Bacterial contamination of platelet products in Dongguan Blood Center, Guangdong Province of China

Ziyi He, Jialin Che, Qing Wang, Shaobin Chen, Qingkai Chen, Lin Yu, Jiaoli Zou, Yingming Hu

Department of Transfusion Research, Dongguan Blood Center, Dongguan 523006, China

Contributions: (I) Conception and design: Z He, J Che; (II) Administrative support: J Che; (III) Provision of study materials or patients: Q Wang, S Chen, Q Chen, L Yu; (IV) Collection and assembly of data: Q Chen, L Yu, J Zou; (V) Data analysis and interpretation: Z He, Y Hu; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Ziyi He. Department of Transfusion Research, Dongguan Blood Center, Dongguan 523006, China. Email: zyhe_8@163.com.

Background: Due to the importance of their preservation and collection methods, it is critical to assess accurately the risk of bacterial contamination of pooled platelets and apheresis platelets. The incidence of bacterial contamination was observed after four preventive measures (FPM) (including: sterilizing donation environment, screening donors, depleting white blood cells from pooled platelets, and removing the first 15 ml of collected platelet) were taken.

Methods: Platelet product samples (pooled and apheresis platelet products) from Dongguan Blood Center were tested by bacterial cultures including initial culture, subculture and identification. If initial culture was positive, subculture would be performed, and if subculture was positive, bacterial identification would be done. 3073 platelet samples were examined in 2006. Platelet samples were collected in 2006 and in 2007 until 2016 after the introduction of FPM. Recipient's blood and transfused platelets were tested for bacterial cultures when adverse reactions occurred after platelet transfusion.

Results: In 2006, 0.72% and 0.47% bacterial contamination were found in pooled platelets and apheresis platelets, respectively. A total of 63 out of 28,711 (0.22%) bacterial contaminations were detected from 2006 to 2016 in pooled and apheresis platelets. From 2007 to 2016, the positive rates of contaminated platelet products declined significantly to 0.33% (pooled platelets) and 0.14% (apheresis platelets). Only 44 positive samples could be identified after the introduction of FPM. In 50 patients with post-platelet transfusion adverse reaction, no bacterial contamination could be identified.

Conclusions: Our study demonstrated the improvement of platelet transfusion safety by FPM, The rate of bacterial contamination in pooled platelets is higher than that of apheresis platelets.

Keywords: Platelet; bacterial contamination; preventive measures

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Introduction

Bacterial contamination of platelet products was the second most common cause for transfusion-related deaths in the USA where septic reactions from bacterial contamination of blood products are considered to be the most frequent and serious infectious outcomes of transfusion during the period between1985 and 1999 (1). In order to avoid the risks, the American Association of Blood Banks (AABB) established a standard that required transfusion service departments to detect and limit bacterial contamination in all platelet products (2). Source of bacterial contamination of platelet products from the surface of the skin during needle stick into the vessel is one of the common routes of entry (3). A report showed that the rate of transfusion reactions due to bacterial contamination of platelet products was about 1 in 25,000 platelet units (4), but another report indicated 1 in 1,000 to 2,000 platelet units to be infected in aerobic bacterial cultures (5).

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Bacteria culture of blood showed that the positive rate varied from 2% to 6% (2). The actual rate of bacterial contamination of platelets ranged from 0.03% to 0.3% in recent prospective studies (6). A few blood centers have implemented the demonstration of bacterial contamination of platelet products in the mainland China. Due to the short shelf life, most of bacterial contamination will not be identified prior to the platelets being issued. During storage of platelet products, bacteria would proliferate from relatively low undetectable levels at the beginning of storage period, to relatively high bacteria titers at the end of storage period. After transfusion of bacteria-contaminated platelet products, patients may develop fever, hypotension and chills at the time of transfusion or shortly after the completion of transfusion. Sometimes the symptoms may take 2 weeks to develop, and a number of patients have shock and hypotension, even death (7). Platelet-septic reactions mainly result from low concentrations of bacteria that escape initial detection (8,9). To prevent this situation, we have employed the demonstration of bacterial contamination in platelet products in Dongguan Blood Center since 2006, and four preventive measures (FPM) were taken from 2007 to today. The purpose of this study was to assess the incidence of bacterial contamination of platelet products before and after FPM.

