been claimed that the risk of clerical error is practically non existent if blood collection and patient are at the same site and reinfusion is conducted without the blood having left the patient side (9). There are, however some contraindications to the use of perioperative salvage (infection, cancer) and some medical controversial hazards (coagulation derangement after reinfusion of salvaged blood).

Infection in the operative field is widely regarded as an absolute contraindication to perioperative blood salvage. Indeed, no existing system of blood filtering or washing can completely eliminate bacteria. Although some reports refer of positive outcome of patients receiving contaminated salvaged blood the use of blood recovered from a contaminated field is justified only for life-threatening bleeding with no available banked blood.

The use of blood salvage is regarded as contraindicated in cancer surgery as concern exists that tumour cells harvested during perioperative salvage would be reinfused to the patient and promote metastatic disease (10). Although an increased incidence of recurrence or metastasis in cancer patients receiving salvaged blood during cancer resection surgery has not been documented, the safety of the technique has not been established and the transfusion of blood contaminated with malignant cells should be avoided. Recently, very promising results have been obtained with blood irradiation. Experimental studies have shown that blood irradiation with 50Gy is very efficient in eliminating cancer cells that contaminate the surgical field. This effective strategy suffers from relevant problem of feasibility (availability of the blood irradiator close to the operating room; special transfusion bags) and exposes to an increased risk of mistaken exchange; however several hospital in Europe are now utilising successfully blood irradiation for intraoperative salvage in cancer surgery (11).

A long standing controversy focuses on the coagulation risk to the patient who receives unwashed salvaged blood as the product is partially hemolyzed and defibrinated and may contain high concentration of cytokines, vasoactive contaminants, activated clotting factors and fibrin degradation products. Moreover when large volume of unwashed salvaged blood are reinfused the amount of anticoagulant (heparin or ACD) may be clinically relevant (10). A number of animal and human studies addressed the issue of whether or not it is safer to wash salvaged blood prior to reinfusion but no conclusive results have been obtained. Taking the different studies together it can be concluded that although unwashed blood may contain potentially harmful soluble products, its use appears to be safe if transfusion is limited to small quantities (< 1000-1400mL of whole blood) and to appropriate circumstances, avoiding transfusion of unwashed blood in the presence of shock, acidosis or hypoperfusion (12,13).

One of the major advantages of perioperative salvage is that is logistically easier to organise than other autotransfusion technique and it is not affected by cancellation of operation and is applicable in emergency cases. The salvaging of blood does not in itself involve any manipulation of the patient's physiology and it is therefore applicable in patients where acute normovolemic hemodilution and PABD are not, for example when the patient is already anemic. However, specially when washing systems are utilised, to ensure a quality blood component for transfusion, a well-designed program and an appropriately trained staff are necessary.

When the efficacy of technique is concerned it can be observed that it provides a ready supply of blood that is available in proportion to the losses that are occurring and, in the event of massive haemorrhage, its use may occasionally be lifesaving if the rate of blood loss outstrips the availability of the allogeneic supply. Moreover, numerous studies have shown that perioperative salvage reduces allogeneic blood transfusions, especially in high-volume blood loss situations such as liver transplantation, extensive scoliosis repair, and complex cardiac (coronary artery graft and valve replacement) and major vascular surgery (9). More controversial is the efficacy of perioperative salvage in other major orthopedic work as major joint replacement and trauma (14,15). In our Institute it has been calculated that, in orthopedic surgery, the recovery varies between 30% and 45% of the blood lost during operation time (tab 1) and constitutes the 5% - 32% of all the blood transfused in patients undergoing different major orthopedic procedures.

Tab. 1 Total perioperative RBCs loss, RBCs loss the day of surgery and mL of RBCs salvaged during surgery and in the early postoperative period (mean ± standard deviation) in different major orthopedic surgical procedures

Type of Surgery	*n° Pts (F/M)*	*Total perioperative RBcs loss (mL of RBCs)*	*RBCs loss the day of surgery (mL of RBCs)*	*Perioperative RBCs salvage (mL of RBCs)*	*% of RBCs salvaged*
Total Hip Replacement	614 (414/200)	866 ± 316	592 ± 255	176 ± 138	29
Hip Revision	58 46/12)	1276 ± 484	959 ± 473	421 ± 265	44
Bilateral Hip Replacement	38 (34/4)	1831 ± 449	1357 ± 562	464 ± 190	34
Total Knee	84 (66/18)	766 ± 224	509 ± 218	178 ± 124	34

The subject of cost-effectiveness for intraoperative and postoperative salvage, including washed versus unprocessed blood, is a complex one, and has not been adequately addressed in any large prospective controlled study. Most researchers have sought to show whether or not the technique achieves cost equivalence with allogeneic blood as the determining measure of its effectiveness. With the use of automated cell-washing devices, it is generally agreed that the equivalent of at least 1.5 – 2 units of blood needs to be recovered in order for the method to be cost-effective (16,17). Thus selective use of the method in situations in which large perioperative blood loss are anticipated would improve the cost-effectiveness of the procedure, but such blood losses are difficult to predict. Indeed, the amount of blood that is lost during surgery and that can be recovered depends on a number of unpredictable variables, beside the type of operation. Consequently the identification of the cases in which the salvaging procedures have to be performed may be erroneous when based only on the type of operation.

To offer all the patients the benefit of salvaging their own blood but maintaining a favourable cost-benefit ratio the "stand-by procedure" is utilised. It consists in mounting the collection set in all the procedures where transfusion is expected and proceed to the washing cycle only if enough blood has been recovered. However, the estimation of the volume of RBCs that can be actually rendered available for transfusion may be fallacious when it simply relies on the volume collected into the reservoir. To estimate the volume of RBCs that can be saved and transfused before proceed to the washing cycle we defined a mathematical approach (18) that takes into account the total volume collected into the reservoir (Vol in reserv) the volume of anticoagulant solution (anticoag), the volume of solutions used to irrigate the surgical field (irrig solut), the patient's preoperative hematocrit (preop Hct), and the expected hemolysis, expressed as a ratio, occurring throughout the process (hemolis ratio); according to the following formula:

Expected volume of salvaged RBCs =

= Š(Blood in reserv - anticoag - irrig solut) x Preop HctĆ x (1 - hemol ratio)

We prospectively compared the estimated volume of salvaged RBCs (calculated with the formula assuming an hemolisys ratio of 0,3 Š30%Ć) with the volume of RBCs actually salvaged in 99 patients undergoing different orthopedic surgical procedures. An optimal correlation between the estimated and the actually collected salvaged RBCs was obtained ($r = 0,957$). Out of 27 cases where the expected RBCs yield was > 180mL only in 3 cases (11%) we actually obtain less than 180mL, while out of 72 cases where the estimated yield was < 180mL of RBCs only in 8 cases (11%) the actual yield was higher (Pearson's chi square = 54.3; $p=0.000$). The formula seems to represent a simple and precise method to estimate the volume of RBCs that can be saved and can be used during a "stand by" procedure to base the decision to process the collected blood, thus improving the cost-effectiveness of the technique.

Acute normovolemic hemodilution (ANH)

Acute normovolemic hemodilution (ANH) is the technique in which whole blood is removed from a patient while the circulating blood volume is maintained with acellular fluid shortly before a surgical procedure that is anticipated to result in significant blood loss. In adults the technique is most commonly used when blood loss of > 1 litre is anticipated, and usually moderate hemodilution is employed, the target hematocrit at commencement of surgery being 0,25- 0,3 (19,20).

The rationale of its use is that the blood lost during surgery after hemodilution has a lower hemoglobin concentration, which decreases the amount of hemoglobin lost and thus potentially decreases the need for allogeneic transfusion.

The proponents of ANH observe that the technique can be safely performed in a large number of patients without significant hemodinamic changes because when normovolemia is preserved, the reduction in RBCs results in a decreased blood viscosity and systemic vascular resistance that are associated with preservation of O_2 delivery.

However ANH carries the potential for a variety of adverse effects, even when the use is limited in extent (Hct>0,20). These effects include the occurrence of peripheral edema, and an increase in lung water when crystalloid is used for replacement. The latter effect may have implications for wound healing and post-operative lung function, although no studies have been reported (20).

The most significant potential risk with ANH is that of myocardial ischemia, the risk of which increases with decreasing hematocrit, in patients with impaired compensatory mechanisms to anemia. In patient with abnormal ventricular function ANH may induce ischaemic ECG changes and in patients with cardiovascular diseases the risk of

silent myocardial ischaemia in the perioperative period can be possible. It has been found that myocardial ischaemia is frequent in this group of patients even in the absence of hemodilution(21). At even greater risk are the patients with pre-existing heart diseases. However in one randomised study of patients with coronary artery disease undergoing aortic reconstruction it appeared that ANH-treated patients were less likely to develop myocardial dysfunction at the time of cross-charging than controls (22).

Another relevant issue regarding the safety of ANH is the chance of clerical errors. While many Authors claim that ANH minimise the risk (as the blood units generally remain in the operating room) concern exists on proper and safe management of blood units when many procedures are performed daily at the same time and from each patient a relevant number of blood units are collected (and some of them have to be transfused in the recovery room). Consequently an initial training, performed by the personal of the blood transfusion service, can be necessary for blood collection, management of the bags, patients and units identification and storage

There is no doubt that ANH has several logistic advantages over other modalities of autologous transfusion. Scheduling difficulties may preclude the use of PABD in urgent or emergent circumstances while are not limit to the use of ANH. Moreover when PABD is undesiderable or impossible (e.g. there is a potential for bacteremia or too little time for donation) ANH may be the appropriate solution. ANH can also be considered when malignancy or infection at the operative site precludes the use of perioperative salvage. Finally, ANH may also be convenient for patients and saves them from having travel to the centre to make donations.

It has been claimed that ANH is simple to perform, has not impact on staffing because usually is performed by anaesthesiologist and does not prolong operating room time (23-25). The latter, however, is an argument of debate. As ANH can be performed in awake and anaesthetised patients it can be implemented both in a surgical "prep" area- or in the OR. In order not to impact overall OR time, by delaying the onset of surgery, it is suggested to initiate ANH immediately following tracheal intubation and complete it after the induction of anaesthesia, during the initial period of the operation when blood loss is minimal. However taking into account that approximately 10 minutes are required to collect one unit of blood, when extensive hemodilution is carried out the time required to collect the required amount of blood may be not compatible with the surgical timetables. When ANH is performed an adequate preoperative evaluation of patient's cardiovascular condition and a careful monitoring during hemodilution are mandatory. The monitoring required depends upon hemodilution and the physical condition of the patient. Placement of a pulmonary artery catheter is usually indicated if extreme hemodilution is to be employed; it is not necessary for moderate hemodilution. However, the procedure must be performed by experienced personnel. ANH requires vigilance, clinical expertise, and an understanding of the physiologic consequences.

The efficacy of ANH in reducing allogeneic blood requirements is highly controversial. Early studies claimed to document the ANH effectiveness in allogeneic blood conservation, however many of these studies used small group of patients, historic or literature controls and were accompanied by changes in transfusion practice, with lower final hematocrit levels in ANH group compared with control.

A recent metaanalysis of 24 randomized, prospective studies of ANH in 1218 patients concluded that ANH reduced the likelihood of allogeneic exposure and the total number of allogeneic blood transfused. However, in trilas using a protocol to guide transfusion, ANH failed to show benefit (26).

Interesting results have been obtained in studies utilising mathematical modelling to evaluate the clinical efficacy of ANH (27-28). These studies suggest that moderate hemodilution to maintain a preoperative hematocrit of 25% results in the preservation of small volumes of RBCs (equivalent to 0.5 – 1 unit of blood) when the perioperative

blood loss is in the range of 1 – 1.5 litres of whole blood. Only when more substantial hemodilution (Hct <20%) is performed in patients with greater blood loses the savings become more substantial. However such a severe hemodilution requires the collection of very large volume of blood that involves safety concerns in a relevant numeber of patients.

Even more difficult is to define the cost-effectiveness of ANH. As indicated above, studies of ANH are few in number, with small numbers of patients and poorly selected controls. It seems unlikely that studies large enough to determine the relationship between the risks of ANH and the benefits of the reductions in allogeneic blood use achieved by its use will ever be carried out. ANH is a relatively inexpensive form of autologous blood transfusion. However its cost-effectiveness seems questionable as a results of theoretical and observational studies showing that the ability of the procedure in reducing allogeneic blood transfusion is limited.

Presently ANH seems safe, efficacious and cost-effective only when undertaken very aggressively (target Hct<20%) in healthy, young patients undergoing surgery with large (higher than 2 liter) expected blood losses. Such extensive hemodilution cannot be applied in elderly patients because in this case has the potential for adverse event. ANH should therefore be reserved for patients under 40 or for patients over 40 who are at low risk of ischemic heart disease unable to deposit preoperatively sufficient blood to meet their transfusion need or for whom allogeneic blood is unavailable.

Conclusions

In conclusion different strategies to reduce perioperative RBCs loss are currently available whose knowledge is very important to achieve the best from their use. The choice of the most appropriate techniques to be used in the specific patient should be based on the clinical condition of the patient, the type of surgery the patient is undergoing, the logistical conditions and on the availability of the different strategies in the specific setting, their efficacy and cost-effectiveness. As the different strategies to reduce perioperative RBCs loss involve the activity of different medical specialists, a strict co-operation between them is of paramount importance to obtain successfully clinical results without wasting precious resources.

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Techniques to increase tolerated blood loss

F. Mercuriali

Introduction

The requirement for blood transfusion during surgery depends on two major variables:

1.) The volume of perioperative blood loss, which is related to the type of surgery, the adequacy of surgical hemostasis and the surgical and anaesthetic techniques used;

2.) The volume of blood loss that the patient can tolerate before transfusion is indicated,

Thus the reduction of the transfusion requirement and of the use of allogeneic transfusion can be obtained by adopting two different strategies:

1.) Reducing of intra and post-operative blood loss; or

2.) Increasing the tolerated blood loss.

Tolerated blood loss can be increased by following guidelines for a correct indication of blood transfusion, lowering intra and post operative transfusion trigger or expanding the circulating RBCs mass of the patients through the preoperative correction of anemia with ematinics, utilizing preoperative blood donation, or stimulating erythropoiesis with rHuEPO treatment.

Indication for blood transfusion in surgery

The objective of blood transfusion in the majority of surgical and traumatic patients is to prevent or correct tissue hypoxia following acute blood loss. For many years has been internationally debated the definition of the values of Hb/Hct to be considered as transfusion trigger. Although there is a general agreement that the decision to transfuse depends not only on the values of Hb or Hct but has to be the conclusion of a thorough clinical evaluation, it is accepted that blood transfusion is rarely necessary when Hb is higher than 9 g/dL, most patients should receive blood transfusion when Hb is lower than 7 g/dL and when Hb is between 9 g/dL and 7 g/dL the decision to transfuse should be based on clinical judgment (1-3).

Recently proposals to lower transfusion trigger have been discussed based on the results of studies performed in critical care patients comparing restrictive versus liberal RBCs transfusion policy, and on the experience acquired in patients refusing blood transfusion. In critically ill patients no difference in mortality at 30 day, organ dysfunction score, length of stay in intensive care unit and total hospital stay between the two groups has been documented (4). Moreover in patients who refuse blood transfusion it has been shown that when Hb is < 5 g/dL in most cases mortality is due to anemia but when Hb is > 5 g/dL there is a lack of substantial rate of mortality due to anemia (5). This might reassure clinicians in their decision to consider lower transfusion triggers. However transfusion at a rigid Hb threshold without consideration of the patient's general clinical condition should become an increasingly infrequent event because there are many conditions limiting the ability to anemia (table 1). Patients at greater risk of undertransfusion are reported in table 2.

Table 1 Conditions limiting the ability to adapt to anemia

Age = impairment of cardiovascular and respiratory adaptation.
Cardiopathy limiting cardiac output adaptation capacity
aortic stenosis;
obstructive cardiopathy, cardiac insufficiency;
fixed-frequency cardiac stimulator, auricular fibrillation;
Coronary insufficiency = patients in whom myocardial ischaemia can be induced by a reduction of circulating Hb.
Chronic hypoxemia = respiratory insufficiency.
History of cerebrovascular accidents.
Assumption of drugs interfering with adaptation mechanisms.

Table 2 Patients at greater risk of undertransfusion

Intensive care patient
High fluctuation of Blood Volume (BV)
Pre-term infants
Variable BV according to clamping time
Elderly "medical" and "post-surgery" patients
Edematous critical care patients
Hypovolemia generally unrecognized

The Policy adopted in our hospital and agreed upon with surgeons and anesthesiologist is reported in table.3.

