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LETTER TO THE EDITOR

The use of red cell units containing additives in large volume neonatal transfusion in neonatology units in the USA

R. Pyles,[1] J. Lowery[2] & M. Delaney[3,4]

[1]*SSM Health Cardinal Glennon Children's Hospital, St. Louis, MO, USA*
[2]*American Red Cross, Durham, NC, USA*
[3]*Seattle Children's Hospital, Bloodworks Northwest, Seattle, WA, USA*
[4]*Department of Laboratory Medicine, University of Washington, Seattle, WA, USA*

Dear Editor,

Red blood cell products (RBCs) are often stored in a solution of adenine, dextrose and mannitol. The purpose for the additive solutions is to provide adenine and dextrose for intracellular metabolism and mannitol to diminish RBC lysis during storage [1]. The additive solutions extends the shelf life of an RBC unit, allowing storage up to 42 days. Although RBC additive use is widespread, there has been lingering concern about the constituents in additive solutions (AS) being potentially detrimental to neonatal patients' developing organ systems, most notably the renal and hepatic systems [1]. Due to the concern about increasing donor exposure and potassium exposure, several studies were undertaken to observe if the use of RBCs with AS cause harm. The authors found that, in the low volume transfusion setting (10–15 ml/kg dose), RBC products containing additives are safe and well tolerated in neonatal patients [2–8]. Furthermore, additional survey data have been collected supporting the use or willingness to use AS containing RBCs for small volume neonatal transfusion [9]. However, the question of whether using AS RBCs in the large volume transfusion setting (≥20 ml/kg), which will deliver relatively more AS to the patient, is unanswered. In fact, the dose of additive solution judged in theory to be toxic for neonatal patients during common large volume transfusion settings (≥20 ml/kg) is difficult to estimate accurately for several reasons. The clinical setting, duration of exposure to additive solutions, bioavailability of solutes, intracellular trapping of solutes and dispersion to extracellular compartments of solutes, combined with the patient's renal and hepatic status all complicate toxic dose calculations [1].

Due to the lack of evidence and the concerns cited above for large volume (≥20 ml/Kg) transfusion settings, many US-based paediatric transfusion services manage two red blood cell (RBC) inventories for neonatal patients; the first composed of low or additive free RBCs, such as CPD or CPDA RBCs, often meant to be used for large volume transfusions, and the second composed of AS-1, AS-3, or AS-5 RBCs for older paediatric patients or to use when small volume transfusions are being ordered. The goal of the survey was to assess neonatal transfusion practice at a subset of US-based institutions concerning RBC additive of choice in a variety of large volume transfusion settings.

An electronic survey was sent to 78 facilities throughout the United States identified as being associated with professional organizations such as the College of American Pathologists or the American Association of Blood Banks. Our objective was to assess neonatal transfusion practice at a subset of institutions concerning RBC additive of choice and product manipulation that may potentially decrease the additive dose in a variety of large volume transfusion settings. To standardize some terminology and for the purposes of data collection, neonates were defined as <4 months of age, small volume transfusion was defined as <20 ml/kg, and large volume transfusion was defined as ≥20 ml/kg. Responses were collected over a 1-month time period.

There were 21 centres that responded to the survey (27% response rate), 24% were paediatric only, and 76% were both adult and paediatric. The majority (90·5%) of responding centres identified as academic facilities. The median neonatal intensive care unit (NICU) size was 46 beds (range 15–604). For large volume transfusions in neonatal patients, 43% of responding centres use AS-3 RBC units, 29% use AS-1 RBCs and 28% use CPD or CPDA RBC units.

A large proportion of centres provide fresh AS RBCs in large volume transfusion settings, presumably to mitigate the risk of transfusion-associated hyperkalaemia, although we did not specifically ask about the rationale for RBC modifications (Table). Participants were asked to provide their definition of fresh stored RBCs from a

Correspondence: Ryan Pyles, SSM Health Cardinal Glennon Children's Hospital, St Louis, MO, USA.
E-mail: ryan_pyles@ssmhc.com

Table 1 Additional AS-RBC product modifications for use in different neonatal large volume transfusion settings

Clinical setting of large volume transfusion	Fresh (%)	Washed (%)	Supernatant reduced (%)	No modifications (%)
General surgery (n = 13)	61	8	8	23
Cardiac surgery (n = 12)	75	8	0	17
ABO incompatible heart transplant (n = 7)	29	43	14	14
Extra corporeal life support (n = 10)	80	10	0	10
Exchange transfusion (n = 13)	69	15	8	8

choice of less than <5, <7, <10 and <14 days; <10 days old was selected as the median of responding centres. The highest proportion of washed AS RBCs are provided in centres with ABO incompatible heart transplant programmes; in this setting, the removal of isohaemagglutinins is the target. Further modifications of AS units are generally infrequent (Table 1).

In conclusion, our survey shows that a significant proportion of responding centres use AS containing RBCs in large volume neonatal transfusions, and that most are considering the age of the product. The results suggest that there is enough usage of large volume AS RBCs transfusion to support future study of the physiology of this clinical scenario. A pragmatic comparative effectiveness study design may be an advantageous way to approach study of large volume neonatal RBC transfusions, due to the range of practice found in US centres.

Conflict of interests

The authors RP and JL declare no conflict of interests. MD received honoraria from Janssen (one time advisory board) and one time consulting SIO Capital, LLC.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1 Survey of the use of red cell additive solutions and special attributes in neonatal patients.