

14. Transfusion-Associated Circulatory Overload (TACO)

Definition

Transfusion-associated circulatory overload includes any four of the following occurring within 6 hours of transfusion:

- acute respiratory distress
- tachycardia
- increased blood pressure
- acute or worsening pulmonary oedema
- evidence of positive fluid balance.

DATA SUMMARY							
Total number of cases		40	Implicated components		Mortality/morbidity		
			Red cells	25	Deaths due to transfusion		1
			FFP (untreated)	3	Deaths <i>probably/likely</i> due to transfusion		3
			Platelets	1	Deaths <i>possibly</i> due to transfusion		2
			Multiple components	11	Major morbidity		15
Gender		Age		Emergency vs. routine and core hours vs. out of core hours		Where transfusion took place	
Male	13	≥18 years	40	Emergency	16	A&E	2
Female	27	16 years to <18 years	0	Routine	20	Theatre	3
Not known	0	1 year to <16 years	0	Not known	4	ITU/NNU/HDU/recovery	6
		>28 days to <1 year	0				
		Birth to ≤28 days	0	In core hours	15	Wards	25
		Not known	0	Out of core hours	9	Community	1
		Total	40	Not known	16	Outpatient/day unit	2
						Not known	1

A total of 33 questionnaires on TACO were received; 1 was transferred in from the ATR section, 2 from TAD and 4 from the TRALI section, resulting in a total of 40 cases, which are analysed in this chapter.

Definition

Cases were assessed by the reviewer for probability for a diagnosis of TACO based on the ISBT definition, available on the SHOT website (www.shotuk.org).¹ Cases that fulfilled these criteria but occurred between 6 and 24 hours were also included.