Tab 3 Transfusion trigger in different operative period

During general anesthesia:	The reduction in metabolic needs reduces the risk of O2 transport insufficiency (Hb = 7 g/dL are well tolerated).
Awakening period:	O2 demand increases (Hb = 8-9 g/dL).
Postoperative period:	Depends on the possible continuation of hemorrage on the energy needs for the reeducation and convalescence (Hb=8-10 g/dL according to cardiovascular considerations).

Relationship between anemia and transfusion requirement

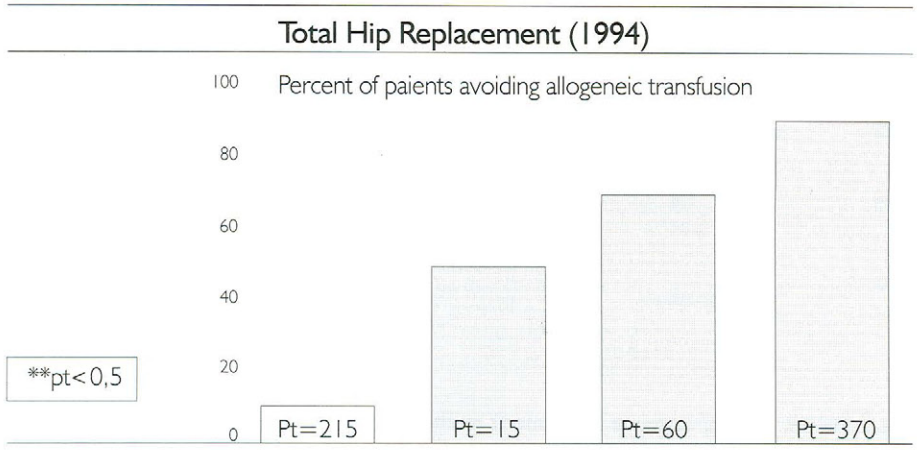
Tolerated blood loss is mainly affected by the clinical conditions of the patient, particularly by the cardiopulmonary condition and the haematological status. Low baseline hematocrit has been shown to be a critical parameter in affecting transfusion requirement. The incidence of preoperative anemia is relevant in many categories of patients but particularly in patients with anemia of chronic diseases [ACD] (1,2). The patients more interested by this type of anemia are those with cancer and rheumatoid arthritis (6,7).

Anemia is common in cancer patients, especially in those with more advanced stages of progressive tumor growth (8) and represents an important component of the morbidity related to the malignancy. Few data are available on the frequency of anemia, however it has been reported that about one half of patients with cancer are anemic, the frequency varying on type of cancer, stage and chemotherapy or radiation therapy used. The pathophysiology of the anemia associated with malignancy is multifactorial and not completely understood. However in the majority of cases the ACD plays a major role. The anemia generally develops slowly and is usually mild to moderate in

severity with hemoglobin values in the 8-10 g/dL range. However, specially in patients receiving chemotherapy values can be < 7 g/dL. It has been reported that the percentage of patients requiring transfusion ranges from 20 to 50% (8). The percentage dramatically increases when patients undergo cancer surgery: in a meta-analysis of 14 studies in colorectal cancer it was calculated that allogeneic blood transfusion was given in 45-84% of subjects (9).

As for cancer patient, anemia is one of the most frequently occurring extra-articular manifestations of rheumatoid arthritis. Although iron, vitamin B12 and folic deficiencies are quite prevalent as indeed is the anemia arising from complications during anti-rheumatic drug therapy, ACD is one of the major underlying causes of low hematocrit values in these patients. The anemia is usually mild and relatively well tolerated (generally no more than 10% of the patients have a severe anemia) (10). However when progression of the disease requires major orthopedic surgery, anemia can preclude the collection from the patient of sufficient blood to cover his or her transfusion needs.

Low baseline hematocrit values, however, have been found detrimental also in surgical patients without underlying diseases candidate to elective orthopedic surgery (11). Indeed it has been demonstrated that in patients enrolled in predonation program the inability to donate the optimal number of autologous units is the major cause of allogeneic transfusion (fig. 1).



	Salvage only	1 AB Pred	2 AB Pred	3 AB Pred
Blood loss (mL rbc)	630	620	643	782
HB units tranf.	2,48	1,23	0,43	0,22 **
Baseline Hct	39,3	40,5	40,1	41,1
Hct 3 days postop	28,2	26	28,3	28,3
Hct 7 days postop	29,9	28,9	27,8	29,2

Fig. 1 Percentage of patients avoiding homologous blood (HB) transfusion, mean perioperative blood loss, mean number of homologous blood units transfused and mean hematocrit values at baseline, 3 days and 7 days after surgery in 660 patients undergoing primary total hip replacement subdivided according the number of autologous blood units predeposited.

The volume of blood that the patient can predeposit during the period before the operation is a function of the total circulating red blood cells (RBCs) mass and the rate of recovery of Hct after collection. A low baseline hematocrit not only preclude the possibility of predonation when is below 34%, but also significantly affect the quantity of blood that can be donated. For each unit of autologous blood (350-450mL) collected, a mean decrease of 1g/dL of hemoglobin and 3 points of hematocrit is observed. With the collection of 3 units of blood the Hct value is reduced by about 10 points. Consequently in a relevant percentage of patients with baseline Hct below 39-40 % the value drops below 34% (threshold value for donation) after the collection of

the first or second bleeding. It has been estimated that anemia precluded the enrolment into the donation program of 10% of surgical patients and limited the number of units collected in 31% of the patients (11).

To define the critical Hct value below which the patients would be at higher risk of receiving allogeneic blood transfusion we correlated the number of units actually predeposited by the patients and the need to integrate autologous blood with allogeneic blood to the baseline Hct value. We found that when baseline Hct values were lower than 37% the blood that the patients could predeposit (0-1 unit) was generally insufficient to cover their transfusion need; when Hct values were included between 37% and 40% autologous blood donations covered transfusion requirement in approximately 56% of cases, while when Hct values were higher than 40% the patients could predeposit 3 or more units of blood and were exceptionally exposed to the risk of being transfused with donor's blood. (11) (fig3).

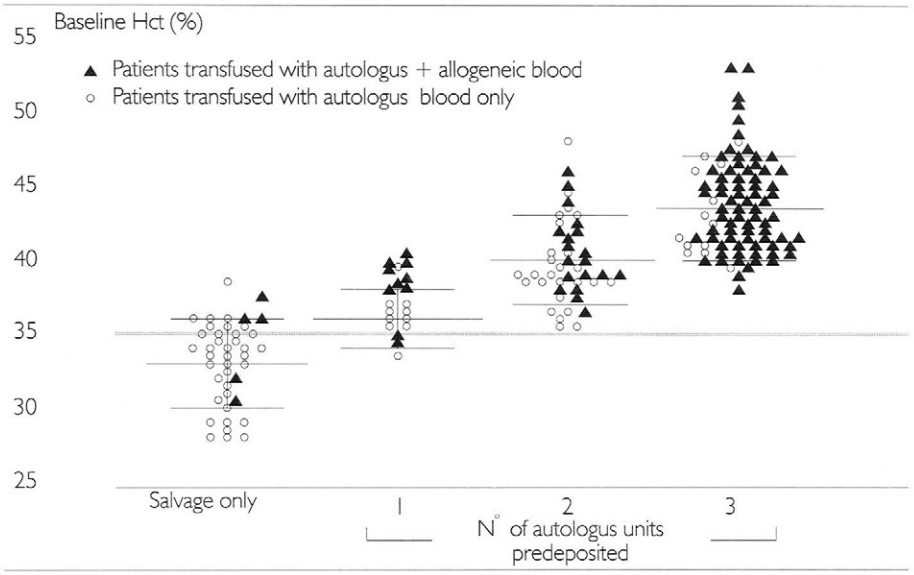


Fig.3 Relationship of baseline hematocrit to the number of autologous units collected and the ability to cover transfusion needs exclusively with the use of autologous blood

To better define the distribution of the baseline Hct values in the orthopedic surgical patients population we analysed the data from 2183 patients candidates to different orthopedic surgical procedures in the Orthopedic Institute of the University of Milan.

Patients have been subdivided into different classes according to the baseline Hct value and the underlying disease conditioning the need for surgical intervention (tab.4). Out of 2183 evaluated patients, a total of 381 patients (18%) had a baseline Hct lower than 34%, value that prevents the use of PABD, method of proven efficacy to reduce the use of allogeneic blood in surgical patients. Moreover a total of 1010 patients (46%) had baseline Hct values between 34% and 40% and are at high risk of allogeneic blood transfusion when undergoing to major orthopedic surgical procedures with expected transfusion need of 2-3 units. Only 792 patients (36%) had optimal baseline values (higher than 40%). As expected the incidence of baseline Hct values lower than 34% was only 7% in patients whose underlying disease was arthrosis but increased to 25%, 30% and 42% in patient with rheumatoid arthritis, cancer or sepsis, respectively. In trauma patients the incidence of such a low value resulted to be 35%.

The last 1034 have been thoroughly examined for iron deficiency. In 73 patients (7%) an iron deficiency has been documented. Sixty of these patients have been treated with intravenous administration of iron sucrose (700-900 mg of elemental iron). In 30 day an increase of Hct from 35.4% + 2.7 to 37.6% + 2.0 was documented with a mean RBCs production of 135 ml.

Tab 4. Distribution of baseline hematocrit in orthopedic surgical patients operated at the Gaetano Pini Orthopedic Institute in 1997

	20.5% - 29.9%	30% - 33.9%	34% - 39.9%	40% - 55.9%	TOTAL
N°of Pts (% of total)	129 (6)	252 (12)	1010 (46)	792 (36)	2183
Female	99 (6.5%)	203 (13.3%)	831 (54.6%)	389 (25.6%)	1522
Male	30 (4.5%)	49 (7.5%)	179 (27%)	403 (61%)	661
Arthrosis	19 (1.5%)	70 (5.5%)	624 (48%)	585 (45%)	1298
Rheumatoid Arthritis	6 (7%)	16 (18%)	42 (52%)	19 (23%)	82
Cancer	14 (14%)	17 (16%)	39 (38%)	33 (32%)	103
Sepsis	8 (14%)	16 (28%)	17 (30%)	16 (28%)	57
Trauma	78 (13%)	126 (22%)	264 (45%)	113 (20%)	581
Other	4 (6%)	8 (13%)	24 (39%)	26 (42%)	62

Accordingly to the analysis a consistent proportion of patients undergoing major surgical procedures can be expected to be unable to face perioperative transfusion need exclusively with the use of autologous blood obtained utilising the currently available autotransfusion techniques (PABD, perioperative blood salvage and ANH). In these patients the administration of recombinant human erythropoietin (rHuEPO) may be a valuable adjunct to increase the efficacy of all the autotransfusion techniques (12,13).

Several studies have evaluated, in different group of patients, the efficacy of rHuEPO in enhancing the collection of autologous blood in patients candidate to elective surgery, in correcting anemia before surgery and in accelerating postoperative erythropoietic response thus reducing the use allogeneic blood (14-20). In all the clinical studies considered, rHuEPO was found to be effective in stimulating erythropoiesis and increasing new RBC production (although this was found to vary considerably 250 to 900 mL) and the number of units predeposited. It was also effective in correcting anemia induced by blood collection.

The increase in the amount of blood deposited correlated fairly well with the dose of rHuEPO administered. The most common treatment protocol used involved IV administration twice weekly for 3 weeks together with oral iron supplements. Total doses of less than 600 IU/Kg were ineffective in promoting sufficient erythropoiesis to significantly increase the volume of predeposited blood. Higher doses yield a dose-dependent production of new RBCs ranging from 250 mL for total doses of 600 IU/Kg to more than 900 mL for doses of 3,600 IU/Kg. It should be noted that, despite oral iron supplementation, the effect of rHuEPO therapy in autologous donors is very often restricted by iron depletion. Intravenous iron administration allows a more adequate iron supply for erythropoiesis, with either an increased Hb response to the same dose of rHuEPO or a reduction in the dose of rHuEPO required. With the use of IV iron sucrose, RBC regeneration and volume of predeposited blood were identical when total rHuEPO doses of 1,800 and 3,600 IU/Kg were compared. The effectiveness of the SC route for rHuEPO has been shown in several studies. In our experience (Fig

4), SC administration for rHuEPO combined with intravenous iron is highly effective in autologous blood donation and, compared with intravenous administration, allows a marked reduction (approximately 55%) in the total rHuEPO dose (26).

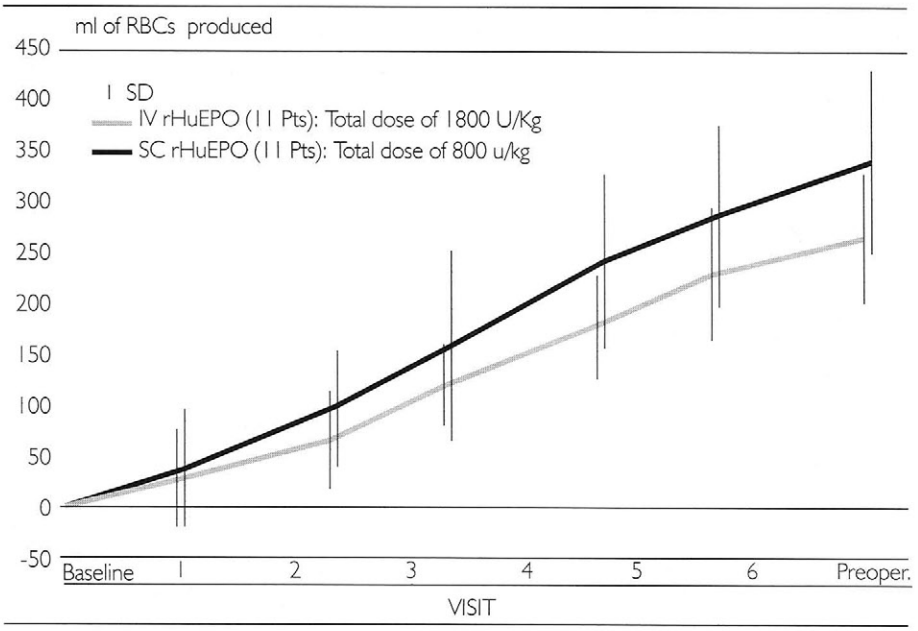


Fig 4 Production of new RBCs in patients treated with IV rHuEPO at a total dose of 1800IU/kg and in patients treated with SC rHuEPO at a total dose of 800IU/kg. Both groups received IV iron supplementation

Recently, some studies have also evaluated the role of rHuEPO in those subgroups of patients for whom preoperative autologous blood donation is not feasible (28). These include patients with anemia or other disorders precluding donation, patients with limited time to surgery, and individuals who are unwilling to participate in an autologous blood donation program because of logistical problems or religious beliefs. For example, postponing the operation in cancer patients or candidates to heart surgery might be more detrimental than receiving allogeneic blood transfusion. In one such study, (29) three different doses of r-HuEPO were used (3000, 6000 and 9000 i.v. 3 times a week for 2 weeks before and after surgery) combined with intravenous iron treatment. In a later perspective placebo controlled double blind study, (30) 2 different doses of r-HuEPO (300 IU/Kg and 150 IU/Kg) were administered subcutaneously for eight consecutive days during the pre-operative period (from day -5 to day +2). A reduced transfusion requirement was evident in both studies.

Perisurgical use of rHuEPO in patients undergoing elective hip replacement reduced from 74% to 33% the portion of patients requiring transfusion when their baseline Hb was less than 13.5 g/dL . (31) Two additional studies have shown significant reduction in transfusion rates with perisurgical use of rHuEPO in subjects undergoing orthopedic surgery with baseline Hb levels between 10 and 13 g/dL. (32,33)

A short-term perisurgical treatment was used in a pilot study at our institute. Sixteen patients for whom predeposit was contra-indicated for various clinical reasons and who were about to undergo major orthopaedic surgery with a predicted transfusion requirement of 2-3 units of blood were enrolled in the study. The protocol involved subcutaneous administration of r-HuEPO at a daily dose of 100 IU/Kg beginning 4 days before surgery (day-4) up to the second day following surgery (day + 2). On the first day of treatment, one 200 IU/Kg bolus was also administered intravenously. Intravenous iron sucrose was administered concomitantly at a total dose of 600 to 1000 mg, according to baseline iron reserve levels. The treatment produced a 2% to 7% in-

crease in Hct, with average increase in circulatory RBC mass of some 100mL (from 0 to 245) before surgery. Twelve of the 16 patients did not require allogeneic transfusion, whereas a total of 6 units of blood was transfused in the remaining 4 patients (34). Although preliminary these findings suggest that rHuEPO administration together with IV iron during a pre-operative period of 4-5 days is able to stimulate erythropoiesis significantly, expand the circulatory red cell mass and reduce the transfusion requirement in patient who, for clinical or logistic reasons (heart surgery and cancer patients) are not able to deposit autologous units prior to elective surgery. Because of the short time period, this protocol could also be offered to a proportion of accident patients about to undergo surgery, when surgery is planned to take place 4-5 days after injury.

