16 Acute Transfusion Reactions (Allergic, Hypotensive and Severe Febrile) (ATR) n=253

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Definition:

Acute transfusion reactions are defined in this report as allergic, hypotensive and severe febrile reactions, occurring up to 24 hours following a transfusion of blood or components, for which no other obvious cause is evident.

Introduction

These reactions are classified according to the International Haemovigilance Network/International Society for Blood Transfusion (IHN/ISBT) definitions which are summarised in Table 16.2, available on-line (ISBT/IHN 2011) and have been adopted by the British Society for Haematology (BSH) (BSH Tinegate et al. 2012).

Cases of acute reaction due to incorrect component transfused, haemolytic reaction, transfusion-related acute lung injury (TRALI), transfusion-associated circulatory overload (TACO), transfusion-associated dyspnoea (TAD) or those due to bacterial contamination of the component are excluded.

Key SHOT message

- A reduction in the number of ATR reported corresponds with the decrease in blood components issued. This relationship is most evident for commonly-used components such as red cells and platelets and provides support for the message that only patients likely to benefit should receive blood

Recommendation

- Platelets suspended in platelet additive solution (PAS) are associated with a reduction in allergic response (BSH Estcourt et al. 2017). Hospitals should consider preferential use of readily available pooled platelets suspended in PAS in patients with a history of allergic reactions. This should include paediatric patients where apheresis platelets are usually the platelet component of choice. If reactions continue, despite antihistamine cover, then platelets resuspended in 100% PAS can be supplied

Action: Hospital Transfusion Teams (HTT)

- Give appropriate targeted treatment and if needed, preventive cover for future transfusion (BSH Tinegate et al. 2012), as indicated below:

Action: HTT

Table 16.1: Targeted treatment for future transfusion reactions

Reaction	Treatment	Prevention of recurrent reactions
Febrile	Paracetamol	Paracetamol 60 minutes before anticipated time of reaction
Allergic	Antihistamine (steroid should not be used routinely) If anaphylaxis, adrenaline is essential	If previous reaction with apheresis platelets try pooled platelets in PAS If recurrent, give antihistamine before transfusion If recurrent, consider washed platelets/red cells; for fresh frozen plasma (FFP) try a pooled component e.g. solvent-detergent treated plasma

Key recommendations from previous years can be found in the supplementary information on the SHOT website www.shotuk.org.

	1 = Mild	2 = Moderate	3 = Severe
Febrile type reaction	A temperature ≥38°C and a rise between 1and 2°C from pretransfusion values, but no other symptoms/signs	A rise in temperature of 2°C or more, or fever 39°C or over and/or rigors, chills, other inflammatory symptoms/signs such as myalgia or nausea which precipitate stopping the transfusion	A rise in temperature of 2°C or more, and/or rigors, chills, or fever 39°C or over, or other inflammatory symptoms/signs such as myalgia or nausea which precipitate stopping the transfusion, prompt medical review AND/OR directly results in, or prolongs hospital stay.
Allergic type reaction	Transient flushing, urticaria or rash	Wheeze or angioedema with or without flushing/urticaria/ rash but without respiratory compromise or hypotension	Bronchospasm, stridor, angioedema or circulatory problems which require urgent medical intervention AND/OR, directly result in or prolong hospital stay, or Anaphylaxis (severe, life-threatening, generalised or systemic hypersensitivity reaction with rapidly developing airway and/or breathing and/or circulation problems, usually associated with skin and mucosal changes
Reaction with both allergic and febrile features	Features of mild febrile and mild allergic reactions	Features of both allergic and febrile reactions, at least one of which is in the moderate category.	Features of both allergic and febrile reactions, at least one of which is in the severe category.
Hypotensive reaction		Isolated fall in systolic blood pressure of 30 mm or more occurring during or within one hour of completing transfusion and a systolic blood pressure 80 mm. or less in the absence of allergic or anaphylactic symptoms. No/minor intervention required.	Hypotension, as previously defined, leading to shock (e.g. acidaemia, impairment of vital organ function) without allergic or inflammatory symptoms. Urgent medical intervention required.

Table 16.2: Classification of reactions

Number of reactions and reaction rates n=253

Deaths n=0

There were no deaths related to the transfusion reaction.

Major morbidity n=76

Severe reactions, as classified above, are used to define major morbidity reactions.

