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An Overview on the Regulatory Aspects of the Haemovigilance in UK and Australia

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ABSTRACT

In this era, the need of blood transfusion is expanding due to the increase in the disease conditions resulting into the deficiency of the blood components. Blood transfusion process is ceaselessly associated with some level of infectious or non-infectious risks/adverse reactions. Thus it is essential to monitor adverse reactions occurring due to the blood transfusion process. It is likewise important to prevent the occurrence and recurrence of this reactions affecting to the human health. Haemovigilance is a continuous process of data collection and analysis of transfusion-related adverse reactions in order to investigate their causes and outcomes, and prevent their further incidence.Regulatory requirements for haemovigilance in different countries are varying from each other, so it is challenging for regulatory authorities to develop haemovigilance compliance strategies that comply with the requirement of the different countries.Haemovigilance incorporates the identification, reporting, examination and analysis of adverse reactions and events in recipients and blood donors as well as incidents in manufacturing processes.Haemovigilance concerns blood components: whole blood, thrombocytes concentrates, erythrocytes concentrates & fresh frozen plasma. Haemovigilance in transfusion medicines concern plasma derivatives: clotting factor concentrates albumin, immunoglobulins and other fractionated products. It infers methods for identifying errors, adverse events and reactions, examination of complaints, traceability systems and audits of practice. Haemovigilance assists the regulatory authorities to monitor and take the necessary actions for safe therapy and to set up systems, which work, despite persistent obstacles.

Key Words: *Haemovigilance, Blood transfusion safety, Blood product regulation.*

INTRODUCTION

Since most recent 4 Centuries, blood transfusion is in practice as the methodology of receiving blood products into one's circulation intravenously. Transfusions are used for various restorative conditions to replace lost components of the blood. Early transfusions utilized entire blood; however present day restorative practice ordinarily utilizes just components of the blood, such asred blood cells, white blood cells, clotting factors, plasma, and platelets.

Blood transfusion is constantly associated with some level of infectious risk. Other than the infectious risks, transfusion may be associated with complications related to exposure to foreign antigens, altered chemical/temperature balance and hypersensitivity. Haemovigilance is a consistent process of data collection and analysis of transfusion-related adverse reactions/ events in order to investigate their causes, and prevent their occurrence or recurrence.

Haemovigilance is a tool to improve the quality of the blood transfusion chain, principally concentrating on safety of human health. In spite of the fact that it is a compelling practice connected with the safe transfusion around the world, there is a need of harmonization between all the nations in regards to the haemovigilance framework.

Haemovigilance:

Haemovigilance is a set of surveillance procedures covering the whole transfusion chain (from the collection of blood and its components to the follow-up of 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 or recurrence [1].

The real necessity of any transfusion is 'zero risk' to the recipient, as the aftermaths of any error during transfusion is huge.

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The risks associated with blood transfusion are HIV, sepsis from bacterial contamination, hepatitis& trauma. So there is a need for the haemovigilance system which can assure patient safety and promote public health. Haemovigilance is a mode to change the ethicalness of the blood transfusion chain, establishing the safety of the process. The products, which are under surveillance in haemovigilance system are chiefly blood components [2].

A system of haemovigilance is lying on: traceability of blood and blood products from donors to recipients; spontaneous reports of transfusion adverse events; and inflexible management of association related to the transfusion process [2].

The information obtained through this system is a key to: introduce required changes in the transfusion policies; reform transfusion standards; follow up in the formulation of transfusion guidelines; and to enhance the safety and quality of the whole transfusion process. Haemovigilance have a noteworthy part to play in optimal blood usage and patient blood management initiatives, key areas for the 'Blood Service' [2].

A haemovigilance system is an essential part of quality management in a blood system and is required for the continual improvement of the quality and safety of blood products and the transfusion process. Haemovigilance is fundamental to identify and prevent the occurrence or recurrence of adverse reactions and undesirable events, and to increase the safety, efficacy and efficiency of blood transfusion. It covers all processes of the blood chain, vein-to-vein, from donor to recipient [2].

History:

The word 'haemovigilance' (he´movigilance in French) was first introduced in France in 1991 in analogy to the already existing term 'pharmacovigilance'. Haemovigilance, as a safety concept, appeared in the beginning of the 1990s. It was initially developed by the French Blood Agency as a national system of surveillance and alert, from blood collection to the follow-up of the recipients. Haemovigilance systems now have been implemented globally in most developed countries, to monitor the adverse events and incidents associated with blood donations and transfusions [3].

On European level, Haemovigilance started around 1995. The European Council published its data in 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 [4].