Finally rHuEPO administration ha been investigated also in surgical patients with ACD. In a pilot study carried out in our Centre, 11 rheumatoid arthritis patients candidates to major orthopedic surgery were selected for their inability to donate blood for autologous use because of anemia (Hct <34%) and received rHuEPO 300 IU/Kg in combination with iv iron sucrose (100 mg of elemental iron) twice a week for 3 weeks (35). Transfusion treatment was compared with that of 12 untreated patients with anemia of comparable severity. The study demonstrated the safety and efficacy of rHuEPO in stimulating erythropoiesis, allowing preoperative donation of blood for autologous use and reducing exposure to allogeneic blood in anaemic rheumatoid arthritis patients. Indeed control patients could not preoperatively deposit any blood unit for autologous use, while all but one of the rHuEPO treated patients deposited 2 or more units. The control group received more allogeneic units than control patients (mean 2.6 + 1.6 vs 0.8 + 0.8, $p=0.009$). Moreover 50% of rHuEPO treated patients as compared with 8% of controls completely avoided allogeneic transfusion.

Recombinant EPO has been shown to be effective in combination with ABD in patients undergoing transurethral resection of the prostate for treatment of prostate cancer (36). Of the 266 patients who took part in the study, 134 predeposited blood. The rate of allogeneic blood transfusion was 6.7% in this patient group, compared with 14.7% among patients who did not donate autologous blood preoperatively. Furthermore, in 6 patients who received concomitant rHuEPO therapy during preparative ABD, the reduction in Hb level during the predonation period was significantly less marked than among untreated patients (-0.4 g/dl vs - 1.9 g/dl; $p<0.05$). Another study involved the inclusion of rHuEPO (150 IU/Kg subcutaneously three times weekly) into the intensive neoadjuvant chemotherapy regimen of 15 patients with sarcomas, in order to prevent the development of anaemia and allow preoperative ABD (37). Twelve patients with identical neoadjuvant chemotherapy acted as controls. In total, 14 rHuEPO-treated patients (93%) donated autologous blood; one patient could not donate as a result of severe iron-deficiency anaemia. No patient in this group required blood transfusion during chemotherapy, compared with 8 patients (67%) in the control group. Hence, rHuEPO was found to be effective in reducing the incidence of anaemia and transfusion frequently associated with intensive chemotherapy. In addition, treatment with rHuEPO permitted patients to donate autologous blood preoperatively, thereby reducing the risk of exposure to allogeneic blood.

Owing to the high cost of rHuEPO treatment, its routine use is unlikely to be cost-effective. To better select those patient who are very likely to benefit from this treatment we defined a more personalised approach to calculate the expected transfusion need for each single patient (38).

We retrospectively applied the algorithm to 577 patients each of whom predonated 2 or 3 units of autologous blood prior to total hip replacement surgery and subdivided the patients according to the calculated transfusion requirement (tab.5). It can be observed that in patients with calculated transfusion need higher than 500 mL of RBC (representing less than 5% of total evaluated patients), in spite of the utilisation of all

the currently available autotransfusion techniques only 68% of the patients avoided the use of allogeneic blood while this figure was more than 95% in the group of patients with calculated transfusion need lower than 200 mL of RBC. In this group of patient with low calculated transfusion requirement an overcollection of autologous blood has been documented as demonstrated by the wastage of about 20% of the autologous units collected.

Tab.5 Transfusion results in 577 patients operated for total hip replacement subdivided according to the expected transfusion requirement calculated with the algorithm (38)

Transfusion requirement	*< 0*	*0-100*	*100-200*	*200-300*	*300-400*	*400-500*	*>500*
NO of Pts (% of total)	50 (8,7%)	48 (8,3%)	67 (11,6%)	90 (15,6%)	139 (24,1%)	156 (27%)	27 (4,7)
% male	98	93	77	39	6,5	1,3	0
Units predeposited (unit / Pt)	103 (2,0)	109 (2,2)	155 (2,3)	230 (2,5)	355 (2,5)	372 (2,4)	64 (2,4)
Units not transfused	20 (19,4)	21 (19,2%)	29 (18%)	33 (12%)	28 (8%)	19 (5%)	0 (0%)
Pts transfused only auto	98%	98%	95%	85%	82%	80%	68%
Pts with discarded units	16 (32%)	16 (33%)	22 (32%)	26 (28%)	25 (18%)	17 (11%)	0 (0%)
Pts transf. with all AB units with postop Hct<27 %	7 (14%)	9 (18%)	10 (15%)	22 (24%)	51 (37%)	74 (47%)	18 (66%)

If we had applied the algorithm for the choice of the most appropriate blood conservation strategies we would have been avoided unnecessary collection of AB in patients with low transfusion requirement thus saving resources that could have been utilised for a rHuEPO treatment in patients at higher risk to require allogeneic blood transfusion because of low baseline Hct values..

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Transfusion alternatives in orthopaedic surgery

Peter Earnshaw

Extracted from article "Transfusion Alternatives in Orthopaedic Surgery"

Summary

The volume of orthopaedic surgery is large and growing – over 200,000 hip and knee arthroplasties were performed in the USA alone last year – and these patients are at particularly high risk of requiring a blood transfusion. Orthopaedic surgeons can significantly reduce the amount of allogenic blood transfused by following simple guidelines. Accurate data gathering has allowed us to better target those most at risk. A wide range of strategies is available including, but not limited to, review of transfusion triggers, autologous predonation, haemodilution techniques, blood salvage and the use of perioperative erythropoetin. Some techniques are particularly suited to orthopaedic surgery and the use of an algorithm can help us to select the best approach for the individual patient.

CHAPTER SUBHEADINGS

INTRODUCTION

The problems of allogenic transfusion are already well documented both in the reduced availability of blood and the multitude of potential risks with its use. Orthopaedic surgeons along with cardiac/vascular surgeons are probably the biggest users of blood products. Even small changes to routine procedures can lead to enormous benefits for patients, physicians, hospitals and society in general.

Until recently the true scale of the problem has been very difficult to elucidate. Simple questions such as " How much blood is lost in hip replacement surgery?" or "How much does a unit of packed cells cost?" have been impossible to answer. An amazingly wide range of figures is quoted from different sources. How can the problems be solved without this basic information? Recently, greatly improved data collection has clarified such information giving us a better starting point when trying to address the problems

Orthopaedic surgery can be divided into the fields of elective orthopaedics and trauma. The elective aspects, particularly joint replacement and spinal surgery, are well suited to the many techniques available to help reduce the use of allogenic blood. Trauma by definition is acute, unpredictable and a much bigger challenge.

The day to day practise of orthopaedic surgery varies widely between countries, hospitals and even individual surgeons. There are many choices and often difficult decisions to be made - Which type of surgery? Which anaesthetic? Is a predonation programme available? Is erythropoetin cleared for use by the regulatory bodies? What are the cost benefits of any of these programmes?

Much of the recent literature in the field of transfusion alternatives has come from orthopaedic departments in Europe and N. America. All are agreed on the necessity of reducing the exposure to allogenic blood but there still remains a great deal of controversy on the best way to do it. This chapter will set out the options available and attempt to provide a consensus on today's žbest practice' for the orthopaedic community.

THE SCALE OF PROBLEM - DATA COLLECTION

Orthopaedic surgeons make high demands on blood banks. In the USA each year as many as 300,000 people sustain a hip fracture. Almost all of these require surgery and a high percentage require transfusion of allogenic blood. This is only a single part of the increasing volume of trauma seen in most orthopaedic centres. As our population ages and our technology improves we have seen an explosion in the amount of elective orthopaedic work, particularly in the field of joint replacement and spinal surgery. In the United Kingdom last year nearly 100,000 hip and knee arthroplasties were performed with perhaps half of these patients receiving allogenic blood.

Surprisingly, it is only recently that useful data has been collected on a large scale. Until then the data was usually from individual surgeons or units. This data allows us to see the scale of the problem. 330 Orthopaedic surgeons across the USA combined the information of blood management for patients having hip or knee arthroplasty. In the USA, the "standard of care" is usually to offer autologous predonation. A transfusion (autologous or allogenic) was given to 46% of the 9482 patients. The prevalence was higher in hip arthroplasty (57%) than knee arthroplasty (39%) Despite the high collection rate of autologous blood, only 55% of these units were actually given back to the patient. Unilateral knee arthroplasties, primary and revision, were associated with the most wastage. Breakthrough transfusions of allogenic blood in patients who had predonated blood were necessary in 9% of patients. As expected this was most likely with revision hip arthroplasty.

In formulating a strategy for blood management, it is important to identify the patients most at risk. This allows the treatment to be tailored to the individual. Not only is this beneficial in the clinical setting but also in providing the most cost-effective solutions. It seems rather simplistic to state that a patient with a lower preoperative Hb is more likely to need a transfusion. Nevertheless, many studies have detailed the likelihood of transfusion based upon the patient's preoperative status. Most institutions use the maximal surgical blood order schedule (MSBOS). This certainly improves the efficiency of blood ordering practices but only deals with the group as a whole not the individual.

Estimated blood loss, age, weight and aspirin use are all indicators but by far the strongest predictor is the preoperative Hb level. Whenever this falls in the range of 10 – 13g/dl the patient has a significantly higher risk of requiring allogenic blood. By utilising this simple data it was possible in one Orthopaedic centre to reduce the amount of blood crossmatched for total hip arthroplasty from 676 units to 265 units, a decrease

of 61% with significant cost savings. Put another way, the crossmatch to transfusion ratio was reduced from 1: 3.14 to 1: 1.23. More recently, the use of an algorithmic approach has been suggested

Unfortunately, despite this data collection, there are still many as yet unexplained variables Even with a well-defined situation i.e. primary total hip arthroplasty, the transfusion rate can vary between hospitals from as low as 25% to nearly 100% (Table 4).

TECHNIQUES APPLICABLE TO ORTHOPAEDIC SURGERY

These techniques are discussed in more detail in other chapters but it is helpful to remind ourselves of the available options. Although there are many choices, it is quite rare to find an orthopaedic centre that can offer the whole range. In the USA and many European countries predonation of blood for autologous transfusion is perhaps the most widely utilised method.

Lowering Transfusion Triggers

This is the simplest method of reducing the use of allogenic blood. Too often blood is given to patients on an empirical basis. In my own institution, for many years, blood was ordered and given to over 60% of patients undergoing hip and knee surgery, usually on the basis that "most patients need it anyway". At times patients undergoing total knee arthroplasty with a tourniquet inflated were transfused even before any blood was lost! It is essential to educate the relevant staff members who may order this transfusion. This may be the anaesthetist, the junior surgical staff or, not infrequently, the surgeon himself who is unwilling to change his practice despite overwhelming evidence to the contrary. By realising and acting upon the simple fact that the majority of patients can tolerate haemoglobin of 8 or 9gm we were able to halve our transfusion rate almost overnight.

Choice of Surgical Procedure

Some choices are obvious and mainstream now. The use of closed techniques for nailing long bone fractures significantly reduces blood loss. Similarly, the use of external fixators for unstable pelvic fractures not only reduces blood loss but at times can be life saving. Early open surgery is not infrequently associated with catastrophic blood loss.

Preoperative Planning

It is essential that the surgeon is familiar with the patient, the procedure, the instruments and the implants. Preoperative planning and rehearsal can save valuable time and reduce blood loss

Modification of surgical techniques

This is another very simple and cost effective way of reducing the use of allogenic blood. Adherence to good surgical principles will lower the blood loss often dramatically. This may involve taking more time to identify and control bleeding vessels before the surgery proceeds. Many procedures have their own potential problems. Perforating branches of profunda femoris artery are often injured when approaching the shaft of the femur. Branches of the circumflex vessels are at risk with a posterior approach to the hip. The superior lateral geniculate artery may be cut during knee surgery. A few extra seconds to locate and avoid or control these arteries can make a big difference to overall blood loss.

Positioning

Appropriate positioning can help lower blood loss. This is particularly helpful in spinal surgery where the intra-abdominal pressure can be lowered with the use of special frames or supports thus preventing congestion of the epidural veins.

Choice of Anaesthesia

It has long been recognised that spinal anaesthesia for total hip replacement surgery can have significant advantages. More recently the beneficial effect of hypotension on intraoperative blood loss during total hip surgery under epidural anaesthesia has been reported. Using this technique led to significantly lowered blood loss, improved bony surfaces for implant fixation and shorter surgical time. The surgical blood loss was reduced from 700ml to approximately 250ml.

Perioperative Use of Pharmacological Agents

There is only limited experience in the use of these agents in orthopaedic Surgery. It is suggested the use of Desmopressin with Harrington rod spinal fusion surgery can reduce blood loss by 32.5%. No benefit was noted with total hip surgery however. Aprotinin has been reported to reduce blood loss in total hip arthroplasty.

Preoperative Optimisation of Medical Status

The majority of patients undergoing orthopaedic surgery have a number of comorbid conditions, which need to be addressed preoperatively. Probably half are hypertensive. Many are taking aspirin, non-steroidal anti-inflammatory agents or anticoagulants. Coagulopathies should be recognised and treated.

Perioperative Erythropoetin

A large number of studies have recently been completed confirming the safety and efficiency of erythropoeitin. Used alone in the perioperative period or as an adjunct to maximise a predonation programme, red blood cell production is increased and allogenic transfusions are reduced. Recent studies are helping to define more clearly the patients who will most benefit from the use of this agent.

Predonation of Autologous Blood

Predonation has been the" standard of care" in many orthopaedic units across the world for a number of years. Although generally effective there are increasing concerns related to cost factors, the increase in preoperative anaemia and the large number of wasted units.

Haemodilution Techniques

As yet there is only limited information available in the orthopaedic setting. There are probably indications for its use when blood loss is expected to be moderately high and the patient has no coronary artery, renal, hepatic or pulmonary disease. Skill levels need to be high and the time and costs need to be considered.

Blood Salvage – Intra and Post operatively

Simple drainage systems which collect, filter and reinfuse shed blood postoperatively are very popular and will be discussed further in relation to specific procedures. It is possible to reinfuse an average of 437ml after primary total hip replacement and 883ml

after primary total knee replacement. Intraoperative salvage is much more costly in the use of time and staff and has more limited applications. It is perhaps useful for extensive spinal surgery. Blood salvage does reduce the need for allogenic blood transfusion but not in all cases. It is particularly effective when combined with other techniques such as predonation or perioperative erythropoeitin.

Blood Substitutes

Perfluorocarbons and haemoglobin solutions may yet have a significant role to play but are still in the phase II testing stage. Minimal data is available in the field of orthopaedic surgery.

RECENT STUDIES AND RECOMMENDATIONS FOR SPECIFIC ORTHOPAEDIC PROBLEMS

Primary Total Hip Replacement

Total hip arthroplasty (THA) is one of the commonest elective procedures in orthopaedics. Current data suggests over half of these patients will receive a transfusion of allogenic or autologous blood. The true blood loss is hard to accurately assess and this causes problems when trying to compare reports from different sources. The measured loss – suction, sponge weighing and drainage – is invariably much lower than the true loss if this is calculated using the pre and postoperative Hb levels. The true loss is variable and depends upon both the patient and the surgeon with an average around 1600ml. Overall 53% of patients received a transfusion, on average 2 units.

The majority of patients participate in a predonation programme (65%). In the remainder, with no predonated blood, 32% received an allogenic transfusion compared to a 16% breakthrough rate in the predonation group. There is also a great increase in the transfusion rate when preoperative anaemia is present.

A predonation programme obviously does decrease the need for allogenic blood in primary THA. However, there are still some serious concerns:

1.) Autotransfusion is not completely žsafe'. Clinical errors and infection can still occur.
2.) There is a high level of wastage. About half the units are not used.
3.) Preoperative anaemia is more likely with predonation. The erythropoeitic response to phlebotomy is unexpectedly rather poor.
4.) Predonation is neither cheap nor easy to arrange.

The usual recommendations of performing the procedure adhering to good surgical principles in a timely fashion need not be repeated.

The use of hypotensive epidural anaesthesia has been shown to reduce the blood loss significantly and is used in many orthopaedic centres routinely.

Acute haemodilution is safe and effective but probably not required for the majority of primary THAs. It requires a high level of skill and is time consuming.

There is some debate concerning the effect of different implants. 25 matched pairs of THAs, half uncemented and half hybrid or cemented, were compared. There was no significant difference noted in the blood loss and transfusion rate.

Intraoperative salvage is costly in time and staffing and rarely warranted in primary THA. Postoperative reinfusion drains can be used but most blood loss is intraoperative and the trend is now to avoid the routine use of drains.

