Avoidable, Delayed or Under/Overtransfusion (ADU) and Incidents Related to Prothrombin Complex Concentrate (PCC) n=285

12

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Key SHOT messages

- The increase in reports of delayed transfusion is of concern
- Poor communication is a major cause of delays
- Major haemorrhage events should be audited, protocols reviewed, and drills used to embed in practice
- Gaps in staff knowledge and training need to be addressed so that haematinic deficiencies are recognised and treated appropriately

Abbreviations used in this chapter

AAA	Abdominal aortic aneurysm
ADU	Avoidable, delayed or under/overtransfusion
AIHA	Autoimmune haemolytic anaemia
BMS	Biomedical scientist
BP	Blood pressure
BSH	British Society for Haematology
CMV	Cytomegalovirus
ERCP	Endoscopic retrograde cholangiopancreatography
ED	Emergency department
FBC	Full blood count
FFP	Fresh frozen plasma
GI	Gastrointestinal
Hb	Haemoglobin
HSE	Handling and storage errors
ICH	Intracranial haemorrhage
ICU	Intensive care unit
INR	International normalised ratio
IV	Intravenous
LIMS	Laboratory information management system
MCV	Mean cell volume
MH	Major haemorrhage
MHP	Major haemorrhage protocol
MHRA	Medicines and Healthcare products Regulatory Agency
NCA	National comparative audit
NPSA	National Patient Safety Agency
PCC	Prothrombin complex concentrate
RECOVERY	Randomised Evaluation of COVID-19 Therapy
SOP	Standard operating procedure
TACO	Transfusion-associated circulatory overload

Recommendation

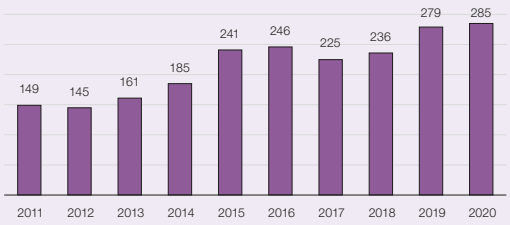
- Problems arising during major haemorrhage indicate a continuing need for review of major haemorrhage protocols (MHP) and regular drills. This has increasing importance with fragmentation of clinical care and management by multiple teams

Action: Medical directors and hospital transfusion teams

Headline data 2020

Number of reports n=285
Deaths n=13
Major morbidity n=6

ADU reports by year



Demographic data

Male n=130
Female n=147
Unknown n=8

Adults n=244
Paediatric n=35
Unknown n=6

Blood component data

Red cells n=201
Platelets n=29
Plasma n=22
Multiple Components n=14
PCC n=17
Unknown n=2

Overview of ADU cases

- **Delayed transfusions n=133**
- **Avoidable transfusions n=110**
- **Under or overtransfusion n=25**
- **Cases related to PCC n=17 (9 in 2019)**

Near miss cases n=21 (not included in the total above)

There were 12 near miss avoidable transfusions including 2 patients nearly given O D-negative units (when crossmatched or group-specific units were available) in the context of major haemorrhage activations. There was 1 near miss delay, 1 PCC nearly given to wrong patient, 6 potential overtransfusions (4 in children; 1 adult female with iron deficiency and 1 patient who had altered the request form themselves from 'group and screen' to 'transfuse 2 units') and 1 undertransfusion of platelets to a child.

Deaths n=13

There were 12 deaths related to delays: 1 definitely related, 3 probably related and 8 possibly related to the delayed transfusion.

One death was possibly related to undertransfusion.

Major morbidity n=6

These were all related to delays in transfusion.

Delayed transfusion

The increase in reports of delayed transfusion, with 12 deaths (2 in 2019), is of concern. Bleeding that is not visible (e.g. GI, ruptured ectopic pregnancy) is more likely to be associated with delayed recognition. Two deaths occurred in infants after elective biopsy. Massive blood loss can occur very quickly in obstetrics and some surgical procedures, so MH procedures need to be slick and efficient. This requires preparedness and practice.

Issues with MH procedures n=41

- Delays were reported for 26 cases of MH, 25 where the MHP was activated and 1 in a child where it was not
- Avoidable transfusions were reported in 11 cases of MH, 9 potentially avoidable use of group O D-negative red cells, and transfusion of red cells to 2 Jehovah's Witnesses
- Overtransfusion was reported in 4 cases of MH, with post-transfusion Hb levels ranging from 173 to 202g/L

Learning points

- Major haemorrhage protocols (MHP) need to be practical and work efficiently. All cases of activation should be reviewed to learn from each event
- The MHP may vary between hospitals and between departments, e.g. ratios of red cells to plasma may be different for obstetric haemorrhage compared with trauma. Staff need to be aware of local protocols and know how to access components in an emergency

MHP Drills

It is difficult to perform drills with all relevant staff at the same time; some hospitals have used simulation suites to set up a mock emergency and this can be used to drill all parts of the activation process such as taking blood samples. Some also recommend activation of the cardiac arrest call at the same time to alert other senior staff who can assist, particularly in wards or areas of the hospital where haemorrhage activations are rare. It is important to include laboratory staff in these drills, for example to see how long it actually takes to get components from the laboratory to the emergency department. A suggested audit is to walk around wards and simply ask staff of all grades if they know where their protocol is and how to activate it. In one hospital this resulted in placing laminated protocols on each resuscitation trolley on wards as this was the one place that gets checked daily and that staff run for when a patient is very unwell.

MHP Audit

Audit of activations can be very useful. The following questions can be included in audit templates: What can be learned or improved? Positive aspects of the management of a major haemorrhage are important; what went well and why?

Conclusion

Delays in transfusion are associated with about a quarter of all deaths reported to SHOT. These should be preventable.

Recommended resources

NICE. Acute upper gastrointestinal bleeding in over 16s: management. Clinical Guideline 141 (2012).
https://www.nice.org.uk/guidance/CG141/chapter/1-Guidance#timing-of-endoscopy

NICE. Major trauma: assessment and initial management. Clinical Guideline 39 (2016).
https://www.nice.org.uk/guidance/ng39

North West Regional Transfusion Committee Steering Group Major Haemorrhage Guidelines Group. Toolkit for the Management of Major Haemorrhage.
https://www.transfusionguidelines.org/uk-transfusion-committees/regional-transfusion-committees/north-west/policies/massive-haemorrhage-toolkit

SHOT educational video about transfusion delays in major haemorrhage can be accessed at this link
https://www.shotuk.org/resources/current-resources/videos/

12a Delayed Transfusions n=133

Definition:

Where a transfusion of a blood or blood component was clinically indicated but was not undertaken or was significantly delayed or non-availability of blood components led to a delay with impact on patient care (not restricted to emergency transfusion).

