14 Acute Transfusion Reactions (ATR) n=343

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Definition:

Acute transfusion reactions are defined in this report as those occurring at any time up to 24 hours following a transfusion of blood or components excluding cases of acute reactions due to incorrect component being transfused, haemolytic reactions, transfusion-related acute lung injury (TRALI), transfusion-associated circulatory overload (TACO), transfusion-associated dyspnoea (TAD) or those due to bacterial contamination of the component. However, the possibility that a reaction could belong to one of these serious reaction categories must be kept in mind during recognition, initial assessment and treatment.

Note that for the purposes of the European Union (EU) legislation, serious adverse reactions (SAR) are defined as any reactions in patients that are 'life threatening, disabling or incapacitating, or which result in or prolong hospitalisation or morbidity.' These must be reported to the Medicines and Healthcare products Regulatory Agency (MHRA) (a legal requirement). In the SHOT category of ATR the following reactions are included:

- Anaphylaxis / hypersensitivity
- Febrile non-haemolytic reactions (FNHTR)

Key SHOT messages

- The treatment of reactions and management of subsequent transfusions should be directed by recognised guidelines e.g. the British Committee for Standards in Haematology (BCSH) Guidelines on the investigation and management of acute transfusion reactions (BCSH Tinegate et al. 2012)
- SHOT has a role in identifying trends in reactions and events, including the monitoring of new components. If reactions are related to washed red cells or platelets in additive solution (PAS) (60-70%), or the forthcoming component 'washed platelets (100% PAS)' the reporter should indicate this on the appropriate implicated red cell or platelet component question

Introduction

There were 343 acute transfusion reactions analysed. The reactions included in this analysis are febrile type, allergic and hypotensive reactions for which no other obvious cause is evident. These are classified according to the International Haemovigilance Network/International Society for Blood Transfusion (IHN/ISBT) definitions which are summarised below in Table 14.1, available online (ISBT/IHN 2011) and which have been adopted by the British Committee for Standards in Haematology (BCSH) (BCSH Tinegate et al. 2012).

	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 14.1: Classification of reactions

Types of reactions

Reactions have been classified as follows:

	Moderate	Severe	Total
Febrile	117	27	**144**
Allergic	81	58*	**139**
Mixed allergic/febrile	16	9	**25**
Hypotensive	4	0	**4**
Unclassified	21	10	**31**
Total	**239**	**104**	**343**