Suggestions

Predonation is very popular but it is very wasteful for all patients to participate. If an individual insists upon participating then 1 unit would usually be adequate rather than the usual 2 units. The management must be tailored to the individual. If he is otherwise healthy with a Hb > 13gm/dl then transfusion is very unlikely. For the anaemic patient or one who is unwilling or unable to predonate blood, a perioperative course of erythropoeitin is appropriate. Erythropoeitin alone may be as effective as a predonation programme. Postoperative drains are not routinely indicated.

Revision Hip Replacement

Revision surgery is accounting for an increasing percentage of hip arthroplasty. The implants inserted in the 70s and 80s are now reaching 15-20yr follow up and the failure rate is rising significantly. Revision surgery is much less predictable than primary surgery and preoperative planning is more difficult. At times the surgery is no worse than a primary procedure, but more likely there will be problems with dense scar tissue, large areas of exposed bone, osteolysis and fractures and a greatly increased operative time. All this adds up to increased blood loss, typically 50-100% greater than a primary procedure. Typically 3 units of blood are transfused. Breakthrough allogenic transfusion with a predonation programme is highest with revision hip surgery at 21% in one series.

Suggestions

As with primary surgery, it is still important to optimise the preoperative status and stop aspirin and non-steroidal agents well in advance. Meticulous surgical technique is even more important. Templating and rehearsal of the procedure and familiarity with the instruments and implants are vital. Hypotensive epidural anaesthesia is usually preferred.

Predonation remains the standard for many orthopaedic surgeons. On top of the usual problems is the need to provide more units of blood than primary surgery. Typically 4 units have been ordered but 2 or possibly 3 would be adequate for the vast majority. For higher predonation levels, erythropoetin supplementation has repeatedly been shown to improve the yields of donated blood.

Erythropoetin alone has been shown to be safe and effective in reducing the exposure to allogenic blood. A dosing schedule of 600iu/kg x 4 weekly doses seems most efficient. A study comparing perioperative erythropoeitin with a predonation programme in total joint arthroplasty involved 490 patients. Erythropoeitin treated patients had a mean rise in preoperative Hb of 1.5g/dl compared to a 1.2g/dl decrease in the predonation group. This led to a total transfusion of 53 units of allogenic blood in the erythropoeitin group compared to 325 units (79 allogenic) in the predonation group.

Haemodilution techniques may be particularly helpful in these situations of higher blood loss but are not widely available. Similarly intraoperative salvage techniques can be helpful when the loss is high but the salvaged blood is often of poor quality. There is usually contamination of the blood with irrigation fluid and the general debris of cement, polyethylene and metal. Of more concern is the occasional presence of infection, which would prevent reinfusion. As before, postoperative drains are probably of only limited value.

Primary Total Knee Arthroplasty

In 100 consecutive primary total knee arthroplasties at Guy's Hospital in 1998 the measured blood loss ranged from 50 – 2590ml with an average of 780ml. When calculated (based upon pre and postoperative Hb and the transfusion given) this average was closer to 1300ml. The average loss in males was much higher than in females

980ml vs. 650ml. Typically the loss and transfusion rate is less than total hip arthroplasty but a 40-50% rate is not uncommon. In a study of 477 patients only the preoperative Hb was a predictor of transfusion risk. If > 13.5g/dl there was only a 2.8% risk but if < 10g/dl this rose to 33%. When predonation is utilised there is high wastage – often at least 50% but in one study as high as 80%. Another approach is to give back all the predonated blood whatever the loss.

This actually could produce a lower complication rate but is not generally accepted as good practise.

Haemodilution and intraoperative salvage are not appropriate for most primary TKAs as many are performed under tourniquet and the blood loss and transfusion rate is not particularly high in most cases.

Suggestions

For most patients simply lowering the transfusion trigger is enough to avoid the need for transfusion. Predonation is generally not warranted in primary knee replacement. As with total hip surgery, if the patient insists upon predonation then a single unit is sufficient unless anaemia is present preoperatively. Perioperative Erythropoeitin is effective for use in the anaemic patient.

Postoperative reinfusion drains are becoming increasingly popular. Some claim there to be no benefit but many recent studies show a marked reduction in transfusion rates, in our unit from nearly 50% to as low as 3%.

Revision Total Knee Arthroplasty

The blood loss is not much different from that seen in primary surgery. The rate of transfusion and the number of units given are higher but not greatly so. Most recommendations for primary knee arthroplasty apply in these cases.

Bilateral Knee Arthroplasty

The blood loss is significantly higher than that seen in unilateral cases leading to an increased transfusion rate. In patients with no predonation this rises from 18% to 57%. This necessitates the application of one or more techniques to avoid allogenic blood.

Suggestions

As before, predonation of autologous blood remains the choice in many orthopaedic centres. Frequently 4 units are drawn and, not unexpectedly, the problems of predonation are magnified. If this technique is used, in the great majority of cases, a single unit for each knee is more than adequate. Erythropoeitin is again very effective in these patients both alone and to improve the yield of the predonation.

Postoperative salvage and reinfusion is also particularly useful but one must exercise care when large volumes are involved. We try to restrict our total reinfusion to 1500ml, usually within the first 6 – 8hrs.

Spinal Surgery

The blood loss in spinal surgery is very variable. The loss ranges from negligible amounts in minimally invasive procedures to as high as 20litres in multilevel, revision or fusion procedures. Bone graft harvest is a further source of blood loss. Coagulopathy is found in a high percentage of these cases perioperatively. The main predictors of transfusion include low preoperative Hb, tumour surgery, and the number of levels operated on. Data is still relatively sparse but hypotensive anaesthesia has long been recognised to be of value. Erythropoeitin used alone in 178 patients reduced the transfusion rate from 24% to 4% in surgery for idiopathic scoliosis.

Normovolaemic haemodilution can be very effective but its use is not widespread and data is still limited.

Suggestions

Autologous predonation is commonly utilised (typically 2-4 units are collected). There are problems collecting larger amounts and supplementary erythropoeitin is of value, often raising the yield by 30%. Erythropoeitin alone may be just as effective but well controlled studies are still rather limited.

Care with the operative technique is vitally important. This would include careful sub-periosteal elevation of tissues, meticulous haemostasis and the use of hot or laser scalpels.

This is probably the most useful area for intraoperative salvage despite the costs in time and manpower and an estimate that only 30% of the blood may be utilised. Postoperative drains may be of supplemental benefit.

Paediatric Spinal Surgery

Generally speaking the problems are similar to those seen in adult surgery. The blood volume is lower and any loss is much more significant as a percentage of total volume.

There are real problems trying to obtain large volumes of autologous blood in children both physiologically and from the trauma of repeated visits and phlebotomies. Early studies of perioperative erythropoeitin (10,000u x 3 weekly doses) and iron suggests the costs and efficiency compare favourably with a predonation programme and may even reduce the length of stay.

Orthopaedic Infection

The problems of orthopaedic infection are particularly difficult to manage. Typically, the orthopaedic surgeon has to deal with an infected joint prosthesis or osteomyelitis not infrequently associated with a fracture. The patients are often chronically ill with a refractory anaemia and multiple comorbidities.

The treatment of an infected total knee prosthesis usually involves a two stage reimplantation. The transfusion rate is extremely high. In an ongoing study, 80% of patients required transfusion at the time of prosthesis removal and 82% at reimplantation. Only 12% of patients escaped allogenic transfusion. This causes great concern not least because of the immunomodulation effects of allogenic transfusion and risk of further infection. Most modalities of treatment are not possible in these patients. Predonation is difficult due to the pre-existing anaemia and salvage techniques are inappropriate in the presence of infection.

Suggestions

Erythropoeitin seems particularly suited to these problems. 40,000u of erythropoeitin sc. with iron supplementation are given at the time of removal of the prosthesis. The treatment continues until after reimplantation, typically 6-8 weeks later. Early results show promise with a rise in Hb from 1.5 to 6.2g/dl (av. 3.3) and a reduction in transfusion rate to 35% [35].

Orthopaedic Oncology

Two major problems are associated with the surgical treatment of oncology cases. First is the chronic anaemia present in a high percentage of cases. This is due to the disease itself and also the effects of chemotherapy and radiotherapy. This anaemia obviously has potential for surgical problems but it also adversely affects the efficacy of the therapies used. Secondly, the immunomodulation effects of an allogenic transfusion are known to cause an increase in tumour recurrence rates and reduce survival

times. Orthopaedic literature is rather sparse but soft tissue sarcoma survival can be greatly reduced after allogenic transfusion. The five-year rate drops from 85% to 63%. Even the number of units seems important.

Suggestions

Predonation of autologous blood remains the favoured option in many centres. The anaemia can adversely affect the yield. Normovolaemic haemodilution is probably effective but experience is limited. Salvage techniques are contraindicated due to the risk of haematogenous spread of the tumour cells. Erythropoeitin has been shown to be effective as part of the general medical treatment of malignancies. The level of Hb was seen to rise in patients undergoing radiotherapy from 11.9 to > 14g/dl in 80% of cases (5% with placebo). Studies have recently started on the use of erythropoeitin in the perioperative setting particularly to help accelerate the time to surgery.

Orthopaedic Trauma

This is a particularly difficult area for effective blood management. The numbers involved are huge and rising; some 300,000 hip fractures occur each year in the US alone. Many patients are elderly and frail with multiple comorbidities and not infrequently are anaemic at the time of the injury. Many of these cases require transfusion of allogenic blood. Pelvic fractures are associated with major blood loss with transfusion requirements ranging from 3.6units to 14.8units (5.9av.) Acetabular fracture fixation is associated with transfusion in over 50% of cases. After initial stabilisation, early fixation of long-bone fractures will reduce the blood loss as well as reducing other complications particularly to the lungs. Closed techniques and the use of fixators will reduce the operative blood loss. Further surgery is often required during the first few days with further blood loss. Later, the problems of rehabilitation arise. Much work is now being done on the effects of anaemia on postoperative recovery, vigour, length of hospital stay and costs.

It is increasingly clear that allogenic transfusion can have detrimental effects on the overall condition of the patient. The infection rate is probably doubled, not just the orthopaedic wound but also the rate of chest and urinary tract infection.

Unfortunately the nature and timing of these injuries precludes the use of many modalities. Predonation is obviously impossible and haemodilution and hypotensive techniques can be risky in these patients.

Suggestions

Allogenic blood is still necessary in a number of cases despite the potential drawbacks. This may be given in the acute phase i.e. pre or intraoperatively or later to correct the problems associated with severe anaemia.

Blood salvage can be of value in cases of high blood loss such as pelvic fracture fixation. Most blood loss will occur intraoperatively but postoperative salvage drains can be of additional help with up to half the loss recoverable.

Erythropoeitin may have great potential in orthopaedic trauma but studies are still limited. Early studies suggest a reduced transfusion rate when given as 5 daily doses to hip fracture patients undergoing operative fixation. In more major cases it could only be used in the post-operative period but should also help reduce the transfusion rate by improving the erythropeitic recovery and help to avoid the complications, particularly the increased infection rate.

The Future

It has taken many years for orthopaedic surgeons to realise the importance of an effective blood management programme. Even now many centres have minimal planning and rely heavily on allogenic blood. It has been clearly shown that even the sim-

plest techniques such as lowering the transfusion trigger can, at times, halve the transfusion rate or better. In the immediate future, much can be achieved with good education making surgeons better aware of the dangers of allogenic transfusion and the options already available to reduce its use. Attempts will continue to make allogenic blood safer with more effective screening but this is only part of the problem.

Predonation programmes will likely continue in the foreseeable future but much can be done to refine them. It is unacceptable to spend so much time and effort only to discard half of the units obtained. An algorithmic approach, which can more accurately predict the expected blood loss in an individual, should be very helpful. It is only after studies involving the gathering large amounts of data that we realise who is really at risk-certainly not the primary knee replacement in an otherwise healthy individual. In more difficult cases requiring large predonations, erythropoeitin will become more commonplace in improving the yield.

Erythropoeitin in the perioperative period has many potential benefits. A large number of studies will be completed in the next one or two years and these should further clarify the individuals most likely to benefit and also the most effective dosing regime. There is still concern about the cost of this treatment but it appears it may be cheaper than a predonation programme for some patients.

There is still a great deal of confusion when trying to compare different treatments. Most methods work to a greater or lesser extent but some are much more time consuming or difficult to set up. Some are potentially very costly and require a large input from highly trained staff. More studies are underway to help with these comparisons, both the efficacy of the treatment and increasingly the costs to the individual and society.

Blood substitutes have gone through a long and difficult testing and validation process. There have been a number of "false dawns" but many of the earlier limitations and side effects seem to have been overcome and early clinical testing is underway.

The process of disseminating this knowledge should become simpler. The Internet and electronic publishing will provide an easily accessible source of information which can be rapidly updated. Laptop or hand-held computer based algorithms are being developed for use in general clinical practice and also as research tools.

Conclusions

It will be some time before the concept of "bloodless surgery" is finally realised but great strides have already been made, particularly in the last ten years. The initial problem of making the orthopaedic community aware of the risks of allogenic transfusion is being solved with better education. A wide array of treatment options are now available and the indications for and effects of each are being defined more accurately. The future is increasingly exciting, as blood substitutes become available. Until that time, we must strive to make the best use of the techniques already available in order to achieve the best possible outcome for our patients.

Key Points

1.) Orthopaedic surgeons are amongst the biggest users of blood products

2.) Extensive data is now available setting out the likelihood of transfusion in specific orthopaedic procedures

3.) A number of treatment options are available including Predonation of autologous blood, haemodilution, modifications to anaesthesia and surgical technique, intra and post-operative salvage and the use of pharmaceutical agents such as erythropoeitin.

4.) The results of recent studies are discussed in detail showing how the use of these techniques can be tailored to individuals and specific operations to effectively reduce the need for allogenic blood

Obveščenost bolnika in pristanek na avtotransfuzijo Pojasnilna dolžnost izbranega zdravnika

Patient s informed consent for autotransfusion

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Ključne besede: Bolnik - zdravnik, pravice in dolžnosti, etična odgovornost, dobrobit, konzultacija
Key Words: Patient - Doctor, Rights and Duties, Etihcs, Benefit, Consultation

Izvleček

Avtotransfuzija je nadomestilo za transfuzijo pri programiranih operacijah. Prinaša za bolnika in zdravnika številne prednosti, saj je varnejša od transfuzije, ni pa cenejša. Pri odločitvi bolnika za avtotransfuzijo mora izbrani zdravnik opraviti svojo pojasnilno dolžnost. Ob pristanku bolnika je pomembno, da je informiran o prednostih in pomanjkljivostih metode. Razgovor z bolnikom in njegov pisni pristanek morata biti zavedena v njegovi zdravstveni dokumentaciji. Obrazec s kratkim pojasnilom o nameravanem posegu, s katerim se zahteva pacientovo privolitev in podpis, v tem primeru ne zadošča.

Abstract

Autologous transfusion becomes more frequent in planned operations. We must inform the patient and the doctor about the benefits of it and with the incoveniences also. The role of general practitioner is very important as well as the good relationship between pacient and doctor. The obligation of the doctor is to give the patient much more than a simple information. "Informed consent" is not in off. The whole proceeding must bee recorded in the medical documentation about the patient.

Uvod

Transfuzija krvi je varen in učinkovit način nadomestnega zdravljenja. Zaradi vedno večje potrebe po nadomeščanju krvi in različnih dejavnikov tveganja ob transfundiranju homologne krvi, ki so se pojavili v 80-tih letih, zlasti virusne infekcije in prionske bolezni, je bolj varno in smotrno nadomestiti izgubljeno kri z transfuzijo avtologne krvi, ki jo imenujemo avtotransfuzija.