Importance: [12]

Haemovigilance is a tool to improve the quality of the blood transfusion chain, primarily focusing on safety. In this review we discuss the history and present state of this relatively new branch of transfusion medicine as well as some developments that we foresee in the near future. The top 10 results and conclusions are:

1. 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.
2. The majority of the serious adverse reactions and events occur in the hospital.
3. The majority of preventable adverse reactions are due to clerical errors.
4. Some adverse reactions such as anaphylactic reactions often are not avoidable and therefore have to be considered as an inherent risk of blood transfusion.
5. Well-functioning haemovigilance systems have not only indicated how safety should be improved, but also documented the success of various measures.
6. The type of organisation of a haemovigilance system is of relative value, and different systems may have the same outcome.
7. International collaboration has been extremely useful.
8. Haemovigilance systems may be used for the vigilance and surveillance of alternatives for allogeneic blood transfusion such as cell savers.
9. Haemovigilance systems and officers may be used to improve the quality of aspects of blood transfusion other than safety, such as appropriate use.
10. Haemovigilance systems will be of benefit also for vigilance and surveillance of the treatment with other human products such as cells, tissues and organs.

International Perspective of Haemovigilance: [5]

Scope of Haemovigilance:

The scope of haemovigilance varies according to jurisdictions. It may include only fresh blood components or both fresh blood components and plasma derivatives. Plasma derivatives are treated under pharmacovigilance (or drug post-market surveillance) in many countries.

Haemovigilance can be divided in three broad categories: donor, process and recipient.

- ***Donor haemovigilance:***

  Surveillance of adverse effects of blood donations has not been traditionally part of haemovigilance activities. It is however now recognized as an integral part of haemovigilance. Donor haemovigilance also addresses patient safety:

  1) Surveillance of prevalence of infectious disease markers in first time donors and surveillance of exclusion factors will to better target blood drives;
  2) Surveillance of incidence of infections in repeat donors will provide data for residual risk estimation for patient counselling.

- ***Process haemovigilance:***

  This refers to surveillance of errors in the process of both the production of blood components and the transfusion of the blood components and blood products. Many blood centres have error tracking systems in place and this is part of the quality control process. Some systems, like the MERS-TM system, provide some standard classification schemes for errors and near misses at the blood centre.

  The analysis of errors provides information in order to improve the process of production. Systematic surveillance of errors at the hospital level relating to the transfusion process is not as well implemented as in blood centres. This surveillance also provides very important information and it is important that it is being done in a blame free environment that encourages reporting of errors without the fear of disciplinary measures. Through such systems it is possible to identify the system deficiencies in order to correct them and to target educational activities. Traceability of blood products is also a transfusion safety issue and its monitoring is an integral part of haemovigilance.

  Surveillance of blood utilization could also be considered part of the field of haemovigilance. Inappropriate blood utilization is certainly a patient safety issue. For example, the French Haemovigilance System has monitored not only adverse transfusion reactions over the years but has also shown that there was a significant reduction of blood component utilization over the past decade, France issuing almost 500,000 units less in 2004 than in 1994.

- ***Recipient haemovigilance:***

  Surveillance of adverse transfusion events is the cornerstone of the majority of haemovigilance systems. It encompasses many aspects like: (1) identification of transfusion-transmitted infections. Alternate methods have been proposed like systematic post-transfusion screening of recipients but the yield of such an activity was very low. Some experiences are underway to match recipient databases with reportable diseases databases in order to identify transfusion-transmitted infections more comprehensively; (2) surveillance of adverse transfusion reactions, either only the most serious ones like in the Serious Hazard of Transfusion (SHOT) scheme in the UK or all reactions like in the French or the Quebec Haemovigilance System. Identification of long term effects of transfusion like immunomodulatory effects or recipient survival are usually more in the scope of research than of haemovigilance. However haemovigilance systems could extend their activities in that field through matching of recipient databases with death and tumour registries or with hospital discharge databases.

Settings and requirements for recipient haemovigilance:

Haemovigilance can be conducted at the hospital level. There needs to be dedicated people to blood safety at the hospital that will have the role of investigating and reporting the reactions. Many hospitals have positions like transfusion safety officers to take on this responsibility while in others the chief technologist or the blood bankdirector will have this role. The presence of transfusion committees that should be multidisciplinary in nature are essential to look at the local haemovigilance data and propose the appropriate preventive measures. Haemovigilance can also be conducted at the regional or national levels.

The key point for a system is standardization of the data elements that are collected for reportable adverse events. A central body in a haemovigilance system is a key element for data validation and analysis. Regular feedback to those who report must be done by the central body. Some systems are based on mandatory and other on voluntary reporting. The key point however, irrespective of the system, is that there is dedicated personnel for investigation and reporting of adverse events.

