16 Febrile, Allergic and Hypotensive Reactions (FAHR) n=284

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Definition:

To reduce confusion, the title of this chapter has been changed to reflect the reactions assessed i.e. isolated febrile type (not associated with other specific reaction categories), allergic and hypotensive 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 below in Table 16.2 (ISBT/IHN 2011), and have been adopted by the British Society for Haematology (BSH) (BSH Tinegate et al. 2012).

Key SHOT messages

- For febrile reactions alone, give paracetamol
- For allergic reactions give an antihistamine as first line; give adrenaline if anaphylaxis is suspected. The effect of steroids is delayed by several hours, will have no immediate effect, and should only be used to prevent a late recurrence. The use of steroids may further immunosuppress already immunocompromised patients and increase the risk of side effects such as infection

Key recommendations from previous years

- 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 re-suspended in 100% PAS can be supplied
- Give appropriate targeted treatment and if needed, preventative cover for future transfusion (BSH Tinegate et al. 2012), as indicated in Table 16.1:

Table 16.1: Targeted treatment for febrile and allergic 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 reactions continue, give pre-transfusion antihistamine If reactions continue, consider washed platelets/red cells; for fresh frozen plasma (FFP) try a pooled component e.g. solvent-detergent treated plasma

- Outpatient departments and day care units, including those in the community, should ensure patients have information about what to do if they experience a reaction after leaving the unit
- The treatment of reactions and management of subsequent transfusions should be directed by recognised guidelines e.g. BSH guidelines on the investigation and management of acute transfusion reactions (BSH Tinegate et al. 2012)

Action: Hospital Transfusion Teams (HTT)

- Reporters should report cases fully, including clinical data such as temperature and blood pressure prior to, and during, a reaction, especially if fever or hypotension are features. The International Haemovigilance Network/International Society for Blood Transfusion (IHN/ISBT) classification should be used to grade severity (Table 16.2)
- SHOT has a role in identifying trends in reactions and events, including the monitoring of new components. It is therefore important to identify the implicated component e.g. standard/washed red cells; pooled/apheresis and/or washed or human leucocyte antigen (HLA)-matched platelets; standard/virally inactivated (including type) plasma

Action: SHOT reporters

- Patients who have experienced transfusion reactions should only be tested for platelet or granulocyte antibodies within guidelines such as those set out in England by the National Health Service Blood and Transplant (NHSBT) in their Histocompatibility and Immunogenetics user guide (NHSBT 2015/16). The main indication, other than platelet refractoriness, is persistence of severe reactions despite the use of platelets where the plasma has been removed and replaced by suspension medium

Action: HTT, Histocompatibility and Immunogenetics laboratories

- Transfusions should only be performed where there are facilities to recognise and treat anaphylaxis, according to UK Resuscitation Council (UKRC) guidelines (Resuscitation Council 2008). This recommendation is also relevant for other transfusion-related emergencies such as respiratory distress caused by transfusion-associated circulatory overload (TACO) or transfusion-related acute lung injury (TRALI). When supplying to community hospitals or for home transfusions, providers must ensure that staff caring for patients have the competency and facilities to deal with reactions. This is particularly relevant in the light of proposals to increase patient treatment outside secondary care

Action: HTT, Royal College of General Practitioners

Table 16.2: Classification of reactions

	1 = Mild	2 = Moderate	3 = Severe
Febrile-type reaction	A temperature ≥38°C and a rise between 1 and 2°C from pre-transfusion 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 mmHg or more occurring during or within one hour of completing transfusion **and** a systolic blood pressure 80 mmHg 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

Number of reactions and reaction rates n=284

Deaths n=0

There were no deaths related to the transfusion reaction.

Major morbidity n=71

Reactions have been classified as shown in Table 16.3. Severe reactions, as classified above, are used to define major morbidity.

Table 16.3: Classification of FAHR in 2017

	Moderate	Severe	Total
Febrile	119	21	**140**
Allergic	55	44	**99**
Mixed allergic/febrile	30	5	**35**
Hypotensive	9	1	**10**
Total	**213**	**71**	**284**

NB: in 25 of the 71 reactions classified as severe this was primarily because the patient was admitted

The percentage of severe reactions remains similar to previous years, 71/284 (25.0%) of all reactions. Many reactions, largely of febrile type, continue to be difficult to classify because 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.

