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Problem of bacterial contamination in platelet concentrates

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ABSTRACT

Bacterial contamination of blood is being recognized more frequently now and is one of the serious complications of transfusion. Use of integrally attached collection systems and strict standards for skin preparation, collection and storage of blood and components have reduced but not eliminated the risk of bacterial contamination. As bacteraemia may be part of acute or sub acute infections, strict donor selection is warranted. The longer the storage time, the greater is the number of organisms and amount of endotoxin present in the unit and associated with transfusion reactions. Importance of haemovigilance system and awareness among clinicians on the potential complications will go a long way in reducing patient morbidity. New approaches for detection of bacterial contamination, pathogen reduction and developments in the field of platelet biology will increase blood safety.

1. Historical overview

Numerous reports were published in the medical literature for over 60 years documenting the occurrence and clinical importance of bacterial contamination of blood. As early as 1939, a publication detailing the risk of bacterial contamination of blood appeared in JAMA [1]. In this, Novak advised that careful attention be given to the potential for bacterial contamination of stored blood. He noted an estimated 5% of blood that had been stored for 10 days at 4–6 °C were grossly contaminated. He even suggested a possible solution for reducing the occurrence of this problem with the addition of antibiotic to the stored blood to improve transfusion safety. The earliest report of a transfusion reaction associated with bacterial contamination of a blood component has been attributed to four patients manifesting a severe febrile reaction after transfusion from pooled plasma, subsequently shown to be contaminated with gram positive bacilli [2]. The FDA, Center for Biologics Evaluation and Research began investigating, monitoring and tracking the problem of bacterial contamination of blood over 50 years ago. Two reports, one in 1945 and a second in 1953, from the Public Health Service, Laboratory of Biologics Control, indicated that bacterial contamination of blood products was clearly a cause of concern [3,4]. Since then numerous instances of bacterial contamination and cases of transfusion-associated sepsis were identified and reported in the medical literature as platelet transfusion therapy emerged as an important treatment modality [5,6]. Buchholz and coworkers were instrumental in identifying the seriousness of this problem and reported two cases of PLT transfusion transmitted Enterobacter cloacae sepsis [7]. A follow-up investigation by them [8] revealed six instances of repeatedly positive cultures of a total of 3251 units sampled (0.18%). Based on their clinical observations and lab findings, they advised that caution should be exercised in the use of platelet products stored at room temperature, especially in recipients with impaired host defense mechanisms [9].

2. Current challenges

The exact incidence of bacterial contamination of blood products is unknown because different studies use variable methods of bacterial detection. Based on surveillance methods employing sensitive culture methods, 1 in 2000 platelet units (apheresis and random units) are contaminated with bacteria [10,11]. Bacterial contamination of blood is the most prevalent infectious risk of blood products in the US. Current risk of receiving bacterially

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contaminated PC may be 10 to 1000 times higher than the combined risk of transfusion transmitted infection with HIV, HCV and HTLV [12]. Bacteria rather than viral transmission remain the major cause of acute morbidity and mortality following post transfusion infection. Bacteria can proliferate from low concentration (<1 CFU/mL) at the time of collection to very high concentration ($>1 \times 10^8$ CFU/mL) during liquid storage period of blood components. Since platelets (PLTs) are stored at 20–24 °C, they constitute an excellent medium for bacteria. In the US, bacterial sepsis is considered the second most common cause of death overall from transfusion (after ABO incompatibility), with reported mortality rates ranging from 1/20,000 to 1/85,000 donor unit exposures [3]. In a seven year period from 1995–2002, 26 bacterial transmissions were reported to SHOT surveillance system in the UK [14]. Platelet related bacteremia occurs at a frequency approximately 50 times greater than that for RBCs [15]. In a comparison with RBC transfusions, Perez et al. reported that the risk of sepsis is increased threefold following platelet transfusions, with a markedly higher risk of sepsis following transfusion of pooled platelet concentrates (PCs) than of apheresis PCs [16]. Results of standardized sterility testing in Germany showed that the bacterial contamination rates for single-donor PCs derived from WB (0.210%) and apheresis (0.156%) were comparable. Pooled PCs produced from buffy coats using sterile docking procedures showed a significantly higher contamination rate of 0.604% compared with single-donor PCs derived from WB and apheresis. PCs are subjected to bacterial contamination more frequently than red blood cell concentrates ($p < 0.001$) or fresh plasma ($p < 0.001$) [17]. Several factors are contributory for the persistence of bacterial contamination of blood. The most important is an apparent lack of recognition of frequency of this problem. Other factors are poor clinical recognition of the problem because of the highly variable accompanying signs and symptoms and because patients receiving blood products have severe underlying diseases, obscuring the clinical identification of a septic transfusion reaction. Compared with available data on the bacterial contamination of cellular blood products, the frequency of clinically apparent septic transfusion events due to contaminated products is considerably lower and present only one end of the clinical spectrum of transfusion-associated septic transfusion reactions. Thus the actual prevalence may be much higher than reported. Septic reactions go unrecognized because it mimics the initial signs and symptoms of the febrile non-haemolytic transfusion reactions that occur following transfusion of platelets. Infrequency of clinical events reporting could be due to non-pathogenic bacteria, insufficient numbers of bacteria to cause clinical sequelae, premedication with steroids/antipyretics, patients already on antibiotics and in immuno suppressed condition [18]. Clinical severity of a transfusion-associated septic reaction can vary considerably depending on the species of bacteria in the unit, number of bacteria infused, its rate of propagation and recipient characteristics.

