

HAEMOVIGILANCE – WHY ?

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Introduction

The treatment of patients with blood and blood products has become an important issue in quality care medicine. Blood transfusions are often taken place as part of the treatment of a great number of hereditary and acquired diseases, are prescribed by almost all medical specialities, but imply potential dangers like immunological reactions and viral infections. However, administration of a blood product is easily to document. But above all, blood is donated by voluntary and non-remunerated blood donors which imposes an important responsibility on those professionals who prescribe blood as a treatment.

A blood supply of high quality and quantity requires apart from the contribution of voluntary blood donors, a well organised system of donor selection, blood drawing, safety and compatibility testing, controlled production at high quality, and not at the least, optimal usage of blood and blood products in clinical care, and vigilance of adverse events – haemovigilance-.

Although several reports have been published on adverse events, including transfusion-associated deaths, the relative risk based on the number of actual cases divided by the number of units of blood products issued or transfused, is relatively low. From the public but also from the medical-scientific point of view, however, the perception of risks related to blood seems to be not correlated to the actual magnitude of the risk. This might be explained by the history of the transmission of blood borne viruses, by the social and legal consequences of these viral transmissions mainly for patients and their relatives but in some cases also for politicians and professionals in the field of blood transfusion and transfusion medicine, by inadequate responses from blood banks and blood transfusion centres and by lack of communication. Already in 1990, it was advised that "management systems for transfusion facilities should be created or revised to include the specific identification of personnel eligible to administer transfusions, to provide written guidance and appropriate training, including recognition and management of errors, and to implement measures that target safe transfusion practice" (1). With the focus on blood safety mainly to safety measures preventing the potential transmission of micro-organisms, and more recently also regarding unknown risks like the transmission of prions, still questions regarding clinical safety in transfusion medicine are not (sufficiently) answered and need to be addressed.

If errors are taken place at the beginning of the handling process in the hospital, the effect on the clinical outcome might be dramatically. Reports of transfusion incidents in the State of New York in 1990-2000, and in the United Kingdom in 1996-1998 and in 1996-2000 showed that more than 50% of the reported incidents were caused by administrative failures (2,3). Of these administrative failures, 10-50% was the result of a wrong blood drawing or of wrong identification of the blood sample. Further, in 10% of the errors, it was forgotten to order an irradiated or leuco-depleted blood product. These studies showed that 1. not well-identified blood samples are an important source of errors in blood transfusion incidents, and 2. the blood product, which is really required, is not always requested.

The risk that inappropriate blood component transfusion is given depends of a great number of variables. Identification errors, notably administrative errors play an important part.

Haemovigilance

The aim of haemovigilance is to detect and to analyse all untoward effects of blood transfusion in order to correct their cause and to prevent recurrence, and to improve the safety of blood transfusion..

Haemovigilance is defined as: "a set of surveillance procedures covering the whole transfusion chain (from the collection of blood and its components to the follow-up of its recipients), intended to collect and assess information on unexpected or undesirable effects resulting from the therapeutic use of labile blood products, and to prevent their occurrence and recurrence" (4). The word haemovigilance is derived from the word pharmacovigilance, which encompasses activities and systems to collect information useful in supervising medicinal products, with particular reference to adverse drug reactions in human beings, and to evaluate such information scientifically. Adverse reactions are defined as reactions which are harmful and unintended and which occur at doses normally used in man for the prophylaxis, diagnosis or treatment or the modification of physiological function(s). Haemovigilance concerns blood components: whole blood, erythrocytes concentrates, thrombocytes concentrates and fresh frozen plasma. Pharmacovigilance in transfusion medicine concerns plasma derivatives: clotting factor concentrates, immunoglobulins, albumin and other fractionated products. Since January 1, 1993, in European legislation plasma derivatives are considered to be pharmaceuticals, and the manufactures have to comply with the European regulations on pharmacovigilance (5).

History of Haemovigilance

The pioneer work on haemovigilance started in France in 1991, with the set up of monitoring systems by Blood Transfusion Committees followed by the start of the Centre National d'Hémovigilance in 1992 (6). Since 1993, multiple definitions of haemovigilance have been formulated. In some definitions, only focus was laid on the transfusion act, while in other countries haemovigilance started from the very first part of the blood collection process. Further, some systems focussed on the follow-up of only immediate adverse events, others on long-term adverse events, and others on both. Because of the complex interactions in the transfusion chain, the scope of haemovigilance is all levels of potential transfusion hazards, i.e. from the selection of potential donors to the transfusion to the recipient. To reach this goal: the core of haemovigilance, as a system of public health surveillance, is a prospective surveillance and alert system.

