The haemovigilance: the best quality management system of the transfusion chain?

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Background and Objectives Haemovigilance is an integral part of blood safety worldwide. Many haemovigilance systems are already in place or are developing, and national or regional haemovigilance systems have been implemented in several countries. In 2016, the WHO Global Database on Blood Safety reported that national haemovigilance system had been established in 70 countries, among which 38 countries were members of the International Haemovigilance Network by the end of August 2017. In this review, we retrospect the development and current status of haemovigilance to outline its function in transfusion chain.

Materials and Methods Through contrasting the evolution of haemovigilance definition in different periods, by analysing its scope and breadth, and with the illustrating its achievements and challenges, we retrospect the development and current status of haemovigilance to outline its function in transfusion chain.

Results Haemovigilance is becoming an important aspect of transfusion medicine, could be used as quality indicator for monitoring the blood transfusion safety, contribute significantly to evidence-based transfusion medicine and results in improved policies, procedures and practices in the blood transfusion chain.

Conclusions The scope of haemovigilance may cover the whole transfusion chain, from collection of blood and its components to follow-up of recipients. Haemovigilance is an essential component of quality management in a blood system and haemovigilance is the best quality management system of the transfusion chain.

Key words: haemovigilance, haemovigilance system, quality management, transfusion safety.
and untoward effects of blood transfusion can be better understood and the quality and safety of transfusion chain have been improved. So, the World Health Organization (WHO) recommends the development of haemovigilance systems to monitor and improve the safety of transfusion processes, in December 2007.

**Haemovigilance evolution**

Haemovigilance is an important aspect of transfusion medicine. This concept of 'haemovigilance' was probably first coined in France in 1992 to function in the same way as the term 'pharmacovigilance' does for drugs [4]. Through the evolution of haemovigilance definition in different periods, we can find its scope and breadth as well as its important contribution in ensuring the safety of blood transfusion. The first French official definition of haemovigilance dates back to 1994 [5, 6], as 'a component of transfusion safety', and it is consisted of three contents for each unit of blood product and component prepared as follows: (1) the alert of any unexpected or unwanted effects related to or likely to be related to the therapeutic use of this product; (2) the collection, preservation and accessibility of information of the blood sample; (3) the use, as well as the effects mentioned above; (3) the evaluation and the use of such information to prevent the occurrence of any unexpected or unwanted effects resulting from the therapeutic use of blood products and components. This definition indicates that its primary aim is to insure the monitoring of blood transfusion, to collect and assess data on all side-effects related to blood transfusion from the collection of blood and to the use of a blood product and of preventing their occurrence, so as to increase the safety and quality of the entire transfusion process.

In 2003, the European Directive has extended to the European Union the concept of haemovigilance, the major emphasis of the EU Directive 2002/98/EC is on haemovigilance (Article 3 and article 14, chapter V) by defining ‘Haemovigilance’ as ‘a set of organised surveillance procedures relating to serious adverse events or unexpected events or reactions in donors or recipients and the epidemiological follow-up of donors’. In addition to the bidirectional traceability from donor to recipient and vice versa, any serious adverse events (accidents and errors) related to the collection, 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 required to notify to the competent authority and the epidemiological follow-up of donors have been added to haemovigilance activity [7].

A little more complete definition of haemovigilance is given by the International (previously European) Haemovigilance Network, as ‘A set of surveillance procedures covering the whole transfusion chain (from the collection of blood and its components to the follow-up of recipients) [8], 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 or recurrence’. Furthermore, in present opinion of WHO, ‘Haemovigilance’ is required to identify and prevent occurrence or recurrence of transfusion-related unwanted events, to increase the safety, efficacy and efficiency of blood transfusion, covering all activities of the transfusion chain from donor to recipient [9]. These above definitions witnessed the evolution of haemovigilance and implied that haemovigilance had been not only surveillance procedures covering the entire transfusion process, but also an effective tool for improving transfusion practice. The concept of haemovigilance has steadily expanded as follows: it started the initial processes concentrating on observation of untoward effects in transfused patients; then it broadened its scope on the entire process of transfusion chain; finally, it has become a crucial part of the blood safety concept as well as an integral tool of blood safety worldwide to help improve quality and safety of blood transfusion.

**Haemovigilance system**

The haemovigilance system is a continuous and standardized system for observing, recording, reporting, analysing, monitoring and intervention: it covers all processes throughout the entire transfusion chain, from blood donation, processing and transfusion to patients for the monitoring, reporting, investigating and creating corrective actions for any nonconformity, when something goes wrong in the blood transfusion chain, using the lessons learned to avoid that problem going wrong again. With co-ordination among all relevant stakeholders, such as the blood transfusion service, professional organizations, hospital laboratories and clinicians, hospital transfusion committees, regulatory agency and health authorities, it monitors and evaluates the processes involved in the transfusion chain, indicates where the main problems and measures for improvement of the safety are, and develops transfusion triggers, guidelines and policies aiming at the rational, evidence-based standards and practice of transfusion.

