What is haemovigilance? The European Haemovigilance Network (EHN).

P.F.W. Strengers

Introduction

Blood transfusion is one of the safest invasive medical procedures. 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. In general, the risk is poorly documented. 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 like blood borne viruses, bacteria, spirochetes, 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.

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. Long term experience with the therapeutic usage of blood products is widespread and knowledge of the occurrence of adverse effects is available, but still a structural surveillance on safety in clinical care is not put in place in many countries. Despite the life-saving effects of blood transfusion, the demonstration of effectiveness is not very concrete and based on surrogate markers. Huge differences in therapeutic protocols exist and the knowledge about the best application of a product in a specific indication and the optimal utilisation of blood components still limited. To increase this knowledge, from the basis, collection of epidemiological data has to be the first goal.

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” (2). 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 (3).

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 (4). Since 1993, multiple definitions of haemovigilance have been formulated differing from one country to another. In some countries, 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 exchange 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 (5). 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 (6).

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, a first meeting was organised 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.

It might be a surprise why so many discussions were needed. Blood was considered to be safe. The prime objectives of haemovigilance, however, are quite complex. It involves:
1. to identify Adverse Events (AEs); to document the nature, the seriousness, the etiology, and the frequency of AEs; and to assess the maintenance of the overall benefit / risk profile.
2. to identify vulnerable sub-groups of patients at risk of AEs; and to identify risk factors.
3. to document the safety of a blood product under wider conditions of use.
4. to conduct a scientific evaluation of AEs (true or false positive).
5. to take action in order to correct or to prevent an identified risk; and to inform those concerned.

And finally, to be able to compare the collated data, uniform definitions and procedures should be used. These objectives required a change in opinion 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 therapeutical 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 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 (7). 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.

Ten Members 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 Members 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 tool for optimal connection and information exchange, the Internet web-site [www.ehn-org.net](http://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. 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.

EHN Seminars are organised almost every year to discuss in Working Parties and plenary sessions question 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 meeting will be organised in Amsterdam, February 6-7, 2003.
References: