

## The indications of leukodepleting blood or blood products, and the importance of using bedside blood-product filters during neonatal transfusion

Morudu LJ, SHERQ Officer, Quality Assurance Coordinator

Clinix Health Group, Tshepo-Themba Hospital Private Hospital, Soweto; and University of Pretoria

Correspondence to: Letennwe Morudu, e-mail: tmorudu@clinix.co.za

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### Abstract

Transfusion therapy remains one of the most commonly used regimens to treat critically ill neonates. Neonatal intensive care professional nurses have a responsibility to ensure that the procedure is as effective, and as safe, as possible. This article aims to provide neonatal intensive care professional nurses with knowledge of the effects of leukodepletion of blood or blood products, the various available bedside blood-product filters, and the role played by the filter pore size in preventing transfusion related reactions in neonates.

### Introduction

During the past few years, concerns regarding the lack of efficiency of blood transfusion to treat critically ill neonates have been compounded by high-profile occurrences of undesirable transfusion-induced effects.

Often, when faced with the responsibility of transfusing neonates with blood or blood products, neonatal professional nurses are faced with the responsibility of deciding which blood or blood-product filter to use. This poses a challenge, as most of them lack knowledge regarding leukodepletion of blood products, of the various blood or blood-product filters available in the market, what pore size beside blood or blood-product filters have, the role played by pore size, as well as a general understanding of leukodepletion of blood or blood products. Leukodepletion is a process that minimises transfusion-associated reactions or complications.

The objective of this article is to provide neonatal intensive care professional nurses with knowledge that will enable them to make relevant, quality clinical decisions regarding the use of bedside blood or blood-product filters, when they have to transfuse neonates with blood or blood products.

### Background

Leukodepletion is a process whereby donor leukocytes are reduced to the level of  $> 5 \times 10^8$  (7-8

million) red cells per unit of packed red cells, and  $> 5 \times 10^6$  (5 million) red cells per unit of platelets.<sup>1,2</sup>

According to universal leukodepletion policy, the highest level of leukodepletion should be less than  $1 \times 10^6$ , which is 10 million white blood cells per unit of blood. In other words, if it is to be considered safe and incapable of producing transfusion reactions in its recipient, more than one million white cells should be removed per unit of blood product.<sup>3,4</sup>

### *Leukocyte counting*

The most accurate measure of leukocyte removal is by examining the absolute number of leukocytes remaining after filtration. Seghatchian maintains that when leukodepletion is performed, pre-storage leukodepletion is the one criterion preferred and advocated by most of the developed and developing world.<sup>3</sup>

Pre-storage leukodepletion is the removal of donor leukocytes from the blood products immediately after the donor has been bled, i.e. on the day of collection.<sup>3</sup> Post-storage leukodepletion is performed a few days after obtaining the blood products from the donor.<sup>4</sup> This is especially applicable when leukodepletion is performed at a central institution, away from the blood collection point. Blood products undergo fragmentation, and tend to release their intracellular contents within minutes of being removed from the body.<sup>2,3,5</sup>

### *Indications and advantages*

In the past, research denoted an increased appreciation of white cell depletion from the red cells and platelets to prevent potential adverse effects, and to reduce the transmission or reactivation of the cytomegalovirus (CMV), human immunodeficiency virus (HIV), Hepatitis A, B, C and other viruses.<sup>3,6-8</sup> The CMV is one of the viruses that is known to be transmitted by blood transfusion, as CMV may be found within the white cell of donated blood products.<sup>7</sup>

Chu mentions that the transfusion of blood or blood products may cause immune deviation towards the secretion of cytokines, which may down regulate cellular immunity.<sup>9</sup> Neonates and paediatrics are often immunocompromised and the unintentional immunosuppressive effects of blood transfusion will only compound this predicament.<sup>10</sup>