Table 16.4 identifies the total number of cases submitted for review into the category of FAHR over the last 4 years and demonstrates that the percentage of cases excluded is consistent. The number of cases included in the report is therefore correlated to the total number of cases reported.

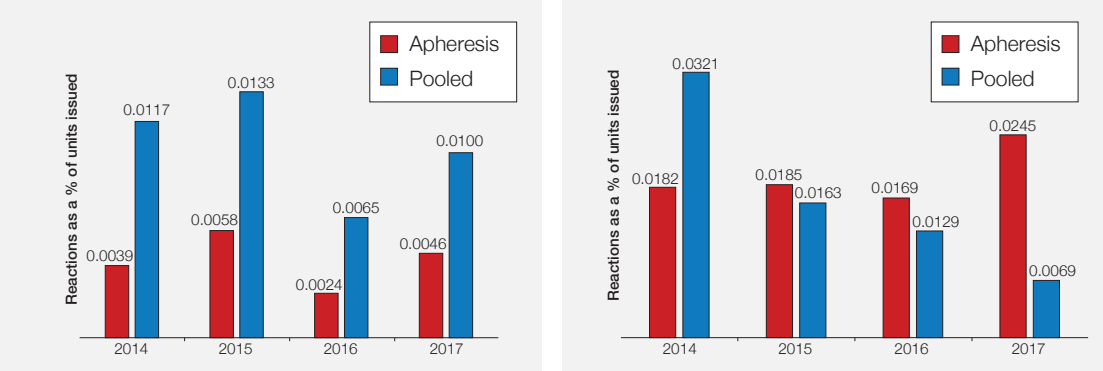
Cases reported	2014	2015	2016	2017
Total reported	434	407	357	390
Included	312	296	253	284
Excluded (withdrawn or unclassifiable)	122	111	104	106
% Excluded	28.1%	27.3%	29.1%	27.2%

Table 16.4: Total FAHR cases reviewed over a 4-year period

The incidence of allergic reactions linked to pooled platelets (suspended in PAS) continues to be lower than the incidence of allergic reactions linked to apheresis platelets and this is likely associated with the reduction in plasma content (Cohn et al. 2014, Tobian et al. 2014). The incidence of febrile reactions continues to be higher with pooled platelets compared to apheresis. Overall pooled platelets are associated with fewer reactions than apheresis platelets as the incidence of febrile reactions to platelets is lower than allergic reactions (Figures 16.1a and b). Reactions to platelets are at least in part caused by release of substances from the platelets themselves and therefore cannot be completely eliminated (Garraud et al. 2016, Maurer-Spurej et al. 2016).

a: Febrile type reactions

b: Allergic reactions



Figures 16.1: Percentage of reactions to apheresis and pooled platelets 2014 to 2017

Type of reaction by component

These remain similar to previous Annual SHOT Reports; Figure 16.2. Red cells are usually associated with febrile type reactions (~70%) whereas plasma and platelets more commonly cause allergic reactions (~80% and ~60% respectively). Three reactions were associated with solvent detergent (SD)-FFP and there were no reactions associated with methylene-blue treatment.