On European level, haemovigilance started around 1995. The European Council published its Resolution of June 2, 1995 and a Communication on "Blood Safety and Self-Sufficiency in the Community" with the aim to improve public confidence in the safety of the blood supply. The word "haemovigilance" appeared in documents of the European Commission, and an invitation to tender was published to carry a feasibility project on the establishment of a haemovigilance network in the European Community. The results of the project should be threefold: a. identify objectives, methods and means related to the establishment of a Community-wide haemovigilance network which would also serve to improve exchanges of information between the Member States; b. promote co-operation between the Member States on the systematic monitoring of risks and hazards associated with blood collection and transfusion and provide guidance in this respect; c. determine the measures that add value to the actions and measures of Members States and which need to be proposed to the European Commission in order to enhance the safety of the blood chain. In the same year and for the first time on ISBT Congresses, at the ISBT 5th Regional (4th European) Congress in Venice, Italy, a haemovigilance symposium "Haemovigilance procedures in Transfusion Medicine" was organised. The conclusion of this symposium was that haemovigilance should be considered as part of the

quality assurance process in transfusion medicine. Collection of data is the key to quality assurance in medicine, but it was recognised that not all data are equally important and that those, which are really important, should be brought to the surface (7). In 1996, the European Commission organised at an informal meeting of Ministers of the European Commission in Adare, Ireland, a Colloquium on Blood, which resulted in the document "Blood Safety and Self-Sufficiency: an Agenda for the European Community". Six areas of action were defined and one of them was haemovigilance. In the United Kingdom, the Serious Hazards of Transfusion (SHOT) scheme was launched, which receives and collates reports of death or complications of transfusion of blood or components on a voluntary confidential basis. In SHOT's first annual report the findings indicated that blood itself is extremely safe, but it draw attention to the need to direct resources towards the development of novel systems to ensure that it is correctly administered (8).

In 1997, the first European Seminar on Haemovigilance was organised by the Agence Francaise du Sang in Bordeaux, France. This inventory meeting was very inspiring and as a result in February 1998 in Paris, the initiative was taken to set up of a European Network on Haemovigilance. In the same year, the second European Seminar on Haemovigilance was organised in Lyon, France. In 1999 the European Commission issued the report on the feasibility of a haemovigilance network (the Haeman Report). In 2000 and 2001, the 3rd and 4th European Seminars on haemovigilance took place.

At the European Seminars, discussions were organised on the organisation of haemovigilance systems (voluntary or compulsory), the required (type of) data, the data on blood donors, the data on the usage of blood components or also on plasma derivatives, definitions, materio-vigilance and on the security of systems. Further the set up-of an alert system and a web-site as a tool of communication was discussed intensely.

Haemovigilance and the European Blood Directive

In European legislation, adverse event reporting in transfusion medicine is prepared. In the Draft Directive 2002 EC, the need for a common procedure for notifying serious adverse reactions and events and notification format is mentioned in two articles (9).

Article 15:

1. Members States shall ensure that:

- any serious adverse events (accidents and errors) related to the collecting, testing, processing, storage and distribution of blood and blood components which may have an influence on their quality and safety, as well as any serious adverse reactions observed during or after transfusion which may be attributed to the quality and the safety of blood and blood components are notified to the competent authority,
- blood establishments have in place a procedure accurately, efficiently and verifiably to withdraw from distribution blood or blood components associated with the notification referred to above.

2. These serious adverse events and reactions shall be notified in accordance with the procedure and notification format referred to in Article 29(i).

Article 29:

The following technical requirements and their adaptation to technical and scientific progress shall be decided in accordance with the procedure referred to in Article 28(2):

- (i) Community procedure for notifying serious adverse reactions and event and notifying format

These objectives require a change in approach of professionals in blood transfusion. Most blood banks are producing blood components, deliver these precious products to the hospitals, provide advice if needed on the usage, but have no real insight in the actual therapeutic use of the products in clinical care. Further, the use of blood components in the hospital is wide spread, in many different departments, for elderly, adults and children, and in many different clinical indications. Finally, most blood banks and blood centres have not sufficient access to hospitals. Discussions on haemovigilance have clarified that most blood banks and blood transfusion centres were not taking part in regular transfusion medicine. So, the new initiative required a new approach.