Key SHOT messages

- Serial delays at different transfusion steps are cumulative and can result in harm or death
- Good communication between clinical and laboratory staff is essential
- Many different groups of staff will be involved in the management of major haemorrhage; ensure the learning is done involving teams
- Patient transfer between departments and clinical teams is associated with delays in transfusion
- A haematologist should be contacted at the earliest opportunity for advice about patients with irregular antibodies and can enable timely concessionary release
- Gastrointestinal bleeding can be deceptive, the severity is often masked, diagnosis may be delayed; hypotension and tachycardia are important clinical signals
- Elderly patients are often on anticoagulants exacerbating the severity of bleeding
- Obstetric haemorrhage can be rapid and massive; it is vital that major haemorrhage protocols work smoothly and quickly. Training and drills are essential
- Staff should be familiar with local protocols. In the event of major haemorrhage all the necessary components may not be available at the same time. Red cells should be quickly available but fresh frozen plasma and cryoprecipitate take time to thaw; platelets may have to be sourced off site

Recommendations

- Clinical staff involved in frontline care must be trained to recognise major blood loss early and know when to activate/trigger the local major haemorrhage protocol and take prompt and appropriate action (NCA 2018)
- Major haemorrhage protocols should be regularly reviewed and practiced with drills particularly in areas of greatest risk, i.e. emergency departments, obstetrics, and operating theatres
- Transfusion laboratories should ensure they have a robust procedure for concessionary release to avoid deaths from bleeding or anaemia
- Ensure that all communication channels function well particularly the correct pathway for activation, including means of contacting porters and transfusion laboratory staff
- Major haemorrhage activations should be regularly audited to ensure lessons are learned

Action: Hospital transfusion teams

Abbreviations used in this chapter

HDFN	Haemolytic Disease of the Fetus and Newborn	**NW**	North West
NICE	National Institute for Health and Care Excellence	**NWRTC**	North West Regional Transfusion Committee

Introduction

The number of reports of delayed transfusion has increased in 2020 (133 compared with 129 in 2019) with 12 deaths (3 in 2019, 1 of these was due to delay in PCC administration) and 6 cases of major morbidity. The reports illustrate many problems with communication and delayed recognition of the severity of haemorrhage. Overall, transfusion was urgent or emergency in 80/133 (60.2%).

Delays were associated with the MHP in 25/133 (18.8%) with features as described in previous years (poor communication, lack of knowledge and failure to follow the correct procedure). There were 4 cases of major obstetric haemorrhage. The principles described in the BSH guidelines (Hunt et al. 2015) should be followed. Several useful resources are available, including the North West RTC toolkit (NW RTC Steering Group 2013) and NICE guidance (links are provided in the recommended resources section). A recent comprehensive protocol has been published from Canada (Callum et al. 2021).

The NCA of major haemorrhage (826 cases) reported that 28% were associated with surgery, 21% with obstetrics, 20% with GI bleeding and 17% with trauma (NCA 2018). This recommended that 'clinical teams must be trained to recognise major blood loss early, and to know when to activate and stand down the major haemorrhage protocol'. In some cases reported to SHOT, recognition of bleeding severity was delayed, particularly when 'concealed' with catastrophic outcomes.

The increase in both total number of reported delays and deaths is of concern. Recurring themes over these 10 years include delayed recognition of serious bleeding, use of the wrong activation phrase when contacting switchboard, bleep failures (laboratory and porters), sample mislabelling, and failure to follow the MHP. Serial delays occur during transfer of patients between departments and teams. Poor communication is a major problem (see below). In major haemorrhages every minute counts and delays should be avoided. Patients should not die from bleeding.

Components may not all be available at once. Delays may be reduced when staff know how to access the emergency group O D-negative and D-positive red cells. These should be available within minutes. In hospitals that do not keep pre-thawed FFP (the majority), the thawing process can take up to 40 minutes. Platelets are usually required later in the treatment of major bleeding; they may or may not be available on site.

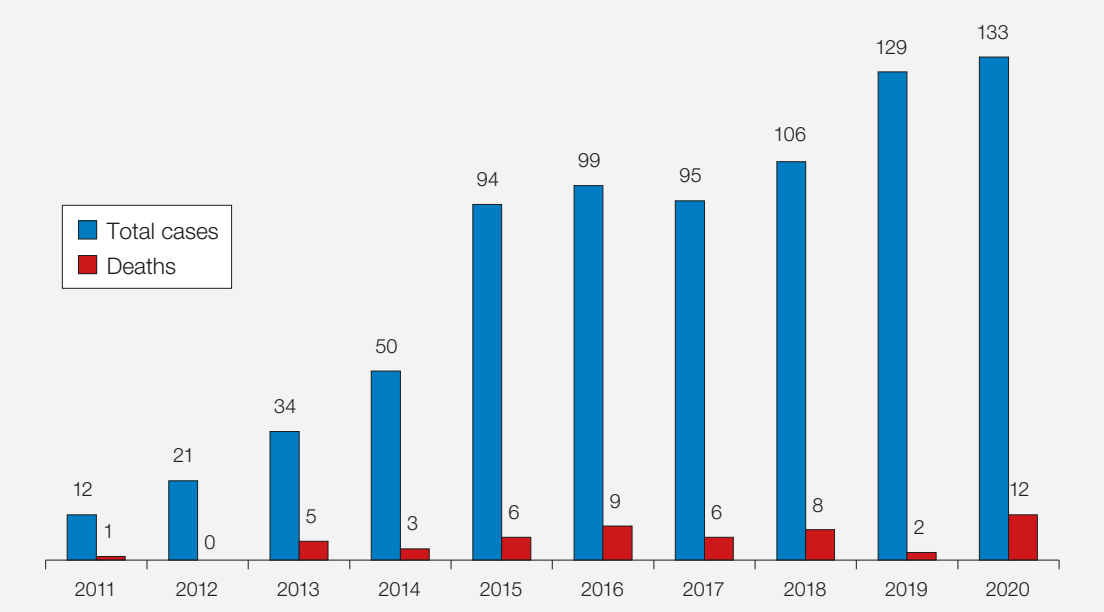


Figure 12a.1: Delayed transfusion reports and deaths by year 2011 to 2020 (n=775, deaths n=53)

Deaths n=12 (2 in 2019)

Imputability: one death was 'definitely' related (imputability 3), 3 'probably' related (imputability 2) and 8 'possibly' related (imputability 1) to the delay in transfusion.

Two infants died from haemorrhage after elective biopsy (liver biopsy and rectal biopsy). This is a very rare complication. In both cases there was delayed recognition of the severity of haemorrhage and delay in activating the major haemorrhage procedures. These are described in Chapter 23, Paediatric Cases.

