Qality control and quality management of blood safety

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Transfusion medicine is a part of medical sciences. The primary objective of transfusion medicine is the treatment of patients with various blood components prepared from human blood.

Transfusion service prepares blood components from human blood by use of simple physical procedures. Blood components differ from the drugs manufactured by pharmaceutical industry.

The production of blood components is regulated by a special by-law. Blood components are not described in pharmacopeia. They differ from plasma derivatives and pharmaceuticals in a number of features. Very few blood components are made from a blood unit obtained from one individual blood donor. Each blood component is a single and unique lot. It is impossible to measure the potency of active substance, to determine the safety, toxicity, pyrogenicity and sterility, and to perform the procedure of virus inactivation in each blood component. In contrast, plasma derivatives are agents identical to the drugs manufactured by pharmaceutical industry, and they are described in pharmacopeia.

There are several definitions of quality. According to some of them, quality is described as fitness for use, fitness for purpose, or customer satisfaction (1). However, in transfusion medicine quality is defined as an adequate number of blood components for transfusion therapy, provided that blood components are efficacious and safe. Each link in the chain of blood preparation and transfusion treatment should meet the set requirements in order to achieve the required quality.

A number of different subjects is involved in the preparation of blood components and the transfusion treatment of patients. In Croatia, promotion of voluntary blood donation and donor selection is organized by the Red Cross and/or the transfusion service. Blood collection, laboratory testing, preparation, storage and release of blood components are completely in charge of the transfusion service. Transport and pretransfusion testing are organized by respective hospitals or hospital transfusion units or blood banks, while the ward physician, is the one responsible for the transfusion treatment of a patient. Thus, the responsibility for the preparation of blood components and for transfusion therapy is divided between a number of subjects, i.e. the Red Cross, transfusion units and hospitals. This may cause problems in the work, the more so, as neither the duties nor the responsibilities of each of the subjects have been well defined and demarcated, nor have any respective mutual agreements been made in writing. Such a situation entails difficulties in achieving the required quality of transfusion therapy, especially in solving misunderstandings that are due to transfusion side effects.

The quality of a blood product depends on the requirements set for the respective product, inherent features of each substance used in product preparation, technological characteristics of the laboratory or preparation process, the quality of work of the personnel involved, and the performance of critical steps in the process of blood component preparation or transfusion treatment of patients, i.e. it depends on the Red Cross or transfusion service promotion activities; transfusion service performance in blood collection and blood component preparation and pretransfusion testing; the work of the ward physician who is in charge of the patient treatment, such as transfusion therapy prescription, choice of a blood product, administration of blood transfusion, patient follow-up upon the completion of blood transfusion, and

identification and management of transfusion side effects. The desired quality is not always possible to achieve. Therefore, the requirements stated in the definition of transfusion treatment quality cannot always be met either. These considerations are exemplified below.

The required number of blood donors is ensured by promotion. The goal of blood donation promotion is to recruit donors without any form of risk behaviour, i.e. those free from an increased risk of blood products prepared from their blood being a cause of transfusion transmitted diseases. This goal is quite difficult to achieve, as undetected risk behaviour is still found in a relatively large percentage of blood donors and their blood may induce transfusion transmitted diseases in the transfused patient. For example, in 6% to 7% of all blood donors in the USA, the main reason for donating blood is testing for blood transmissible disease markers rather than a humanitarian motivation (2). In Germany, 10 of 186 examined donors were found to have used or to currently use narcotics at the time of the blood donation (3).

Neither blood donation promotion, nor donor selection, nor laboratory testing can detect all donors whose blood is infectious. Blood products prepared from the blood of an infected donor will cause transmission of the causative agent of transfusion transmitted diseases, with consequential infection of the majority of patients. Testing of blood donors certainly was and remains the most important procedure in reducing the risk of infection due to transfusion therapy. However, not even the most sophisticated laboratory testing can guarantee that the patient will not be infected with the viruses for the markers of which the donor has been tested, or with some other viruses, bacteria, or other agents found in the donor's blood, the presence of which has not been tested in the donor's blood. Laboratory testing can detect markers of infectious disease agents in the donor's blood only after a certain period of time has elapsed since his/her infection (the so-called window period). The time between the donor's infection and the occurrence of markers for transfusion transmitted diseases depends on the type of causative agent and the quality of the screening test used. This period is reduced by test improvement or by the introduction of new tests. However, even the best of tests currently used are burdened with a window period during which the donor's blood and blood preparations are infectious. Thus, with the introduction of NAT, the window period has been reduced from 29 to 11 days for HIV, from 59 to 34 days for HBV, and from 66 to 23 days for HCV (4). This is a real improvement in the safety of blood preparations concerning infection with most severe transfusion transmitted diseases; however, it only applies to the agents the blood is tested for, whereas other viruses, bacteria and other agents that may also cause transfusion transmitted disease remain undetected.

Improvement in the quality of testing in transfusion medicine has reduced the rate of morbidity and mortality due to transfusion therapy (5). Hepatitis and AIDS have ceased to be the most common risks of transfusion therapy, having been replaced by immune hemolytic reactions, bacterial infections, TRALI and GvHD as the main transfusion-related causes of death. The prevalence of ABO incompatibility has leveled off with the prevalence of hepatitis (5).