**Anaphylactic/severe allergic*

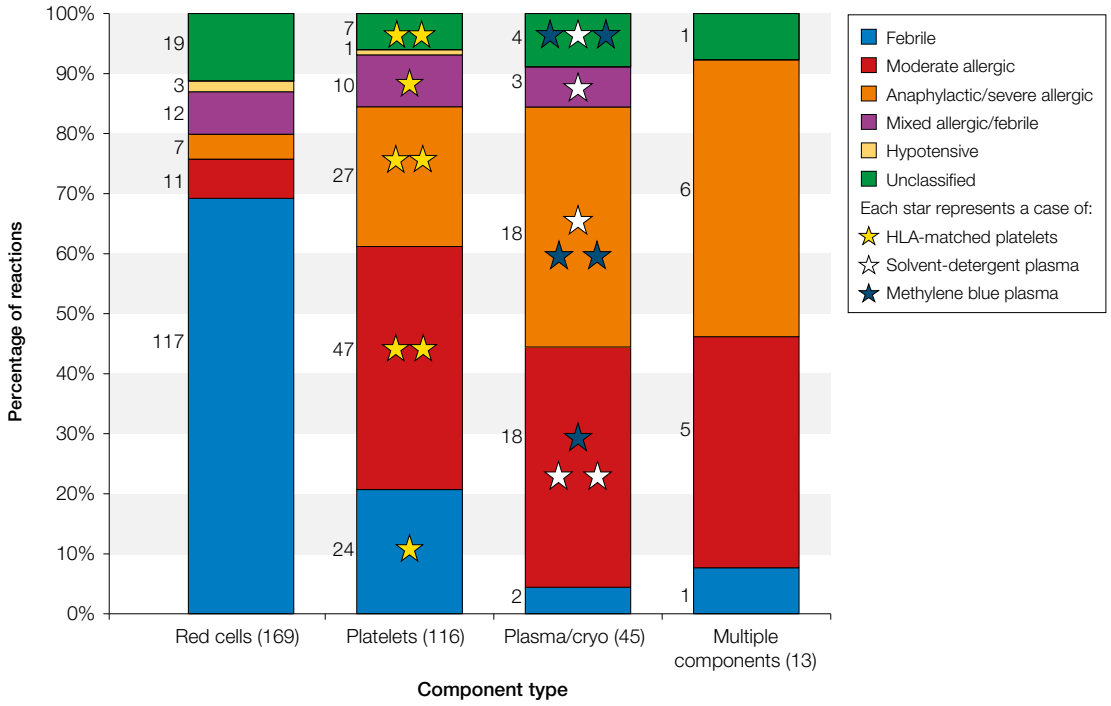
Table 14.2: Types of reactions

Comparison with previous reports

Similarities

The pattern of reactions remains similar to previous reports, Figure 14.1: Reactions by component type. Red cells are usually associated with febrile type reactions (~70%), plasma (including methylene blue-treated fresh frozen plasma (MB-FFP) and solvent detergent-treated FFP (SD-FFP)) with allergic reactions (~80%) and platelets cause more allergic (~60%) than febrile type (~20%) reactions but the percentage difference is less marked. As in previous years, many reactions were difficult to classify as a result of insufficient information, the IHN/ISBT grade of reaction severity not being used and because of the difficulty distinguishing true transfusion reactions from symptoms and signs associated with the patient's underlying condition.

Figure 14.1: Reaction by component type



Analysis of reactions also remains comparable in the following:

Table 14.3: Characteristics of ATR

Characteristic	Occurrence
Age distribution	~90% 18 years or over and 1-2% under 1 year
Gender	Similar numbers of male and female cases
Urgency of transfusion	70% were given routinely
Timing of transfusion	50-60% occurred within standard hours
Location	~20% in outpatients/day units, 50% on wards

Differences

There has been a progressive change in the last few years in the percentage of reactions associated with each blood component, Figure 14.2. This is likely to reflect discontinuation of data collection for mild reactions, a reduction in red cell use and increase in platelet and plasma use over this time period. The number of cases associated with either MB-FFP or SD-FFP has also increased (10 in 2014, 4 in 2013) which may be related to their increased use (see Chapter 20 Paediatric cases for discussion of MB-FFP cases) but the numbers are small. In addition there has been a steady increase in the number and percentage of cases considered to be severe (104 in 2014, 66 in 2013) Figure 14.3. This may represent an alteration in reporting, changes in the definition of reaction severity or a modification in the method used to analyse and classify these reactions.