European Haemovigilance Network

The objectives for a European Haemovigilance Network (EHN) are aiming to increase blood safety at a European level (10). Early detection of an adverse event is needed. The aim of EHN is to develop and maintain in Europe a common structure with regards to safety of blood and blood products aimed on haemovigilance of blood transfusion and transfusion medicine. To assess the real risk, information should be pooled, and epidemiological data should be collecting systematically to evaluate differences between countries and the reasons for the differences. Information should be harmonised. At the same time, focus should be laid on materio-vigilance because it was recognised that the same material could be used in different countries. A first inventory showed that legislation in the field of haemovigilance was not equal and that not in all countries regulation concerning haemovigilance exists by law. In Austria, France, Germany, Netherlands, Sweden and Switzerland, notification of AEs to the authorities is mandatory. In Denmark, only notification of viral infection by blood is required. However, at the same time, it was recognised that in a mandatory system AEs are not always reported and that underreporting exists. Notification on a voluntary basis is implemented in Belgium, Greece, Ireland, Luxembourg, Russia, Sweden, and the United Kingdom.

EHN has the following objectives:

1. favour exchange of valid information between members
2. increase rapid alert and / or early warning between the members
3. encourage joint activities between the members
4. undertake educational activities in relation to haemovigilance.

Further:

1. standardisation of processes and forms, by developing common 'mother' matrixes.
2. compilation and analysis of European data, generated by national systems
3. assistance in the implementation of the European Blood Directive, in relation to legal provisions.

Adverse event reporting

One of the objectives of haemovigilance is notification of side effects and /or incidents related to the clinical use of labile blood components. Adverse event reporting in blood transfusion and transfusion medicine is complex. It depends on the collaboration between blood banks or blood transfusion services with clinicians and hospitals. It implies knowledge of blood banking, transfusion medicine and routine clinical care of all gender and ages, of potential hazards of transfusion, of immune-haematology, of microbiology, and of epidemiology. An adverse event may have its cause in every single part of the chain from donor to recipient. In adverse events reporting, reference may take place to a proven problem, a potential problem, or to a justified doubt

In almost all blood transfusion centres, a single donation of a donor will be processed into a number of different products, i.e. an unit of red cell concentrate, an unit of platelets, an unit of Fresh Frozen Plasma, and these units might be divided or processed

into more products. Blood components are produced from whole blood or apheresis donations, and depending of the blood drawing and processing techniques, a high number products with different specifications are prepared. The shelf life of these products are not equal and therefore the moment in time of actual use of each unit prepared from the same donation may differ. In case the unit of platelets harms the recipient, for example because of a bacterial transmission, a rapid alert can warn the blood bank, the blood transfusion service or the ward of the hospital in order not to issue or to transfuse the unit of red cells or the unit of FFP prepared from the same donation because of the potential adverse reaction, which was detected during or after the transfusion of the first unit used.

This example shows that a notifying system has to consists of two components:

1. A Rapid Alert / Early Warning system, and
2. A Reporting system for Adverse Reactions to Blood Component Transfusion.

The European Haemovigilance Network (EHN) has developed reporting forms for Rapid Alert reporting and for Adverse Reaction to Blood Component Transfusion reporting in order to standardise the information process needed to take appropriate action to prevent the occurrence or recurrence of unexpected or undesirable effects resulting from the therapeutic use of labile blood products. The draft reporting forms developed in work shops and intensely discussed at plenary sessions at the Seminars of EHN, and have been endorsed by all EHN members at the 4th EHN Seminar in Athens in 2001. It was decided that each member should advocate for the use of these documents in the haemovigilance organisation in their home country, aiming for implementing only one format of adverse events reporting documents in all European haemovigilance systems.

Rapid Alert System

The objectives of a Rapid Alert System (RAS) are enabling to make corrective actions in the shortest period of time. RAS is being used for signalling the appearance of clusters of clinical signals after transfusion, hidden or apparent defects of disposable materials used in the chain of blood transfusion, such as leakage of filter housings, holes in blood bags, defects in apheresis material, problems with equipment, and others. RAS allows quick and safe transmission of correct and precise data to quality assurance responsible persons in blood transfusion centres and to competent authorities allowing to decide on possible action in order to maintain or improve safety in blood transfusion. Quick transmission of information, potentially important for the safety, quality and efficacy in a structured predefined way is needed for passing information from one actor to another.