Four deaths in elderly patients were associated with GI bleeding; 3 of these patients were on anticoagulants for atrial fibrillation.

Case 12a.1: Death from GI bleeding with serial delays and miscommunications

An elderly woman on anticoagulants was admitted with a history of melaena. She was pale with hypotension, blood pressure 88/55mmHg, and tachycardia, and was assessed within 3 minutes of arrival. She was noted to be in shock from blood loss. Her Hb on the blood gas machine on admission was 41.8g/L. The MHP was not activated. Transfusion was delayed for almost 7 hours from admission and she died shortly after it was started.

The investigation noted that:

- There was no clear line of responsibility for delivering care and limited resources in the ambulance bay. A hospital pre-alert would have resulted in a 'fast-track' to resuscitation
- There was failure to escalate due to poor communication when the patient was moved from the ambulance bay to resuscitation, and a lack of communication between doctors and nurses in the resuscitation area
- Computer blood prescribing was noted to be complex and 'a common source of clinical error'
- The medical consultant was working in an unfamiliar and understaffed environment with an unfamiliar clinical condition with staff he did not know
- Handover to the registrar resulted in decisions being made without seeing the patient
- Mandatory transfusion training for medical staff should take place

Case 12a.2: Death related to GI haemorrhage with multiple points of delay

An elderly man had a prolonged admission for renal problems. His anticoagulant for atrial fibrillation and omeprazole were discontinued. Two months later after successful treatment he was awaiting discharge. His anticoagulant had been restarted. Unexpectedly he developed large volume melaena. A group and screen sample taken at 10:01 was received in the laboratory at 13:15 (portering delays) but not processed due to incorrect labelling. The clinical team did not know this due to the LIMS not interacting with the patient information system. The FBC sample was clotted, requiring repeat. At 16:26 Hb 66g/L was noted and transfusion of two units requested. The repeat sample for transfusion was delivered to the laboratory at 17:09 (diagnosis anaemia rather than GI bleeding) requesting blood for 20:00. However, at 19:00 he had a large rectal bleed and died.

The review concluded that:

- There were significant delays in obtaining a valid Hb in a patient with GI bleeding together with mislabelling and rejection of the transfusion sample
- There was failure to recognise the signs: the patient had a sustained tachycardia but maintained normal BP. 'Clinicians should be aware of potential need for urgent transfusion and resuscitation in a bleeding patient with tachycardia, even if the BP is within normal limits'

Case 12a.3: Delayed transfusion despite severe anaemia and GI bleeding

An elderly woman presented to the ED with lethargy and a history of dark stools. She was taking apixaban for atrial fibrillation. Her Hb was 36g/L. Two units of blood were prescribed but not ordered from the laboratory. There was delayed medical review. She had a massive GI bleed after transfer to the ward and died without transfusion after a 9-hour delay.

Learning points

- Gastrointestinal (GI) bleeding can be difficult to recognise and assess, and can be particularly severe in elderly patients on anticoagulants
- Where it is recognised that a patient requires urgent transfusion, delays must be avoided. Every effort must be made to ensure prompt transfusions, which should be commenced without waiting for transfer of patients to other departments

Major morbidity n=6

A patient suffered serious bleeding after a total hip replacement requiring inter-hospital transfer, and transfusion was delayed.

Two patients with GI bleeding suffered delay:

- A patient had a 45-minute delay in provision of components after the MHP was called because there were no trained staff able to collect these (in the operating theatre and out-of-hours). Hypovolaemic shock resulted and the patient required admission to the ICU
- A patient with Hb 41g/L had a 7-hour delay before transfusion and suffered cardiac arrest but survived

Case 12a.4: Ruptured ectopic pregnancy with delayed diagnosis

A young woman presented with vaginal bleeding and three syncopal episodes at 17:45. Her BP 62/30 improved with fluids to 95/53mmHg. She was referred to gynaecology who were unable to review her in the ED, so she was transferred to the ward at 20:15. The diagnosis of ruptured ectopic pregnancy was then considered but not escalated. She became increasingly hypotensive over the next 2 hours with tachycardia and Hb 51g/L on venous gas. When taken to surgery at 23:55 she was haemodynamically unstable, systolic BP 45mmHg, tachycardia of 160bpm. It took more than 1.5 hours to stabilise her and secure venous access. The estimated blood loss was 5-6L. She was admitted to ICU and made a full recovery. The review noted that there had been failure to recognise how sick she was and there was delayed MHP activation.

Two delays resulting in major morbidity occurred as a result of antibodies (see Case 12a.6).

Delays related to presence of antibodies n=8

In 8 cases transfusions were delayed for between 9 and 36 hours due to difficulty in crossmatching. These patients were seriously ill; three died and two suffered myocardial ischaemia due to delay. One death was possibly related to the delay. Three patients had AIHA with severe anaemia and 5 others had antibodies detected on screening. Delays occurred due to the need to send samples to external specialist laboratories for investigation and crossmatch. Poor communication was a notable feature.

Case 12a.5: Death related to failure to transfuse in timely manner in a patient with AIHA

An elderly man with chronic lymphocytic leukaemia complicated by autoimmune haemolysis (diagnosed in 2015) was on a small dose of prednisolone. He was recently noted to have critical aortic stenosis and presented with shortness of breath, dizziness, and blackouts. His Hb was 76g/L and red cells were requested. Transfusion was delayed. Due to a positive antibody screen (AIHA) the blood had to be crossmatched at the specialist red cell immunohaematology laboratory. The correct procedure was not followed exacerbating the delay. The urgency of transfusion was not communicated to the referral service. The next day was a bank holiday. The samples arrived out-of-hours (could be 2 hours by taxi but took longer as sent using a Blood Service driver). The local hospital made available the least incompatible units (ABO Rh-compatible and Kell-negative). Over the course of the next day the Hb result of 59g/L was delayed as samples were marked 'routine', the blood was not given, the patient deteriorated and died. The units were available from the Blood Service within 4 hours of the discussion about urgency. The available local hospital units were 'not

collected as the ward environment was considered too unsafe to give a transfusion' because of high level of patients needing intense input. The transfusion laboratory was understaffed.

Multiple factors contributed to the delay in this case, for example, poor communication, deviation from correct procedures, inadequate staffing in the laboratory and clinical area, all of which could be prevented.

Case 12a.6: Newly diagnosed autoimmune haemolysis results in delayed transfusion

A patient with chronic lymphocytic leukaemia developed severe anaemia (Hb 53g/L) due to new autoimmune haemolysis. Blood samples were obtained at 19:00. A 20-hour delay in obtaining red cells resulted because the samples needed to be sent out to a specialist laboratory. There was poor communication with failure to escalate to haematology consultants and misunderstanding about the concessionary release policy. The patient sustained myocardial ischaemia due to the anaemia (major morbidity).

