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Setting up haemovigilance from the very first step. The Indian perspective

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Background and Objectives Setting up a national haemovigilance programme requires meticulous planning, and the following issues need to be addressed: whether reporting will be voluntary or mandatory, what is to be reported and by whom, reporting formats and resources to sustain the programme. With this in view, it was aimed to set up a national haemovigilance programme in India.

Materials and Methods The Ministry of Health and Family Welfare, Govt. of India had launched the national Pharmacovigilance Programme (PvPI) in July 2010, with oversight by the Indian Pharmacopoeia Commission. Adverse Drug Reaction (ADR) Centres were set up in 90 medical institutes in the country, and trained staff was recruited for data collection and submission. After the successful establishment of PvPI, the haemovigilance programme was initiated as a collaborative venture between National Institute of Biologicals (NIB) and Indian Pharmacopoeia Commission with the coordinating centre at NIB. Five expert subgroups with defined responsibilities will analyse and collate data and make evidence-based recommendations to the regulatory authorities for blood safety initiatives and their compliance.

Results The initial focus is on reporting the adverse reactions as defined by the Working Party of the International Society of Blood Transfusion, reporting is voluntary, and a Guidance Document and the TRRF have been made available to the medical institute blood banks. The reporting is online through software, 'Haemo-Vigil'. Reporting commenced from February 2013 and till date 731 reports of adverse reaction have been submitted.

Conclusion A well-structured programme of haemovigilance has been initiated in India.

Key words: adverse transfusion reaction, reporting formats, haemovigilance in India

Introduction

Haemovigilance is recognized as an important tool for improving blood safety. Haemovigilance data have given valuable information on adverse reactions in recipients of blood transfusion, complications in donors, errors and deviations in processes related to blood product preparation, near-miss events and rapid alerts for withdrawal of defective items or contaminated blood products. It 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

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occurrence and recurrence' (http://www.ihn-org.com) [1]. Haemovigilance may be performed in a hospital to improve blood transfusion practices, but this does not create a system. A haemovigilance system comes into existence only when data of adverse transfusion events are collected through an organized network for reporting to a central office where the data are collated and analysed by experts and appropriate recommendations are made and evaluated for blood safety.

Haemovigilance systems around the world

Haemovigilance systems have been organized mostly within the existing network for collection of data related to blood transfusion, for obvious logistic reasons. France started haemovigilance through legislation as a component of the Blood Transfusion Safety Act in 1993. As per the Act, notification of transfusion incidents is mandatory [2]. In the United Kingdom, a system of voluntary reporting of transfusion-related events the Serious Hazards of Transfusion (SHOT) was established in 1996 [3]. It is funded by the four UK Blood Services. The strategic direction of SHOT comes from a steering group represented by medical, nursing and laboratory staff. Presently, it is mandatory to report all serious adverse blood reactions and events to UK Competent Authority for the blood safety. A similar voluntary system has been functioning well in the Netherlands [4]. Many European countries set up haemovigilance systems, and the European Haemovigilance Network was formed in 1997. The network began with five member countries and increased to a strength of 28 members, some from outside Europe. The network is now named the International Haemovigilance Network (IHN) and is an important platform for information exchange between member countries [1]. The IHN organizes an annual symposium in one of the member countries each year. In the US, haemovigilance was developed as a module within biovigilance, which itself is a component of the National Healthcare Safety Network (NHSN) of the Centers for Disease Control [5].

Blood transfusion services in India

Blood is categorized as a 'drug' as per the Drugs and Cosmetics Act, 1940. Ministry of Health and Family Welfare, Government of India and Blood banking services are regulated by the rules therein, amended from time to time [6]. India is an enormous country with a population of almost 1·2 billion. There are 2545 licensed blood banks [7]; most of these are hospital based. 981 (38·5%) are in the public healthcare sector, and the remaining 1564 are either in private hospitals or managed by charitable/voluntary organizations. The average annual blood collection is 7–8 million units [8]. The modernization of blood banks in public and charitable healthcare settings was undertaken by the government through Blood Safety division of National AIDS Control Organization (NACO). The National Blood Policy was formulated in 2002 with an Action Plan on Blood Safety in 2003. Objective 5·7 of the Action Plan stated the development of a national programme of haemovigilance [9]. However, blood safety priorities that drew attention were improving voluntary blood donation, upscaling blood component preparation, manpower training and quality assured blood testing. Data on blood collection and seroprevalence of transfusion-transmitted infections are submitted to NACO, and compliance is obviously better from NACO-supported blood banks. There is no national database for information related to numbers of blood units or recipients transfused. Given the diverse management and highly decentralized blood transfusion services in the country, implementation of haemovigilance was a highly complex and challenging task.