Ob avtotransfuziji se pojavljajo novi vidiki na pravnem, etičnem in biološkem področju, ki terjajo pretehtano delo z bolnikom. Pomemben premik ob uvajanju avtotransfuzije, je pojasnilna dolžnost izbranega zdravnika na primarni ravni. Da bi bolnik pristal na možnost avtotransfuzije, je potrebno uveljaviti partnerski odnos med zdravnikom in bolnikom, ki temelji na zaupanju, informiranju in odločitvi bolnika (1). Sicer bi sicer ga težko prepričali o dobrobiti oddajanja lastne krvi, če lahko dobi tujo kri. Marsikdo bo imel odpor do odvzema pomembne količine krvi. Ob informaciji o prednostih in škodljivostih avtotransfuzije bo pacient nujno želel vedeti, kakšna je njegova dobrobit v primeru, da se odloči za avtotransfuzijo. Bolnik mora imeti možnost, da v toku razgovora z zdravnikom zastavlja določena vprašanja in da ta vprašanja dobi tudi zadovoljujoč odgovor. Vse to ni možno, če mu ponudimo v podpis obrazec o obveščenem pristanku. Avtotransfuzija je specifičen način zdravljenja in je uvrščena med "invazivne postopke" v medicini in se zahteva za njo poseben pristanek bolnika. Po proučevanju različnih etičnih in pravnih vidikov in razgovorov z različnimi strokovnjaki iz tega področja, avtorica ugotavlja, da z vidika pojasnilne dolžnosti izbranega zdravnika in obvešèenosti bolnika, ni potrebno, da bolnik pri izbranem zdravniku podpiše standardni obrazec. Zadošča,

da je iz bolnikove zdravstvene dokumentacije razvidno, da je bil z bolnikom opravljen pojasnilni pogovor, da mu je bila na podlagi anamneze, kliničnega pregleda in vrste programiranega kirurškega posega, svetovano nadomeščanje izgubljene krvi z avtotransfuzijo. Podpisan obrazec o "obveščenem pristanku" bolnika, zdravnika ne ščiti v primeru odškodninske tožbe, če nastanejo komplikacije v škodo bolnika. Natančen zapis v zdravstveni dokumentaciji je dokaz, da je zdravnik ravnal vestno in odgovorno in da je bolnik seznanjen s prednostmi in škodljivostmi avtotransfuzije.

Prebivalstvo Slovenije se stara, vedno večja je tista starostna skupina, v kateri so najpogostejši programirani kirurški posegi. Potreba po nadomestnem zdravljenju s krvjo je vedno večja. Avtotransfuzija je metoda izbora pri sicer zdravih osebah, ki so predvidene za programirani kirurški poseg.

Zakaj avtotransfuzija?

Vemo, da je transfuzija varen in učinkovit način nadomestnega zdravljenja s krvjo. Se pa pri prejemnikih transfuzije pojavljajo tudi različni neželjeni učinki. Največkrat sta to le zvišana telesna temperatura in mrzlica, možni pa so tudi zapleti z usodnim izidom za bolnika. Vsako transfuzijo spremlja določeno tveganje, saj nekaterih stranskih učinkov ne moremo niti predvideti, niti preprečiti, drugi nastanejo zaradi strokovnih napak (2).

Poleg transfuzije krvi se uporabljajo krvni nadomestki, ki zmanjšujejo uporabo alogeničnih pripravkov krvi in avtotransfuzija. Za varčevanje s krvjo so se razvile različne nove tehnologije, kot je prestrezanje pacientove krvi med samo operacijo, ki jo primerno obdelano vrnejo pacientu. Intraoperativno in pooperativno zbiranje pacientove krvi ima lahko nepričakovane stranske učinke, kot je razsoj tumorskih celic, bakterij, možne so motnje strjevanja krvi, hemolitične reakcije. Preoperativno, intraoperativno in postoperativno zbiranje pacientove krvi za avtotransfuzijo je tehnološko, organizacijsko in finančno zahteven poseg (3).

Da bi avtotransfuzija postala popularna in uspešna metoda nadomeščanja krvi, je nujno, da so bolniki in zdravniki primerno informirani, potrebna je sprememba odnosov med bolnikom in zdravnikom. Izredno pomembna je pojasnilna dolžnost izbranega zdravnika, ki bo ob natančnem poznavanju svojega bolnika, njegove diagnoze in potrebe po načrtovanem kirurškem posegu, lahko suvereno svetoval poseg za katerega meni, da je za bolnika najboljši in ki ga je ta sposoben in pripravljen sprejeti (4).

Avtotransfuzija in socialno medicinski pristop

Populacijsko drevo iz leta 1995 nam kaže, da je v Sloveniji 190.000 ljudi v starosti od 55 do 75 let. V tem starostnem obdobju se veča število kroničnih in degenerativnih obolenj, zlasti bolezni "obrabe", ki se odražajo na kostno-mišičnem sistemu. Skoraj vsak človek v tej starosti ima obrabljene velike sklepe, kot so kolki in kolena. Vzporedno s tem se veča tudi število načrtovanih kirurških posegov, pri katerih pride do velike izgube krvi, ki jo je potrebno nadomestiti.

Avtotransfuzijo so prvič pričeli uporabljati v 80-tih letih, ko se pričela pojavljati zavest o nevarnosti transfuzije s tujo krvjo. Širile so se okužbe z virusom HIV, Hepatitisa B in C. V 90-tih letih se je temu pridružila še nevarnost prionskih bolezni. Narkomani so pričeli prodajati svojo kri, da bi tako prišli do denarja za nabavo drog. Vedno težje je bilo zagotoviti neoporečno kri tujega dajalca. Potrebni so bili pomembni premiki v transfuziološki praksi. Po svetu se je prenehalo z odkupovanjem krvi. Kri se pridobiva izključno na krvodajalskih akcijah od neplačanih krvodajalcev, uporabljajo se strogi kriteriji in testiranje krvi. Medicinska stroka je razvila kirurške posege pri katerih je potrebno nadomestiti veliko izgubo krvi, kot je na primer operacija kolka, razliene operacije na odprtem srcu, operacije različnih malignomov (5).

Kaže se nujnost zbiranja lastne krvi pri programiranih operacijah na sicer zdravih ljudeh. Potrebno je informirati širšo javnost o avtotransfuziji in lečeče zdravnike na primarni ravni. V laični in strokovni javnosti je potrebno ustvariti mišljenje, da je avtotransfuzija pomembna za dobrobit bolnika in družbe.

Pojasnilna dolžnost izbranega zdravnika

Avtotransfuzija je predmet velikega zanimanja s strani bolnika in zdravnika, ko se oba znajdeta pred nujnostjo njene uporabe. Kot vsaka novost vzbuja občutke strahu in odpora pri bolniku. Ker gre za poseg v telo, je tudi tukaj pomembna obveščenost bolnika in njegov pristanek. Če analiziramo vse dejavnike, ki so v igri pri posegu avtotransfuzije, se izkaže, da dosedanja oblika privolitve bolnika s pomočjo podpisanega obrazca "obveščen pristanek" z dodatkom standardne informacije za pacienta, ni dovolj.

Samo zdravnik, ki bolnika dobro pozna, lahko presodi, katere informacije je pacient sposoben sprejeti, kaj mu je dobro povedati in katere sila redke komplikacije mu kaže zamolčati. Od dobrega partnerskega odnosa bolnika in zdravnika je odvisno, kako bo bolnik zdravnikova pojasnila sprejel in kakšna bo njegova telesna, duševna in čustvena pripravljenost, da se bo odločil za avtotransfuzijo. Zadovoljstvo bolnika s takim zdravnikovim ravnanjem je merljivo (6). Tabela 1.

Zdravnik se mora pri tem ravnati po etičnih načelih, ki ga obvezujejo veliko bolj kot pravne norme. Za razvoj pravega partnerskega odnosa med zdravnikom in bolnikom je potreben čas. "Konzultacija" pacienta z zdravnikom je tista oblika komuniciranja, ki jo poznajo v razviti Evropi že danes, pri nas pa ni možna zaradi omejenih časovnih normativov za "zdravnikove storitve". Angleški izraz "Commitment to the pacient" dobro izraža partnerski odnos in predanost zdravnika svojim bolnikom (7). Ker ustreznega slovenskega izraza nisem našla, naj pojasnim s primeri:

Žena srednjih let, z doraščajočimi otroci, ki se nahaja v terminalnem štadiju zaradi adenokarcinoma pankreasa, vas je izredno prizadela. Skupaj z njeno družino in njo podoživljate katastrofo. Njenemu možu ste dali svojo domačo telefonsko številko z

navodilom, da vas lahko pokličejo kadarkoli.

Prijetna, vendar kronično anksiozna učiteljica z napadi panike, ki se stopnjujejo. V svoji grozi vas kliče zelo pogosto ravno takrat, ko imate največ dela in se želi pogovoriti z vami o svojih problemih. Z velikim razumevanjem za njene težave ji ponudite čas, ko niste v službi.

Besedo Commitment razumem kot žrtvovanje svojega prostega časa za bolnika, ki to potrebuje.

Pogoji za uspešno opravljeno pojasnilno dolžnost zdravnika so predstavljeni v tabeli 1.

Da bi izbrani zdravnik lahko izpolnil pojasnilno dolžnost do bolnika, mora osvojiti nova znanja iz področja biomedicinskih in socialnih znanosti, mora postati človeško sočuten in razumevajoč zagovornik bolnika in dober medicinski strokovnjak (8).

Na srečanje bolnika z zdravnikom moramo gledati kot na srečanje dveh med seboj odvisnih in enakopravnih človeških bitij. Usoda bolezni in bolnika je njun skupni problem (9).

Pri pojasnjevanju avtotransfuzije z namenom svetovanja bolniku in pojasnilno dolžnostjo zdravnika je zlasti **pomembna bolnikova pravica do obveščenosti.**

Bolniku morajo biti dostopne vse informacije, ki je vsebuje zdravstvena dokumentacija: diagnoza bolezni, način zdravljenja, prognoza zdravljenja. Seznanjen mora biti s svojim zdravstvenim stanjem in vedeti mora ali je sposoben dobro prenesti načrtovan poseg in kakšne so najverjetnejše posledice. Informacijo moramo posredovati **na primeren** način ob upoštevanju bolnikove izobrazbe, kulture, psihičnega in čustvenega stanja. Samo zdravnik, ki bolnika dobro pozna je zmožen oceniti, koliko je v tem trenutku bolnik zmožen prenesti in sprejeti (10).

Privolitev v poseg je pravno relevantna samo v primeru, če je dana na podlagi popolne informacije o bolezni, možnosti zdravljenja z namenom in potekom predvidenega posega, verjetnostjo uspeha in običajnim tveganjem, povezanim s posamezno metodo zdravljenja. Samo v tem primeru lahko govorimo o "obveščenem pristanku" (11). Pojasnilna dolžnost zdravnika je mnogo širši pojem, ki temelji na razmerju bolnik-zdravnik.

Poleg pojasnjevanja in svetovanja bolniku ima zdravnik dolžnost sodelovanja pri ozaveščanju in izobraževanju bolnika in javnosti ter aktivno sodeluje pri izvajanju programa avtotransfuzij (tabela 2).

Avtotransfuzija in dobrobit bolnika

Bolnik upravičeno želi izvedeti, kakšne so prednosti avtotransfuzije, ko se zave, da mu bo odvzeto približno 1000 mml krvi, saj ne gre za majhno količino, sprašuje se, zakaj krvi ne more dobiti od drugega dajalca, "tako kot vsi drugi".

Ob tem je dobro vedeti, kakšne so koristi za bolnika:

Prejel bo lastno kri, tako ni izpostavljen okužbam z razlienimi virusi (Hepatitis B in C, HIV), ki so prenosljivi s krvjo. Izogne se imunskim reakcijam na tuje beljakovine, tuje levkocite, odpade senzibilizacija na različne snovi, ki se nahajajo v krvi dajalca. V primeru, da gre za redko krvno skupino in pacientu ne moremo zagotoviti skladne krvi je avtotransfuzija neizbežna. Pacient se na ta način izognezapletom, ki lahko nastopijo ob transfuziji inkompatibilne krvi. Prednosti odtehtajo škodo, ki bi jo utegnil utrpeti zaradi zmanjšanega volumna krvi in prehodne anemije, ki nastopi po odvzemu lastne krvi. Tabela 3 prikazuje prednosti in pomanjkljivosti predoperativne avtotransfuzije.

Zavedati se moramo škode, ki jo lahko avtotransfuzija bolniku povzroči! Odvzem krvi za avtotransfuzijo lahko povzroči slabokrvnost ali zmanjšan volumen krvi. Med lokalnimi reakcijami, ki niso zanemarljive se najpogosteje pojavlja lokalni hematom, tromboflebitis in poškodba živca. Med splošnimi reakcijami na odvzem krevi so najpogostejši padec krvnega tlaka in kolaps. Ob transfuziji avtologne krvi so neželeni učinki zelo redki. V določenih primerih lahko nastanejo hude posledice, ko se zamenja kri za avtotransfuzijo. Neustrezno shranjevanje in ravnanje s krvjo za avtotransfuzijo lahko privede do razmnoževanja bakterij v krvi .

Ali je bolnik sposoben za avtotransfuzijo določi njegov lečeči zdravnik in transfuziolog v primeru predoperativne avtotransfuzije.

Razgovor z bolnikom

V našem primeru gre za bolnika, starega 65 let, ki mu je zaradi obrabe desnega kolka potrebno kolčni sklep zamenjati z umetnim kolkom. Pacient je sicer zdrav, tehta 50 kg, odvzeli mu bodo 450 ml krvi, kar pomeni 13 odstotkov krvnega volumna. Pri njegovi telesni teži ima 3.500 mml krvi ali 70 mml krvi na kg telesne teže. Deset dni pred programiranim kirurškim posegom mu bodo na zavodu za transfuzijo odvzeli 450 mml krvi in 3 dni pred posegom še 450 mml krvi. Njegov organizem bo tako izgubo krvi nadoknadil v treh dneh.

Pacient se z izvidi ortopeda in transfuziologa oglasi na razgovor. Vznemirjen je zaradi operacije, ki ga čaka in nekoliko zmeden, ker ne ve, zakaj bodo ravno njemu pred operacijo odvzeli kri, da bi izgubljeno kri nadomestili z njegovo lastno krvjo. Gre za povprečnega bolnika s srednjo izobrazbo, ki je psihično urejen, s katerim do sedaj nisva imela nesporazumov in sva se glede postopkov zdravljenja ves čas strinjala. Rezultati zdravljenja so bili za pacienta zadovoljivi in lahko trdim, da sem si sčasom pridobila pacientovo zaupanje.

Pacientu povem, da bo operiran na določen datum in da je zamenjava kolka operacija, ki povzroči precejšnjo izgubo krvi, podrobnosti mu prihranim, povem, da bo potreboval kri. Razložim mu, da kri lahko dobi s transfuzijo, kar pomeni, da mu bodo infundirali kri drugega človeka z isto krvno skupino, ali pa lahko dobi svojo lastno kri z avtotransfuzijo s tem, da bomo to kri pričeli zbirati 10 dni pred predvidenim posegom. Prvo vprašanje pacienta je, kako bo odvzem skoraj enega litra krvi vplival na njegovo stanje med operacijo in po njej. Potem ga zanimajo prednosti avtotransfuzije in kakšno je tveganje. Tudi to mu pojasnim.

Vprašanje pacienta je, za kakšno obliko nadomeščanja krvi bi se sama odločila, če bi šlo zame. Povem mu, da bi se na podlagi treznega premisleka odločila za avtotransfuzijo, ki pomeni veliko manjše tveganje kot transfuzija krvi tujega dajalca.

Kot zaključek najinega razgovora vprašam, ali privoli, da vsebino razgovora na kratko zapišem v zdravstveni karton in ali je pripravljen svojo odločitev potrditi s podpisom.

Namesto zaključka

Kadar opravljamo pojasnilno dolžnost pri bolniku, ki potrebuje avtotransfuzijo, ne moremo mimo sedem osnovnih lastnosti dobrega zdravnika:

Zvestoba zaupanju in obljubi

Dobrodelnost

Odrekanje sebičnim interesom

Sočutje in skrb

Strokovna poštenost

Pravičnost

Preudarnost

Po definiciji Edmunda Pellegrina je zaupanja vreden zdravnik tisti, ki si je svojo poklicno etiko oblikoval po notranjem čutu in razumevanju bolnikove stiske, ne pa po poklicnih kodeksih ali etičnih teorijah.

Tabela 1 - Najpomembnejši kriteriji, odločilni za zadovoljstvo bolnika z zdravnikom
(J. Drinovec po Schmittdiel J. et al. Odnos zdravnik-bolnik - njegovo ocenjevanje in merjenje. Zdrav.vestn 1998; 67:579-82)

1.) Čas, ki ga zdravnik porabi za bolnika (anamneza, pregled, zdravljenje in navodila)
2.) Pojasnitev diagnoze in zdravljenja
3.) Tehnična usposobljenost zdravnika
4.) Osebnostni pristop zdravnika
5.) Uporaba najnovejše tehnologije
6.) Osredotočenost na preventivo
7.) Vpliv na čustveno ravnovesje
8.) Celokupna zadovoljnost
9.) Bi priporočali vašega zdravnika drugim?