The administration of leukodepleted blood products to all neonates has tended to protect these recipients from the abovementioned complications and infections, regardless of their body weight.<sup>11</sup> However, Seghatchian states that leukodepletion alone may not provide complete protection from some viral transmissions, such as non-haemolytic transfusion-related reactions, i.e. CMV and HIV.<sup>3</sup>

### **Problems**

Previously, leukodepletion (with a bedside filter) after storage tended to be the predominant method of delivery, but filtration efficacy turned out to be highly variable, even after only brief periods of storage at 4 °C. Hence, pre-stored leukodepletion has rapidly become the preferred method. However, the majority of pre-storage filtrations still take place after a certain holding period, for example, overnight, and especially where leukodepletion is performed centrally.<sup>3,4</sup>

There is no clear evidence as to the minimum level of residual leucocytes or lymphocytes subsets that are needed to prevent certain immunomodulatory effects, and the transmission of infections including CMV and non-haemolytic febrile transfusion reactions.<sup>12,13</sup> The removal of viruses, particularly the HIV virus, through the leukodepletion process, still has to be adequately researched. Patients have tested HIV positive post-transfusion. The mode of transmission was blood products.<sup>12</sup>

Furthermore, there is some evidence that certain donations, or filter combinations, frequently lead to membrane blockage or filtration failure.<sup>14</sup> This is possibly due to high levels of micro-vesicles or large cells, cellular aggregate, or pinched or structurally abnormal WBCs. This is of particular relevance to sickle cell trait. In order

to establish a national evidence-based policy throughout transfusion therapy, a comprehensive evaluation of donor-related issues, filtration failure and recurrent blockage is urgently needed.<sup>5</sup>

### **Bedside filtration**

Bedside filtration means the application of bedside blood or blood-product filters to administration sets used for administering blood or blood products to neonates, while attempting to remove precipitates.<sup>15</sup> In this article, it refers to contaminating leukocytes and any pathogens, viruses, microbes, debris or microaggregate, that might have been formed or collected during donation and storage, or while preparing for neonatal transfusion.<sup>4</sup>

Compliance with national and international standards requires that all blood components are transfused through an administration set, containing an integral filter. Accorsi et al, and Seghatchian, reiterate that within a few hours of collection, platelet aggregation occurs.<sup>4,6</sup> After a day or more, the leukocytes start losing their viability, and combine with the aggregating platelets. Finally, fibrin precipitation occurs, consolidating the loosely bound structures, and forming stable microaggregate. The size of the microaggregate varies between 10-200 unimicron ( $\mu\text{m}$ ), and is of similar size to precapillary arterioles of the lungs. Inadvertent infusion of the microaggregate within blood products can result in the occlusion of these vessels.

The infusion of microaggregate has been implicated in various transfusion-associated complications. It is believed that microaggregates are able to release biochemically active components which can contribute to the development of respiratory dysfunction.<sup>16</sup> Leukocytes are regarded as the core component of a microaggregate. The transfusion of chronically ill and immune-comprised patients, of whom neonates form a major part, often requires a greater level of leukocyte depletion. Recent developments in this field have enabled leukocyte depletion by filtration to be performed, either at the patient bedside, or in the blood bank.<sup>6</sup>

The clinical complications associated with transfusion therapy can, to a large extent, be prevented by the use of appropriate bedside blood or blood-product filters.<sup>17</sup>

### *Types of bedside blood-product filters*

Presently, two types of blood-product filters are available for bedside use during neonatal transfusion, namely leukodepleting and microaggregate blood filters. The pore size for a leukodepleting bedside blood-product filter is normally between 20-40  $\mu\text{m}$ , while microaggregate filters are between 170-240  $\mu\text{m}$ . The pore size of the bedside blood-product filters plays a crucial role in preventing even smaller pathogens and debris, such as microscopic air and viruses, from entering the neonate's circulatory system.<sup>2,8</sup>

### *Leukodepleting bedside blood-product filters*

Leukodepleting bedside blood-product filters can be used to:

- Remove small blood clots formed during storage and debris found within the collection bag.
- Remove residual donor white cells from blood products, and trap microscopic air and viruses prior to transfusion.

These filters commonly have a smaller  $\mu\text{m}$  size, which not only reduces or prevents incidences or complications associated with transfusion therapy, but also traps and prevents microscopic air from entering the neonate's circulatory system during transfusion.<sup>17</sup>

### *Microaggregate bedside filters*

Microaggregate bedside filters are capable of removing only microaggregate, blood clots and debris that may have collected within the blood bag during storage. They only trap larger pathogens that would otherwise pass through the standard 170  $\mu\text{m}$  intravenous (IV) administration set filter. They contain a sieve-like filter, and operate on one of two principles: screen filtration or depth filtration.<sup>17</sup>

### *Indications and advantages of bedside blood-product filters*

Introducing inadvertent particles such as microscopic air or microemboli, fibrin threats, or microaggregate to neonates is profoundly dangerous during neonatal blood transfusion. This can lead to the development of potentially life-threatening complications, such as pulmonary embolism, and even death. Although there have been cases involving peripheral venous access, the risk is even higher when central or umbilical catheters are used.<sup>16</sup>

The filter attachment point also plays a role in preventing particles from entering the neonatal circulation which might be found in the administration set, or those having entered the set during the priming period. Kunac et al note that it has been claimed that the placement of an in-line filter proximal to the cannula, but distal to the administration set, may protect the patient from being transfused with particulates because it allows filtration of the fluid as it is delivered to the patient.<sup>18</sup> These filters normally have a pore size of 40  $\mu\text{m}$  and less.<sup>19</sup>

The bedside blood-product filter, that is attached proximal to the administration set, cannot trap any plastics or small plastic particles that may be found within the administration sets.<sup>20</sup> The other disadvantage associated with bedside blood-product filters attached proximally is that personnel tend to reuse them to the point of administering clear intravenous solutions, leading to the

unloading and detaching of filtered particles or debris from the filter into the neonate's circulatory system.<sup>20</sup>

When professional neonatal nurses have insufficient knowledge about leukodepletion and bedside blood-product filters, it is difficult for them to decide which bedside blood-product filters to use during neonatal blood transfusion, with regards to the specific type of blood or blood products that have been prescribed.

## **Conclusion**

It is of paramount importance that neonatal professional nurses who are responsible for transfusing neonates with blood or blood products have sufficient knowledge regarding leukodepletion of blood or blood products, as well as the various types of bedside blood-product filters to use with specific blood products. The sufficiently knowledgeable neonatal nurse will be able to make the appropriate decision, and enhance transfusion efficacy, as well as prevent neonatal morbidity in response to the effects of leukodepletion.

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## **References**

1. British Committee for Standards in Haematology: transfusion task force. Transfusion for neonates and older children: guidelines. Oxford: Blackwell Scientific Publications; 2004.
2. South African Blood Transfusion Services. Clinical guidelines for the use of blood products in South Africa. 3<sup>rd</sup> edition. Johannesburg: Adcock Ingram Critical Care, 2003; p. 9.
3. Seghatchian J. Universal leukodepletion: an overview of some unresolved issues and highlights of lessons learned. *Transfus Apher Sci.* 2003;29:105-117.
4. Soli M, Blanco L, Riggert J, et al. A multicentre evaluation of a new filtration protocol for leukocyte depletion of high-haematocrit red blood cells collected by an automated blood collection system. *Vox Sang.* 2001;81(2):108-112.
5. Llewelyn CA, Taylor RS, Todd AAM, et al. The effects of postoperative infections on length of stay in elective orthopaedic and cardiac surgery. *Transfusion Practice.* 2004;44(4):497-500.
6. Accorsi P and Iacone A. Selective or universal leukodepletion: the Italian experience. *Transfus Sci.* 2000;22(1-2):65-67.
7. Pall Medical. Leucocyte depletion for neonatal and paediatric care: filtration, separation, solution. Clinical update. Portsmouth: Europa House; 2000.
8. Pall Medical. Leucocyte removal and post operative infections: filtration, separation, solution. Clinical update. Portsmouth: Europa House; 2000.
9. Chu, RW. Leukocytes in blood transfusion: adverse effects their prevention. *Hong Kong Med J.* 1999;5(3):280-284. [homepage on the Internet]. Available from: [http://hkmj.org/article\\_pdfs/hkm9909p280.pdf](http://hkmj.org/article_pdfs/hkm9909p280.pdf)