Methods

Sample source and bacterial culture

A total of 28,711 platelet samples were examined from 2006 to 2016. The study included the screening of 1,794 samples of pooled platelet products and 1,279 samples of apheresis platelets from platelet donors collected in 2006. FPM have been taken since 2007, including (I) carefully and properly sterilizing donation environment (skin disinfection), (II) strictly screening of donors, (III) completely depleting leukocytes from pooled platelets, and (IV) removal of the first 15 mL of collected platelet. Strictly donor selection includes enquiring the medical history, health examination, leukocyte count and classification, excluding potential bacterial sepsis and bacteremia. A total of 4,488 samples of pooled platelets and 21,150 apheresis platelets were tested based on the following methods from 2007 to 2016. Initial culture and subculture were applied to these samples.

After 12 hours of apheresis platelets and pooled platelets prepared, aliquots of 5 mL of platelet product were added to aerobic and anaerobic culture medium (BacT/ALERT, France Biomerier), respectively, and incubated for 7 days at 37 ℃ by automatic bacterial culture monitoring system culture system (BacT/ALERT 3D system, France Biomerier). The color of the indicator at the bottom containing the samples would change if bacterial metabolites were detected. If there was any color change, the positive bottles were subculture. Biochemical method was used to identify bacteria. If a product was suspected to cause bacterial contamination adverse reaction, the product would be immediately reserved for bacterial culture, and the samples from the patients after transfusion were also kept for bacterial culture. Bacteria isolated from cultures of the recipient and product would be reserved for further investigation (see below). If any adverse reaction occurred after platelet transfused, bacterial cultures of recipients and transfused bags were performed to determine the cause.

This study was approved by the Ethics Committee of the Dongguan Blood Center and all aspects of the study complied with the Declaration of Helsinki.

Bacterial identification

The positive samples in subcultures were sent to Humen Hospital, Dongguan, China for identification of bacteria. The macroscopic and microscopic properties of bacteria were examined. The color and appearance of colonies were noted. The Gram-staining method and conventional biochemical tests in bacteriology were used.

Results

A total of 63 bacteria-contaminated samples were identified from 28,711 platelet samples in this study. The infection rate was 1 in 456 samples tested (0.22%), in which the infection rate was (0.62%, 19/3,028) prior to the FPM and 0.17% (44/25,638) after the FPM were taken. The positive rate of pooled platelet products was higher before than after the FPM were taken (*Table 1*).

After FPM were taken, the positive rate of pooled platelets for the initial culture (1.67%) was higher than that of apheresis platelets (0.82%) ($P<0.01$). In pooled platelet products, the positive rate of single anaerobic culture (0.25%) was higher than in apheresis products (0.02%) ($P<0.01$), and the positive rate of both aerobic and anaerobic culture (0.31%) was also higher than in apheresis products (0.13%) ($P<0.01$). The positive rate of subculture in pooled platelets (0.60%) was higher than in apheresis products (0.21%) ($P<0.01$). Positive bacterial identification rate in pooled platelets (0.33%) was higher than in apheresis

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(0.14%) (P<0.01) (*Table 2*).

In 44 cases of positive bacterial identification, there were 21 cases of coccus, 19 cases of bacillus, 2 cases of anaerobic bacteria, 1 case of fungi and 1 case of monocyte-bacteria, The major aerobic bacteria were coccus and bacillus, in which mostly being Staphylococcus epidermidis and gram positive bacillus (*Table 3*), they were all non-pathogenic. Among them, Staphylococcus epidermidis, coagulase negative staphylococcus, Klebsiella pneumoniae ozaenae, Micrococcaceae, and Brevundimonas vesicularis were conditioned pathogens, the ratio is 31.82% (14/44).

From 2006 to 2016, about 50 patients with adverse reactions occurring after platelet transfused, but none of them were bacteria-culture positive.

Discussion

Although the risk of infections transmitted through transfusion is less today than the past, bacterial infections still occur after platelet product transfusion. In the past, transfusion-related infections remained an important cause of morbidity and mortality in many developed countries (10). In our study, the infection rate was 1 in 161 (0.62%) platelet samples tested before FPM were taken. In order to reduce the risk of bacterial contamination, FPM has been taken since 2007. The risk of bacterial infection transmitted through transfusion was reduced, the rate of bacterial contamination in pooled platelets was 0.33%, but in apheresis platelets was 0.14%. The positive rate of anaerobic culture was 0.25% in pooled products and only 0.02% in apheresis platelets. The positive rates of aerobic and anaerobic culture were 0.31% in pooled products and 0.13% in apheresis platelets.

