16 Paediatric Summary

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Definition:

Paediatric cases comprise all reports for patients under 18 years of age, including all paediatric cases from the other chapters in this report. Paediatric reports have been subdivided by recipient age group: neonates ≤28 days; infants >28 days and <1 year old; children ≥1 year to <16 years and young people aged 16 to <18 years.

Key SHOT messages

- There were several cases of adult emergency O D-negative red cell units having been used for neonatal resuscitation despite availability of neonatal emergency packs. Local measures should be in place to help guide staff to select the correct component in emergency situations
- A total of 5 reports related to babies undergoing neonatal exchange transfusion; one died and another had severe clinical deterioration. Exchanges are invasive procedures now performed rarely. They require special components with a short shelf-life with which staff may be unfamiliar. Babies undergoing exchanges are by definition vulnerable
- Laboratory errors result from inadequate neonatal pre-transfusion testing or failure to provide phenotyped blood, which in the context of other laboratory errors reported to SHOT suggest the need for increased support and training for laboratory staff
- The increased reporting of transfusion-associated necrotising enterocolitis (NEC) cases is encouraged in order to improve understanding of this condition in the United Kingdom (UK)

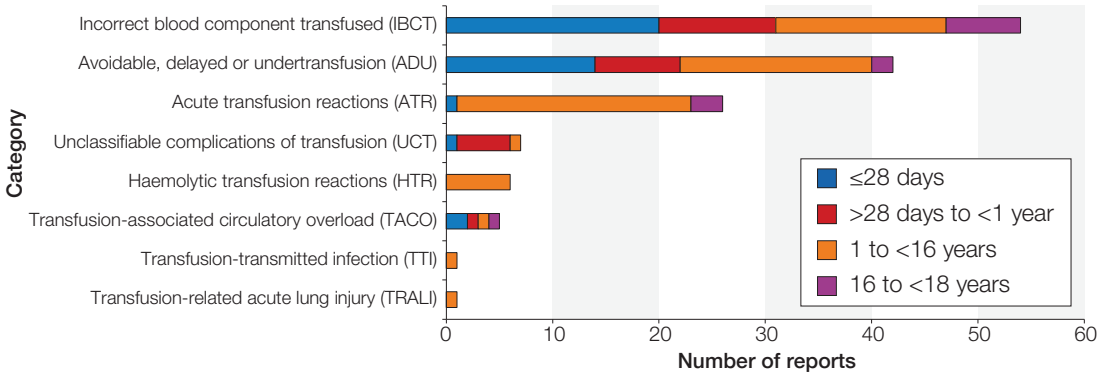

Figure 16.1: Summary of paediatric cases 2015 by most frequent category and age

Introduction and overall trends

Paediatric reports have increased from 221 in 2014 to 274 in 2015. These contributed 162/1858 (8.7%) of incident reports in 2015, and the total of 274/3288 (8.3%) when near miss (NM) and right blood right patient errors (RBRP) are included.

Six cases of transfusion-associated necrotising enterocolitis (NEC) were reported (discussed in Chapter 15, New or Unclassifiable Complications of Transfusion (UCT)).

Deaths where the transfusion contributed n=6

In total there were 18 deaths (12 unrelated to transfusion) in the paediatric age group, of which 14 were neonates or young infants consistent with the vulnerability of this young population.

Of the 6 deaths that were assessed as being related to transfusion, there were 2 cases of transfusion-associated circulatory overload (TACO) possibly related, 3 cases of necrotising enterocolitis (NEC) possibly related, and 1 Anti-D immunoglobulin (Ig) failure which was probably related (Case 1 in Error Reports: Human Factors section).