Blajchman et al. describes leukocyte removal as a possible option for reducing the risk of contamination [19]. However, filtration to achieve leucodepletion does not prevent bacterial growth, but reduces the quantity of contaminating bacteria, and possibly the risk of bacterial sepsis [20,21]. The effect of blood filtration on the reduction of bacterial contamination appears to vary greatly with bacterial species [22], with strains among the same species, bactericidal activity of donor blood and even the physical properties of the filter [20]. Pooling of blood components from several whole blood donations, the contamination risk is carried over into the end product and if the contamination rate of pooled PCs is lower than expected rate, this is probably attributed to self sterilization [23]. Major source of contamination is skin derived. Bacterial contamination in platelet concentrates (PC) is mainly donor phlebotomy arm related. Donor bacteraemia, contaminated collection equipment and contamination occurring during processing and storage of blood, the phlebotomist and the environment including air and equipment also have an impact. The mean prevalence of bacterial contamination in whole blood derived platelets is 33.9/100,000 units and that for apheresis platelet units is 51.0/100, 000 units [13]. Reactions are commonly noted and more severe with platelets stored for greater lengths of time. In the UK, serious hazards of transfusion (SHOT) reported that potentially 80% of bacterial transmissions, in which source was identified, were derived from donor's arm [24]. Implementation of improved donor arm disinfection, application of principles of GMP, diversion and bacterial screening have shown substantial benefit. Several studies have investigated the potential for the diversion of the first 10–40 mL of blood to flush out organisms from skin flaps entering the collection container [25,26]. The use of pH monitoring, Gram stain, glucose measurements and inspection of swirling have all been used for the detection of bacterial contamination in PCs. Swirling can be performed in seconds and has been used to detect bacterial levels of $>10^7$ CFU/mL in platelet components. Platelet cease to swirl when contaminated with high levels of bacteria because the declining pH in the unit causes asymmetric platelets to become spherical [27,28]. All these have been attempted, but are not sensitive or specific to interdict contaminated units. Frequency of contamination was greatly reduced with the advent of closed sterile systems for collection and storage of blood. Adverse effects related to transfusion-associated bacterial contamination, besides the systematic detection of bacteria or bacterial metabolic products in blood, the promising use of agents capable of inactivating microorganisms in blood, modification of transfusion practices, all of which help reduce the risk of bacterial contamination [29–32]. Phlebotomy needle passing through the skin may take a small fragment of skin containing viable bacteria which enter the collection bag. Dimpled phlebotomy sites make effective cleansing of the area difficult. Although it has been shown that "best practice" donor arm disinfection techniques can substantially reduce the bioburden on the upper layers of the skin, it is virtually impossible to disinfect the lower layers [26]. Bacterial bioburden may be considerable at the antecubital fossa and Mc Donald et al. indicated that more than 50% donors have 10^5 organisms per cm^2 at the venepuncture before disinfection [33].Donors who are asymptomatic or with low grade chronic infection or in the incubation period have