As platelets are stored in aerobic environment, cultures of anaerobic bacteria seem to be irrational. However, Ahmed *et al.* reported that 15 out of 16 organisms were aerobic microbes and 1 was an anaerobe (11). In our study, the positive rate of bacterial contamination from both the initial culture and subculture was higher in pooled platelets than in apheresis platelets, apheresis platelets were collected from a single donor, and the whole process was totally closed, so it is safer. Before the confirmatory assays were performed, the initial results might have a high false positive rate due to either the poor specificity of culture-based tests or laboratory contamination of the culture system. A true contamination of platelet product is often because of the skin flora, the environment, or the donor who was having bacteremia or transient bacteremia. Gram-negative bacterial are often due to occult bacteremia and are significant, but gram-positive organisms are likely to originate from either skin or environmental exposure.

Because culture-based tests are time-consuming, bacterial contamination is usually identified after the products have been issued, so it is thus important to identify the

Table 1 Comparison of bacterial contamination before and after FPM

Blood products	Before prevention measures		After prevention measures	
	n	Positive (%)	n	Positive (%)
Pooled platelets*	1,794	13 (0.72)	4,488	15 (0.33)
Apheresis platelets†	1,279	6 (0.47)	21,150	29 (0.14)

*, χ^2=4.35, P<0.05; †, χ^2=8.48, P<0.05 before prevention measures *vs.* after FPM. FPM, four preventive measures.

Table 2 Comparison the positive rate of bacterial culture between pooled platelets and apheresis platelets after FPM

Variable	Pooled platelets	Apheresis platelets	χ^2	P
n	4,488	21,150	–	–
Initial culture (%)	75 (1.67)	174 (0.82)	27.03	<0.01
Aerobic culture (%)	2 (0.04)	13 (0.06)	0.01	>0.05
Anaerobic culture (%)	11 (0.25)	5 (0.02)	25.60	<0.01
Aerobic and anaerobic culture (%)	14 (0.31)	27 (0.13)	7.84	<0.01
Subculture (%)	27 (0.60)	45 (0.21)	19.83	<0.01
Positive bacterial identification (%)	15 (0.33)	29 (0.14)	8.36	<0.01

Pooled platelets *vs.* apheresis platelets. FPM, four preventive measures.

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Table 3 The results of bacterial identification after FPM

Classification	Apheresis platelets	Pooled platelets	Total
Cocci coccus [21]			
Staphylococcus epidermidis	4	5	9
Hemolytic Staphylococcus	2	/	2
staphylococcus aureus	1	/	1
Warner Staphylococcus	3	/	3
Staphylococcus simulans	1	/	1
Staphylococcus warneri	1	/	1
Squirrel coccus	1	/	1
Coagulase negative staphylococcus	1	1	2
Micrococcus	1	/	1
Bacillus [19]			
Klebsiella ozaenae	1	/	1
Brevundimonas vesicularis	/	1	1
Gram positive bacillus	9	7	16
Gram-positive corynebacterium	1	/	1
Sphingomonas paucimobilis	/	1	1
Aspergillus	1	/	1
Anaerobic bacteria	2	/	2
Total	29	15	44

FPM, four preventive measures.

bacteria in the contaminated platelets prior to issue. In our study, the main strains of bacteria identified were coccus, bacillus, most of which were staphylococcus epidermidis and Gram positive bacillus. Hillyer *et al.* (12) found that isolated bacteria from contaminated platelets mainly came from the skin flora and most of them were Gram-positive cocci. Brecher and Hay (5) demonstrated that Gram-negative bacteria were the main reason for the deaths due to transfusion of infected blood products (59.7%). A question is why about 6,000 units of platelet products were transfused one year in Dongguan city, but there was no case of bacteremia occurred in recipients. Usually, bacterial contamination of a blood component is not considered in diagnosis as signs and symptoms, including fever, rigors and hypotension, resemble those expected either from transfusion reaction or from sepsis due to other causes (13). Gram-positive bacteria found on skin are the most frequent contaminants of platelets. Although gram-negative bacteria are less commonly recognized as contaminants, they may cause severe and often fatal infections. We consider the amount of contaminated bacteria is very small in the platelets supplied, so that the immune system may destroy the small amount of bacteria quickly after platelet transfusion to recipients.

In our study, 44 cases of contaminated platelet products were identified which could potentially cause complications, but 30 cases were unconditioned pathogen and only 14 cases were conditioned pathogen all the bacteria identified in platelet products mainly came from the skin or environment. Clinical follow-up showed no bacteremia occurring after transfusion.

In conclusion, FPM can help reduce the rate of platelet bacterial contamination; the bacterial contamination rate of pooled platelet was higher than that of apheresis platelets. The necessity of platelet bacterial cultures remains doubtful.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/aob.2018.08.01). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional/

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regional/national ethics committee/ethics board of the Dongguan Blood Center (No. 201801) and written informed consent was obtained from all patients.

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