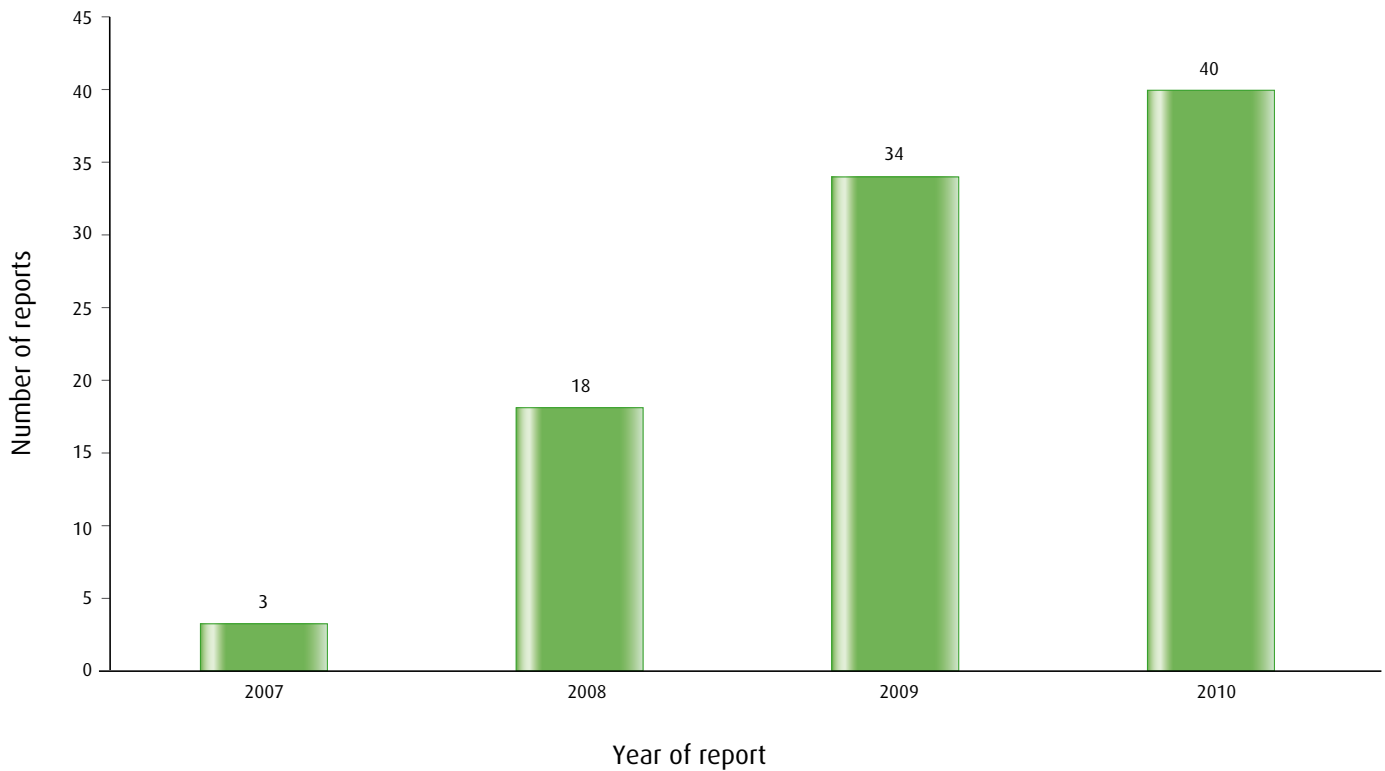
Patients

There were 13 men and 27 women. The age range was 27–91 years, with 23 patients (57.5%) 70 years or more and 7 patients <50 years. There were no patients under 18 years.

Table 45
TACO case probability based on ISBT criteria

TACO case probability (ISBT criteria)	No. of cases
Highly likely	13
Probable	20
Possible	7
Total	40

Figure 14
Number of cases of TACO reported to SHOT each year



*TACO was introduced as a SHOT reporting category in 2008.

Mortality *n* = 6

There were 6 deaths where the transfusion was contributory: imputability ≥2 in 4 (Cases 1, 3, 4 and 5) and 2 where the possibility that TACO had contributed to death could not be excluded: imputability 1 (Cases 2 and 6). These are detailed below.

Case 1

TACO following RBC transfusion to elderly male with renal impairment and cardiac failure

An 83-year-old male with refractory anaemia related to CRF received 2 units of RBCs, each over approximately 1.5–2.5 hours. He had continuing bradycardia during the second unit. He remained stable, but the bradycardia persisted at 40–45 beats per minute (bpm). Within 15 minutes of the start of the third unit of RBC, he became unresponsive with no assessable cardiac output. An arrest call was put out and resuscitation commenced, which was ultimately unsuccessful. A post-mortem examination showed acute left ventricular failure (LVF), hypertensive heart disease with mitral valve prolapse and hypertensive nephropathy.

Case 2

TACO in elderly patient with hypoalbuminaemia and fluid overload

A 73-year-old female with a chronic anaemia associated with gastric malignancy and pulmonary embolism (PE) was admitted to hospital. She had hypoalbuminaemia and fluid overload. She was given a 2 unit RBC transfusion and became SOB 85 minutes into the second unit of RBC. She also developed tachycardia, pulse 140 bpm with BP 177/82, nausea and back/chest pain. The O_2 saturation was 66% on 3 L of oxygen and she had pulmonary oedema. She was given IV furosemide and hydrocortisone, and transferred to the HDU. TACO was considered to be highly likely. The following day she developed a haemothorax. Two days post transfusion she was documented to have further minor PEs, a lower respiratory tract infection and pulmonary oedema. She was transfused 4 further RBC units with careful fluid management and diuretic cover, apparently uncomplicated, on the cardiac care unit. Four days after the development of TACO her condition deteriorated through the night and she died.

Case 3

TACO after RBC transfusion to elderly female with pre-existing cardiac failure

An 86-year-old female with chronic anaemia associated with chronic myeloid leukaemia (CML) received a 2-unit RBC transfusion in the haematology day unit over approximately 5 hours. She had pre-existing cardiac failure with pitting oedema up to the level of her buttocks. On getting up to go home she became breathless, tachycardic (pulse 140 bpm) and hypertensive (BP 192/80), with a reduced O_2 saturation of 78%. The jugular venous pressure (JVP) was raised at +5 cm, and she had bilateral basal crepitations. The CXR appearances were consistent with pulmonary oedema. Treatment included oxygen support with continuous positive airway pressure (CPAP), but she subsequently died.