Case 12a.7: A dangerous antibody in pregnancy

An anti-K antibody in a pregnant woman found at booking (at about 12 weeks) was not reported in a timely manner and was noted by the midwife 4 weeks later when the titre was 1 in 512. This delay impacted referral to the fetal medicine unit. Serial intrauterine transfusions were required starting at about 18 weeks for anaemia.

The antibody result should have been communicated immediately by the laboratory staff to the relevant teams as this is a well-recognised cause of fetal anaemia. The clinical team have a responsibility to follow up the results of blood tests in a timely manner and take appropriate actions.

Case 12a.8: Delay in providing blood for neonatal exchange transfusion due to multiple factors

A neonate with HDFN required an exchange transfusion. Blood was requested from the Blood Service but was not received within the expected timeframe (2.5 hours). When blood was finally delivered 4.5 hours from order time, there were further delays in the hospital laboratory due to problems with the maternal sample and staff misunderstanding of results.

Learning points

- Patients with autoimmune haemolytic anaemia or irregular antibodies are more difficult to crossmatch. Timely and clear laboratory to clinician communication is essential
- Procedures should be in place for concessionary release of red cells for patients with atypical antibodies in an emergency, including early involvement of a haematologist
- Maternal antibodies can cause serious harm to the fetus during pregnancy. Where these are detected and deemed to be clinically significant, appropriate timely actions must be taken to reduce the potential of such harm. When there is doubt or confusion regarding antenatal testing, immune prophylaxis or referral to the fetal medicine unit, laboratory or transfusion medicine experts must be contacted for additional guidance
- Neonatal exchange transfusion for HDFN is an emergency and delays must be avoided to prevent adverse outcome

Concessionary release

In situations of emergency haemorrhage or severe anaemia with haemolysis, blood components that do not meet patient specific requirements may need to be released from the laboratory. This is generally termed concessionary release (BSH Milkins et al. 2013).

Laboratories should have robust procedures for concessionary release of components in these situations that ensure the clinical team treating the patient are aware of the potential risks of transfusion and can balance them against the risk of blood loss. This should include, as a minimum release of:

- D-positive red blood cells for D-negative patients of childbearing potential (risk of production of anti-D that can cause HDFN in future pregnancies)
- Antigen-positive red cells for a patient with clinically significant atypical red cell antibodies (very small risk of delayed transfusion reaction)
- ABO/Rh/K matched red cells to patients with AIHA without exclusion of alloantibodies (very small risk of delayed transfusion reaction)
- Components that do not have specific requirements such as CMV-screened negative or irradiated (very small risk of patient developing CMV infection or transfusion-associated graft versus host disease)

The involvement of a consultant haematologist at the earliest opportunity is vital for concessionary release but should not delay provision of components in massive haemorrhage. If not contactable at the time of the event consultant haematologists must be made aware that a concessionary release has been completed so that the patient can receive appropriate follow up. Use of a script within the concessionary release form that covers the potential risks can help to guide conversations between the laboratory and clinical teams and support the safe provision of blood components. Concessionary release events should be reported, monitored and subject to trend analysis in accordance with local protocols. The patient should not die from bleeding or anaemia.

Near miss case n=1

A woman for an elective caesarean section with high risk of bleeding was not eligible for electronic issue. Prior to the operation the transfusion laboratory was contacted, and a two-unit crossmatch requested. The BMS confirmed that they had an appropriate sample and would do it straight away. The operation proceeded uneventfully but as the patient was returned to recovery (1 hour 15 minutes later) a BMS telephoned to request another sample before crossmatch could go ahead as the sample they had was no longer valid. No blood had been required during surgery, but none would have been available.

The investigation noted a shortage of trained staff in the transfusion department and that there was miscommunication between the different BMS. The BMS who took the first call did what he thought was right but had not been trained in crossmatching and the provision of blood and other components.

Main factors leading to delay

Multiple factors often contribute to delayed transfusion, particularly communication failures. These were primary in 37 reports but contributory in a further 34, altogether cited in 71 reports of delays. The correct procedures were not followed in 55 (43 clinical and 12 laboratory).

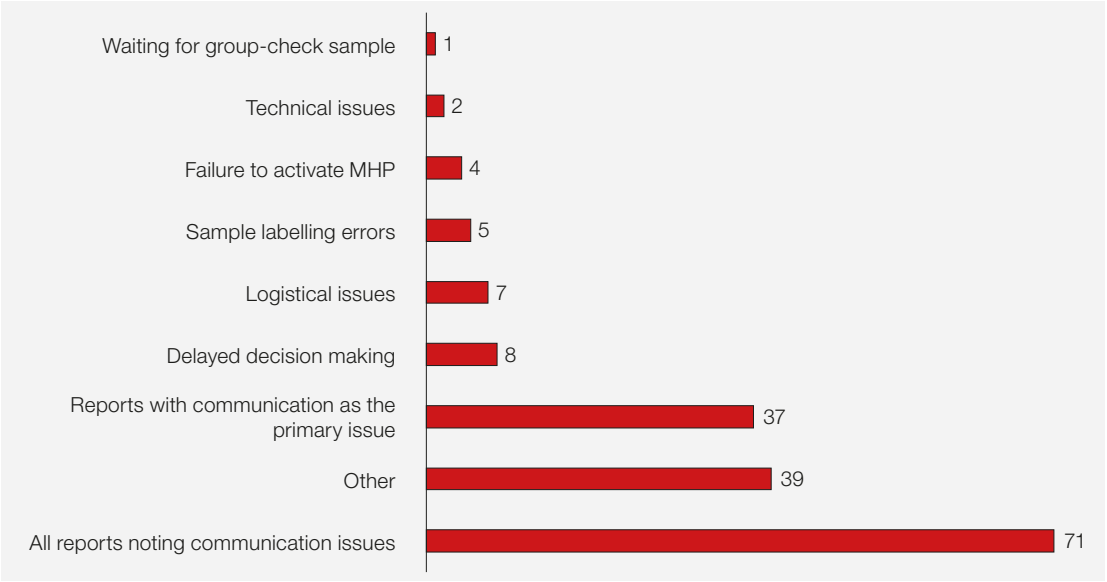


Figure 12a.2: Errors contributing to delayed transfusion

Conclusion

The number of reported delayed transfusions continues to increase each year. The deaths related to this should be preventable with improved communication and attention to the correct activation and actions in the MHP. More than 10 years on from the NPSA rapid response report it is disappointing to see many instances of MHP delays with poor communication. Delays in recognition and treatment of GI bleeding are reported year on year. The safety of patients is compromised by these factors and likely compounded by staff shortages and challenges over the past year.