Critical points concerning blood product quality are also to be found in the process of blood product preparation. For example, in the Croatian Institute of Transfusion Medicine the training of the personnel and the performance modifications carried out from 1998 till 1999, reduced the number of ill welds in the device for sterile tube connection from 0.17% to 0.11%, the number of expired and discarded blood product units from 8.02% to 6.20%, the number of aggregates in platelet concentrates from 8.79% to 7.88%, the rate of package damage from 0.37% to 0.23%, and the rate of nonsterile platelet concentrates from 0.72% to 0.089% (6). In the year 2000, the favorable trend of the production quality improvement has continued, so that ill welds were observed in not more than 0.03%, platelet concentrate aggregates in 6.08%, and container damage in 0.24% of cases only (6).

Year by year, transfusion service provides clinicians with blood products of ever higher quality (7). In spite of this, the side effects and deaths due to transfusion therapy have been reported (8). In their study of the location of errors, Linden et al. (9) showed that the majority of reasons for post-transfusion side effects were generated at hospital locations of transfusion therapy use or in the interface between the transfusion laboratory and the clinical ward, rather than at the blood bank or transfusion centre (9). The cause of only 25% of post-transfusion reactions originated from a blood bank or a transfusion unit, and 17% were due to errors common to both the transfusion unit and the hospital ward (9). Accordingly, errors made at the hospital ward accounted for as many as 75% of post-transfusion reactions (9). The SHOT (serious hazards of transfusion) study of the causes of post-transfusion reactions from Great Britain has provided recommendations for the improvement of safety of the transfusion treatment (10). Most of these recommendations refer to the work at clinical departments.

The crucial question is whether a better quality of transfusion treatment can be achieved and if so, how to realize it. The quality is not incorporated in the product nor will it ensue by itself. The achievement of a desired quality level requires organized and systematic work on its improvement. Currently, it could be rephrased as the need for proper quality management.

There is a considerable lack of understanding, or a confusion among laymen and health professionals not closely engaged in the quality issues, concerning the terms quality control, quality assurance, quality system, and quality management. Therefore, definitions of these terms are given below, with a note that they differ according to the scope of activities and resources they involve. Quality assurance also includes all the procedures involved in quality control, while quality system includes both quality control and quality system.

Quality control defines operational techniques and activities that are used to fulfill requirements for quality (1).

Quality assurance defines all the planned and systematic activities implemented within the quality system and demonstrated as needed to provide adequate confidence that an entity will fulfill requirements for quality (1).

Quality system defines organization, structure, procedures, processes and resources needed to implement quality management (1).

Quality management defines all activities of the overall management function that determine the quality policy, objectives and responsibilities, and improvement means such as quality planning, quality control, quality assurance, and quality improvement within the quality system (1).

One of the most widely used quality systems in the world is ISO 9000 (1). It is expected to be soon substituted by ISO 2000. The system practically covers all fields of activities and work in the firm or organization except for accountancy, book-keeping, and some other administrative fields. According to this system, relationships between organizational units and among the people involved must be clearly explained, so that there is no overlapping of thear duties and responsabilities. Each individual process must be described. Every segment of the work with substantial impact on the product quality must be accompanied by written operation procedures. Workers should be properly educated to be able to follow the written operation procedures without deviations. Each result must be recorded, along with the name of the person who performed the work. Documentation must be regularly kept and stored according to in-house instructions or respective by-law. Instructions for work are modified upon analysis and evaluation of the results, and workers are re-educated to be able to follow the new ones. The objective of the system is to achieve such a level of the workers' performance which will be consistent with the written instructions for work,

thus producing uniform results of the work, avoiding errors, and controling changes in the work and the working process. The system cannot guarantee that errors will not occur; however, when an error does occur and its cause is identified, measures can be taken for the error not to recur, thus creating a spiral that yields a continuous quality improvement. The main goal of the quality system introduction is to influence the product quality. However, some other effects are also produced, e.g., reinforcement of the customer's or user's confidence, economic savings, etc.

Quality system management is achieved by defining organization and management responsabilities, education and training, analysis of work, analysis of nonconforming products and procedures and complaints, internal control, and implementation of corrective measures. The basis of successful system implementation is proper education of all workers and full adoption of the system by all the personnel involved.

ISO 9000 has been implemented at the Croatian Institute of Transfusion Medicine. To date, 52 procedures and 430 standard operating procedures, more than 170 specifications for starting material, intermediate and final products, and more than 300 various forms have been identified and described (6). The system implementation took several years; however, it has resulted in products of a considerably higher quality. The analysis of some inconsistencies has indicated that savings have already paid off the cost of the system introduction in the Croatian Institute of Transfusion Medicine.

The quality of transfusion therapy depends on a number of factors, and can only by influenced upon and improved by use of the quality system and quality management. Today, the critical location for quality of the transfusion therapy is the clinical ward and its interaction with the transfusion unit.

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