Case 4

TACO after oral diuretics withheld in elderly patient with cardiac failure because 'nil by mouth'

An 84-year-old male with congestive cardiac failure (CCF) associated with IHD, on oral furosemide, isosorbide mononitrate and enalapril, was admitted with melaena. The Hb was 7.9 g/dL. He was transfused 3 units of RBC, each over 3 hours. However, because he was nil by mouth for endoscopy, his oral medication was withheld. No parenteral diuretic was substituted. He developed pulmonary oedema with pO_2 6.3 kPa, and received CPAP and diuretic therapy, but he died.

Case 5

TACO following RBC transfusion to elderly female with renal impairment and cardiac failure

A frail 91-year-old female with a history of CRF and CCF had anaemia, Hb 8.1/dL, associated with intermittent rectal bleeding. She was stable with pulse 70 bpm, BP 110/50 and good oxygen saturation. She became SOB, pO_2 8 kPa, during transfusion of a unit of RBC given over 5 hours and covered with furosemide 80 mg IV. The next morning a second RBC unit was transfused, making her progressively unwell with 15 L of oxygen required to maintain normal saturation. She arrested and later died.

Case 6

TACO following RBC transfusion to elderly female with chronic anaemia secondary to myeloma

An 85-year-old female with stage 3 myeloma and chronic anaemia, Hb 6.5 g/dL, became SOB during transfusion of the second unit of a 2-unit RBC transfusion. Each unit was given over 4 hours. The transfusion was stopped. She became tachycardic (pulse 110 bpm), hypertensive (BP 203/110) and hypoxic, with mild to moderate LVF. She was transferred to the coronary care unit, but her renal function deteriorated and she died 11 days later.

Learning point

- TACO is potentially avoidable in many cases. Doctors should undertake pre-transfusion clinical assessment, taking into account concomitant medical conditions that increase the risk of TACO (cardiac failure, renal impairment, hypoalbuminaemia, fluid overload) and consider diuretic cover (e.g. furosemide).

Major morbidity $n = 15$

There were 15 cases of major morbidity. Thirteen of these 15 patients required ITU or HDU admission and/or ventilation. The remaining 2, who were already on ITU, required increased ventilatory support after the development of TACO.

Of the remainder ($n = 19$), 12 were administered O_2 , 2 had CPAP and 13 were stated to have received diuretic therapy.

Clinical details and transfused fluids in TACO cases

Details of the rate of transfusion were reported in 30/40 cases (75%). In 10 of 16 cases where RBC were transfused in the absence of suspected haemorrhage, the mean duration of transfusion/RBC unit was approximately 2 hours 30 minutes; in 3 cases it was 4 hours and in 3 cases it was not stated or not recorded. Details on fluid balance were supplied by the reporter in 11/40 (27.5%) and not recorded, not stated or incomplete in the remainder.

The median time between the transfusion and the onset of symptoms was 0–2 hours in 19/40 cases (47.5%), 2–6 hours in 16 cases (40%), and between 6 and 24 hours in the remainder (13.1% (5/40); 6–12 hours in 3 and 12–24 hours in 2 cases).

Twenty-three of the 40 patients (57.5%) had 1 or more concomitant medical conditions that increase the risk of TACO: cardiac failure, renal impairment, hypoalbuminaemia, fluid overload (not stated in 1 case).

Learning points

- Nurses should monitor the rate of transfusion and fluid balance as these factors influence the risk of a patient developing TACO.
- SHOT reports indicate that TACO can occur up to 24 hours after the transfusion, therefore the patient should be monitored accordingly, as advised in the BCSH guidelines on the administration of blood components.²

Acute haemorrhage cases in which more than 1 component was transfused $n = 7$

There were 7 cases of TACO in which RBC plus other blood components were administered for major acute haemorrhage: post-partum (3), postoperative (2) and GI haemorrhage (2).

Case 7

TACO following transfusion for massive obstetric haemorrhage

This female had a PPH post Caesarean section. She received 7 units of RBC, 2 units of FFP and 1 pool of platelets transfused rapidly, following which she starting coughing up frothy white sputum. The O_2 saturation dropped to 85%, and she became hypotensive, tachycardic (140 bpm), temperature 39°C (pre-transfusion temperature unavailable), acidotic pH 7 and pO_2 11 kPa on 100% oxygen. A CXR indicated pulmonary oedema. Furosemide and noradrenaline were given with a good response. An ECHO later showed good ventricular function.

