Automation in Blood Centre: Its impact on Blood Safety

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Safety of blood and blood components is the major concern of every blood centre. Blood centre needs quality systems and state of the art infrastructure to maintain good laboratory practices in spite of heavy workload. Therefore recruitment of voluntary donors, proper collection and component separation process and screening of collected blood for transfusion transmissible infections (TTI) are the essential requirements of the blood safety. Immunohaematology laboratory functions 24 hours, 365 days and responsible for supplying compatible blood. To prevent manual errors this laboratory should preferably have automation.

Donor's Blood Collection

1. Whole Blood Collection

Blood Safety begins with the donor. Regular voluntary donor's blood is the safest source of blood for transfusion. Blood centre is committed to recruitment of dedicated volunteer blood donors. In order to select safe donors a series of questions are asked covering health and lifestyle.

Even if the phlebotomist is skilful drawing donor's blood is a challenge as sometimes there is difficulty in accessing donor's vein and multiple punctures are made. Vein illumination device uses near infrared light to illuminate subcutaneous veins on skin surface.[1] AccuVein, VeinViewer, Venoscope and Veinite are some of the major brands available in the market.

Blood component quality depends on the methodology used for whole blood collection. Random donor platelets cannot be prepared if 450 ml blood collection is not within seven minutes. Automatic electronic blood collection monitor (BCM) or blood mixers help in good quality blood collection suitable for Blood component preparation.[2] It provides smooth and gentle rocking of 5 to 10 RPM for homogenous mixing of blood with CPD-A1 solution. Instrument displays the time taken for blood collection and keeps record of time of each donation. These monitors apart from displaying weight and volume of blood have motor activated clamping at the end of collection. Thus there is no risk of excess blood collection. There are audio visual alarms to monitor collection process. If the flow is less than 15 ml/min instead of 50 to 70 ml/min it warns the phlebotomist. BCM is portable equipment which could be easily carried in the blood donation camps.

2. Collection of Components on Cell Separator

Automated blood donation allows the Blood Centre to target certain blood components during donation to better meet patient needs. In an Apheresis procedure cell separator machine collects blood from a healthy donor, the needed component is separated and the remaining blood is returned to the donor.[3-7] Products such as platelets, leukocytes, RBC (two units), neocytes, peripheral blood stem cells and plasma can be collected from the donor. The cell separator could be employed for therapeutic purpose also. The most commonly used cell separators adopt either intermittent flow centrifugation or a continuous flow centrifugation using single arm or two arm procedures respectively with single or double needle access. Machine ensures donor safety all the time during the operation. All cell separators use pre packed disposable sets of sterile bags, tubing and centrifugal device unique to cell separator. Depending on the type of component procedure and device used the total aphaeresis time varies from 30 minutes to a few hours. Most commonly available cell separators are manufactured by Haemonitics Corporation (MCS-LN 9000/MCS-LN8150), Baxter (CS-3000/ Amicus), Fresenius Kabi (Com. TEC), Cardian BCT (Trima Accel), Terumo BCT (COBE Spectra) and Johnson and Johnson (THERAKOS™ CELLEX™).[3-7]

The advantages of these machines are:

- The product quantity is more hence full effective dose of component is given at a time.
- There is a reduced multiple donor exposure thus reducing risk of alloimmunization and transfusion transmitted infections.
- Purity and quality of the product is better than the manually collected component.

Studies are available for automated portable systems for double RBC units' collection.[8-11] Wiltbank and Giordas[8] compared 1,023,682 whole-blood collections with 249,154 two-unit aphaeresis

RBC collections and concluded that it is safe to collect two units at a time and donor reaction rate is significantly lower than that observed in the manual whole blood collection. Other studies[9-11] have also confirmed this fact.