SHOT
Serious Hazards of Transfusion

References

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BSH Milkins C, Berryman J, Cantwell C, et al. Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories. *Transfus Med* 2013;**23(1)**:3-35. http://onlinelibrary.wiley.com/doi/10.1111/j.1365-3148.2012.01199.x/full [accessed 25th March 2021].

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NCA. National comparative audit of major haemorrhage. 2018. https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/19130/2018-major-haemorrhage-audit-full-report.pdf [accessed 27 April 2021].

Avoidable Transfusions n=110

12b

Definition:

Where the intended transfusion is carried out, and the blood component itself is suitable for transfusion and compatible with the patient, but where the decision leading to the transfusion is flawed.

Key SHOT messages

- Inappropriate management of haematinic deficiency continues and indicates an ongoing need for better education of medical and nursing staff
- Group O D-negative units are a precious resource and D-positive units may be used in an emergency in women over 50 and men over 18 years of age
- Unexpected low platelet counts should trigger careful review of the blood count and diagnosis before prescribing platelets

Abbreviations used in this chapter

AoMRC Academy of Medical Royal Colleges

NBTC National Blood Transfusion Committee

Recommendation

- Hospitals should review their use of O D-negative units and ensure that group O D-positive units are used when possible in emergencies in older patients as advised by guidelines (NBTC 2019)

Action: Hospital transfusion committees

Introduction

The number of avoidable transfusions has increased compared to the previous year. The causes are similar and are discussed below. Where recorded, 48 red cell transfusions were considered to be indicated by BSH guidelines. These included 19 where group O D-negative unit transfusion could have been avoided, and 2 Jehovah's Witnesses. Overall, 46 avoidable transfusions were not in line with BSH guidelines.

Deaths n=0

Major morbidity n=0

Avoidable transfusion of red cells

Key features are considered below.

Haematinic deficiency n=8

Eight patients with B12 (n=3) or iron deficiency (n=5) received unnecessary transfusions. A woman with B12 deficiency was given five units of red cells (Case 12b.1). An elderly man under regular follow up with a history of autoimmune haemolysis was found to be anaemic at a clinic visit so transfusion was arranged; however, the blood findings suggested a diagnosis of iron deficiency on this occasion.

Case 12b.1: Inappropriate management of anaemia

A woman in her 60s with minimal symptoms was found to have Hb 62g/L. She was transfused with three units of red cells without checking the Hb until afterwards when it was 103g/L. She was then found to have B12 deficiency. Three days later when Hb was 89g/L she was given another unit, and a further unit the next day when Hb was 94g/L.

Correct practice for any case of anaemia is to review the MCV on the presenting blood count and to check the haematinics. A raised MCV is a characteristic feature of B12 and/or folate deficiency. While she might have warranted transfusion of a single unit there was no reason to continue to a total of five. The bone marrow responds rapidly to replacement with the missing vitamin. Excessive transfusion can be dangerous in haematinic deficiency. This case (discovered by audit) suggests a lack of knowledge about anaemia and its causes.

Avoidable use of group O D-negative red cells n=25

There were 25 reports of avoidable use of O D-negative red cells; 9 were associated with MH procedures. Four patients had crossmatched units available and the other 5 could have received group-specific units. More than half the individuals could have received group O D-positive red cells, 15/25 (60.0%). This included 9 men (age range 54 to 74 years) and 6 women over the age of 50 years. The 2018 NCA of major haemorrhage procedures (NCA 2018a) showed that 36/67 (54%) males and 22/26 (85%) females over the age of 50 were transfused with group O D-negative red blood cells where group O D-positive could have been given. Group O D-negative blood is a scarce resource, and hospitals should review their local practices in accordance with national guidelines (NBTC 2019).

The NCA of group O D-negative use showed that 6% were transfused in an emergency to females aged over 50 years and males. At that time (NCA 2018b) 31% of sites did not have a policy to provide O D-positive red cells in an emergency to unknown males and females aged over 50 years. If this policy had been applied to all potential recipients in this audit, transfusion of 10% (504/4970) of O D-negative red cells during the audit period could have been avoided.

Case 12b.2: Get the blood sample details right first time – potentially avoidable use of O D-negative blood at delivery

The initial sample from a woman's booking visit to the antenatal clinic was successfully grouped without incident (A D-positive), however a subsequent sample taken 6 months later gave a different result (O D-positive). This discrepancy was flagged on the analyser but was not acted on correctly by the member of staff processing the samples, instead the result was amended manually and transmitted. Three weeks later the group was again O D-positive but was now flagged as a wrong blood in tube. The next grouping sample was clotted. The fifth sample was taken when the woman was in the delivery suite. By now there were two records of A D-positive and two that were O D-positive. Emergency O D-negative blood was issued as the blood grouping results did not match either of the previous results. Neither the acceptance of the discrepant result on the analyser or its subsequent amendment on the LIMS were in accordance with laboratory SOP.

Further information was provided in the investigation report submitted by the reporter. It stated that the provider of LIMS systems was subsequently contacted, and a call logged to investigate whether it would be possible to limit access to the grouping results editor function to higher level staff. On this occasion the member of staff had used this function instead of following documented laboratory procedures. LIMS access rights could not be restricted.

Case 12b.3: Avoidable transfusion of group O D-negative units in an emergency

The MHP had been activated for a patient on the obstetric delivery unit. The porter arrived in the

laboratory to collect the shock pack. The BMS selected a bag containing two units of red cells from the refrigerator, signed them out and handed them to the porter. They were transfused and retrospectively assigned to the patient. This occurred towards the end of a shift. When the next BMS on duty came to replace the shock pack they noticed that although the O D-positive units were signed out and allocated, the O D-negative shock pack was actually given to the porter and had been transfused. The patient's group was O D-positive, this had been checked before the shock pack was collected and was the reason the BMS intended to give the O D-positive units instead of the O D-negative units. On realising the mistake, the BMS allocated the correct units to the patient.