Cases in which RBC transfusion was implicated $n = 34$

RBC were transfused in 34 cases. In 16 of these RBC were transfused for acute haemorrhage, in 7 cases together with (an)other component(s) (detailed above). In a further 18 cases RBC were administered in the absence of suspected acute haemorrhage. In these 18 cases, TACO occurred after >3 units in 1, after ≤2 units in 15 and after ≤1 unit in 2. In 12 of these 18 cases (66.7%) patients were ≥70 years (mean 81.8 years). Five of the remainder (not stated in 1) who were <70 years (range 42–68 years) had risk factors that increase the risk of TACO: fluid overload (3), hypoalbuminaemia (1) and fluid overload, hypoalbuminaemia and renal impairment (1). In 4 of these 18 cases the mean transfusion duration/RBC unit was 4 hours and in a further 10 it was approximately 2 hours 15 minutes (range 1 hour 30 minutes–3 hours 45 minutes). In 4 cases the duration of transfusion was not stated or recorded.

Learning points

- TACO can occur after transfusion of small volumes of RBC, even ≤ 1 unit.
- Patients >70 years are particularly at risk of TACO following RBC transfusion in the absence of suspected acute haemorrhage.
- Patients <70 years are also at risk of TACO, particularly in the presence of factors that increase the risk of TACO: cardiac failure, renal impairment, hypoalbuminaemia and fluid overload.

Cases in which FFP was transfused $n = 13$

There were 13 cases in which FFP was implicated in TACO, of which 8 occurred in the context of acute haemorrhage. Of the remaining cases (5/13), in 2 cases FFP was transfused pre-procedure because of abnormal coagulation tests, in 2 cases FFP was transfused to patients with hepatic disease and in 1 case 1200 mL FFP was transfused without plasma exchange (PEX) to a 77-year-old male diagnosed to have thrombotic thrombocytopenic purpura (TTP). A volume of >1000 mL was transfused in 7 cases (volume unstated in 2).

Learning points

- There are few proven indications for FFP, but if FFP is indicated, the BCSH guidelines state that the conventional dose is 10–15 mL/kg, with the dose dependent on the clinical situation and its monitoring.³
- Plasma exchange (PEX) with FFP replacement (rather than FFP transfusion without PEX) is the mainstay of the treatment of TTP and has led to a reduction in mortality from $>90\%$ to approximately 20%. Patients diagnosed as having TTP should be transferred to a unit that can provide PEX as soon as is feasible, with FFP transfusion while this is being organised. SD FFP should be used (see Commentary).

Cases in which platelets were transfused $n = 8$

There were 8 cases in which platelets were transfused, of which 4 occurred in the context of acute haemorrhage. In 7 cases other components were also transfused, and in 1 case platelets only were transfused.

Procedural review

In 16/40 (40%) the case had been reviewed by the HTC and in 3/40 the case had been reported to the Trust clinical risk committee, with review stated to be pending in the remainder.

COMMENTARY

This year TACO has been implicated in 6 deaths (4 imputability ≥ 2 ; 2 imputability 1) and 15 cases of major morbidity, with these serious outcomes together comprising 52.5% (21/40) of cases analysed. While TACO may occur in approximately 6–8% of critically ill patients on ITU,⁴ only 2 reported cases occurred in the ITU setting.

The number of cases of TACO reported has reached a plateau. Eleven of the 40 patients had haematological conditions, suggesting awareness of TACO among haematologists, but TACO probably remains under-reported.

Patients >70 years are particularly at risk of TACO following RBC transfusion in the absence of suspected acute haemorrhage. Patients <70 years are also at risk of TACO, particularly in the presence of factors that increase the risk of TACO: cardiac failure, renal impairment, hypoalbuminaemia and fluid overload. These factors occurred in 57.5% (23/40) of cases overall. The BCSH guidelines on the administration of blood components² do not address clinical assessment prior to transfusion, including for the risk of TACO, and measures to decrease the risk of TACO.