Major morbidity n=22

(ATR n=11, HTR n=3, IBCT WCT laboratory n=3, UCT n=2, transfusion-associated circulatory overload (TACO) n=1, transfusion-related acute lung injury* (TRALI) n=1, TTI n=1)

*this case was thought to be unlikely TRALI

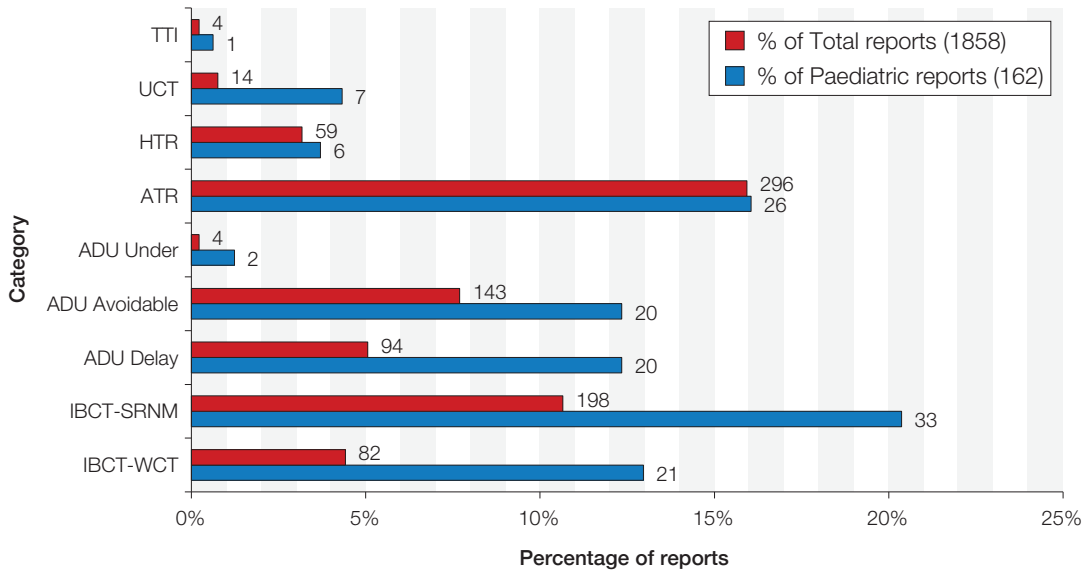

Figure 16.2: Percentages and numbers of paediatric and total reports in key categories

TTI: transfusion-transmitted infection; HTR: haemolytic transfusion reaction; ATR: acute transfusion reaction, IBCT: incorrect blood component transfused; SRNM: specific requirements not met; WCT: wrong component transfused

Error-related reports n=112

(IBCT, handling and storage errors (HSE), ADU and anti-D)

These were 112/162 (69.1%), compared to 71/122 (58.2%) in 2014. There was an increase in paediatric cases (42/162) in the ADU category (Figure 16.2). Almost half (20/42, 47.6%) were reports of delays to transfusion.

A total of 45/112 (40.2%) errors originated primarily in the laboratory (9 wrong components transfused (WCT), 20 specific requirements not met (SRNM), 6 HSE, 8 ADU, 2 anti-D Ig).

Charts showing trends in paediatric reports over time can be found in the supplementary information on the SHOT website www.shotuk.org.

Incorrect blood component transfused (IBCT) n=54

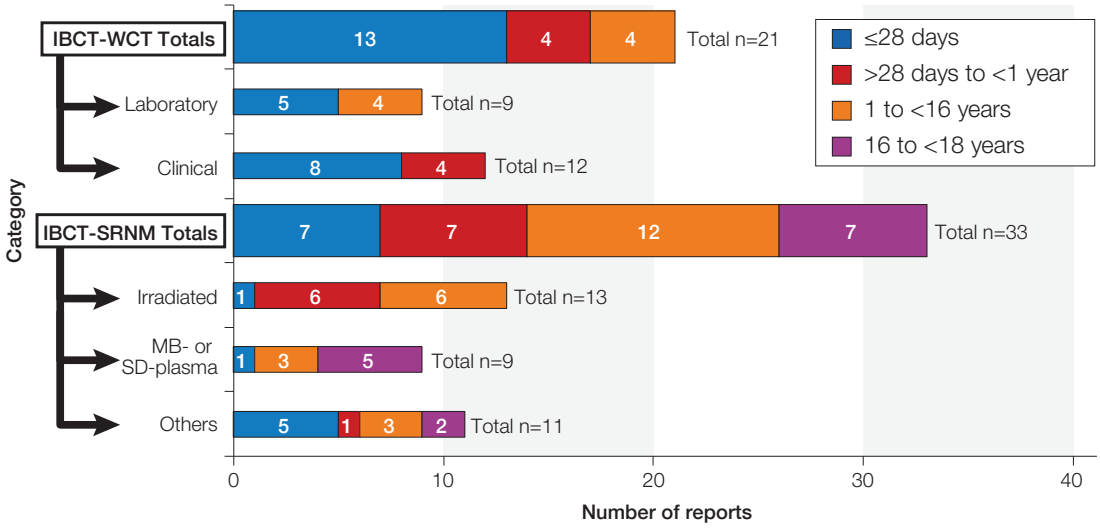

Figure 16.3: Reports of an incorrect blood component transfusion: type and age group