Many haemovigilance systems are already in place or are developing, and national or regional haemovigilance systems have been implemented in several countries. According to WHO Global Database on Blood Safety report, 39% countries (70 of 180) have a national haemovigilance system: across WHO regions, the European region has the...
highest percentage of countries with haemovigilance systems (33 of 43 countries, 77%), followed by South-East Asia (five of 11 countries, 46%), the Eastern Mediterranean (seven of 20 countries, 35%), the Western Pacific (eight of 25 countries, 32%), Africa (12 of 42 countries, 26%) and the Americas (five of 35 countries, 14%) [10].

Many different national haemovigilance system models exist, for example, blood transfusion safety systems may be managed either by Competent Authority (e.g. France, Germany, and Switzerland), Blood manufacturers (e.g. Japan, Singapore, and South Africa), Professional organizations (e.g. Netherlands, UK), Public Health Authority (e.g. Canada), or by Private/Public Partnership (e.g. USA) [3]. But, there are important differences between regions/countries when it comes to the implementation of regional/national haemovigilance programmes, reflecting the diversity of health systems and blood systems in different countries, for example, types of haemovigilance system may be passive or active, voluntary or mandatory, centralized or decentralized; notification may be devoted to severe adverse reactions and events or to all adverse reactions and events; all levels of imputability or confirmed and highly probable case may be reportable.

Classically, two different ‘poles’ of systems are cited as follows: the French scheme is implemented nationwide, in which reporting all adverse events despite their severity is mandated by law; while the British haemovigilance scheme (SHOT), started as a voluntary system and compulsory and/or partly mandatory reporting systems required by the UK Blood Safety and Quality Regulations (2005), in which only limited errors and serious reactions are reported. These two systems represent two different directions in both thinking and acting; many countries consult with learning from the lessons generated by the two systems and take a hybrid approach when they are developing their own haemovigilance systems. Haemovigilance, mainly in Europe, has led to similar effects, namely reduction in the number of deaths and fewer instances of serious adverse events from transfusion. Despite the different types of haemovigilance systems, confidentiality and nonpunishment policy should be the basic principles.

International co-operation on haemovigilance is imperative and crucial to make exchanges and meaningful comparisons of data between different haemovigilance systems. Collaboration in haemovigilance has been achieved by networking systems and experts in new or existing organizations, such as the IHN, the ISBT Working Party on Haemovigilance and the WHO. With the concerted and tremendous efforts of all sides, standard definitions of ‘recipient adverse reactions’, ‘complications of blood donation’, ‘a limited number of types of incident in the transfusion chain’, ‘noninfectious hazards’ and the international haemovigilance database (ISTARE project) have been developed [11, 12].

Achievements and challenges

The ex-President of IHN, Prof. Dr René R. P. De Vries, summarized 10 results and conclusions of haemovigilance practice in 2011 on the occasion of the Vox Sanguinis’s 100th issue [5]. He pointed out that ‘Haemovigilance systems have shown that blood transfusion is relatively safe compared with the use of medicinal drugs and that at least in Europe blood components have reached a high safety standard’, that ‘The type of organization of a haemovigilance system is of relative value, and different systems may have the same outcome’, that ‘Well-functioning haemovigilance systems have not only indicated how safety should be improved, but also documented the success of various measures’, that ‘Haemovigilance systems and officers may be used to improve the quality of aspects of blood transfusion other than safety, such as appropriate use’, that ‘Haemovigilance systems will be of benefit also for vigilance and surveillance of the treatment with other human products such as cells, tissues and organs etc., it turns out that haemovigilance has made great achievements to improve quality and safety of entire transfusion process.

Data from well-functioning haemovigilance systems show the success of various measures to even further improve the transfusion safety. For example, (1) the Swiss, French, Belgian and Cerus Corporation HV data characterize the effectiveness of amotosalen/UVA treatment to prevent septic transfusion reaction [13]. (2) French and Dutch haemovigilance systems observed that the introduction of the deviation pouch used during blood drawing could minimize the risk of contamination by skin bacteria [14, 15]. (3) French system identified the potential hazard of anaphylactic reactions to methylene blue-treated plasma; a new gravity level of grade 0, aiming at reporting and analysing the blood transfusion chain dysfunction was created [16, 17]. (4) Data of SHOT and French system demonstrated the effectiveness of using only male donor’s plasma for transfusion-related acute lung injury reduction and universal leukoreduction may decrease post-transfusion purpura and transfusion-associated GVHD in immune-competent transfusion recipients [18–20]. (5) Quebec Haemovigilance System implemented the diversion segments and postcollection culturing of PLTs to reduce bacterial infection transmissions; besides, it prompted increased clinician education about the condition, and additional clinical attention to the TACO’s complication lead to a decline in its frequency [18, 21]. Haemovigilance is now considered to be used for other important objectives, such as the transfusion education, the
implementation of PBM and donor haemovigilance programme, the development of clinical guidelines. In France, the percentage reduction in blood components transfused is 1.4 for RBC and 9.7 for plasma between 2015 and 2016 [22], and many examples demonstrate that the most common measure of success of patient blood management programmes is the percentage reduction in the number of blood transfusions together with the reduction in costs observed after implementation of the new practices [23, 24].