Haemovigilance Programme of UK:

Haemovigilance includes organized surveillance procedures relating to serious adverse or unexpected events or reactions in blood donors or recipients, and the epidemiological follow-up of donors& recipients. The overall aim of this is to improve transfusion safety [7].

The UK was one of the first countries to implement such a system and since 1996 the Serious Hazards of Transfusion (SHOT) scheme has successfully undertaken those aspects of Haemovigilance relating to recipients [7].

SHOT is the United Kingdom's independent, professionally-led haemovigilance scheme. Since 1996 SHOT has been collecting and analysing anonymised information on adverse events and reactions in blood transfusion from all healthcare organisations that are involved in the transfusion of blood and blood components in the United Kingdom. Where risks and problems are identified, SHOT produces recommendations to improve patient safety. The recommendations are put into its annual report which is then circulated to all the relevant organisations including the four UK Blood Services, the Departments of Health in England, Wales, Scotland and Northern Ireland and all the relevant professional bodies as well as circulating it to all of the reporting hospitals. As haemovigilance is an ongoing exercise, SHOT can also monitor the effect of the implementation of its recommendations [7].

SHOT consists of the SHOT office team, the Working Expert Group (WEG) and the Steering Group (SG)[8].

Act to Access the Data: [13]

1. ***The Data Protection Act:*** Details of reported events or reactions may be disclosed, personal identifying details of patients and/or reporters will not in accordance with this act.

2. ***The Freedom of Information Act:*** It bound the MHRA to respond to requests for information which it holds and is recorded in any form, and creates a right of access to that information.

3. ***The Public Interest Disclosure Act (PIDA):*** As a result of having disclosed information, you may be punished by your employer or that may lead to your dismissal. But this act will protect your employment position. PIDA protects workers who make a protected disclosure of information, concerning certain types of matters relating to their employment, from being dismissed or penalized by their employers as a result of the disclosure.

Reporting to SHOT (Serious Hazardsof Transfusion): [13]

Reporters use the SABRE (Serious Adverse Blood Reactions and Events) system to initiate a report to SHOT at the notification stage. SABRE will then prompt the SHOT database to create a record for you and to send you an automated email link to the database. You will then be asked to log in separately to the SHOT Dendrite system and complete their online form.

Reporting to SABRE: [13]

To report an adverse event to SHOT you must first make a report to SABRE (Serious Adverse Blood Reaction and Events) and then tick the "Share this Report with SHOT" box or the "SHOT only report" box. SABRE will then notify the SHOT Dendrite database and create a record for you to complete and then send you an automated e-mail with a link to the database. Please note that this not a "real time process" and it may be a day or so before you receive your e-mail from the SHOT database.To login into the SABRE, you will need to use your Email address, Password, and registration number which will have been sent to you by Dendrite.

Haemovigilance Programme of Australia: [9]

The National Blood Authority (NBA) has developed reporting and governance frameworks for the National Haemovigilance Program for Australia. It reports on serious transfusion related adverse events occurring in public and private hospitals. National Safety and Quality Health Service Standard 7 on Blood and Blood Products requires health service organisations to participate in haemovigilance activities conducted by the organisation or state or national levels and to ensure that adverse events are included in incident management and investigation systems.

The NBA's national haemovigilance program is informed by the ***Haemovigilance Advisory Committee***. The Haemovigilance Advisory Committee comprises experts in transfusion medicine, science, nursing and epidemiology from both the private and public health care sectors. This group provides advice to governments on adverse event reporting originating from health service organisations and on national transfusion safety priorities. The committee also oversees the national reporting and governance frameworks.

The NBA is a member of the International Haemovigilance Network (IHN) and coordinates Australia's contribution to the ISTARE international database

ISTARE International Database: [10]

ISTARE stands for ***International Surveillance of Transfusion-Associated Reactions and Events***. Its purpose is to record national haemovigilance data using common definitions. This allows international comparisons, information sharing and benchmarking.

It aims to capture all adverse reactions and incidents (events) in recipients of blood and blood products that can certainly, probably or possibly be imputed to blood transfusion. It also records adverse events in blood donors.

National Safety and Quality Health Service Standards of Australian Commission: [11]

The NSQHS Standards, which were introduced by the Australian Commission on Safety and Quality in Health Care in 2011, include safety and quality measures for use of blood and blood products. They provide important blood management principles for all clinicians, and compliance with the Standards is required for hospital accreditation. The Standards direct institutions to implement, monitor and improve systems for use of blood, including cellular components, fractionated blood products and recombinant agents.