Avoidable transfusion of platelets n=9

Nine cases were reported:

- In 5 cases, patients had spurious low platelet counts due to platelet clumping. A blood film should be examined before issuing the result
- In 1 case the count was low due to a partial clot in the sample which had not been detected in the blood count sample but was noted in the biochemistry samples
- In 3 cases platelets were not necessary (a young woman presenting with immune thrombocytopenia for which platelet transfusions are the wrong treatment; platelets were requested only for standby at caesarean section for another woman but were given). In the 3rd case platelets were transfused in excess of requirements (an elderly woman with lymphoma receiving cover for hip replacement following fractured neck of femur)

Learning points

- An unexpected low platelet count should prompt review of the sample for clots
- Laboratories should explore rules and algorithms within analyser, middleware or laboratory information management systems that can be used to suppress reporting of platelet counts below the lower limits of normal in the presence of analyser flags indicating clumping. The presence of platelet clumps can then be verified by reviewing a blood film and confirmation of a normal platelet count using a sample taken in a citrate tube

Avoidable transfusion of FFP n=4 or cryoprecipitate n=2

- An elderly man on apixaban for atrial fibrillation required a laparotomy. Advice was sought from a haematologist who recommended PCC, but the patient received two units of FFP
- A young woman with liver failure received a single unit of FFP to cover drain insertion but this was not indicated
- Two other patients received FFP which was not indicated
- Medical staff wrongly prescribed cryoprecipitate as part of fluid replacement for plasmapheresis
- Communication confusion resulted in inappropriate transfusion of cryoprecipitate to cover emergency laparotomy. Four units of cryoprecipitate were erroneously ordered, issued from the lab, prescribed and administered by the theatre team when only one unit was originally intended to be transfused to ensure safe fibrinogen levels. Communication was further impacted by a hyperdynamic situation in a busy theatre during the pandemic, compounded by use of wireless telephones with unreliable reception

Near miss cases n=12

An overview of these 12 cases are detailed here:

- In 2 cases, inappropriate transfusion of red cells was avoided by repeat testing in the laboratory when initial analyser results were erroneous

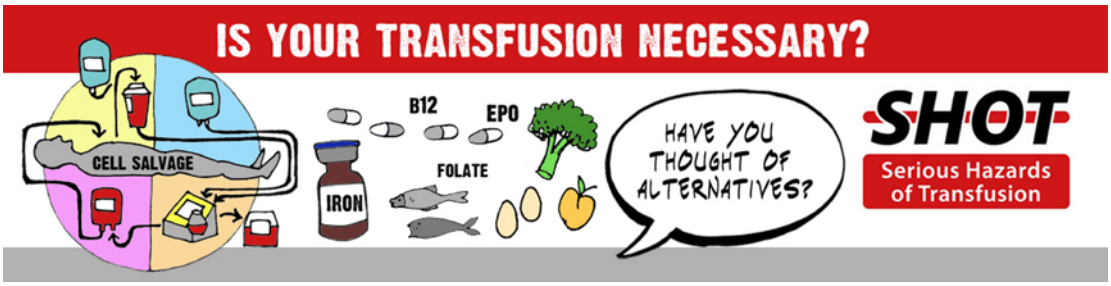
- Six transfusions were avoided because staff recognised that the low Hb results were probably wrong and repeated them
- Transfusion of an additional unit was avoided when staff realised the transfusion was complete, but the second unit had not been recorded on the prescription chart
- There were 2 cases related to miscommunication during MHP activations
- One patient was nearly transfused convalescent plasma for COVID-19 instead of the monoclonal antibody treatment to which they had been randomised

Conclusion

Avoidable transfusions continue to be reported to SHOT and the causes for these remain similar year on year. Transfusions are a valuable and scarce resource and every effort must be made to avoid unnecessary transfusions. This also will help ensure that patients are not put at unnecessary risk of exposure to blood components. Clinicians should be familiar with the 'Choosing Wisely' recommendations for transfusion and ensure that medical and nursing staff receive appropriate education and training about anaemia and its management. Haematinic deficiencies can be detected before severe anaemia develops and primary care teams can help address this before patients are admitted with severe symptomatic anaemia. The Evidence-Based Interventions Proposed List 2, drafted by the independent Expert Advisory Committee to the Evidence-Based Intervention programme and endorsed by the Academy of Medical Royal Colleges (AoMRC 2020) supports the use of red cell transfusions only where indicated and then in single units, unless there are exceptional circumstances. While transfusions are safe there are inherent risks and unnecessary transfusions must be avoided wherever possible.

Recommended Resources

O D-negative red cell tool kit
https://hospital.blood.co.uk/patient-services/patient-blood-management/o-d-negative-red-cell-toolkit/



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Under or Overtransfusion n=25

12c

Definition:

A dose/rate inappropriate for the patient's needs, excluding those cases which result in transfusion-associated circulatory overload (TACO). Infusion pump errors leading to under or over transfusion (if it did not lead to under/over transfusion then it is reportable under handling and storage errors (HSE)).

Key SHOT messages

- In the setting of major haemorrhage, it can be difficult to estimate the quantity of blood lost and the effect of fluid resuscitation
- During the management of haemorrhage regular monitoring of haemoglobin and other parameters is recommended
- Point-of-care testing should be quality assured with oversight from the laboratory, and dubious results confirmed by standard laboratory tests
- Errors continue to be made in paediatric prescribing
- A Blood Assist app is now available (developed by the NHS Blood and Transplant Patient Blood Management team) which gives information for all aspects of blood transfusion (see recommended resources)

Abbreviations used in this chapter

JPAC Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee

Recommendation

- In instances where allogeneic blood components and cell salvage have been used, regular checks of haemoglobin (quality assured point-of-care tests or standard laboratory tests) should take place to avoid over or undertransfusion
- All staff responsible for authorisation of blood component transfusion must be aware of the different component indications and the appropriate dose calculations for fresh frozen plasma and cryoprecipitate for all age groups

Action: Hospital transfusion committees

Introduction

Quantitative transfusion errors leading to overtransfusion are made mostly in paediatric patients due to errors in calculation or pump setting. Overtransfusion and undertransfusion are both risks in major haemorrhage where it can be difficult to assess the balance of gain versus loss.

Deaths n=1

Two deaths were reported in patients who were overtransfused. Both occurred in the management of ruptured AAA with major blood loss during surgery. One death was 'possibly related' to the overtransfusion but the other was unrelated. This is a serious condition with a high mortality rate.

Case 12c.1: Overtransfusion in a case of AAA (1)

A man in his 80s collapsed at home. He was found to have a ruptured AAA and proceeded to surgery receiving a total of more than 3L of red cells and cell salvage material.

The postoperative Hb was 202g/L. He died later the same day (death 'possibly related' to transfusion).

Case 12c.2: Overtransfusion in a case of AAA (2)

This case was associated with estimated blood loss of more than 10L and a postoperative Hb 181g/L. The review (death unrelated to transfusion) noted that reliance was placed on Hb estimation from serial blood gases and formal laboratory tests (FBC, clotting screen and fibrinogen) were not undertaken until the patient was admitted to the ICU postoperatively.

Overtransfusion might have been avoided if near patient testing had been supplemented by formal laboratory blood tests during surgery. However, the case review noted that 'the patient was cardiovascularly unstable with catastrophic blood loss and corresponding aggressive fluid replacement which meant that accurate assessment of fluid balance would have been challenging whatever means of assessment were used'.