Tabela 2. Pogoji za uspešno opravljeno pojasnilno dolžnost izbranega zdravnika

1.) pravilen odnos med bolnikom in zdravnikom
2.) poznavanje postopka
a. organizacijske in tehnične podrobnosti programa avtotransfuzijskega zdravljenja
b. indikacije za avtotransfuzijo (vrste in značilnosti posegov)
c. vrste in značilnosti posameznih načinov avtotransfuzije

d. značilnosti predoperativnega odvzema krvi
e. prednosti in pomanjkljivosti avtotransfuzije
f. korist ali dobrobiti za bolnika
g. posledice sprejetja ali odklona
h. nujnost in narava pisnega pristanka na avtotransfuzijo
3.) poznavanje bolnika
a. zgodovina bolezni in psihosocialne značilnosti
b. splošno zdravstveno stanje
c. osnovna bolezen

Tabela 3. Dolžnosti izbranega zdravnika

1.) Pojasnilna dolžnost izbranega zdravnika
a. pojasnjevanje in svetovanje
b. vodenje zdravstvene dokumentacije
2.) Vključitev in sodelovanje v programu avtotransfuzij
3.) Ozaveščanje in izobraževanje bolnika in javnosti

Tabela 4. Prednosti in pomanjkljivosti avtotransfuzije

a. Prednosti
i. Preprečevanje prenosa virusnih okužb
ii. Preprečevanje nastanka aloimunizacije
iii. Preprečevanje nelkaterih reakcij po transfuziji krvi
iv. Vir krvi za bolnike z multiplimi protitelesi
v. Stimulacija eritropoeze
vi. Dodaten vir pri preskrbi s krvjo
b. Pomanjkljivosti
i. Reakcije na dajanje krvi
ii. Povečani stroški
iii. Zastaranje krvi v primeru prestavitve operativnega posega

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Akutna normovolemična hemodilucija

Neli Vintar, Breda Starc

UVOD

Akutna normovolemična hemodilucija (ANH) je metoda, s katero zmanjšamo oziroma nadomestimo transfuzijo homologne krvi med operacijo. Z ANH odvzamemo bolniku kri tik pred uvodom v anestezijo ali takoj po njem. Odvzeto kri nadomeščamo z kristaloidnimi in koloidnimi raztopinami. S tem razredčimo bolnikovo kri do vrednosti hematokrita, ki je majhna, vendar mora biti še v fiziološko sprejemljivih mejah. Tako se ob kirurški krvavitvi izgublja kri z manjšo vsebnostjo eritrocitov, kot če je ne bi prej razredčili. Odvzeto kri vrnemo v bolnika, ko je narejena kirurška hemostaza ali že prej, če je krvavitev večja in moramo vzdrževati najmanjšo še sprejemljivo vrednost hematokrita (1,2).

METODA

Prednosti ANH

Z ANH zmanjšamo absolutno izgubo eritrocitov med operacijo. Vzemimo primer da bolnik med operacijo izgubi 1 liter krvi. Bolnik s Ht 0,45, izgubi 450 ml eritrocitov, bolnik s Ht 0,25 pa le 250 ml eritrocitov. Z ANH zmanjšamo tudi viskoznost krvi, predvsem zaradi zmanjšanega števila eritrocitov, v manjši meri pa tudi zaradi zmanjšane koncentracije plazemskih proteinov. Zmanjšana viskoznost krvi izboljša tkivno perfuzijo, kar je najbolj izrazito pri Ht 0,30 (3).

Uporaba v klinični praksi

Čeprav mnogi klinični zdravniki uporabljajo ANH le pri zdravih odraslih operirancih, jo lahko uporabljamo tudi pri otrocih in starejših. Prvič se je metoda začela izvajati pri operacijah na srcu, ko so namesto heparinizirane krvi za polnjenje naprave za zunajtelesni krvni obtok uporabili kristaloidne in koloidne raztopine. ANH je učinkovita pri celi vrsti operacij. Poleg operacij na srcu, se pogosto uporablja pri ortopedskih bolnikih (operacija endoproteze kolka), uroloških (radikalna prostatektomija) in onkoloških bolnikih. Študije so pokazale, da je metoda klinično učinkovita pri odraslih, ki imajo Ht več kot 0,34 in pri katerih pričakujemo več kot 1 l izgube krvi med operacijo (1,4).

Kontraindikacije

Anemija je največja kontraindikacija za ANH. Pri hemoglobinu 110 g/l ANH ni več smiselna. Bolniki z zmanjšano ledvično funkcijo, ki ne more izločiti velikih količin tekočin, niso primerni za ANH, ravno tako ne bolniki z zmanjšano plazemsko koncentracijo koagulacijskih faktorjev. Posebna previdnost velja pri bolnikih z ishemično srčno boleznijo. Celo pri bolnikih, kjer ta bolezen ni znana, se lahko razvije ishemija, kadar se vrednost Ht zmanjša pod 0,30. Bolniki s periferno žilno boleznijo imajo običajno tudi ishemično srčno bolezen, zato niso primerni za ANH (1)

Kompenzatorni mehanizmi

Zmanjšanje Ht ob ANH sproži kompenzacijske mehanizme. To so reološke in hemodinamske spremembe ter povečana ekstrakcija kisika iz hemoglobina. Transport kisika je odvisen od minutnega volumna srca (MVS) in vsebnosti kisika v arterijski krvi V mirovanju pri normalnem Ht je transport kisika približno štirikrat večji od porabe.

Torej je rezerva velika tudi brez kompenzacijskih mehanizmov, seveda če je celotni volumen cirkulirajoče krvi normalen. Večina študij kaže, da se MVS poveča pri anesteziranem bolniku od 16 do 50%, če se Ht zniža na 0,25 do 0,20. MVS naraste zaradi povečanega utripnega volumna in ne povečane srčne frekvence. Povečana srčna frekvenca ponavadi kaže na nezadostno anestezijo ali hipovolemijo. Ob povečanem MVS se pri majhnem hematokritu arteriovenska diferenca vsebnosti kisika poveča. Torej se poveča ekstrakcija kisika iz krvi. Glavni faktor za povečanje MVS je zmanjšana viskoznost krvi. Z manjšo viskoznostjo se zmanjša periferni upor in poveča venski dotok (1,2,5).

Stranski učinki

Z ANH se razrečijo vse sestavine plazme, tudi tiste, ki so pomembne za koagulacijo krvi. Zato sta protrombinski in trombinski čas ob ANH zmerno podaljšana, kar pa naj nebi vplivalo na kirurško krvavitev. Število trombocitov se z ANH zmanjša, vendar se le-ti hitro mobilizirajo iz kostnega mozga. Trombociti v odvzeti bolnikovi krvi ostanejo funkcionalni, saj odvzete krvne enote običajno ne hladimo (2,3) .

Protokol ANH

Bolnikovo kri odvzamemo tik pred uvodom oziroma takoj po uvodu v anestezijo, tako da kaniliramo kubitalno veno in uporabljamo vrečke, ki vsebujejo 63 ml konzervansa CPDA. V vrečko spustimo najmanj 300 in največ 450 ml krvi. Kri lahko odvzamemo tudi preko arterijske kanile. Ob jemanju krvi bolniku skozi drugo vensko kanilo simultano z odvzemom infundiramo kristaloidne raztopine (3 ml na 1 ml odvzete krvi) ali koloidne raztopine (1 ml na 1 ml odvzete krvi). Eno enoto krvi odvzamemo v 7-10 minutah. Bolnika moramo ob tem postopku seveda ustrezno monitorizirati. Poleg spremljanja EKG krivulje (kjer smo posebno pozorni na ishemijo miokarda), sistemskega arterijskega pritiska, respiratornih parametrov, je priporočljivo vstaviti tudi arterijsko kanilo, s pomočjo katere jemljemo vzorce krvi za določitev Hb, Ht, oksigenacije krvi in acidobaznega ravnotežja ter neposredno merimo arterijski pritisk.

Volumen krvi, ki ga lahko odvzamemo preračunamo po formuli:

$V = EBV * (Ht_O - Ht_1)/Ht_{AV}$

EBV je pričakovani volumen krvi, Ht_0 je začetni hematokrit, Ht_1 je želeni hematokrit, Ht_{AV} je povprečni hematokrit.

Pričakovani volumen krvi pri moškem srednjih let je 70 ml na kg telesne teže. To je približno 5 l. Če je začetni Ht 0,45 in želeni 0,35, lahko odvzamemo 1250 ml krvi. Če pa je želeni Ht 0,25 pa lahko odvzamemo še 1 l krvi. Zato ponavadi odvzamemo 3-4 enote krvi. Vsako enoto krvi moramo opremiti z bolnikovim imenom, zaporedno številko in časom odvzema. Po odvzemu vsake enote krvi, določimo Ht. Kri ostane v operacijski dvorani pri bolniku na sobni temperaturi, zato da ohranimo funkcijo trombocitov. Po preteku 6 ur, damo kri v hladilnik in jo hranimo pri +4°C do 24 ur. Krvne enote vračamo v bolnika v obratnem vrstnem redu, kot smo jih odvzeli. Torej bolnik dobi najprej enoto z najbolj razredčeno krvjo, razen če predvidevamo, da ne bo dobil vse odvzete krvi. Takrat dobi najprej prvo enoto. Ves čas operacije skrbno spremljamo Hb in Ht. Če predvidevamo hipervolemijo ob infuziji odvzete krvi dobi lahko bolnik diuretik. Katera najnižja vrednost Ht je še varna, je težko določiti. Odvisna je od ocene bolnikovega splošnega stanja. Pri večini bolnikov je tkivna oksigenacija dobro ohranjena pri Ht 0,20 seveda ob normovolemiji in dobri oksigenaciji arterijske krvi. Večini klinikov se zdi Ht 0,27 spodnja meja varnosti pri bolniku brez spremljajočih bolezni (1).

DISKUSIJA

ANH je dobra metoda za zmanjšanje trasfuzije homologne krvi. Kot tudi pri drugih avtotransfuzijskih metodah se z ANH izognemo transfuzijskim reakcijam, imunosupresiji in prenosu nalezljivih bolezni. ANH je bolj učinkovita, če uporabljamo še suplementarne metode kot so skrbna kirurška hemostaza, uporaba krvnih prevez udov, infiltracija tkiva z adrenalinom in zdravljenje z eritropoetinom pred operativnim posegom.

Učinkovitost ANH pri zmanjšanju homologne transfuzije je kljub številnim študijam, od katerih jih je največ na matematičnih in računalniških modelih, še precej nejasna, kajti kliničnih primerjalnih prospektivnih študij je malo. Če torej strnemo najnovejše študije, potem je največja učinkovitost ANH, kadar jo uporabljamo pri bolnikih s Ht več kot 40% in dosežemo želeni Ht od 0,24 do 0,21 in pričakujemo izgubo krvi okrog 50% krvnega volumna (1,6).

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Perioperativno zbiranje krvi

Prim. Vanda Brubnjak-Jevtč

Nadomeščanje izgubljene krvi med operativnim posegom pri nas temelji na uporabi **homolognih komponent**, zbranih, predelanih in shranjenih na Zavodu RS za transfuzijo oz. transfuzijskih oddelkih. V času operativnega posega, ko izgubo krvi nadomeščamo s homolognimi komponentami, pa le te ne zagotavljajo več **optimalni učinek**. Npr. pri transfuziji trombocitov - čeprav je njihovo število veliko, je učinek manjši, ker se njihova funkcija s časom hranjenja zmanjšuje. Enako je tudi s koncentriranimi eritrociti. Glede nevarnosti prenosa bolezni z izpostavljanjem bolnika homolognim komponentam je govor v drugih prispevkih.

Preoperativno zbiranje lastne krvi in hranjenje do operacije, sicer odstrani nevarnosti prenosa bolezni, ostane pa odprto vprašanje kvalitete shranjene (konzervirane) lastne krvi.

Medoperativno zbiranje krvi (ki bi jo sicer zavrgli) koncentriranje in izpiranje avtologni eritrocitov, oz. pridobivanje ostalih komponent s pomočjo celičnih separatorjev je zagotovo metoda izbora, ki zagotavlja bolniku najboljšo možno kvaliteto komponent.

Zgodovina

Ideja o avtotransfuziji je ponovno zaživela med vojno v Koreji in Vietnamu. Zaloge homologne krvi niso zadostovale za operirance posebej ne za tiste operirane na odprtem srcu.

Vojaški kirurg dr. Klebanoff je s firmo Bentley Laboratories razvil prvi aparat za avtotransfuzijo na katerem temeljijo tudi današnji izpopolnjeni celični separatorji. Pri tem aparatu je obstajala velika nevarnost zračne embolije, zato so ta sistem hitro opustili.

Prvi avtotransfuzijski aparat, ki se je začel rutinsko uporabljat je izdelala firma Haemonetics leta 1976. Aparat se je upravljal ročno. Hitro so sledile izpopolnjene aparature Cell Saver II. in Cell Saver III., ki sta bila polavtomatska. Cell Saver IV. je že popolnoma voden računalniško in je namenjen operativnim posegom z velikimi izgubami. Sledile so mnoge druge firme z aparaturami, ki omogočajo celično separacijo pred operacijo, nadaljevanje z isto aparaturo med in po operaciji. Avtorji (Hood, Potter, Keating...) iz Regionalnega mornariškega medicinskega centra Oacland - California navajajo že leta 1993 primere izgube krvi nad 10000 ml med operacijo na odprtem srcu s pomočjo ZTO, ki so jih izpeljali brez uporabe homologne krvi.

Dosedanje klasične alternative uporabe homologne krvi so: farmakološka priprava bolnika, preoperativna avtotransfuzija, izbor anestezije (regionalna, hipotenzivna anestezija), intraoperativna lega bolnika, intraoperativni odvzem krvi ob nadomeščanju volumna (normovolemična hemodilucija), intraoperativno zbiranje polne krvi in vračanje nazaj preko filtra.

V izogib uporabe homologne krvi in v cilju čim večje uporabe avtologne je najboljše kombinirati več naštetih možnosti. Smiselno je izdelati program avtotransfuzije za posamezne operativne posege. Zakaj? Predvsem zato, ker bolnik ima pravico do večje varnosti, ker mora kri biti takoj na voljo, ker EU zahteva samozadostnost v preskrbi s krvjo in nenazadnje zaradi zmanjševanja stroškov zdravljenja.

Običajni perioperativni avotologni program predstavlja zbiranje krvi med operativnim posegom, koncentracijo in izpiranje eritrocitov.

Kri pomešana z antikoagulantno raztopino - heparin 30000 E/l fiziološke raztopine, se izsrkava iz operativnega polja in preko filtra (40 mikronov) dovaja v rezervoar.

Zbrana kri vsebuje hemolizirane eritrocite, aktivirane trombocite, aktivirani komplement in druge snovi, ki se med operativnim posegom sproščajo v rani. Z filtracijo se sicer

večji delci iz operativnega polja odstranijo, vendar filter ne odstrani škodljivih snovi. Te se odstranijo šele, ko se eritrociti v procesu centrifugiranja koncentrirajo in operejo z fiziološko raztopino. Končni produkt procesa so: KONCENTRIRANI OPRANI ERITROCITI. Del eritrocitov se ob vsrkavanju in centrifugiranju uniči zato je izkoristek aparature približno 70-80%.

Kontraindikacije za uporabo celičnega separatorja so:

maligni tumorji,

kontaminirana kri (sepsa, črevesna vsebina),

amnionska tekočina.

Komplikacije

Nevarnost zračne embolije, ki je bila prisotna pri prvih aparaturah, sedaj ne obstaja več. Sodobni separatorji imajo senzor za odkrivanje zračnih mehurčkov. V primeru, da senzor odkrije zrak, se aparat samodejno ustavi.

V postopku koncentracije in izpiranja eritrocitov se žal skupaj z nezaželenimi produkti odstrani tudi plazma, zato pri večjih izgubah krvi lahko pride do koagulopatije. V tem primeru je pri uporabi te klasične metode potrebno dodatno transfundirati homologne trombocite ali svežo zmrznjeno plazmo.

S sodobnimi celičnimi separatorji je v takih primerih možno zagotoviti program odvzema večjih avtolognih komponent in sicer:

a) preoperativno
   koncentrirane eritrocite,
   plazmo bogato s trombociti,
   plazmo z malo trombocitov,
   koncentrirane trombocite in
   trombocitni tkivni gel,
b) medoperativno
   oprani koncentrirani eritrociti za takojšnjo transfuzijo,
c) pooperativno
   oprani koncentrirani eritrociti za takojšnjo uporabo.

Klinični učinki avtologne komponentnega programa

Vsebina trombocitnega koncentrata je približno $5,5x\ 10^{10}$ in je primerljiva s komponentami pripravljenih na transfuzijskih oddelkih.

Tako pripravljeni trombociti so funkcionalni, sveži, avtologni in po količini primerljivi 10 enotam.

Plazma pridobljena s separacijo vsebuje sveže avtologne koagulacijske faktorje, ki so primerljivi dvem enotam sveže zmrznjene plazme.

Bolnik ni izpostavljen homologni krvi krvodajalca - bolnik je sam krvodajalec.

Tako izpopolnjeni avtologni komponentni program lahko zmanjša porabo homologne krvi za več kot 90%.