One fatal case (Case 4) was associated with failure to continue diuretic therapy in a patient who had known cardiac failure. While Li *et al.* suggest that pre-transfusion diuretic therapy was not found to be protective among medical ITU patients, it was acknowledged that infrequent use of diuretics in 9/51 (17.6%) TACO cases and 12/51 (23.5%) matched controls before transfusion in the study population made it difficult to draw a definite conclusion.⁴

It is of concern that details on fluid balance in the 24 hours prior to the reaction were supplied by the reporter in only 11/40 (27.5%) cases.

In 10 of 18 cases where RBC were transfused in the absence of suspected acute haemorrhage, the mean transfusion duration/RBC unit was approximately 2 hours 15 minutes, and 4 hours in the remaining 4 cases where information was supplied. The transfusion rate influences the risk of TACO, particularly in the elderly and in the presence of concomitant medical conditions that are risk factors for TACO. The *Handbook of Transfusion Medicine* (4th edition) recommends that all blood component transfusions are completed within 4 hours of removal from a controlled temperature environment.⁵ This limit is designed to reduce the risk of bacterial growth and TTI, and is based on data relating to the 'lag phase' before bacteria begin to proliferate after removal from refrigeration. The BCSH guidelines note that the evidence for a strict 4-hour rule 'falls short of that required for a "must" recommendation', and recommend that this rule should continue to be applied in clinical practice wherever possible.²

TACO was associated with the transfusion of relatively modest volumes of RBC and other blood components. It has been suggested that the aetiology of TACO may be more complex than excessive blood volume. In a retrospective analysis in a single centre in the US, Blumberg *et al.* (2010) reported a substantial reduction in the incidence of TACO (to zero) and also of TRALI but not of allergic reactions following the implementation of universal leucodepletion.⁶ In the UK, universal leucodepletion of all cellular components (except granulocytes/buffy coats) was implemented in late 1999.

The majority of cases of TACO occurred within 6 hours of the transfusion, but 13% occurred after 6 hours (6–12 hours in 3 cases and 12–24 hours in 2 cases), suggesting that the 6-hour cut-off for diagnosis of TACO merits consideration. Following last year's main recommendation on pulmonary complications of transfusion, SHOT is participating in a collaborative approach to further define these.

Cases of TACO following major obstetric haemorrhage continue to be reported, with a further 4 cases this year and a total of 7 cases since 2008. Contributory factors are difficulties in estimating actual blood loss, particularly because of the changing blood volume, and circulatory capacity. As a result patients may be over-transfused. There may also be a failure to recognise TACO in these young individuals, who are often regarded to be 'immune' to TACO.

FFP transfusion, particularly volumes >1000 mL of FFP, is a risk factor for TACO. There are few proven indications for FFP, but if FFP is indicated, a limiting factor to administration of an adequate volume of FFP may be the patient's ability to tolerate the volume transfused. The BCSH guidelines state that the conventional dose is 10–15 mL/kg, with the dose dependent on the clinical situation and its monitoring.³ Prothrombin complex concentrates (PCC), in which the volume of a therapeutic dose is small, is the product of choice for urgent reversal of coumarin (warfarin) anticoagulation when

this is indicated. PCC may also be useful in the correction of coagulopathy in non-warfarinised patients with severe bleeding, where substantive data would be welcome.

In 1 case TACO was associated with (untreated) FFP transfusion without PEX. The mainstay of the treatment of TTP is PEX with FFP replacement, which has reduced mortality rates from >90% to approximately 20%. The DH recommends that because of the high donor exposure, adult patients with TTP should be treated with SD-FFP.⁷ SD-FFP, unlike standard FFP, lacks high molecular weight vWF multimers and may be more effective than standard FFP in TTP, and has been shown to be associated with fewer allergic/urticarial and citrate reactions than the use of cryosupernatant in patients with TTP.⁸

Recommendations

- National guidelines are required on clinical assessment pre transfusion, which should include taking into account concomitant medical conditions that increase the risk of TACO (cardiac failure, renal impairment, hypoalbuminaemia, fluid overload) and measures to reduce the risk of TACO.

Action: BCSH

- The rate of transfusion also merits review, particularly in patients >70 years and those with concomitant factors that increase the risk of TACO.

Action: BCSH

For active recommendations and an update on their progress, please refer to the SHOT website.