Regular monitoring of Hb and coagulation during major haemorrhage is recommended in the Transfusion Handbook (JPAC 2013, link to relevant web page is included in the references and has been updated in April 2020) and BSH guidelines (BSH Hunt et al. 2015).

Major morbidity n=0

There were no cases where major morbidity resulted from over or undertransfusion.

Overtransfusion n=18

Two patients in the RECOVERY trial received excess doses of convalescent plasma for COVID-19 infection by mistake. They were each transfused four units instead of two. Patients randomised to receive convalescent plasma were to be given a single unit on day 1 and if tolerated, then also on day 2 as per the trial protocol. In these cases, the prescriptions had been written as recurring daily, and the error was only identified after four units had been administered. All transfusion decisions should be reassessed regularly, and the appropriateness of subsequent transfusions evaluated.

Other cases:

Case 12c.3: Unexpected complication of pregnancy

A woman in her 30s was found to have an unexpected placenta praevia at caesarean section and suffered major haemorrhage. She received massive transfusion of red cells, plasma, platelets, and cell salvage. Her preoperative Hb was 123g/L and postoperative was 173g/L indicating that she had received more red cells than she needed.

In the setting of massive bleeding, it can be difficult to estimate the losses as indicated in the two cases of AAA described above. This hospital is considering introduction of thromboelastography in the management of major haemorrhage.

Case 12c.4: Hb not checked between transfused units

A woman in her 90s presented with breathlessness due to heart failure and was transfused two units of red cells on the basis of Hb 56g/L. Her Hb was not checked between units and post transfusion was 160g/L suggesting the first result had been incorrect. In addition, the pre-transfusion Hb result of 140g/L on the blood gas machine was not noticed. Fortunately, she did not experience worsening heart failure as a result.

Case 12c.5: An excess of platelet transfusions

A young man with leukaemia and history of retinal haemorrhages received excessive doses of platelets (three units). the decision to transfuse had been made taking into account a historical note in the patient's medical records that the platelet target should be 50x10^9/L. The patient was known to have poor increments to transfused platelets. When the case was reviewed after all the three units were given it was noted that these units were avoidable as the patient platelet count was acceptable and the retinal haemorrhages had occurred several days previously so the platelet target was no longer required. This advice had not been updated in a timely manner in the patient's records.

Case 12c.6: Second unit of red cells transfused without authorisation or clinical need

An elderly woman with pelvic fractures following a fall received a unit of red cells with post-transfusion Hb 85g/L. A second unit was subsequently transfused that was not indicated or prescribed due to miscommunication during handover. The nurse administering the second unit saw that there was another unit available for the patient but did not check the medical notes or blood prescription prior to administering the second unit.

Paediatrics n=9

Nine children age range 10 days to 15 years (6 were aged 2 years or less) received excess volumes. Two cases related to platelets, 1 to FFP and 6 to red cells. Prescription errors were made in 3 cases.

Undertransfusion n=7

Red cells n=4

- One premature infant received 7mL instead of 12mL due to problems with the infusion pump and giving set
- Three patients did not receive the intended quantity of red cells, 1 due to clamping the line shut during transfer, 1 due to the pump alarming and the other because the rate was inappropriately slow (3mL/hour)

Plasma components n=3

One report identified two adults who received inappropriately low doses of FFP because they were prescribed as 10mL/kg instead of units. The doses had been calculated by a consultant haematologist. The nursing staff misunderstood the prescription and, in each case, gave only a single unit. BSH guidelines (BSH Green et al. 2018) note that there is no good evidence for what the dose should be, but a starting dose of 15mL/kg is suggested prior to an invasive procedure. The internal review recommended that the calculated dose is converted to units of FFP to avoid confusion.

An additional patient should have received three units of FFP prior to ERCP but only received one. No bleeding complications were reported.

A patient with hepatic encephalopathy received a single pool of cryoprecipitate rather than the two indicated as a standard adult dose. Following this treatment, the fibrinogen was below 1g/L.

Learning points

- Volume errors are most often made in paediatric transfusion
- Fresh frozen plasma should be given in accordance with national and local guidelines
- The standard adult dose of cryoprecipitate is two pools, each adult pool is made up of five single components
- Those authorising/prescribing need to know the appropriate doses for adults and how to calculate for children

Near miss cases n=7

Six patients avoided overtransfusions (4 children) and 1 infant was nearly undertransfused.

- In 1 case a parent of a regularly transfused child noticed that an inappropriate dose of red cells had been prescribed
- One regularly transfused adult changed the request from 'group and screen' to 'crossmatch two units'. This individual was aware that there were often delays as the crossmatch needed to be done at a specialist laboratory and was trying to avoid delay
- An elderly patient with iron deficiency anaemia (Hb 55g/L) was prescribed 1134mL of red cells by a doctor. This was noted and challenged by the BMS
- Three children had inappropriately large amounts prescribed. The FFP prescription for a 1-year-old was calculated as 100mL/kg instead of 10mL/kg. A second child was also prescribed an incorrect amount of FFP. Another excessive dose of red cells was prescribed based on the weight of the wrong patient
- The ward requested a paediatric platelet pack for a 3-year-old. The laboratory staff queried the volume required but this information was not supplied. The unit supplied was 80mL when the unit arrived at the ward the nursing staff noted that the volume was insufficient.

Conclusion

It is difficult to assess the amount of blood lost in severe major bleeding such as AAA and obstetric emergencies. Clinical staff should do their best to continuously evaluate the balance using quality-assured near patient testing (blood gas analysers, thromboelastography) and regular samples sent to the main laboratory. Paediatric patients continue to be at risk of miscalculation and wrong settings on intravenous pumps. All staff responsible for transfusion should understand the different components and their appropriate dose schedules.

Recommended resource

Blood Assist - a blood administration safety app developed by the Patient Blood Management team at NHS Blood and Transplant.
Apple (https://apps.apple.com/gb/app/blood-assist/id1550911130)
Google play (https://play.google.com/store/apps/details?id=uk.nhsbt.bloodassist)
Web based (www.bloodassist.co.uk)

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Incidents Related to Prothrombin Complex Concentrate (PCC) n=17

12d

Definition:

Hospitals are asked to report any issues with prescription and administration of prothrombin complex concentrate. This include delays in administration, inappropriate prescription, or problems with administration. (Allergic reactions should be reported to the MHRA via the Yellow Card scheme)

Key SHOT messages

- Prothrombin complex concentrate (PCC) administration is an emergency treatment and should be started within an hour of the decision being made and before the patient is transferred to other wards or departments
- Emergency departments should ensure they have clear instructions for PCC administration
- Medical and nursing staff working in emergency departments should be trained in the prescription and administration of PCC

Recommendations

- Emergency departments should ensure they have a protocol for prothrombin complex concentrates (PCC) use with clear instructions for dose and administration, and ensure that staff are appropriately trained in their use
- Use of PCC should be regularly audited for timeliness and appropriateness

Action: Medical directors of acute Trusts/Health Boards

Introduction

These incidents occurred in an elderly population (age range 61 to 97 years, median age 82 years), who often have multiple comorbidities. There were 11/17 reports of delayed infusion, 1 inappropriate treatment to a patient receiving heparin and 3 cases where the patient received less than was prescribed. In another case PCC was administered to the correct patient but labelled with an incorrect surname (right product right patient), and in the final case PCC was issued incorrectly by the pharmacy. An electronic prescription was received, and a new pharmacist issued PCC from stores (which were held for the laboratory), when it should only have been issued from the laboratory. The dose issued was also incorrect.