There are several challenges that can affect the implementation of haemovigilance such as (1) variation in terminology and definitions: the umbrella term ‘adverse event’ is problematic [11], the variant definition of the term between different systems is disadvantageous to standardization of definition and its usage, it is very necessary to find an alternative umbrella term. The term of ‘side-effect’ is suggested and used in our haemovigilance system, thus the definition of ‘side-effect’ contains ‘adverse event’ and ‘adverse reaction’, while ‘adverse reaction’ defines as an unintended response in donor or in patient associated with the collection or transfusion of blood or blood components, but ‘adverse event’ defines as any untoward occurrence of transfusion chain unrelated to human response/injury, which contain incident, error and near miss. (2) Underreporting and limited details: more report and sufficient detail contribute to make effective recommendations to improve transfusion practice, so a nonpunitive environment, good education and training are essential to a haemovigilance system. (3) Review and validation of the noncompliance: some results of different system are opposite, such as the clinic evaluation of the methylene blue virally inactivated fresh-frozen plasma, the results of Greek system is positive but that of French system is negative [16], how to look at and analysis these two conclusions? How to find the way to deal with the inconsistent information in network? (4) Donor-management-programmes: such as patient blood management programmes and donor haemovigilance programme are important to improve donor care, data of ‘the relationship between iron depletion and blood donor/donation’, ‘development of osteoporosis and depletion of immune capacity in repeated apheresis donors’ and ‘effect of mobilizing agent to peripheral blood mononuclear cells donors’ should be to help in formulating transfusion guidelines [25].

**Haemovigilance: the best quality management system of the transfusion chain?**

Many blood services and hospitals implemented an ISO 9000 or analogue quality management system throughout the entire organization. The use of such international standards in the healthcare sector should raise the level of quality within an organization or among organizations [26, 27]. Each blood service or hospital is an independent member of transfusion chain, even if each organization can ensure the safety of its product/service with the efficient functioning of its quality management system, the quality and safety of entire transfusion process cannot be fully guaranteed, as every aspect of the transfusion chain is important to the end result of a safe blood transfusion, so the assurance of blood safety depends on the co-ordinated co-operation between the blood transfusion service, hospital clinical staff and transfusion laboratories, hospital transfusion committees, regulatory agency, and health authorities.

Haemovigilance has become an integral part of blood safety worldwide as well as an essential component of quality management in a blood system and is needed for the continual enhancement of quality and safety of blood products and transfusion process using the lessons learned and associated with the use of blood products to take action to avoid that problem going wrong again. Haemovigilance may be interpreted as the ‘check’ step of the PDCA cycle (plan-do-check-act or plan-do-check-adjust), which is an iterative four-step management method used for the control and continuous improvement of processes and products [28], so a well-functioning haemovigilance system could be used as quality indicator for monitoring the blood transfusion safety, and also contribute significantly to evidence-based transfusion medicine [29], and the resulting modifications to transfusion policies, standards and guidelines, as well as improvements to processes in blood services and transfusion practices in hospitals, lead to improved patient safety.

Perhaps haemovigilance is the ultimate quality management system of the transfusion chain. Although the way a system is organized has many variables, common definitions and standardised methodologies are established in bringing together the different national policies by an international effort. An intelligent, Web-based data capture system could display only items pertinent to the case report as it unfolded. In general, haemovigilance system is interfaced with a facility’s systems integrating blood service information, patient medical records and error management. Capturing, exchanging and analysing information may help to make necessary changes in transfusion policies, for amendments in transfusion practices in hospitals and blood services, to enhance transfusion standards, to help in formulating transfusion guidelines and to improve quality and safety of entire transfusion process.

**Conclusions**

Over the past 25 years, haemovigilance systems have developed in countries around the globe with legal and
organizational structures that vary from country to country. There are many changes and outcomes triggered by haemovigilance system, such as significant increase in traceability of blood components; significant decrease in wastage of blood components; significant decrease in recurrence of ABO RBC transfusion errors, TRALI, Allergic reactions, TTBI; significant increase in reporting of TACO, haemodosiderosis, DHTR; significant increase in reporting of serious donor reactions and postdonation informations. Haemovigilance should be a part of quality management systems of blood centres and healthcare institutions and should be the best quality management system of the transfusion chain. The advice and information acquired from haemovigilance facilitate corrective and preventive actions to be taken to minimize the potential risks associated with quality and safety in blood processing and transfusion for donors, patients and staff, resulting in improved policies, procedures and practices in the blood transfusion chain.

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Conflict of interests

The author declares no conflict of interests.

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