IBCT: wrong component transfused (WCT) n=21

Clinical errors n=12

There were 12 clinical errors where adult O D-negative emergency red cell units were collected and transfused instead of emergency units suitable for neonatal use. Most were transfused to neonates within the first few days of life. Four were young infants, all related to the same incident, where adult units were taken from the remote issue refrigerator for the infant transfusions.

Laboratory errors n=9

- Non-neonatal red cells given for neonatal exchange
- See supplementary information on the website for the other 8 cases

Case 16.1: Severe clinical deterioration following neonatal exchange with adult red cells

A neonate, blood group A, with severe ABO haemolytic disease of the newborn underwent a double-volume exchange transfusion, following continuing rise in bilirubin levels despite phototherapy and intravenous immunoglobulin (IVIg). There were no clinical problems noted with carrying out the exchange procedure according to protocol but immediately following exchange, the baby deteriorated and developed multiorgan failure with disseminated intravascular coagulation and evidence of ongoing haemolysis. The baby required resuscitation and multiple blood component transfusions over several days and was also given further IVIg as well as steroids and ongoing antibiotics. The haematology team liaised closely and gave advice on management but unfortunately did not instigate formal investigations for a transfusion reaction. The baby was discharged home well several days later.

Subsequently it was realised that the unit ordered and used for the exchange procedure was an irradiated group O adult unit of red cells suspended in saline adenine glucose mannitol (SAGM), that was not high-titre (HT) negative, containing high-titre anti-A (IgM 1:512). The unit had been requested in the early hours of a Sunday morning by a biomedical scientist (BMS) without previous experience of ordering blood for neonatal exchange transfusion and who had last been rotated into the blood transfusion laboratory 3 months previously. The standard operating procedure (SOP) did not include specific instructions about the correct component to order. The product name for neonatal exchange units on the Blood Service electronic ordering system drop-down menu is 'Exchange Red Cells Irradiated', without specifying 'neonatal'. The BMS was confused by this and selected 'Red Cells Irradiated' instead, ticking several additional optional requirements and adding a line note that the blood was required for neonatal exchange transfusion, HT-negative. The Blood Service staff did

not take account of all the line notes as these did not align with the system-controlled component requested by the BMS.

Comment: The cause of the sudden clinical deterioration is not certain in this complex case. It could not be explained by electrolyte disturbances. Bacterial sepsis was considered by the clinical team but felt to be unlikely as the baby did not behave clinically as expected for sepsis and the C-reactive protein (CRP) was not significantly raised. However, the baby did not have a blood culture sent after deterioration and the blood bag was not cultured so sepsis was not formally excluded.

After careful review it was felt that the least unlikely cause of the clinical deterioration after exchange transfusion was the HT anti-A antibodies in the transfused red cell unit causing an acute haemolytic transfusion reaction (with possible additional bystander haemolysis causing destruction of transfused red cells). However, as only a small volume of plasma was infused in the SAGM unit (approximately 15mL), such a reaction would be very unusual and it was not established that the donor IgM anti-A was lytic in vitro (so low imputability). Moreover, there was already maternal IgG anti-A present (IgG titre of 1 in 8000 in the maternal plasma). The bilirubin was already high due to this, but did not rise much further after exchange transfusion. The neonatal plasma was not inspected for increased haemolysis post exchange. Both IgG and IgM ABO antibodies bind complement and both can cause intravascular haemolysis. IgM binds complement more easily, but neonatal complement levels are usually low. Alternatively, IgM anti-A can cause in vitro agglutination in the absence of complement, and these can become trapped in the sinusoidal circulation but it is not clear which processes were active in this instance.