Perioperativno in postoperativno zbiranje krvi

D. Paškvan
Ortopedska bolnišnica Valdoltra

Zbiranje krvi po kriruških drenih in med operativnim posegom in vračanje tako zbrane krvi bolniku je utečen način avtotransfuzije, je enostavna in cenovno ugodna metoda, katero v naši ustanovi uporabljamo od konca leta 1992. Idejo oziroma povod za začetek te metode avtotransfuzije smo dobili tekom leta 1992, ko smo ugotavljali, da nam počasi zmanjkuje homologne krvi in da postoperativno zgubljamo preveč bolnikove krvi. Na tržišču je v tem času bilo nekaj sistemov, kateri so omogočali zbiranje po operaciji.

Po enoletnem preiskušanju smo se odločili za sistem Haemocell. Sistem je enostaven za uporabo, nudi nam 1200 ml velik zbiralnik. Popolnoma zaprt sistem, ki nam zagotavlja sterilnost, možnost, da naredimo podlak mehansko (ročna pumpa) ali avtomatsko (električna pumpa). Sistem ima enostaven vacuum indikator. Mikrobiološki filter onemogoča kontaminacijo krvi, nepovratni ventil pa ščiti bolnika. Sistem je opremljen s 125 micronskim krvnim filtrom.

Sistem za postoperativno zbiranje se priklopi na kirurške drene na koncu operacije na operacijski mizi, pod sterilnimi pogoji to izvede inštrumentarka. V rezervar vbrizgamo do 30 ml antikoagulantnega sredstva.

V literaturi je opisana uporaba istih sistemov brez antikoagulantnega sredstva. V naši ustanovi smo preiskušali sistem brez antikoagulantega sredstva in nismo ugotovili signifikantne razlike v primerjavi s sistemom s koagulntnim sredstvom. Uporabljamo sistem z antikoagulantnim sredstvom. Pri predaji bolnika v postoperativni nadzor odpiramo sistem in začnemo z zbiranjem krvi. Negativni tlak v sistemu je maksimalno 100 ml stolpca živega srebra (v literaturi se ne priporoča večji negativni tlak). Maksimalni čas zbiranja krvi v naši ustanovi je štiri ure od začetka zbiranja (v literaturi opisujejo maksimalni čas zbiranja do šest ur). Zaradi varnosti in možnosti komplikacij smo se omejili na 4.urno zbiranje na sobni temperaturi, sistem nam pač ne dovoljuje po izpraznitvi zbiralnika naslednje štiri ure zbiranja. Na ta način zbrana kri se vrača bolniku brez dodatne obdelave skozi transfuzijski sistem z 40 micronskim filtrom.

Maksimalne količine na ta način zbrane se v naši ustanovi gibljejo tudi čez 2000 ml. Možne komlikacije: nekajkrat je prišlo do nastanka strdkov kljub temu, da smo v sistem dodali antikoagulantno sredstvo.

Z intraoperativnim zbiranjem bolnikove krvi smo začeli leta 1995 pri večjih ortopedskih posegih (korektivne operacije otroške hrbtenice). Kri zbiramo iz odprte kirurške rane. Sistem za aspiracijo je nenehno vlažen z antikoagulantnim sredstvom (pri zbiranju 1000 ml krvi porabimo 5000 IE Heparina razredčenega v 250 ml 0,9% NaCl). Kri se filtrira skoz 125 micronski filter v zbiralnik. Pomembno je, da kirurg kontinuirano uporablja aspirator.

V naši ustanovi za odvajanje tekočine za izpiranje iz odprte kirurške rane uporabljamo drugi aspirator. Iz odprte kirurške rane zbiramo samo kri. Zbiranje krvi nehamo pred koncem operacije, tako zbrano kri obdelamo na Haemocell Cell-saverju. Praviloma tako obdelano kri bolniku vrnemo še preden je zbujen. Spet s transfuzijskim sistemom opremljenim z 40 micronskim filtrom. Možne komplikacije: hematurija (mikroskopska ali makroskopska).

Zaključek:

Tovrstna avtotransfuzija nam omogoča:

eliminacijo tveganja transfuzijskih reakcij
eliminacijo tveganja prenašanja nalezljivih bolezni
zmanjšanje števila postoperativnih infekcij
eliminacijo tveganja avtoimunizacije na rdeča krvna telesca in ostalo
kirurško obdelavo bolnikov senzibilziranih na homologno kri
zmanjšuje porabo homologne krvi
Cost benefit

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Organization of an integrated autotransfusion program

Prof. Mempel

Blood transfusion "per se" is no therapeutical procedure in most cases but a supportivemeasurement. Since it has risks which can not be neglected it has to be handled very critical.

One way to avoid the risks of allogeneic blood transfusion is the use of autologous in stead of allogeneic blood. However the succes of an autotransfusion program is dependant of the organization. Though autotransfusion consists of several components like intraoperative cell salvage, hemodilution and preoperative donation, I will focus on preoperative donation since this needs the most extensive organization. Autologous preoperative donation only makes sense if the patient has timeenough to replace the erythrocytes he has donated.

The means that predonation must be done at least two weeks before operation, and this means that all doctors and the patient involved must plan in advance.

The driving force for preoperative blood donation mostly comes from the patient because he fears the risks of allogeneic blood.

In Germany there exists a decicion of the supreme court, that any patient who is going to be transfused, must be informed about the risks and must be informed about the possibility to donate autologous blood. But it is necessary to inform the patient in time, otherwise he will not be able to donate the right numbers of blood needed, for the special operation. Normally the general practioner is the first of discuss the problem. The surgeon, when discussing operation modalities has to decide how much blood will be necessary. The blood banker will draw the blood, fractionate and store it until it is delivered to the operation room. The anaesthesiologist will give the blood back to the patient. All these specialists must work together and only if all are cooperative the system of autologous transfusion will work.

Blood for transfusion is a drug (in Germany) that holds true even for autologous blood. Any person who prepares a drug and delivers it must have a permission.

According to the transfusion law which was established 1998 iti is easier to get the permission for autolougos blood than for allogeneic but you must have it. Many of the small hospitals lack the permission, so they must cooperative with a transfusion service.

Autologous blood has to fullfill the criteria of a normal blood unit that means it must be handled the same way. It will be tested for infectious diseases HIV, Hepatitis B, and C; at Least the patient will be tested once before a donation period. If the tests are positiv for HIV or HCV blood will not be taken or if necessary stored under special security conditions.

As a standard; units will be separated in RBC and plasma which is frozen immediately. But since there is rarely a real need of plasma for coagulation disorders, and since a great deal of autologous units are not needed at all; there is a growing discussion weather it would be advantagous to store autologous blood as whole blood. Especially after the establishment of inline filter for leukoreduction an autologous leucodepleted whole blood can be produced which has better storage conditions than a normal whole blood and which is cheaper than a separated unit. Autologous blood must be stored in a separate refrigerator and all precautions must be done to avoid mixing up. Documentation is very essential especially in the patients report, to avoid the risk that the patient will get a homologous unit as long as autologous units are still in reserve. Crossmatching is not necessary, but we do a major blood grouping on the unit before

delivery; so that we can compare it with the blood group of the patient. A bedside test will be done before transfusion. When the blood is not needed it has to be discarded.

Crossover to other patients is not allowed in Germany.

But you have to make a contract with the patient regarding the waste. Otherwise the patient can ask you for this plasma for the time till is outdated (up to 2 years) and your storagecapacity will be full very soon.

For a full success of the program all criteria must be considered, but this is not different to other medical therapeutic procedures.

Results of an integrated program of current autotransfusion techniques

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To face the problems of allogeneic blood transfusion safety and of blood inventory shortage a program of better use of blood and autotransfusion was implement in 1980 at our hospital. During the last two decades a number of measures have been adopted to continuously improve the efficacy of the program and its cost-effectiveness.

The aim of this paper is to present the currently utilized strategies and the results obtained.

The Gaetano Pini Orthopedic Institute is currently composed by 14 surgical wards with approximately 400 surgical beds. Five major objectives have been identified in setting up the transfusion practice in our Institute.

1. Rationalization of the blood component utilization
2. Preoperative hematological evaluation of patients candidates for elective surgery.
3. Reduction of allogeneic blood use through the appropriate use of allogeneic blood alternatives (such as the autotransfusion techniques, erythropoietin).
4. Optimization of cost-effectiveness of the alternatives
5. Improvement of the safety of bedside transfusion practice

I) Rationalization of blood component utilization

A survey carried out at the beginning of the program revealed that the requests made by surgeons were generally in excess of the real needs for intra and postoperative blood transfusion requirements. This represents a relevant problem for blood supply management and forecasting and is a well known cause of high blood component wastage rate and increased costs.

Moreover, the most important cause for inappropriate use of blood component in surgery is the inappropriateness of blood use. Indeed a number of studies have documented a general tendency to overtransfusion in this group of patients. On the basis of these consideration it has been agreed upon to adopt a strict policy for preoperative blood ordering and blood component transfusion indication.

Preoperative blood ordering

For all the procedures performed in a consistent number of cases the recommended blood order (ie. no blood, or the number of units to be reserved for the patient) is defined by the local MSBOS (Maximum Surgical Blood Order Schedule). This guidelines, prepared in cooperation with the surgeons and the anesthesiologist, are approved by the transfusion committee of the hospital and are revised every year on the basis of the current blood usage.

The adoption of the MSBOS procedure actually allowed to reduce the workload due for unnecessary pretransfusion tests. Indeed in the group of patients operated on for a procedure included in the MSBOS, only 16% of the patients for which pretransfusion tests were performed didn't require any transfusion support, while this figure was 46% in the group of patients operated on for procedures not included in the MSBOS.

Moreover the strict application of the MSBOS contributed to limit the wastage of allogeneic blood unit to the value of 1.3%.

Blood transfusion indication

For each blood component, specific guidelines addressing its indication have been developed and approved by the transfusion committee. The compliance to the principle expressed is strictly monitored through concurrent and retrospective audit. The results obtained in 1998 are reported in tab. 1

Tab1. Proper use of blood and blood component in 1998

Parameters	
Pts transfused the day of surgery whose Hct value is > 35% on day 1 postop.	15%
RBCs Units transfused in the postoperative period to pts with pretransfusion	
Hct > 28%. Total:	12,6%
Allogeneic units:	9,2%
Autologous units:	17%
Pts transfused with RBCs and Plasma units	2,7%

As it can be seen from the table there is still a tendency to overtransfuse surgical patient the day of surgery. This is partially due to the difficulty to evaluate the need for transfusion support in this phase, as in the majority of the case the decision to transfuse a patient is based on an evaluation of blood losses occurring during surgery and the early postoperative period. In the postoperative period hypertransfusion differently involved allogeneic and autologous units. Allogeneic units were rarely hypertransfused (9%) while this happened more frequently for autologous units. This indicates a more "liberal" utilization of autologous units in particular aimed to facilitate early rehabilitation program of the patient.

2) Preoperative hematological evaluation

A properly timed presurgery evaluation of patients undergoing major elective surgery by transfusion specialist is of relevance to optimize the patient surgical management.

In our institute we set up a program allowing to evaluate, 25-30 days prior to surgery, the patient's clinical and hematological conditions, its expected transfusion needs and the most appropriate transfusion strategy for the specific patient. According to the protocol all the patients candidates for elective surgical procedure expected to require transfusion support have to be referred to the Transfusion Center for the pre-admission evaluation.

As preoperative anemia is a major factor in conditioning transfusion requirements, patients having low Hct/Hb values are evaluated to define its causes and when possible, to correct them. A special care is devoted to detect iron deficiency conditions.

In 1998 a total of 875 patients (74% of all the patients candidates for major surgical procedures expected to require transfusion support) have been referred for presurgical evaluation. A total of 40 patients (36 females and 4 males) had low baseline Hct values attributable to iron deficiency and were treated with intravenous administration of iron sucrose (average dose 791 $\pm$278 mg of elemental iron) before enrollment into the preoperative autologous blood donation (PABD) program. The treatment allowed to increase the hemoglobin value by a mean of 0.8 g/dl in a mean of 37 days (thus increasing their RBCs mass by 125 ml).

Further 137 patients, despite of good Hb/Hct values, have been detected to have suboptimal iron stores and were supplemented with intravenous iron during the PABD program thus optimizing the efficacy of the technique.

Moreover, 13 patient undergoing major elective surgery were found to have anemia not correctable with hematinics and received erythropoietin treatment. All these pa-

tients could predeposit a sufficient number of autologous blood units to completely cover their perioperative transfusion needs.

3) Alternatives to the use of allogeneic blood

Preoperative Autologous Blood Donation

All the patients undergoing major elective surgery expected to require transfusion support (according to MSBOS) are considered potential candidates for predeposit their own blood. Contraindications to enrolment are fever, severe coronary disease, poor general conditions and anemia (Hct <33%). As previously reported, anemic patients are evaluated to define the causes of anemia and when possible treated. In case of successful treatment, patients are subsequently enrolled into the PABD program.

The number of units to be collected is defined according to the patient's hematological conditions and the expected transfusion need. Donations (normally 400 mL each) are collected in single blood bag at 7 days interval.

Perioperative blood salvage

Recovery of blood lost during surgery or in the early postoperative period, washing and immediate retransfusion is carried out, on a shift basis, by staff members of the transfusion service.

For major orthopedic surgery if the forecast blood loss is greater than 1000 ml, intraoperative salvage is always proposed. Intraoperative blood salvage is not performed in cases of cancer, infected wounds, sepsis, or when the anticipated blood lost is less than 300 ml. In all the other cases the stand-by procedure is utilized a collection set, consisting of reservoir, vacuum line and anticoagulant line is assembled. When the reservoir contains the equivalent of more than 1 unit of blood the washing set is connected, and blood processing commenced. If the amount of RBCs collected into the reservoir is equivalent to less than 1 unit of blood, recovered blood is disposed off unless postoperative salvaging is indicated. As a routine, the surgeons are requested to control suction pressure to as low a level as possible, consistent with efficient aspiration of blood and minimal hemolysis. In tab.2 are reported the guidelines for intra and postoperative salvage utilization adopted in 1998.

Tab.2 Indications for perioperative blood salvage in different surgical procedures at the Gaetano Pini Institute

Surgical Procedure	Intraoperative Salvage	Postoperative Salvage
Total hip replacement	Stand by Optional (*)	Optional (*)
Bilateral hip replacement	Yes	Yes
Total hip prosthesis revision	Yes	Yes
Partial hip prosthesis revision	Stand by	No
Pelvis ostheotomy	Stand by	No
Total knee replacement (with tourniquet)	Stand by	Yes
Vertebral arthrodesis	Yes	No
Osteosinthesys or partial hip prosthesis for femur fracture	Stand by	Optional (*)

(*) : when intraoperative blood loos is particularly relevant

Acute Normovolemic Hemodilution

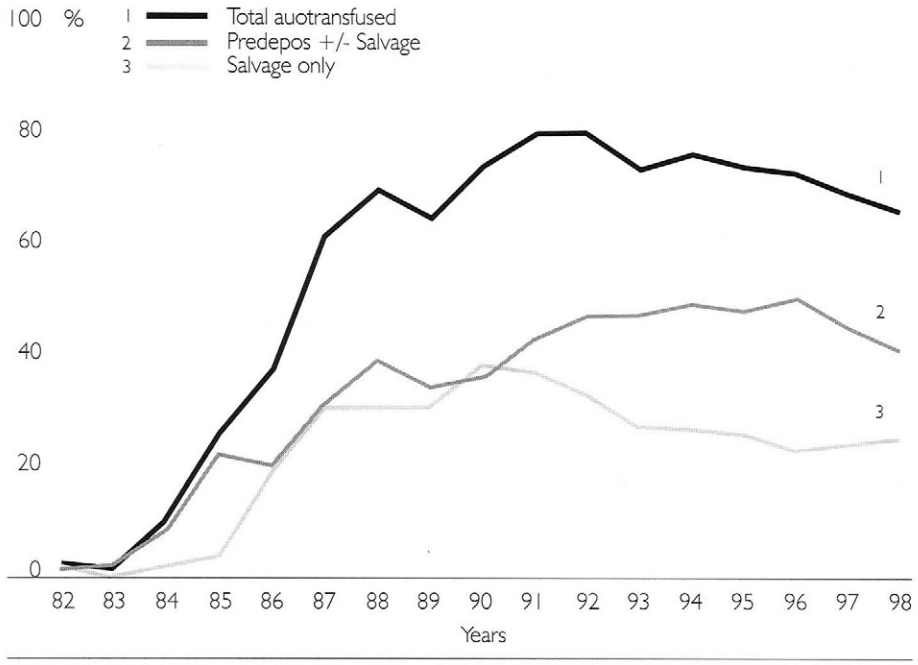
The techniques is not routinely utilized in our Institute but is adopted only in limited and selected cases when other techniques are not feasible.