Implementing haemovigilance

The blood transfusion chain described aptly as 'vein to vein' is a series of multiple processes and procedures commencing with donor blood collection to its final aim-recipient blood transfusion. Setting up haemovigilance system requires meticulous planning to address the following critical issues [10]:

(1) The organizational set-up with defined responsibilities to implement haemovigilance as a national programme.
(2) Which adverse events are to be reported (comprehensive reporting of all adverse events in the transfusion chain vs. restricted reporting of serious adverse reactions in recipients).
(3) Who shall be made responsible for reporting.
(4) What mechanisms should be in place for reporting (uniform definitions, standardized formats).
(5) Mandatory vs. voluntary reporting.
(6) Awareness and training programmes for staff who will participate in haemovigilance.
(7) Availability of adequate financial resources.
(8) Non-punitive approach.

Planning the national haemovigilance programme

The haemovigilance programme was initiated under the overall ambit of Pharmacovigilance Programme of India (PvPI). The Drugs and Cosmetics Act and Rules, Ministry of Health and Family Welfare (MoHFW), Govt. of India regulates the import, manufacture, sale and distribution

of drugs, including blood and blood products [6]. The Central Drugs Standards Control Organization (CDSCO) ensures enforcement of the Act and Rules, and the Indian Pharmacopoeia Commission (IPC) sets standards of drugs in the country. The CDSCO, Directorate General of Health Services under the aegis of MoHFW, Govt. of India in collaboration with IPC launched the PvPI in July 2010. The IPC is the National Coordinating Centre. Adverse drug reaction (ADR)-monitoring centres were set up in a phased manner in departments of pharmacology in medical colleges. Technical, administrative and financial assistance has been provided by the CDSCO to the ADR-monitoring centres in medical colleges. Dedicated staff the technical associates (TAs) were recruited to collect information from clinical units and submit ADR reports to IPC [11]. Each ADR-monitoring centre under PvPI is provided with one TA whose salary comes from the Indian Pharmacopoeia Commission. The National Institute of Biologicals (NIB) is an autonomous institute under the MoHFW, Govt. of India, which ensures quality of biologicals for use in the country. After the successful launch of PvPI, the Haemovigilance Programme (HvPI) was planned as a collaborative venture between IPC and NIB. The National Co-ordinating Centre of HvPI is located at NIB.

The objectives of the programme are to (i) monitor transfusion reactions, (ii) create awareness amongst healthcare professionals, (iii) generate evidence-based recommendations, (iv) advise CDSCO for safety-related regulatory decisions, (v) communicate findings to all key stakeholders and (vi) create national and international linkages. The main characteristics of this programme are in accordance with WHO guidelines for adverse event reporting and learning systems [12]. It is non-punitive, confidentiality of the reporter is maintained, it is independent of punishing authority, data will be reviewed by experts, and the intent is to improve processes and systems and to make the participants responsive to recommendations. A 5-year roadmap, that is, year 2012–2017 with four phases, that is, initiation phase (year 2012–2013); expansion and consolidation phase (year 2013–2015); expansion and maintenance phase (year 2015–2016) and optimization phase (year 2016–2017) has been prepared for implementation of this programme at various levels of healthcare facilities to include public and private sector hospitals and blood banks. The targets for each phase of the programme are defined. A separate budgetary proposal from PvPI is under active consideration within the ministry, for the HvPI. The coordination and operationalization of HvPI will be through five expert subgroups, Core Committee, National Advisory Committee, Signal Review Panel, Quality Panel and a Training Panel, Fig. 1. Core Committee has the following roles and responsibilities:

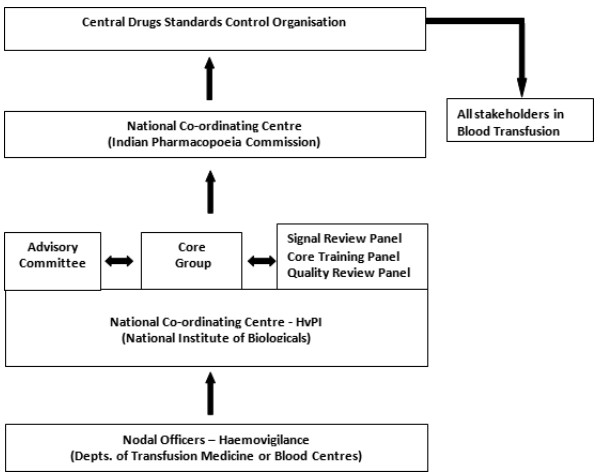

Fig. 1 Organisational structure for flow of information-HvPI

(1) To track adverse reactions/events and incidence associated with blood transfusion and blood product administration.
(2) To help identify trends, recommend best practices and interventions required to improve patient care and safety

The National Advisory Committee has been constituted to carry out the following functions:

(1) To finalize haemovigilance–transfusion reaction reporting form (TRRF) to be introduced in the country.
(2) To give inputs for collection, collation and analysis of haemovigilance data and development of the software for the same.
(3) To monitor the functioning and quality of the data collected by the adverse transfusion reaction reporting centres.
(4) To finalize training modules and guidelines for implementation of haemovigilance.
(5) To develop a roadmap for linking Haemovigilance Programme with IHN.