Deaths n=0

Although 4 patients died, none were related to the PCC incidents.

Major morbidity n=0

There were no complications causing major harm related to these PCC incidents.

Delays n=11

Delays were caused by poor communication, transfer of patients between departments or setting inappropriately long infusion times. Treatment with PCC for anticoagulant reversal is an emergency and should take place within an hour of the treatment decision. Two studies from teaching hospitals (one unpublished) demonstrated the median time to administration was 5-6 hours (Toth et al. 2013). In the Toth study the mean time to PCC for ICH was 3 hours and the mortality from ICH was 22.3%, a reminder of the serious nature of this disease.

Case 12d.1: Three cases of suspected ICH with delayed infusion

- *In a patient on warfarin with a head injury, there was a 4-hour delay while the patient was moved between departments and the prescription was lost*
- *Following a head injury in a patient on apixaban for atrial fibrillation the infusion was set to run at 1mL/hour instead of 1mL/minute. This was recognised after running for 16 hours*
- *A man in his 80s with suspected ICH had delayed administration because each vial was collected separately from the transfusion laboratory rather than all collected together*

Additional factors included unfamiliarity of staff with PCC prescription and administration, the use of infusion pumps calibrated in mL/hour, verbal instructions, and rearrangement of the ED due to COVID-19.

Learning points

- Medical staff working in emergency departments and medical/surgical admissions units should be trained in the indications and ordering of prothrombin complex concentrate (PCC) so that it can be administered without delay for anticoagulant reversal in the face of major haemorrhage
- PCC should be easily accessible, and consideration given to keeping a stock in the emergency department (but this blood product must be fully traceable)
- Where use of PCC is indicated immediate reversal of anticoagulant should take place (and certainly within an hour) especially in cases of suspected intracranial haemorrhage

Comment

Could delays be reduced by using a fixed PCC dose? What is the evidence for fixed dose PCC for warfarin reversal?

Delay in administration of PCC is potentially life-threatening. The mortality related to ICH is high, nearly 34% in the USA (Sweidan et al. 2020). PCC should be kept in the ED with a simple dosing structure independent of the degree of abnormality of the INR (Toth et al. 2013). PCC are blood products and must be traceable, so that the batch number must be recorded in the patient record and transfusion laboratory.

There are no UK guidelines recommending fixed dose protocols, but several papers in the literature support this with variable evidence. Many are not very robust studies (retrospective case series, observational studies) and do not always give the clinical outcome, although clearly demonstrating that the INR can be rapidly reduced. The use of fixed dose may also have financial benefit.

The reported fixed dose was usually either 1000 or 1500IU (some used 2000IU). Some patients needed additional doses to achieve the INR goal. The higher the INR and the heavier the patient, the more likely it is that additional doses will be required. A literature review up to 2018 (Schwebach et al. 2019) noted that patients with a high INR or ICH may need higher doses. A randomised controlled trial is underway to assess the standard variable dose regimen compared with a fixed dose of 1000IU in patients on vitamin K antagonists with extracranial bleeding, and the protocol has been published (Abdoellakhan et al. 2018).

The Oxford University Hospitals NHS Foundation Trust use a simplified and standardised weight-based protocol, Table 12d.1(Oxford University Hospitals 2017). The Royal Devon and Exeter NHS Foundation

Trust use a fixed dose protocol (1000IU), with an additional dose (500IU) given if indicated (Davies et al. 2020). However, it is crucial that treatment is 'immediate' for ICH (NICE 2015). The American College of Cardiology consensus guidelines for anticoagulant reversal include a fixed dose option of 1000IU and 1500IU for ICH (Tomaselli et al. 2020). The use of a fixed dose of PCC simplifies management and can reduce the time to treatment which is an advantage and is easier to organise. Although studies show good reduction of the INR after fixed doses for warfarin reversal, currently there is no clear published evidence of benefit to morbidity or mortality. Whatever dose is given the INR should be checked 15-30 minutes after the dose to confirm the reduction in INR and may guide the need for additional doses. The effect of the PCC will wane and therefore the INR should be repeated over the next few days to confirm satisfactory correction.

The patient on warfarin should always also receive IV vitamin K urgently which will generate increased synthesis of factors 2, 7, 9 and 10 within a few hours providing a longer lasting correction.

PCC may also be used for selected direct oral anticoagulants. The evidence has been reviewed recently (Sweidan et al. 2020). Canadian authors recommend that for a patient on dabigatran consider the specific reversal agent idarucizumab 5g. For a patient on a Xa inhibitor (apixaban, rivaroxaban), give PCC 2000IU; if significant bleeding persists after 1 hour, a second dose of 2000IU of PCC should be considered; while not approved in Canada, a specific reversal agent to Xa inhibitors, andexanet alfa, has also been used in these situations as a continuous infusion (Callum et al. 2021). Reversal of oral anticoagulation in patients with ICH has recently been reviewed noting the importance of rapid treatment (Kuramatsu et al. 2019).

Weight	Dose of PCC
Less than 60kg	1500IU
60-75kg	2000IU
76-90kg	2500IU
Greater than 90kg	3000IU

PCC= prothrombin complex concentrate

Table 12d.1: Warfarin reversal in haemorrhage: dose of PCC (Oxford regimen)

Near miss cases n=1

PCC was requested and issued for the wrong patient. The doctor used an addressograph label from another patient who had been in the same area of the ED earlier whose paperwork had not been fully cleared. The telephoned order should be made from the patient's prescription. The error was discovered at the bedside pre-administration check. Staff went to the correct patient but observed that the product was labelled with the wrong patient's details.

Conclusion

PCC is an important treatment for immediate reversal of vitamin K antagonists and some other oral anticoagulants and should be given immediately after a decision is made. All clinical staff involved in the acute care of patients with suspected serious haemorrhage, particularly ICH, who are eligible for reversal should ensure that they know how to obtain and how to administer PCC. Delay can contribute to death.

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