Results

The results obtained with the utilization of the alternative strategies to the use of allogeneic blood have been evaluated on the basis of the three major objectives enrolment, allogeneic blood conservation and avoidance from the exposure to the use of allogeneic blood.

The systematic and integrated use of the different autotransfusion techniques has allowed to constantly increase the number of patients who benefit from the use of autologous blood (Fig 1).

Figure 1. Enrollment through the years into the autotransfusion program of the patients undergoing major elective surgery at the Gaetano Pini Orthopedic Institute



In 1998, 66% of all the transfused patients have been enrolled into the autotransfusion program (41% of the transfused patients could predeposit their blood in association with perioperative salvage, while the remaining 25% of patients could only benefit from perioperative blood salvage). When the use of each single technique is concerned it can be observed that PABD utilization varied according to type of surgery. Indeed in major elective surgical procedures, PABD was utilized in 64% of the transfused patients while its utilization was significantly lowen in minor elective surgery (28%) and in non elective surgery (0.5%). The most relevant causes preventing the use of PABD were, beside the absence of indications, anemia (37% of the cases), cardiopathy (10%) and inadequate venous access (5%). Organizational reasons averted from using PABD only in 4% of the transfused patients who were actually suitable for predeposit their blood.

The utilization of the perioperative blood salvage is reported in tab. 3. As it can be seen the compliance with guidelines has been satisfying, however in a consistent number of cases it has been performed in absence of indication.

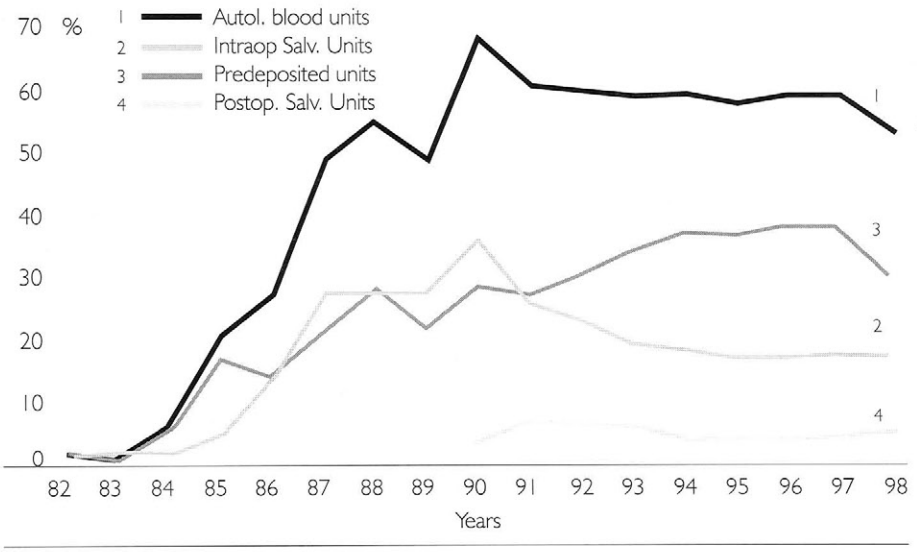
Tab. 3 Utilization of perioperative blood salvage

	IOS (performed / indicated)	*POS (performed / indicated)*
Pts for which salvage was indicated	207/333 (62%)	164/300 (55%)
Pts for which "stand by" procedure was indicated	694/1358 (51%)	0
Pts for which salvage was "optional"	0	194/1190 (16%)
Pts for which salvage was "not indicated"	160/500 (32%)	88/701 (12%)

Pts: Patients; IOS = intraoperative salvage; POS= postoperative salvage

Blood conservation obtained through the use of the autotransfusion techniques is measured by the ratio between autologous blood units transfused and the total units transfused. As it can be seen from fig. 2 in the last 10 years, more than 50% of blood requirement have been covered with autologous units.

Figure 2 Autologous blood units transfsued through the years in elective surgery patients at the Gaetano Pini Orthopedic Institute



The contribution of autologous blood techniques to allogeneic blood conservation according to type of surgery is reported in tab. 4.

Tab 4 Utilization of autologous and allogeneic blood units in different groups of orthopedic surgical procedures in 1998

Type of surgery	*N° of Pts*	*Predep units n° (%)*	*Salvaged units n° (%)*	*Allogeneic units n° (%)*	*Total units n° (%)*
Major elective surgery	1132	1595 (44)	1051 (29)	938 (27)	3584
Minor elective surgery	54	18 (21)	28 (33)	39 (46)	85
Not elective (trauma)	577	5 (0.3)	72 (5.2)	1342 (94.5)	1419
Unclassificable (cancer)	136	63 (13)	88 (19)	315 (68)	466

The use of the autotransfusion techniques, in conjunction with the other adopted strategies, significantly reduced the patient's requirement for allogeneic blood support.

In 1998, 44% of all the operated and transfused patients received their own blood only. This figure varied significantly according to the type of operation (Tab.5).

Tab 5 Patients transfused with autologous blood only, autologous plus allogeneic blood and allogeneic blood only in different type of orthopedic surgery in 1998

Type of surgery	*N° of Pts n° (%)*	*Auto only n° (%)*	*Auto+Allo n° (%)*	*Allo only n° (%)*
Major elective surgery	1132	705 (62)	342 (30)	85 (8)
Minor elective surgery	54	38 (70)	4 (8)	12 (22)
Not elective (trauma)	577	39 (7)	52 (9)	468 (86)
Unclassificable (cancer)	136	55 (41)	34 (25)	47 (34)

The integrated use of PABD and perioperative salvage emerged to have a critical role in limiting the exposure to allogeneic blood. Indeed in major orthopedic surgery if perioperative salvage is used alone the chance of a patient also receiving donor blood is 79%, while the probability of receiving autologous blood only is more than 85% when salvage is integrated with predeposit.

4) Optimization of Cost-Effectiveness of the Alternatives

Autologous blood transfusion, although generally accepted as a standard of care, is considered more costly than allogeneic blood transfusion. Thus, improving the cost-effectiveness of autologous blood transfusion programs is becoming more and more important as financial pressure on the health-care system place great emphasis on the cost-containment and prioritization of medical interventions.

To optimize the cost to benefit ratio of the autotransfusion techniques a number of measures aimed at the reduction of their direct costs and at the improvement of their efficiency have been adopted in our Institute. Some of the adopted measures to reduce the direct cost of autologous blood procurement on:

- the definition of guidelines and flowcharts for the patient's presurgical evaluation and scheduling,
- simplifying the patients interview and donation process
- avoiding serological tests for infectious disease markers
- collecting autologous blood in single collection bag and storing it as whole blood

Moreover a special care has been devoted to optimize the efficacy of the autotransfusion technique, and to avoid the collection.

Optimization of efficacy of the autotransfusion technique

Specific measures have been adopted to optimize the efficacy of both predeposit and perioperative salvage.

It has been clearly demonstrated that to optimize the efficacy of PABD it is necessary to collect autologous blood far in advance to surgery so to allow the production of as many as possible new RBCs. If we don't give the patient enough time to compensate for the collected red cells through the physiologic erythropoietic mechanisms, PABD offers very little advantage to the patient because in this case only a reduction of intra-operative RBCs loss is obtained through the moderate hemodilution induced by blood collection.

For these reasons specific protocols have been adopted to allow a 4 week interval between the collection of the first unit of autologous blood and surgery. This target has been very successfully reached as the mean interval between the starting of the PABD program and surgery resulted to be 26+8 days. The appropriateness of the surgery planning is confirmed by the observation that only 1.5% of the collected units were disposed of because outdated before patient's surgery.

To optimize the cost-effectiveness of perioperative blood salvage, beside the adoption of the "stand-by procedures" it has been recommended to extend salvaging in the post-operative period whenever the intraoperative yield is equivalent to approssimately 1 unit of blood, or higher. Indeed as it can be seen from tab. 6 in the majority of the cases where both intraoperative and postoperative salvage has been performed, more than 1.5 units of blood have been collected and transfused.

Tab 6. Mean number of salvaged units harvested and % of cases in which more than 1.5 units of blood have been harvested in different orthopedic surgical procedure subdivided according to the type of salvaging performed.

	n° of salvaged units					
	IOS		POS		IOS+POS	
Operation	Mean	% 1.5	Mean	% 1.5	Mean	% 1.5
Total Hip Replacement (THR)	0.6	5.1	n.a.		1.5	52
Bilateral THR	n.a.		n.a.		2.6	93
THR Revision	1.6	43	n.a.		2.6	90
Revision of THR component	1.0	20	n.a.		2.6	78
Pelvis Osteothomy	0.5		n.a.		n.a.	
Total Knee Replacement	0.3	35	0.7	8	1.2	34
Vertebral Arthrodesis	0.9	6	n.a.		n.a.	
Osteosyntesis for femur fracture	0.6	0.5	n.a.		2.2	100
Partial Hip Prosthesis	0.5	0	n.a.		n.a.	

IOS = intraoperative salvage; POS= postoperative salvage; n.a.= not applicable because of the limited number of cases

Avoidance from the collection of unnecessary autologous units.

The most relevant cause of the higher cost of autologous units is the wastage of units that are collected and discarded because not transfused.

In our Institute to minimize the wastage rate of predeposited units, preoperative collection has been taken into account only for patients candidates for surgical procedures in which the probability of allogeneic blood transfusion in higher than 10%. Moreover the number of autologous units to be collected from patients who are appropriate candidates to the enrolment into the PABD program has been defined according to the SOPCAB (schedule of optimal preoperative collection of autologous blood) method suggested by Axelrod et al. According to SOPCAB the number of units of autologous units to be collected for any surgical procedures should be calculated in each hospital as the 70-80th percentile of the distribution of the number of units transfused during the whole hospital stay. The adoption of these systems resulted in an overall wastage rate of autologous units of 14%. The wastage rate in some of the orthopedic surgical procedures, compared with the % of patients completely avoiding allogeneic blood transfusion, is reported in tab 7.

Tab 7 Wastage of predeposited units and % of patients transfused exclusively with autologous blood in 1998 subdivided according to the surgical procedure

Operation	*% of wasted predeposited units*	*% of Patients transfused only auto*
Total Hip Replacement (THR)	Male 2; 1 Female 9	87
Bilateral THR	Male 0.4; Female 15	97
THR Revision	9	71
Revision of THR component	8	86
Pelvis Osteothomy	17	96
Total Knee Replacement	18	88
Vertebral Arthrodesis	14	100

The adoption of MSBOS and SOPCAB, although valuable to obtain a correct management of the inventory of allogeneic blood and acceptable results in containing the wastage of AB units, however, suffer from substantial limitations: these methods do not give any indication on the appropriateness of the transfusion indications and more important they do not take into account the different transfusion requirement of the single patients undergoing a specific surgical operation in that particular hospital.

In order to further optimize the utilization of all the alternative to allogeneic blood we are now experimenting with a new and more personalized approach to define both the perioperative blood requirement and the utilization the most appropriate methods to cover the calculated blood requirement. This new approach takes into account the predicted blood loss determined through a constantly update calculation of the real blood loss that occurred in each patient per surgical operation and the volume of the blood that the patient can tolerate to lose before necessitating a transfusion support.

Preliminary results seams to indicate that this method may effectively optimize the management of the transfusion strategy in the surgical patients.

Improvement of the safety of transfusion therapy

As a consequence of the adoption of a number of measures such as stricter criteria for blood donor selection and the introduction of sophisticated tests for infectious diseases markers, blood supply is safer now than any other time in the history of blood banking. However, the occurrence of acute hemolytic reactions, due to the transfusion of AB0 incompatible blood, is still unacceptably relevant. Most incompatible transfusions are the results of clerical errors occurring during specimen collection, issue and transfusion of blood that lead to the transfusion of blood to a patient other than the intended recipient.

To reduce phlebotomy and bedside identification errors, a device, based on the forcing function concept, was proposed by Wenz et al (2). The system (Bloodloc Safety System, Novatek Medical Inc., Greenwich, USA) consists of a coded locking system so that a blood unit cannot be accessed without matching a three letters code that can be found only on the patient's wristband. Any error in patient or blood unit identification would make it impossible to open the lock, and consequently to transfuse the patient, Moreover, all the errors are automatically referred to the transfusion center; this makes possible the identification of all the errors occurring in the transfusion process and the concurrent implementation of a QA/QI program in the bedside transfusion practice.

In our Institute the Bloodloc Safety System and the associated QA/QI program in transfusion practice were implemented in January 1993 with the aim of preventing bedside transfusion errors occurring outside the blood transfusion service.

Up to December 98, 30430 blood units (13749 predeposited autologous blood units

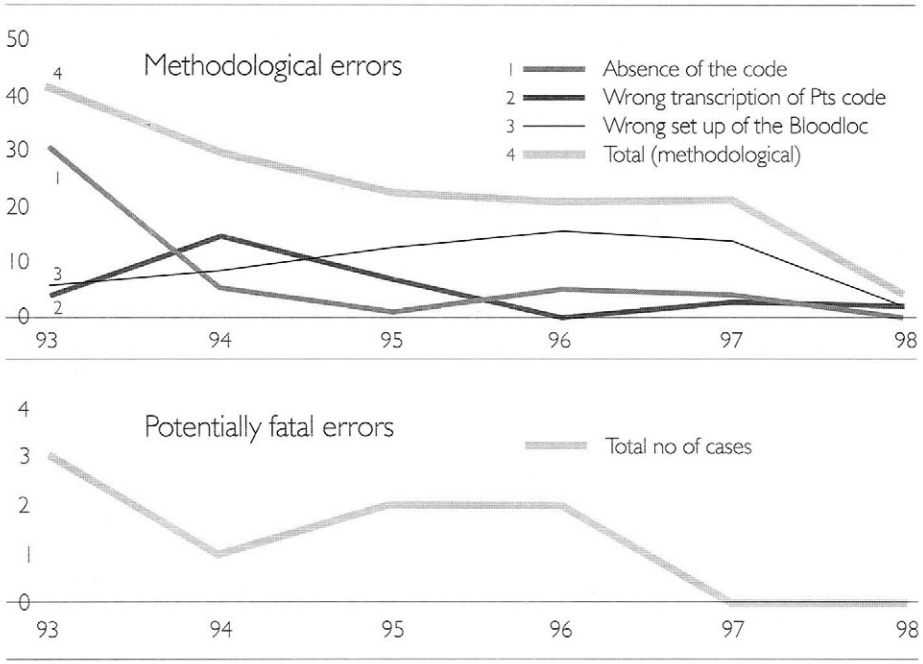
and 16668 allogeneic units) were transfused to 12.154 patients. A total of 143 methodological errors (absence of the three-letter code on the patient's specimen phlebotomist error in transcribing patient's code on the tubes, and improper encoding of the lock by the blood bank) were detected giving an incidence of 1 in every 212 units transfused.

In this period, 8 potentially fatal errors (1 in every 3803 units transfused) occurred, 6 of which were detected and prevented by the use of Bloodloc. The potentially fatal errors detected and prevented by the system included 2 cases of interchange of recipient sample tubes resulting in misgrouping of blood, 3 cases of patient misidentification and 1 case of blood unit misidentification.

Two errors have not been prevented: the first case was the transfusion of a unit of fresh frozen plasma (FFP) to the wrong patient (but in our Institute the Bloodloc is not utilized for FFP and other component because not associated with the risk of fatal hemolitic transfusion reaction); the other error was the transfusion of a compatible properly crossmatched allogeneic blood unit to a patient for whom autologous blood units were still available. The error was determined by omissions in the routine procedure for assignment and transfusion by the physician of transfusion service and the anesthesiologist in charge of the patient.

As it can be seen from Fig.3 the adoption of the Bloodloc system and the associated QA/QI program allowed to constantly reduce the incidence of errors in the transfusion practice in our hospital.

Fig.3 Methodological and potentially fatal errors through the years at the Gaetano Pini Orthopedic Institute



Conclusions

The results obtained through the years indicate that an integrated program of currently available autotransfusion techniques and proper use of blood is feasible and can significantly contribute to improve the quality of the transfusion practice given to the patients. Moreover, it can contribute to solve the problem of donor blood shortege that is becoming a more and more serious problem worldwide.

Critical parameters for the success of such a program are:

- The transfusion policy that must be discussed and developed by all hospital departments that are involved in the program and must give simple and unequivocal indication;
- The organization that must allow the patients to be referred, at least 10-15 days before hospital admission, to the preoperative autologous blood donation program, and the transfusion service must be provided of the logistical structures needed and of qualified physicians to bleed not only blood donors but also patients;
- Finally, it is essential that the results of the program should be monitored to ascertain the compliance. Both the results obtained and the measure eventually required to reach the target of the program should be discussed and analysed with the directors of the other departments involved.

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