Because of the importance of the message and the preciseness of the information to prevent unnecessary and unjustified actions, a number of practical aspects should be taken into account.

1. before using the Rapid Alert System:

- the pertinent information has to be brought to an official qualified person (Blood Safety Officer, BSO),
- the information has to be checked to be correct, and as far as possible complete,
- in case a manufacturer of a device is implicated, written information and/or confirmation should be requested from the manufacturer.

2. using the Rapid Alert System:

- a validated Alert Report Form should be used,
- the requested information should be filled in with special care to lot and batch numbers, and other reference numbers needed for traceability,
- actions considered, suggested, or requested should be described,

- additional information should be attached, like written information and/or confirmation from the manufacturer,
- the information should be dispatched in a predefined way to the Department responsible for blood safety at the National Competent Authority.

3. after using the Rapid Alert System:

- investigations on the adverse event should continue,
- additional information should be dispatched, concerning outcome, impact, consequences, etc.,
- reactions from other informed parties like BSOs from other countries should be collected, compiled and disseminated in order to ensure an overview of actions taken and the follow-up thereafter.

Reporting Form for Adverse reaction to Blood Component Transfusion

The report Form for Adverse Reaction to Blood Component Transfusion is developed by EHN to assist the BSO in the investigation of the clinical adverse event. It may help to assist the physician in order to define the course of action, and in trying to define the adverse event in the (in most cases complex) treatment of the patient involved. In the final report of the adverse event, this document should always be included and signed and dated by both the physician and the BSO.

EHN Web-site

Ten Member States of the European Union – Belgium, France, Denmark, Greece, Ireland, Portugal, Luxembourg, Finland, Netherlands, and United Kingdom - are 10 full members of EHN. Non-EU Member States as Australia, Canada, Switzerland and Norway are associate member, and Brazil, Spain and Romania have expressed their wish to join as associate member.

As a tool for optimal connection and information exchange, the Internet web-site www.ehn-org.net has been developed. This web-site has two zones of information, a public domain with general information on blood transfusion organisations, data on donors, data on donations, data on blood components etc. of each member, and a protected domain with the Rapid Alert System. The Rapid Alert System (RAS), where only one person per country has access to, is used for rapid dissemination of (emerging) threats, clusters of adverse events, materio-vigilance, problems with equipment etc..

EHN Seminars are organised almost every year to discuss in Working Parties and plenary sessions questions to be solved, like: which information is related to immediate security of blood products, what is useful to be exchanged at European level, how to ensure scientific coherence of data, how to compare systems, how to standardise transfusion data, how to establish cross-border traceability and how to harmonise technical support.

The next 5th European Haemovigilance Seminar will be organised in Amsterdam, February 6-7, 2003.

Conclusion

Haemovigilance has an important function in safeguarding transfusion medicine. Errors have to be prevented and improvement in the use of blood products might be achieved through an audit process based on simple indicators, providing the responsible clinicians with continuous feedback of results obtained. Ten years ago, the Sanguis Study already showed that in three year period such an audit programme reduced both excessive preoperative requesting and actual transfusion of red cell units and plasma in elective surgical patients by 22, 20, and 70%, respectively (11).

Continuous feedback of data in laboratory medicine reduce excessive ordering of laboratory test and other resources. And more importantly, intensive “marketing” of

accepted practice guidelines is required to produce changes in clinical transfusion practice.

Uniform Rapid Alert Forms and Adverse Reaction Forms are important means of communication for rapid dissemination of information on adverse events in blood transfusion. Fax, e-mail and the Internet are tools to be used to inform all parties involved and all parties which may benefit from this information. It has to be realised, however, dissemination of this information may imply legal aspects, regarding privacy and liability, if not handled with care. All actors involved in a rapid alert are potentially prone to be hold liable for any damage to one of the parties involved. These legal aspects should be taken into account but in no way it should hold back persons from taking the necessary measures from preventing the occurrence or recurrence of an adverse event.