Reactions have been classified as follows:

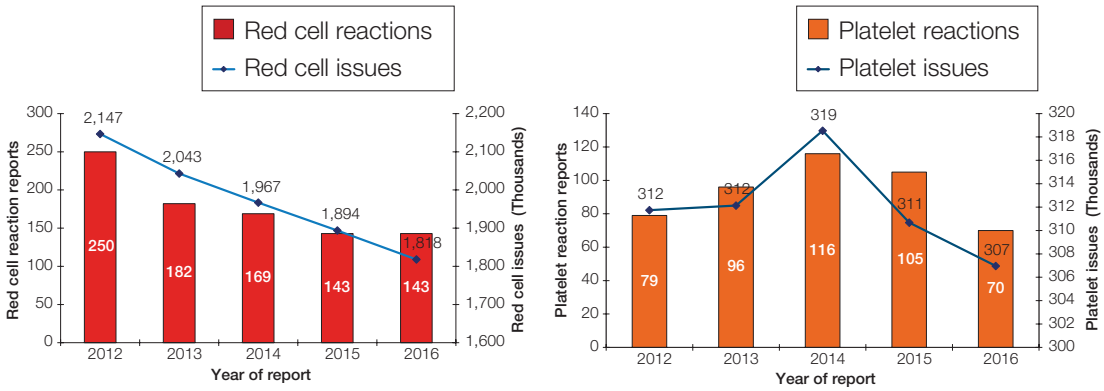
	Moderate	Severe	Total
Febrile	98	26	**124**
Allergic	61	46	**107**
Mixed allergic/febrile	14	4	**18**
Hypotensive	4	0	**4**
Total	**177**	**76**	**253**

N.B. in 40 of the 76 reactions classified as severe this was primarily because the patient was admitted

Table 16.3: Classification of ATR in 2016

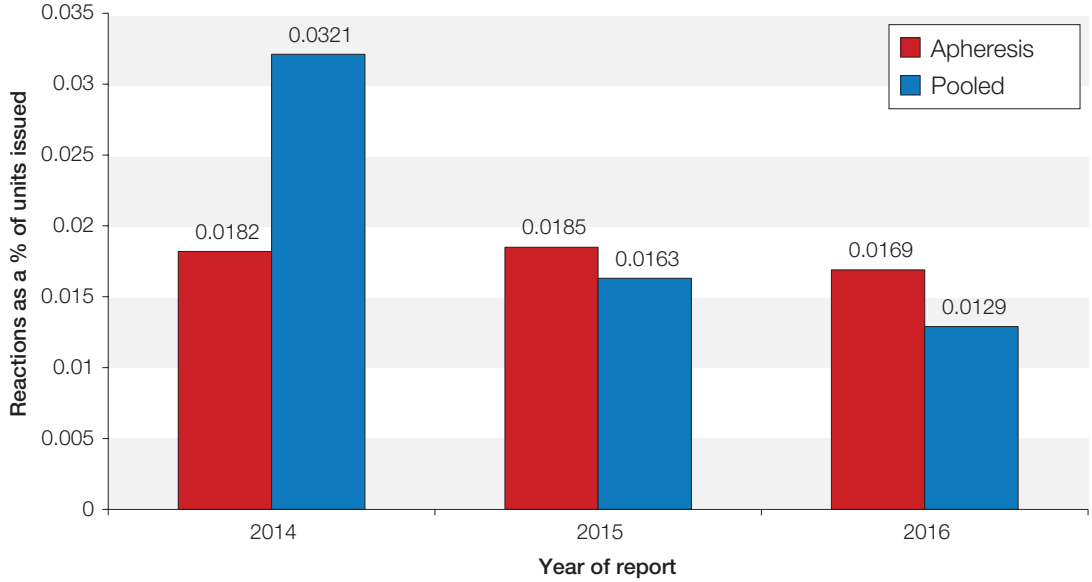
The total number of reactions reported over the last few years has reduced in keeping with the fall in total blood component demand. For the two most commonly used blood components, red cells and platelets, the relationship between units issued and reactions reported is striking; Figure 16.1. There is less correlation with other blood components likely because of the smaller number of reactions reported.

Figure 16.1: Reactions related to the number of issues from UK Blood Services



In addition to the reduction in platelet demand, suspension of pooled platelets in PAS, which is now universal in England and Wales, is also likely to have contributed to the reduction in reactions. This year, in these countries, in keeping with 2015 data, allergic reactions associated with pooled platelets are fewer than with apheresis platelets. This is in contrast to reaction rates in 2014 when both components were suspended in plasma; Figure 16.2.