Red cells other than of neonatal/infant specification are not labelled as negative for high-titre anti-A/B as it is not considered that the small volume of plasma in SAGM red cells constitutes a significant risk (BCSH Milkins et al.).

Learning points

- *Biomedical scientist (BMS) training*

Neonatal exchange transfusions are relatively rarely performed now, and BMS staff may lack knowledge and experience of the specific component required. Staff rotate between laboratories and may only have basic training in blood transfusion. Even where there are specific standard operating procedures (SOP) available giving guidance, BMS staff may not know where to find them. Once a specialised component has been ordered from the Blood Service, hospital laboratory staff should not assume that it has been provided correctly and still need to specifically check the provided product on arrival

- *Computer ordering systems*

When ordering components from the Blood Service, product names are not always consistent between all documents, software and labels (see also Case 6.7 in Chapter 6, Incorrect Blood Component Transfused (IBCT)). When using computer system-controlled drop-down menus, the role of additional explanatory 'line notes' is not always clear as they are not information technology (IT)-controlled in the same way

- *Investigation of suspected transfusion reactions*

Where there has been a significant clinical deterioration during or following a transfusion, local standard procedures and British Committee for Standards in Haematology (BCSH) guidelines (BCSH Tinegate et al. 2012) should be followed for investigation of a transfusion reaction in order not to miss possible transfusion-related events and to ensure adequate investigation e.g. for bacterial contamination, unit incompatibility, and whether an appropriate component was transfused

- *Neonatal exchange transfusion components and procedure*

Neonates undergoing exchange transfusion are vulnerable. There is a need to ensure that the correct component is used for the exchange transfusion and there needs to be meticulous monitoring during and following the procedure, including fluid balance and Hb levels

- *Role of high-titre (HT) antibodies in causing the haemolytic transfusion reaction*

For non-neonatal/infant red cell units, information on HT screening is not considered clinically necessary given the low risk related to the low volume of plasma in standard *saline adenine glucose mannitol (*SAGM) units. However HT-negative is recommended for neonatal/infant specification blood, and is particularly important for neonatal exchange units which contain a higher volume of plasma

Neonatal exchange transfusion has been the subject of a British Paediatric Surveillance Unit (BPSU) survey between October 2014 and October 2015 (BPSU 2015, Gottstein et al. 2016). Little is known about indications and complications of this procedure. Details of the protocol are available at www.rcpch.ac.uk/bpsu/ebt. The results are not yet fully available but data published in abstract reports complete data collection for 93 babies who had 1 to 5 exchanges (total 115), the majority (86%) for hyperbilirubinaemia (secondary to haemolysis). Time to obtain suitable red cells varied from 22 minutes to 17 hours (median 4 hours 35 minutes). Four babies died, one from splenic rupture related to the procedure and 3 from their underlying disease. The outcome will be to develop appropriate guidance.

IBCT: specific requirements not met (SRNM) n=33

Additional details can be found in the supplementary information on the SHOT website www.shotuk.org.

- Clinical cases where requirements were not communicated properly to laboratory: n=13
- Primary error in the laboratory: n=20

Avoidable, delayed or undertransfusion (ADU) n=42

- Delays to transfusion: 20 (various reasons – included three neonatal exchange transfusions due to problems associated with the exchange component: age, shelf-life, irradiation)

Additional details can be found in the supplementary information on the SHOT website www.shotuk.org.

Handling and storage errors (HSE) n=14

- Technical administration error: 4 (pump setting error: 1 transfusion given too quickly; no/incorrect giving set in 3)

Case 16.2: Inappropriate method of administration in an emergency

A 1 year old boy was transferred to the emergency department (ED) from a private clinic with major haemorrhage following circumcision. He was managed by a paediatric trauma team who activated the major haemorrhage protocol resulting in 2 emergency O D-negative adult units being brought to the ED. No paediatric giving sets could be found in the ED so the anaesthetist punctured the blood bag several times with needles and syringes and gave blood directly by peripheral venous access with no blood giving set which would normally incorporate a mesh filter. The punctured bag was found leaking in the sink in the ED. The child recovered fully.