Mechanisms for data analysis

Detailed review of data in the TRRF will be performed by the Quality Review Panel which has the following mandate:

(1) To review quality and completeness of data in the TRRF.
(2) To review the causality assessment of adverse reactions to the blood transfusion and blood product administration.
(3) To make recommendations to the National Haemovigilance Advisory Committee after data analysis by the Signal Review panel.

(4) To devise formats and guidance documents for follow-up actions after implementation of recommendations.

The analysis of the data in the TRRFs will be done by a Signal Review Panel that will be entrusted with the following responsibilities:

(1) Collation and analysis of information from the adverse reactions data submitted to NIB in TRRF.
(2) Define bio-statistical methods to be followed for analysis.
(3) To create standardized post analytical reports that will help understand the information that is derived from adverse reaction data.
(4) To decide on actionable indicators.

To assure the uniformity and quality of data being collected from the enrolled centres, there is a need to train the participating staff. A core Training Panel is under consideration to carry out the following activities in this regard:

(1) Identifying trainers for haemovigilance training programme.
(2) To identify the zone-wise training centres for imparting training to the staff involved in furnishing information in TRRF from the Medical Colleges.
(3) Development of the training modules, manuals and schedules.
(4) Organizing of training programmes.
(5) Interact with international agencies for participation and implementation of training programmes related to haemovigilance.

The Core Committee and National Advisory Committee are already notified and functional. Constitution of the Quality Review Panel, Signal Review Panel and Core Training Panel is under active consideration by the ministry.

The roles and responsibilities of the functional units of haemovigilance programme are depicted in Table 1.

Table 1 Roles and responsibilities of functional units of HvPI

HV units	Role and responsibilities
Reporting units	Generate transfusion reaction reports Causality assessment Submit report through HV software
National Co-ordinating Centre – HvPI	Review quality and completeness of data Collation and analysis Preparation of guidance documents Training and awareness programmes Feedback to reporting units Recommendations for blood safety to NCC – PvPI at IPC
National Co-ordinating Centre PvPI	Forward recommendations of HV – National Advisory Committee to CDSCO
CDSCO–DCGI (Drug Controller General India)	Formulate safety-related regulatory decisions Communication of blood and blood products transfusion-safety-related decisions to stakeholders To monitor compliance

CDSCO, Central Drugs Standards Control Organization; IPC, Indian Pharmacopoeia Commission; PvPI, Pharmacovigilance Programme of India.

HV software, validation, data submission and security

The major challenge for implementation of HvPI was to have an indigenous software to facilitate collection and collation of data in TRRF from various centres across the country and to transmit this data to National Coordinating Centre at NIB. The development of indigenous software entailed its validation, verification, operationalization and hands on training to end-users. The information technology cell comprising of officials from NIB and IPC developed this software and obtained the Security Audit and Compliance Audit through National Informatics Centre (NIC), Government of India. The software – 'Haemo-Vigil' – was hosted on NIB website on 24th January 2013 [13]. The adverse transfusion reaction data collected from the centres enrolled under the programme is secured in the NIC Server.

Reporting of transfusion reactions and preliminary results obtained

Enrolment of haemovigilance-reporting centres was initiated in 90 medical colleges in the country from December 2012 onwards. In the first phase of the programme, it is targeted to include 369 medical colleges in the country out of which 116 (31·4%) have expressed their intention to participate in the programme. Presently, the programme is voluntary and restricted to information of adverse transfusion reactions from recipients. The TRRF has been finalized by the National Advisory Committee. Reporting was initiated for severe transfusion reactions as per the definitions of International Society of Blood Transfusion (ISBT) Working Party for Haemovigilance [14]. However, data on all transfusion reactions were submitted by the reporting centres. Necessary modifications were made in the TRRF after deliberations by the National Advisory Committee, and now all transfusion reactions are being reported. The reactions as listed in the TRRF are as follows: immunological haemolysis due to ABO incompatibility, immunological haemolysis due to other allo-antibody, non-immunological haemolysis, transfusion-transmitted bacterial infection, anaphylaxis/hypersensitivity, transfusion-related acute lung injury, transfusion-transmitted viral infections,

post-transfusion purpura, graft vs. host disease, febrile non-haemolytic transfusion reactions, transfusion-related circulatory overload, transfusion-related dyspnoea and 'others' (mild and/or unclassifiable reactions). A guidance document for definitions and reporting was prepared for the users.