Figure 16.2: Percentage of allergic reactions 2014 to 2016



Type of reactions by component

This remains similar to previous reports; Figure 16.3. Red cells are usually associated with febrile-type reactions (~75%) whereas plasma and platelets more commonly cause allergic reactions (~80% and ~60% respectively). Only one reaction associated with methylene blue treatment was reported. The percentage of severe reactions remains similar to 2014 and 2015 at 30.0% (76/253). As in previous years, many reactions were difficult to classify as a result of insufficient information, the IHN/ISBT grade of reaction not being used and because of the difficulty distinguishing true transfusion reactions from symptoms and signs associated with the patient's underlying condition.

Analysis of reactions remains comparable in the following parameters:

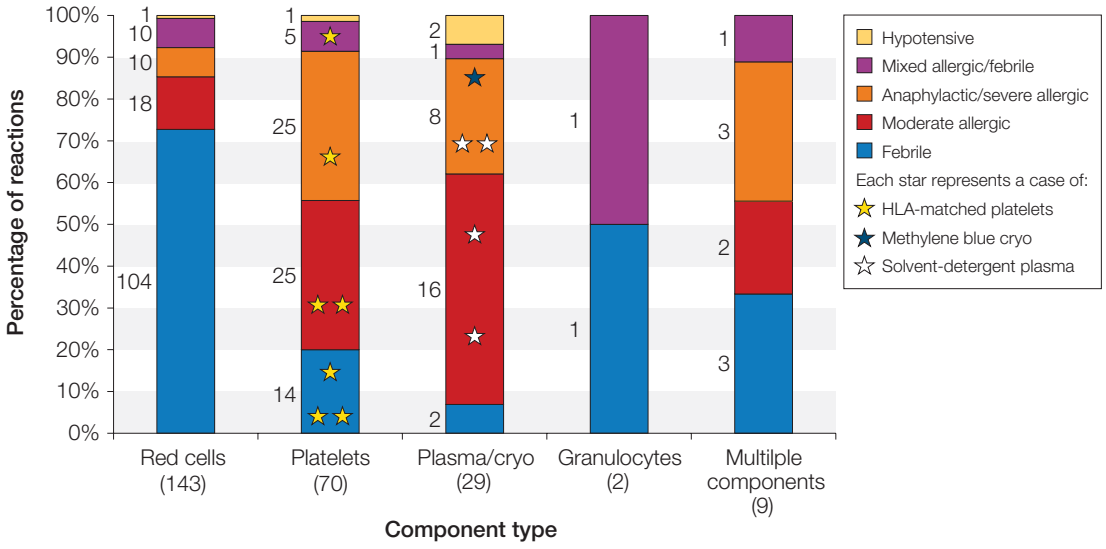


Figure 16.3: Reaction by component type

Characteristic	Occurrence
Age distribution	About 90% of patients were aged 18 years or over
Gender	Similar numbers of male and female cases
Urgency of transfusion	70% were given routinely
Timing of transfusion	About 60% occurred within standard hours
Location	About 50% were on wards and 20% in outpatient/day case units

Table 16.4: Characteristics of ATR

Treatment of reactions

Similar to previous years an antihistamine with or without steroid continues to be a common treatment of reactions with only febrile/inflammatory type symptoms and/or signs; Table 16.5. In addition to no evidence of benefit, the use of steroids may immunosuppress some already immunocompromised patients and increase the risk of side effects such as infection and other adverse events (Waljee et al. 2017).

Following a pure febrile reaction, in cases where details of subsequent management were provided, 42.9% planned use of an antihistamine with or without steroids; Table 16.6.

Given the evidence for reduced allergic reactions to pooled platelets suspended in PAS compared to apheresis platelets, analysis of future management following allergic reactions to apheresis platelets was identified. Thirty-one allergic reactions to apheresis platelets occurred and future management was stated in 18/31. In 10/18 premedication was advised, in 4/18 washed platelets were advised, in 1/18 human leucocyte antigen (HLA)/human platelet antigen (HPA) testing was advised and in only 3/18 were pooled platelet components recommended.