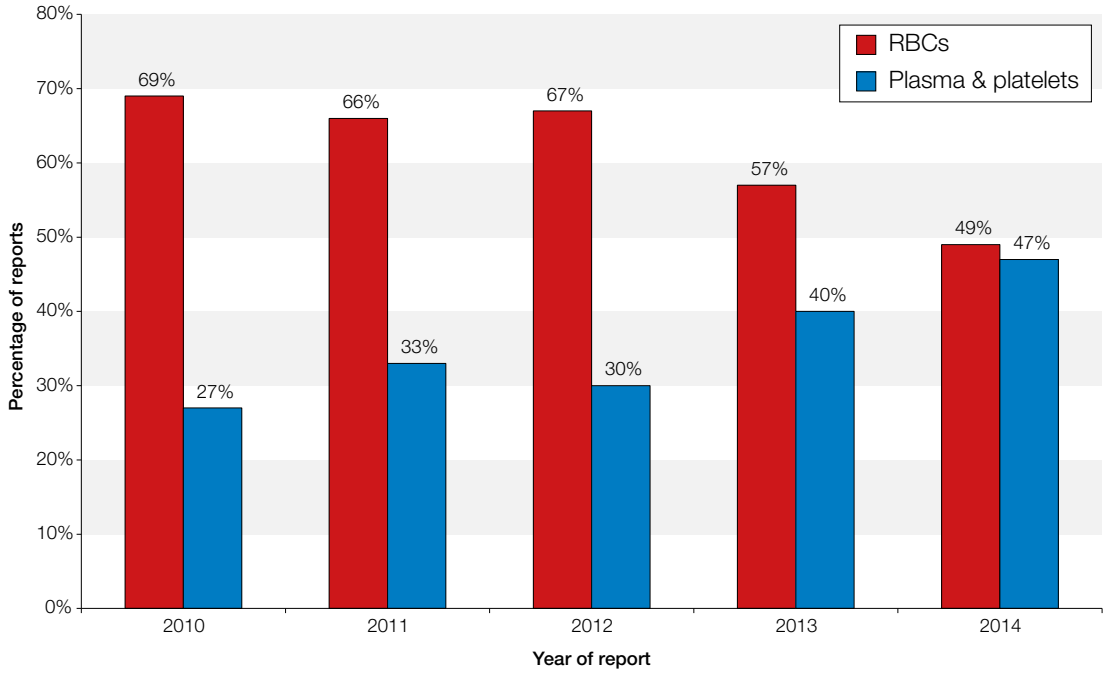


Figure 14.2: Percentage of total cases reported by component, excluding multiple components (2014 actual numbers can be found in Figure 14.1)

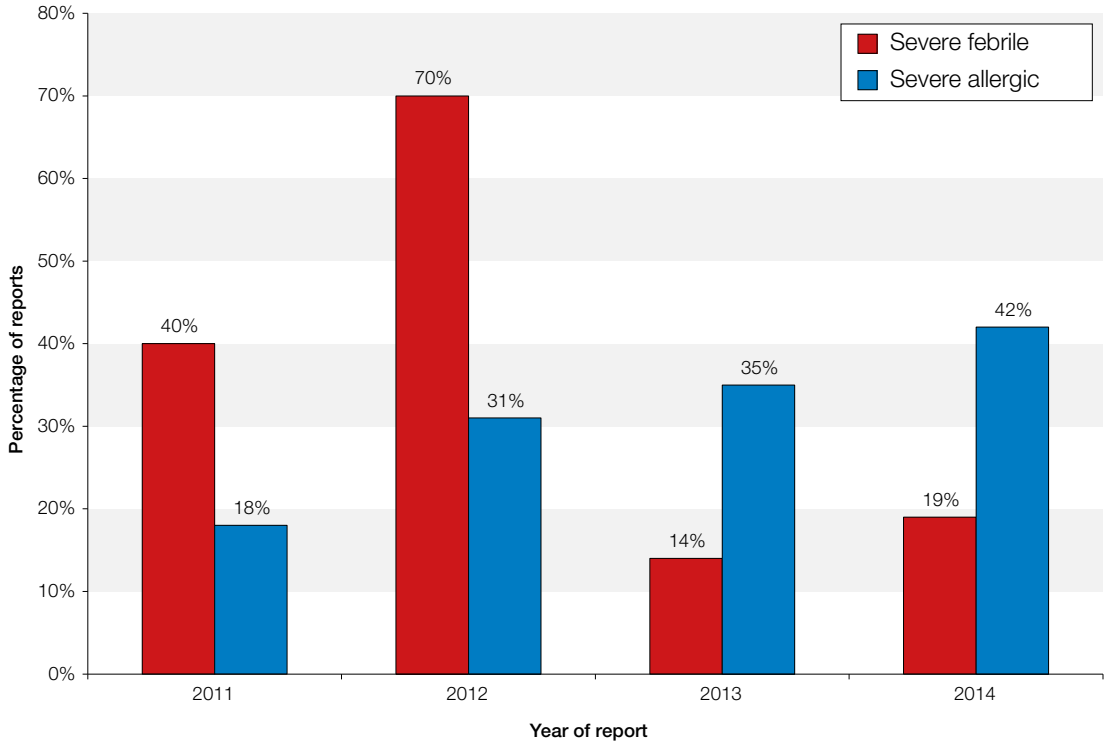


Figure 14.3: Percentage of total cases classified as severe (2014 actual numbers can be found in Table 14.2)

Recognition of reactions and their treatment, and management of subsequent transfusions

The recognition of reactions and their treatment and the management of subsequent transfusion episodes is considered this year, an analysis not performed in previous years.

Recognition of reactions

Continuous monitoring or routine transfusion observations identified most of the reactions. However in 122/343 (35.6%) cases patients themselves alerted staff promptly and in 13 cases this was done by relatives. In at least 10 cases rapid action by staff was felt to have curtailed the reaction severity. Good awareness of reactions by patients, relatives and staff therefore enabled rapid intervention and management which may have limited the severity and hastened recovery.