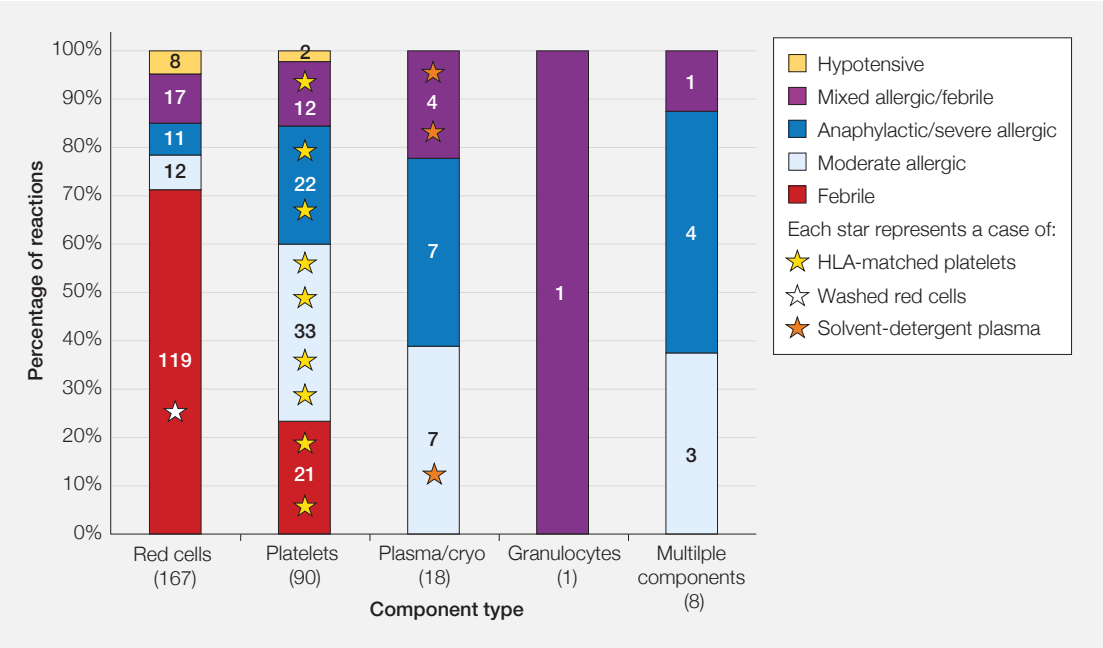


Figure 16.2: Reactions by component type

HLA=human leucocyte antigen; cryo=cryoprecipitate

Analysis of the characteristics of reactions remains comparable to those in previous years.

Table 16.5: Characteristics of FAHR

Characteristic	Occurrence
Age distribution	About 90% of patients were aged 18 years or over
Gender	45% male and 55% female cases
Urgency of transfusion	66% were given routinely
Timing of transfusion	46% occurred within standard hours
Location	59% were on wards and 14% in outpatient/day-case units

Treatment of reactions

An antihistamine with or without steroid continues to be used to treat reactions with only febrile/inflammatory type symptoms and/or signs however this practice may be reducing; Table 16.6. In addition to no evidence of benefit, the use of steroids may further immunosuppress already immunocompromised patients and increase the risk of side effects such as infection.

Table 16.6: Treatment of reported reaction

	Number	Medication stated	Antihistamine +/- steroid
Febrile			
2017	140	121/140 (86.4%)	46/121 (38.0%)
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			
2017	99	97/99 (98.0%)	10/97 (10.3%)
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%)

Following a purely febrile reaction, in cases where information about subsequent plans for management were provided, a lower percentage (22.7%) than in previous years (42.9% in 2016) planned to use an antihistamine with or without steroids. However, the numbers of reporters providing these data were small. It is notable that future treatment with pooled platelets was much more commonly stated to avoid allergic reactions than in previous years.

Illustrative cases

This year cases have been selected to demonstrate good practice.

Case 16.1: A febrile reaction appropriately treated with paracetamol

A patient in their 80s received a red blood cell transfusion to treat ongoing non-severe bleeding associated with a haemoglobin (Hb) of about 80g/L. After 100mL had been transfused (30–60 minutes) the patient experienced rigors, an increase in respiratory rate and the temperature was noted to have risen from a baseline of 36.6°C to 38.3°C. There were no other symptoms or signs. The transfusion was initially slowed and then discontinued. Paracetamol was prescribed and the patient's observations returned to baseline. Bacterial cultures from the patient at the time of the reaction were negative. No change in management was planned for any subsequent blood transfusion.

Case 16.2: A febrile reaction to red cells. To receive iron as future management of iron deficiency anaemia

A patient with menorrhagia and Hb of 50g/L was transfused with red cells. After the first unit her post-transfusion observations identified a pyrexia of 39.6°C (an increase of more than 2°C from baseline) and tachycardia of 120 beats/minute. She was given treatment which included paracetamol and

made a complete recovery with observations returning to baseline over 1-4 hours. Repeat serology was negative and future management was planned with intravenous iron and avoidance of blood transfusion.

Case 16.3: Allergic reaction to apheresis platelets with planned transfusion of pooled platelets suspended in PAS for future management

A child with reversible bone marrow failure and thrombocytopenia received apheresis platelets prior to an operation. Within 10 minutes of the start of the transfusion, periorbital oedema, wheezing and a fall in oxygen saturations to 92% on air occurred. Oxygen therapy, hydrocortisone, chlorphenamine and salbutamol nebuliser were given with complete recovery within 1-4 hours. Investigation did not identify IgA deficiency and mast cell tryptase remained within the normal range. The patient had experienced previous mild reactions to apheresis platelets and so it was agreed that in future platelets suspended in PAS would be used to reduce the risk of a further allergic reaction.

References

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