Table 16.5: Treatment of reported reaction

	Number	Medication stated	Antihistamine +/- steroid
Febrile			
2016	124	102/124 (82.3%)	51/102 (50.0%)
2015	142	101/142 (71.1%)	57/101 (56.4%)
2014	144	97/144 (67.4%)	42/97 (43.3%)
	Number	**Medication stated**	**Paracetamol**
Allergic			
2016	107	101/107 (94.4%)	11/101 (10.9%)
2015	122	106/122 (86.9%)	10/106 (9.4%)
2014	139	112/139 (80.6%)	14/112 (12.5%)

Table 16.6: Planned treatment for subsequent febrile reactions

	Number where treatment stated	Antihistamine +/- steroid
2016	21	9/21 (42.9%)
2015	9	7/9 (77.8%)
2014	24	9/24 (37.5%)

Illustrative cases

Case 16.1: A febrile reaction treated with hydrocortisone and chlorphenamine

An adult male with sickle cell disease attended an outpatient department to receive an exchange blood transfusion. After the first unit of red cells he developed rigors. Observations revealed a temperature of 38.6°C and a rise of 2°C. His blood pressure was also increased compared to pre-transfusion observations but there were no respiratory signs or symptoms. The transfusion was discontinued and he was given hydrocortisone and chlorphenamine. He recovered in less than one hour and was subsequently admitted to the ward for antibiotics to treat a possible chest infection. Repeat serology and blood culture of the patient and implicated unit were negative.

Although admission may have been required to manage a possible underlying infection it is difficult to understand why hydrocortisone and chlorphenamine were considered to be appropriate.

Case 16.2: A moderate febrile reaction resulting in transfer of the patient from a community hospital to a larger hospital with an emergency department

An elderly male with myelodysplastic syndrome (MDS) received two units of red cells in a community hospital. He was known to have anti-C, anti-Kp^a and a non-specific autoantibody. Following transfusion of his second unit routine observations identified a temperature rise from 36.9°C prior to transfusion to 38.7°C. An ambulance was called and the patient transferred to the emergency department at a larger hospital. On arrival he was given paracetamol, his temperature settled and he was discharged home. Repeat serology, and culture of the patient and implicated unit revealed nil significant.

Febrile-type reactions, although not serious, can alarm clinical staff and result in significant time and resource to investigate and manage.

Case 16.3: An allergic reaction to apheresis platelets

An elderly male with MDS and possible sepsis but no bleeding received a unit of apheresis platelets. Ten minutes after starting the transfusion he developed a swollen tongue and was unable to talk. His observations were stable, the transfusion was discontinued and he was given intravenous hydrocortisone. The reaction resolved and a decision made that further platelet transfusion should routinely be covered with both hydrocortisone and chlorphenamine.

A patient with MDS at an increased risk of infection may have benefitted more from prudent use of platelet transfusion and pooled platelets suspended in platelet additive solution as an alternative to premedication for apheresis platelets, if required.

Case 16.4: A severe reaction in a patient with IgA deficiency

An adult female received transfusion of red cells to treat a postpartum bleed on the delivery ward. Within 15 minutes of the start of the transfusion she developed a fever, chest tightness and throat swelling associated with a temperature rise of more than 2°C to 39.7°C, dyspnoea and visible angiodema. She received paracetamol, an antihistamine, hydrocortisone and intravenous adrenaline. After 4 hours her observations settled. Subsequent investigation identified that she was IgA deficient with IgA antibodies and IgA deficient or washed red cells were recommended for any future transfusion.

Reactions associated with IgA deficiency are rare despite a prevalence of IgA deficiency of around 1 in 200. In this case symptoms of allergy were present, which are considered standard, but in addition a fever occurred more typical of a febrile type reaction. A similar reaction was reported last year and included in the illustrative cases.

References

BSH Tinegate H, Birchall J, et al. (2012) **Guideline on the investigation and management of acute transfusion reactions. Prepared by the BCSH Blood Transfusion Task Force.** Br J Haematol 159(2),143-153

BSH Estcourt LJ, Birchall J et al. (2017) **Guidelines for the use of platelet transfusions.** Br J Haematol 176(3), 365-394

ISBT/IHN, Haemovigilance Working Party of the ISBT (2011) **Proposed standard definitions for surveillance of non-infectious adverse transfusion reactions.**
http://www.ihn-org.com/wp-content/uploads/2011/06/ISBT-definitions-for-non-infectious-transfusion-reactions.pdf [accessed 21 March 2017]

NHSBT (2015/16) **Histocompatibility and immunogenetics diagnostic services user guide.**
http://hospital.blood.co.uk/diagnostic-services/diagnostic-user-guides/ [accessed 21 March 2017]

Resuscitation Council (2008) **Emergency treatment of anaphylactic reactions.**
http://www.resus.org.uk/pages/reaction.pdf [accessed 21 March 2017]

Waljee AK, Rogers MAM et al. (2017) **Short term use of corticosteroids and related harms among adults in the United States: population based cohort study.** Br Med J 357 https://doi.org/10.1136/bmj.j1415 [accessed 15 April 2017]