REPORTING FORM FOR ADVERSE REACTION TO BLOOD COMPONENT TRANSFUSION

Patient	sex : M <input type="checkbox"/> F <input type="checkbox"/> ; age : ... file number :		
	Date of transfusion :/...../..... Delay of reaction after transfusion :min / hours / days / years (Others informations are confidential and appears only on the hospital form)		
Transfused component	Type : <input type="checkbox"/> RC <input type="checkbox"/> platelets <input type="checkbox"/> plasma <input type="checkbox"/> granulocytes <input type="checkbox"/> allogeneic <input type="checkbox"/> autologous		
	Preparation : <input type="checkbox"/> whole blood processing <input type="checkbox"/> apheresis Characteristics : <input type="checkbox"/> leucodepleted <input type="checkbox"/> irradiated <input type="checkbox"/> CMV negative <input type="checkbox"/> plasma depleted <input type="checkbox"/> SD treated <input type="checkbox"/> safe quarantine <input type="checkbox"/> antigen matched <input type="checkbox"/> other (specify) :		
Place of distribution	<input type="checkbox"/> hospital <input type="checkbox"/> blood bank		

Symptoms and clinical / biological signs of reaction

Signs	Before	after	Symptoms (1)	Symptoms (2)	biological
Temperature °C	<input type="checkbox"/> discomfort	<input type="checkbox"/> lower back pain	<input type="checkbox"/> positive DAT
Blood pressure (mm Hg)	<input type="checkbox"/> chills	<input type="checkbox"/> chest/abdominal pain	<input type="checkbox"/> Hyperbilirubinemia
Pulse	<input type="checkbox"/> itching	<input type="checkbox"/> nausea/vomiting	<input type="checkbox"/> ALT > 2N
Haemoglobinurea	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> urticaria	<input type="checkbox"/> dyspnea	<input type="checkbox"/> Transfusion refractoriness
Cardiac arrhythmia	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/> redness	<input type="checkbox"/> acute renal failure	<input type="checkbox"/> Other :
Others :			<input type="checkbox"/> rash	<input type="checkbox"/> shock	
			<input type="checkbox"/> jaundice	<input type="checkbox"/> loss of consciousness	
			<input type="checkbox"/> other :	<input type="checkbox"/> others :	

Conclusions or Syndrom (only one for each report):

Immunological

Hemolysis ABO

Hemolysis irreg ab

Immunisation :

RC Granulocyte

HLA IgA

HPA

PTP

allergy (mild)

anaphylaxis

TRALI

Infectious

Component Bacterial contamination

Germ (s) :

HIV

HBV

HCV

CMV

Other agent :

Others

Non Hemolytic Fever T.R

TA-GVHD

Pulmonary oedema (cardiac failure, overload)

Hemosiderosis

Severity

0. no effect

1. immediate, no vital

2. immediate, vital

3. long term morbidity

4. death

Imputability

0. excluded

1. possible, dubious

2. likely, probable

3. certain, proven

Other relevant clinical information :
(e.g. prior condition of the patient)

Patient outcome :

Transfusion process	<input type="checkbox"/> op.theatre, <input type="checkbox"/> Intensive Care Unit, <input type="checkbox"/> medical, <input type="checkbox"/> paediatric,
Location :	<input type="checkbox"/> outpatient clinic, <input type="checkbox"/> other :
Time :	<input type="checkbox"/> working hours, <input type="checkbox"/> night shift, <input type="checkbox"/> week end
Incorrect component transfused : yes <input type="checkbox"/> no <input type="checkbox"/>	where in the process did the error occur : (cross matching laboratory, hospital blood transfusion service, delivery/transfer to the clinical ward, etc...)
Associated involvement	<input type="checkbox"/> materiovigilance <input type="checkbox"/> pharmacovigilance <input type="checkbox"/> reagent-laboratory failure

EHN-4X05

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ALERT REPORT

REFERENCE : ____ / ____ . ____ . ____ / ____ . ____ <small>(country/pays) (date : YYYY MM DD) (time : HH - MIN)</small>	From :
Subject / Objet :	
DESCRIPTION :	
Appended Documents : (documents joints) ***** This report is for your information only and does not suggest any action *****	
If device implication (MATERIOVIGILANCE): Denomination :	Key words / Mots clefs :
Producer address / Adresse Fournisseur :	1.
Product code / code produit :	2.
Batch nr / n° de lot :	3.
Expiry / expiration :	4.
Incidence : (Nr of events/period - Nb d'incidents / période)	5.
To : → this report is automatically dispatched to the members of EHN group.	