Treatment of reactions

In 97/144 (67.4%) of cases where symptoms were limited to a febrile type reaction, medication was given. However, in 42/97 (43.3%) of these this included an antihistamine +/- steroid, which is recognised treatment for an allergic but not a febrile type reaction.

In 112/139 (80.6%) of cases where symptoms were limited to an allergic reaction, medication was given. 14/112 (12.5%) of these included use of an antipyretic such as paracetamol as well as an antihistamine +/- steroid.

Management of subsequent reactions

There were 92 reports which stated that intervention for subsequent transfusions would be used. The most frequent intervention recommended was to use prophylaxis (52/92, [56.5%] of reports), usually with both an antihistamine and a steroid. This included at least 9/24 (37.5%) in which only febrile type symptoms had been reported.

Washed red cells and/or platelets in additive solution were planned for future transfusion in 22/92 (23.9%) and in 6 cases human leucocyte antigen (HLA)-matched platelets were documented to be required. In only one case where HLA-matched platelets were intended was this because of platelet refractoriness. In 5 cases where reactions occurred during plasma exchange, all of which were associated with SD-FFP, a decision was made to change to standard plasma in three, albumin in one, and to abandon procedures in another.

Five reports stated that subsequent platelet transfusions would be with apheresis rather than pooled platelets and three reports mentioned use of a manual rather than electronic crossmatch of red cells, although there was no evidence of haemolysis or red cell antibody formation.

Comment: Treatment with an antihistamine +/- steroid is commonly used for febrile type reactions but is not appropriate. HLA-matched platelets compared to standard platelets are unlikely to reduce reactions and should primarily be used when there is evidence of refractoriness. Similarly decisions to use apheresis rather than pooled platelets to prevent reactions, and manual rather than electronic red cell crossmatch, without haemolysis, are irrational and not evidence-based (BCSH Tinegate et al. 2012).

Illustrative cases

Case 1: Severe febrile reaction

A patient with myeloma, who also had dementia, had a 2 unit transfusion of irradiated red cells. The cannula needed reinserting during the second unit, and during this procedure the patient became very agitated, appeared cyanosed, and began shaking vigorously. She became dyspnoeic and had a slight rise in temperature. She was treated with antihistamine, hydrocortisone and given 100% oxygen. Her symptoms settled after 15 minutes.

Case 2: Repeated allergic reactions from different donors

An adult patient requiring regular platelet transfusions experienced allergic reactions with itch, chest and throat tightness, and mild wheeze, on three successive occasions. No cause was found. Two of these reactions, occurring 10 weeks apart, were reported to SHOT. On the first occasion, the implicated donor was removed from the HLA-matching panel, though this is not required, as it may not recur in that or any other recipient.

HLA-matching would not alter the risk of allergic reactions to platelets.

Cases 3 and 4: Allergic reactions to platelets from the same donation in two different recipients

Two young women were given prophylactic apheresis platelets from the same donor in an outpatient department on the same day. Case 3 experienced a moderate allergic reaction with chest tightness and shortness of breath 10 minutes after the transfusion had finished. Case 4 returned to the department 3 hours after transfusion with an itchy rash on her abdomen and back. Both were given intravenous (IV) chlorphenamine with good effect and discharged home later the same day. Subsequently 9 out of 11 further platelet concentrates from this donor were traced and none of the recipients had experienced a transfusion reaction.

Case 5: Severe allergic reaction associated with inappropriate transfusion

An adult male patient experienced a severe reaction within seconds of starting a unit of FFP, which was being given for warfarin reversal with a life-threatening bleed. Symptoms included chest pain and tightness, dyspnoea with wheeze, and angioedema. The FFP was given in the radiology department, and he had previously received IV contrast medium. No cause for the reaction was demonstrated.

The reporter noted that transfusion of FFP was inappropriate, as prothrombin complex concentrate was available and is the treatment of choice in this clinical setting.

Case 6: Anaphylactic reaction with characteristic mast cell tryptase response

A young male patient who was bleeding from a stabbing injury was given three units of red cells, four units of MB-FFP, and two units of cryoprecipitate, as part of a massive transfusion. During transfusion of one of the units of cryoprecipitate, he developed itch, urticaria, tachycardia and hypotension. Serial mast cell tryptase measurements were performed. The immediate and 12 hour samples were normal, at 7 and 12.1ng/mL while the 3 hour specimen was raised at 30ng/mL, in keeping with anaphylaxis.

References

BCSH 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

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