Automation in Blood Component Processing

Manual Blood Component processing is a tedious process involving many operations such as centrifugation, component separation etc. Automated devices reduce manual operations. Semiautomatic equipment is available for separation of plasma, red blood cells (RBC), platelets, with the advantage of leukoreduced products.[12-14] These component processors use top and bottom or top and top blood bag system. Different models of Optipress manufactured by Baxter Healthcare Corporation, Compomat G4 of Fresinius Kabi, T-ACE of Terumo Penpol and Dual Press of JMS Co Ltd are available in the market. Scientific studies have confirmed the efficiency of these instruments in separating leukoreduced RBC and platelets.[13-16]

An automated cell processing system ACP 215 has been manufactured by Haemonetics Corporation for RBC washing.[17] Component laboratory has to provide saline washed RBC to multi transfused patients. This is laborious job and manual washing poses a risk of contaminating the product. This system is very useful for washing RBC in a closed system. Ackley *et al*.[18] Have used automated cell-processing system for cryopreservation and deglycerolization of red cells.

Automation in Testing

Large blood centres have a heavy workload and therefore there is a risk of errors when operation is manual which compromises blood safety. Often it is difficult to have a skilled staff. Automation eliminates manual errors, reduces manpower requirements and has uniform performance.

1. Immunohaematology Systems

Conventional tube technique though still a Gold Standard, has many limitations, particularly in a blood centre having heavy workload. Inherent short comings of manual tube method are:

a. Variability in red cell concentration in red cell suspension which affects the antigen to reagent/antibody ratio.
b. Elution of low affinity antibodies during the washing by centrifugation.
c. Lack of consistency in reading agglutination reaction.
d. Human errors.

Automation has brought quality in immunohaematology testing because of the following advantages:

a. Barcode system prevents sample identification errors.
b. Prevention of human errors in interpretation of results.
c. Prevention of transcription errors while documenting the results.

Automated platforms available for forward and reverse grouping, red cell antibody screening and identification, cross matching etc are manufactured by:

a. Biorad (Switzerland).
b. Diagast (France).
c. Ortho Clinical Diagnositcs (Jhonson and Jhonson, USA).
d. Immucor (USA).
e. Grifols (USA).

These systems differ in their technical specifications, throughput, turn around time, sample loading operation etc. The devices like micro-plates or gel columns are generally used. The tests performed on these systems include ABO-RH grouping, phenotype, irregular antibody screening and compatibility testing. Fully automatic systems manage all the steps from the sample positioning on the carrier down to the final result (Autovue, Galileo, ID gel station, Qwalys, Tango, Techno) and the semi-automatic systems require intervention of an operator for the phases of centrifugation, stirring and incubation, the reading being automated for all.[19,20] All systems include the possibility of a connection to the central data processing system through an interphase. Biorad, Ortho and Grifols are based on column agglutination technology. Diagast uses the principle of erythrocyte magnetized technology (EMT) which avoids centrifugation and washing steps. Immucor platform is based on principle of solid phase red cell adherence assay.

All immunohaematology systems need validation before adaptation. Sensitivity of the test in these workstations is increased by using low concentration of red cell suspensions (0.5 to 1%) and enhancing media like low ionic strength solution (LISS) or Bromelin. Therefore there is a risk of false positive results in antibody detection. In all instruments optimization of the automated systems implies a specific training of the staff and the strict compliance with the standard operating procedures.[19] The system should not be used without proper validation of results.[21]

2. Electronic cross-matching

Computer cross-matching is an efficient and safe method for assigning blood components, based on Information Technology applied to typing and screening. Micihigan Medical Centre first introduced the Electronic cross-matching.[22] The computer or electronic cross-match replaces the immediate spin crossmatch for detecting ABO incompatibility. It is essentially a computer assisted analysis of the data entered from testing done on donor unit and blood samples drawn from intended recipient. Based on the barcode of the accepted sample, the software prevents the allocation of ABO incompatible blood and checks the congruence of the historical data by controlling the results of tests conducted on different samples and at different times. The software allocates a unit, choosing the one that is most compatible with regards to ABO/Rh blood groups and closest to the end of its shelf-life. Furthermore, at the time of releasing the unit, the programme checks that the allocation label has been attached to the correct bag, by reading the barcodes of the donation code and blood component-bag code which are on the unit, and the unique identification. When offered with fully automated pre-transfusion testing, computer cross-matching offers significant potential for rapid service.[23]

Electronic cross-match can only be accepted as a method of compatibility testing when it is properly designed, validated, implemented and monitored. It reduces the risk of human error through the use of software controlled decision making but high degree of validation is required to ensure accuracy. It can only be used if there is absence of unexpected antibodies in the intended recipient.