10. Red blood cells transfusion in newborn infants: revised guidelines. *Paediatr Child Health*. 2002;7(8):553-558.
11. Sowemimo-Coker SO, Kim A, Brandwein H, Wenz B. Analysis of leukocyte subsets in leukoreduced platelets platelet concentrates. New York: Pall Corporation;1998: p. 5. Pall Corporation. Technical report.
12. Romaine C, Hazlehurst G, Jewell AP. Leukodepletion for transmissible spongiform encephalopathies. *Br J Biomed Sci*. 2004;61(1):52-53.
13. Wilson GS. Anaemia and blood transfusion in ICU. *The Southern African Journal of Critical Care*. 2004;20(1):28-32.
14. Barrowcliffe, TW. Universal leukodepletion : practical and regulatory consequences. *Transfus Sci*.1998;19(4):361.
15. Baillère's neonatal intensive care professional nurses dictionary. London: Balliere Tindall, in association with Royal College of Nursing; 2004.
16. Van Lingen RA, Baerts W, Marquering ACM, Ruisj GJHM. The use of in-line intravenous filters in sick newborn infants. *Acta Paediatr*. 2004;93(5):658-662.
17. Kapadia F, Smith G, Valentine S. The role of blood microfilters in clinical practice. *Intensive Care Med*. 1992;18(5):3-4.
18. Kunac DL, Ball PA, Broadbent RS. Inline intravenous filtration in neonates: help not hindrance. *The Australian Journal of Hospital Pharmacy*. 1999;29(6):321-327.
19. Towns D. Hemolytic disease of the fetus and newborn and perinatal immune thrombocytopenia: emergency transfusion. *Canadian Blood Services*. 2007;113-115.
20. Bird A, Nel T, James M. Administration of blood components: avoiding unnecessary costs. *S Afr Med J*. 2003;93(6):419.

## Neonatology unit at Bara upgraded by SiPAP machine donation

The neonatology unit at Chris Hani Baragwanath Hospital acquired two new SiPAP machines on November 10<sup>th</sup>, which will assist greatly in managing the breathing problems commonly seen in babies with a low birth weight under 2.5 kgs.

Donated by the Neonatology Department of Abbott Laboratories South Africa, the SiPAP machines were sourced by Respiratory Care Africa (RCA) and are more advanced than the standard CPAP machines currently being used by the unit.

According to Prof Sithembiso Velaphi, head of Bara's Department of Paediatrics, two thousand babies are born on average per month at the hospital. Of these, approximately 15% have a birth weight below 2.5 kgs, with 3% weighing less than 1.5 kgs. "It is estimated that 10 percent of the babies between 1.5 and 2.5 kgs will require some assistance with breathing, with the number escalating to 60% of the babies below 1.5 kgs," he says.

"The SiPAP machines will make a big difference to the outcome of the babies weighing below 1,500 gms. The major benefits of the new machines are that they kick in when the baby stops breathing and are less invasive, being attached to the baby via prongs in the nose, rather than a tube."



Prof Velaphi notes that "Bara has a record of over-using equipment because of the high number of patients needing it. The neonatology unit currently needs double the number of CPAP machines in its possession; therefore the new machines will be in use all the time," he says.

"We were touched by the work that Professor Velaphi is doing in his unit," says Lindy Hales, Business Unit Manager of Abbott's Speciality Care Division. "We wanted to help the neonatal unit save more babies with breathing complications and also free the staff up to attend to other tasks."