The number of adverse transfusion reaction reports received by National Coordinating Centre at NIB from 18 participating centres over a period of 10 months is 731. A preliminary analysis of reports reveals that majority of the reactions are mild and comprise of febrile non-haemolytic reactions and allergic reactions. The haemolytic transfusion reactions numbered 42 of 731, and 18 are reported to be of non-immunological causes. Non-immune haemolysis includes those haemolytic transfusion reaction due to storage and handling errors where red cells have been significantly damaged. There was one report of hypotension where this was the only symptom after starting transfusion. The reactions that were included in the 'others' group included chills, backache, headache, abdominal pain, pain at infusion site and mild breathlessness. The analysis is preliminary based on the TRRF category of reaction list. Detailed review of the TRRF forms is scheduled in the first quarter of 2014. Nine reports of transfusion-related dyspnoea were noted, but there is no report of transfusion-related acute lung injury. In India, male donors constitute over 90% of the donor population, and this may be one contributory factor, although underdiagnosis and hence under-reporting cannot be excluded at this stage. Other centres enrolled under Haemovigilance Programme are in the process of being trained about the information and procedures to uplink the adverse transfusion reactions via Haemo-Vigil Software. The types of reactions and their frequency reported till date is depicted in Fig. 2.

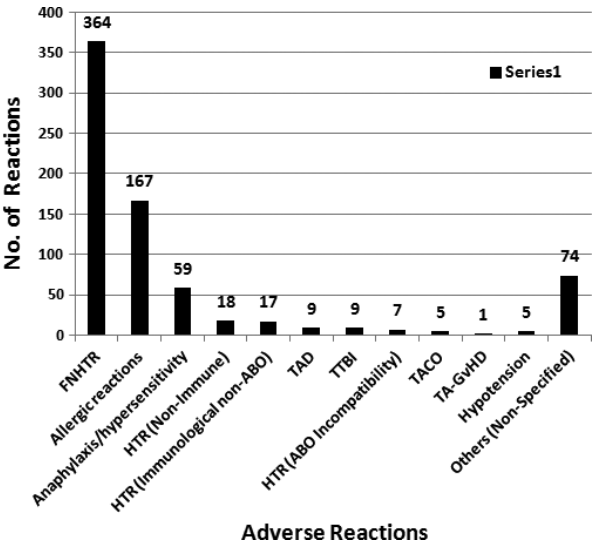

Fig. 2 Adverse Reactions reported from February 2013 to November 2013

Creating awareness

Success of any programme depends upon the degree of awareness created in the relevant stakeholders. A multi-pronged strategy to this effect was prepared for HvPI. The first announcement of the intention to launch this national programme as part of PvPI was made during the national conference of Indian Society of Transfusion Medicine on 24th November 2012 during the ISBT supported session on 'Haemovigilance'. Since then, a series of continuing Medical Education programme (CMEs) are being regularly organized state-wise in the country. The CME contents have been prepared by an expert subgroup and focus mainly on (i) creating awareness about the programme (ii) giving information on what is reportable, how it is defined and documented and (iii) online demonstration of uploading reports using Haemo-vigil software. Eight such CMEs have already been organized in different states located in different regions of the country. The Haemovigilance Newsletter is being published on a biannual basis from the National Co-ordinating Centre. It is posted on the NIB website and also printed for wide distribution. A brief communication about launch of the HvPI was also published in the official journal of the Indian Society of Transfusion Medicine [15]. The above steps are being taken to bring about sensitization and encourage participation by the healthcare professionals in the country.

Challenges ahead

The programme envisages that all the 369 medical colleges, superspeciality medical institutions, private and district hospitals and 2545 blood banks will be included in the centralized Haemovigilance Programme. However, enrolment of reporting centres has been planned in a phased manner. The medical colleges and other tertiary healthcare institutions are being enrolled first as these centres have the necessary expertise for diagnosing transfusion reactions. Constraints are being identified during the initiation phase; the most notable ones are fear of punitive action, additional work and responsibility especially by clinicians, shortage of staff in the blood banks, limited availability of computers and lack of easy access to internet and lack of perception of immediate benefits of reporting. Proposal for sanction of staff (Technical Associate) and computers for haemovigilance-reporting centres has been submitted to the MoHFW, Govt. of India for approval. Review of the programme is ongoing based on feedback from reporting centres and study of well-estab-

lished systems in other countries. It is aimed to become member of IHN. Once the programme gets optimized, it will be expanded to include donor vigilance, surveillance of transfusion-transmissible infections and rapid alerts.

Disclosure

The authors have no conflict of interest to declare.

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