3. DNA Typing of Red Cell Antigens

The number of blood group systems is currently 35, and at present, 44 genes and 1568 alleles have been defined as encoding antigens within the 35 blood group systems. Polymerase chain reaction (PCR) based genomic typing is labour intensive as each sample has to undergo multiple assays. Single nucleotide variant (SNV) mapping to predict blood group antigens is the most commonly performed DNA micro array method.[24] DNA micro array detects all antigens in a single step thus helps in providing antigen matched blood for chronically transfused patients. It reduces the risk of alloimmunization in these patients.

The solid surface of a DNA micro array commonly consists of a chip, wafer or bead, with probes corresponding to various blood group alleles bound to the surface. During the micro array process, allele-specific hybridization occurs between complementary probes and labelled DNA fragments from a sample, and this is measured to determine genotype. There are several commercial DNA micro array platforms currently available for blood group genotyping. The two widely utilized platforms for blood group genotyping are the BloodChip from Progenika (Grifols) and the BeadChip from BioArray Solutions (Immucor). Other available platforms include LIFECODES RBC/RBC-R (Gen-Probe) and ID CORE XT (Progenika) based on Luminex technology, GenomeLab SNP stream (Beckman) the HIFI Blood 96 (AXO Science) and the Hemo ID Blood Group Genotyping Panel (Agena Bioscience).[24]

Automated micro array data analysis processes offer significant advantages over traditional serological and in-house PCR-based tests. This is because for traditional methods, analysis of data is often a more manual and time consuming process and can be subjective. The limitation of all SNV micro array platforms is that they utilize a targeted genotyping approach and thus genotype only alleles incorporated in the micro array. Once new alleles are discovered, this system requires time for specific design and validation. In some cases, genotype does not accurately reflect phenotype.

4. Automated Serological Tests for Transfusion Transmissible Infections

Automated systems generally offer substantial advantages in terms of quality, reproducibility and reduce operational errors. All enzyme linked immunosorbent assay (ELISA) Systems employed by the blood centre need a basic level of automation like automated plate washers and readers. Highly sophisticated automated screening systems are available that can perform all steps including analysis of the results. Most of the workstations are micro plate based "Open" systems. However DiaSorin LIAISON XL and Abbott ARCHITECT platforms are "Closed" systems.[25]

Many fully automatic walk away Systems are available in the market which can perform several types of ELISA and have an open platform. All have barcode system and interphase facility. Most of the systems have either single or dual probe robotic arm. Freedom Evolis (Tecan) has two arms i.e. robotic and analytical and also has the option of washable probes or disposable carbon (graphite) tips. NexGen Four of Adaltis Company also has two robotic arms. Most of the machines process two to seven ELISA plates at a time and all have impendent incubators. Alisei of Radim has rotating platform. The choice of the equipment depends on the number of plates, speed, disposable or washable probes etc. TKA Company has models like Bellini, Vivaldi, Verdi etc having two to 12 microplate processing capacity. These systems have washable probes. Grifols Triturus walk away ELISA analyzer has two probes while DA VI NCI QuaHro of Bimerieux and Mago 4 of Transasia have single robotic arm with a single probe. Automated immunoassays are also available for detection Syphilis and malaria infections.[26,27]

Various automated Chemiluminescence immunoassay analyzers are now commercially available and are replacing conventional enzyme immunoassays. Prominent among them are Architect i2000 system, Vitros ECiQ Immunodiagnostic System, UniCel DxI 800 analyzer, and Cobas e 411 analyzers which have been proved to be an excellent system for diagnostics of HBV, HCV, and HIV infections.[28,29]