Review of this case identified the need for training of paediatric, anaesthetic and ED staff in safe transfusion procedures. Porters needed training to recognise both types of emergency O D-negative units, paediatric and adult. The ED nursing staff were empowered to challenge inappropriate practice by other professionals.

Anti-D Ig n=2

There were no cases related to pregnancy. The two cases were:

- A 3 year old girl who was B D-negative was given B D-positive platelets without receiving prophylaxis with anti-D immunoglobulin. It was a laboratory error which should have been detected by the ward
- A neonate with high bilirubin and probable haemolytic disease of the newborn was born to a mother who had developed immune anti-D (Chapter 9, Anti-D Immunoglobulin (Ig) Errors). The baby died of clinical complications during the exchange transfusion (Case 1 in the Error Reports: Human Factors section)

Transfusion reactions n=50

Acute transfusion reactions (ATR) n=26

This year paediatric ATR made up 26/296 total ATR reports (8.8%). Severe paediatric reactions were reported in 11/26 (42.3%) but there were no deaths. There was only one ATR reported in a neonate (to SD-FFP, see below), and none in infants.

The percentages of ATR shows that the majority were to platelets: red cells 19%, platelets 69%, plasma 8%, granulocytes 4%.

Further details can be found in the supplementary information on the SHOT website www.shotuk.org.

Haemolytic transfusion reactions (HTR) n=6

See Chapter 14, Haemolytic Transfusion Reactions for details; two episodes were reported in the same patient.

Note also neonatal exchange case with possible haemolysis related to HT donor antibodies.

Transfusion-associated circulatory overload (TACO) n=5

There were two cases in neonates. One was severe TACO after a double exchange transfusion, Case 16.3 below. The second was a 25 weeks gestation, 21 day old baby with chronic lung disease who developed increasing respiratory symptoms following a 15mL/kg top-up transfusion.

Case 16.3: TACO following exchange transfusion for hyperbilirubinaemia

A preterm baby aged 6 days was admitted unwell with severe hyperbilirubinaemia and acidosis, requiring ventilation. During the exchange transfusion, the respiratory function deteriorated with decreased oxygen saturations and increased respiratory rate. The Hb increased from 132g/L to 218g/L following the exchange, and the fluid balance was 105mL positive (45mL/kg). The baby developed worsening renal failure, coagulopathy and poor perfusion, had cardiac arrests and died the following day. It was felt that the exchange transfusion was contributory to the deterioration.

The case illustrates the vulnerability of neonates undergoing exchange transfusion and the need for meticulous monitoring of the procedure including fluid balance and Hb levels.

Case 16.4: TACO following a top-up transfusion

A 13kg one year old showed evidence of TACO following transfusion of an apheresis unit of platelets (approximately 20mL/kg) followed by 150mL red cells (approximately 400mL in total).

Unclassifiable complications of transfusion (UCT) n=7

There were 6 babies aged about 1 month with necrotising enterocolitis (NEC) following packed red cell transfusions, of which 4 died. (For further details and the additional case, see Chapter 15, New or unclassifiable complications of transfusion (UCT)).

Transfusion-transmitted infection (TTI) n=1

A 13 year old liver transplant recipient was diagnosed with hepatitis E virus (HEV) infection following a platelet transfusion. This case was identified in the investigation following a confirmed HEV transmission in another adult recipient.

Near miss (NM) n=97 and right blood right patient (RBRP) n=15

Recommendations

- Adult O D-negative units are unsuitable for neonatal emergency use. Dedicated neonatal O D-negative units should be available for emergency use in neonates. Local measures should be in place to help guide staff to select the correct red cell component for neonatal resuscitation in emergency situations
- Particular attention should be provided for laboratory staff training regarding the specification and ordering of neonatal exchange components in hospitals with neonatal intensive care units

References

BCSH Milkins C et al. (2013) **Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories**. Transfus Med 23, 3-35

BPSU survey Gottstein R (2015) **Neonatal exchange transfusion in infants <28 days** https://issuu.com/joballrcpch/docs/annualreport201415_web [accessed 27 April 2016]

Gottstein R, Rennie J et al. (2016) **Neonatal exchange blood transfusion – A 13 month survey in UK and Ireland**. Arch Dis Child 101 (Suppl 1), A254-A255