Transfusion-related clinical governance systems, such as hospital transfusion committees, are important elements of institutional quality improvement. Clinical governance systems for transfusion are now mandated, including establishing local transfusion policy and procedures, monitoring transfusion-related risks, internal and external reporting of adverse events and other quality improvement activities. These systems promote an institutional culture where transfusion safety is viewed as paramount, and they support clinicians and other team members involved in the transfusion process.

The NSQHS Standards recognise the importance of patient involvement in the transfusion process and require informed consent to be obtained and documented. Another component, which is often overlooked, is documentation of patient transfusion history, transfusion indication and outcome, special product requirements and adverse events. This promotes appropriate clinical decision making, improves future practice through audit and investigation of adverse reactions, highlights special product requirements and assists the transfusion laboratory to comprehensively identify antibodies in previously transfused patients.

Future Perspectives of Haemovigilance: [4]

Data from an anaesthesiology survey in France indicated that more peri-operative deaths are due to under-transfusion or delayed transfusion than to adverse reactions of transfusions given in time. In order to give the best advice, haemovigilance systems should broaden their scope in order to give the best advice on the treatment with blood components or blood alternatives.

The main challenge is to generate data on the benefit of transfusion of a blood component in different clinical situations in order to be able to make risk-benefit calculations. It is clear that haemovigilance systems and officers may help to collect and analyse the necessary data. Haemovigilance will have a major impact on optimal blood usage. The awareness that, apart from vital indications, the efficacy of blood transfusions is often unknown, not established or even negative, has resulted in a significant reduction of the use of blood products as documented by many, but not all, haemovigilance systems. In order to understand this development, the surveillance of appropriate or optimal blood use in a more detailed way, e.g. through the collection of a set of indicators that may be provided easily by most hospital information systems, has to be started. Nevertheless, it is expected that existing haemovigilance systems including the haemovigilance officers in hospitals will contribute in the near future also to the surveillance of optimal blood use.

Finally, haemovigilance systems will be a candidate to ensure vigilance and surveillance of other human products that are transplanted, such as cells and tissues and, at a later stage, organs for transplantation. In the USA, the word 'biovigilance' has already been coined for this combined activity.

Table No. 1: Worldwide Adverse Event Reports Related to Haemovigilance [6]

Country	No. of Serious Adverse Reactions cases related to blood transfusion	Special notes	Sources
Australia	913 (year 2009-2011)	Increase in no. of cases till 2013	Australian National Haemovigilance Programme
Europe	527 (year 2012)	60% increase in severe adverse reaction since 2010	Surveillance of Adverse Reactions/Events (STARE)
United	3545 (year 2012)	3.2% increase as compared	Serious Hazards Of Transfusion (SHOT)

Kingdom		with report of 2011	
United States of America	Transfusion related acute lung injury TRALI (35%); ABO blood group haemolytic transfusion reactions (22%); non-ABO haemolytic transfusion reaction (15%); microbial infection (15%) and transfusion associated circulatory volumes overload (TACO) (7%). (year 2008)	Transfusion-related acute lung injury has been the most frequent cause of transfusion associated mortality in the United States for the past several years	U.S. Food and Drug Administration.
Canada	420 (year 2006)	Most common events were: transfusion-associated circulatory overload (46.2% of serious adverse events)	Churchill WH, Schmidt B, Lindsey J, Greenberg M, Boudrow S, Brugnara C. Thawing fresh frozen plasma in a microwave oven. A comparison with thawing in a 37º C water bath.
India	105 (year 2002-2003)		Transfusion-related adverse events at the tertiary care centre in North India: An Institutional haemovigilance effort *Asian Journal of Transfusion Science, Vol. 5, No. 2, July-December, 2011, pp. 164-170*
Singapore	688 (year 2006)		
Germany	702 (year 2010)		Paul-Ehrlich-Institute (PEI)
Japan	653 (year 2007)		Japanese Red Cross Society

CONCLUSION

Haemovigilance is a measure of consistence to and the adequacy of value administration frameworks and a fabulous quality marker for the blood transfusion administration. Without haemovigilance, it is difficult to completely measure the risks associated with a transfusion and hence troublesome for clinicians to survey the benefit/risk ratio and advice pretransfusion patients appropriately. Assessment of information from haemovigilance frameworks ought to structure the premise for advancement of benchmarks and rules for transfusion practice to advance blood safety and utmost improper blood utilization. The primary challenge is to create information on the benifits of transfusion of a blood segment in diverse clinical circumstances so as to have the capacity to make risk-benefit calculations. Haemovigilance frameworks will be a contender to ensure vigilance and surveillance of other human products that are transplanted, for example, tissue transplant, cell transplant and organ transplant.

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