5. Nucleic Acid Amplification Technology (NAT) Assays

Nucleic Acid Amplification Testing (NAT) automatic system tests viral nucleic acid (RNA/DNA) of human immunodeficiency virus (HIV)-1, hepatitis B virus (HBV) and hepatitis C virus (HCV) simultaneously. NAT tested blood increases blood safety as window period infection is generally missed by serological tests. The systems available for NAT are Procleix^{R}, Ultrio^{R} Assay (Chiron Corporation automation), semi automatic Procleix Tigris System (Chiron), Cobas TaqScreen MPX (Roche Molecular Systems) and Zelosx100 automated minipool NAT system of German Red Cross. Assal *et al.*[30] compared Procleix Tigris and Cobas 5201 and found Tigris ID-NAT more sensitive. Makroo *et al.*[31] have carried out multi centric NAT study by Procleix Ultrio assay and reported 0.065 % NAT yield of HIV, HBV and HCV.

Automation for Sterility Test

As per Drugs and Cosmetic rules 1% product should undergo Sterility test. Manual blood culture procedure is lengthily and tedious. Biomerieux has developed BacT/Alert system for this purpose. Based on colorimetric sensor technology the system detects microorganisms by continuously monitoring CO_2 production over a defined number of days. As organisms grow and produce CO_2 the sensor in the culture bottle changes from grey to yellow. Evaluation of BacT/Alert system was carried out by Mastronardi *et al.*[32] Study demonstrated that the system is capable of detecting aerobic and anaerobic bacterial contamination.

Traceability of Blood Products

Large blood centre has a heavy workload and therefore there is a risk of errors in manual operation which compromises blood safety. Mistaken identification of recipients and of the units of blood components to transfuse is still the most frequently reported error to the international haemovigilance systems. Often it is difficult to have a skilled staff. Automation eliminates manual errors, reduces manpower requirements and has uniform performance. The safety of transfusion therapies for patients depends in part on the distribution of the blood products.

International Society of blood transfusion (ISBT) working party on Automaton and data processing recommended code 128 on the symbol for all bar code messages on label[33,34] Besides Barcode system another technical innovation is Radio frequency identification device (RFID). ISBT established working party on

"Information Technology" in the year 2000 to develop guidelines for validation of automation systems in blood banking and maintaining their validation state.[35]

The Blood Bank activities which benefited are:

- Collection and whole blood processing using automated systems like Cell Separator, electronic blood collection monitor, Component extractor etc.
- Laboratory equipment like fully automated ELISA system, Immunohematology system, automated culture system etc.
- Information management systems.

Radio frequency identification (RFID) is a promising technology that has the potential to make the identification, storage, handling and distribution of blood and its products a more efficient and safer process.[36,37] The RFID tag communicates with the RFID reader via radio waves, which sends the identity to the database. Unlike barcode technology, the RFID system can read quickly, accurately and simultaneously. It offers a more secure and traceable solution. Several reports in the literature suggest the there is a potential for RFID technology in Blood Centers.[35-37]

Advantages of radio frequency identification:

- Reduction of human errors by reducing manual steps.
- Improved blood stock management.
- Simplified testing of donor/patients' samples on automatic equipment.
- Improved blood unit identification, distribution.
- Information can be sent directly to the network.
- Saves time.

Future Scope

In the modern blood banking Quality is primary goal to achieve blood safety. Therefore continuous scientific progress coupled with automation and computerization is the future requirement for maintaining highest level of quality in blood bank. According to Petrik[38] the future testing algorithms in blood centre will be combination of new multiplexing techniques with existing blood testing assays. The DNA Micro array technology in transfusion medicine helps in the identification of new genes and to learn more about infectious diseases. It offers a promising tool for high throughput genotyping for red cells and platelet antigens. Tht automated technique for extended blood group genotyping having multiplex analysis potential may dominate future Immunohaematology laboratories.

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