11 Avoidable, Delayed or Under/ Overtransfusion (ADU), and Incidents Related to Prothrombin Complex Concentrate (PCC) n=279

Authors: Paula Bolton-Maggs and Simon Carter-Graham

Key SHOT messages

- Do not delay in asking for help from haematologists when grossly deranged coagulation results are reported. Isolated prolongation of the activated partial thromboplastin time (normal thrombin time and fibrinogen) in a male infant indicates factor VIII or IX deficiency and warrants urgent investigation because appropriate factor replacement may be lifesaving
- There is continued evidence of poor understanding and activation of major haemorrhage procedures resulting in delayed transfusion
- Prothrombin complex concentrate administration remains poorly understood. When indicated this should be infused within an hour
- Children continue to be at risk of errors in volumes transfused
- All staff responsible for any part of the transfusion process must be adequately trained to identify available components and their doses
- Poor communication remains an important feature in delayed transfusion and avoidable transfusion of O D-negative units

Abbreviations used in this chapter

APTT	Activated partial thromboplastin time
AV	Arteriovenous
BMS	Biomedical scientist
CQUIN	Commissioning for Quality and Innovation
CT	Computerised tomography
FFP	Fresh frozen plasma
GCS	Glasgow coma score
Hb	Haemoglobin
HSE	Handling and storage errors
ICH	Intracranial haemorrhage
ICU	Intensive care unit
INR	International normalised ratio
IT	Information technology
IV	Intravenous
MHP	Major haemorrhage protocol
MDT	Multidisciplinary team
NICE	National Institute for Health and Care Excellence
NM	Near miss
PCC	Prothrombin complex concentrate
POCT	Point-of-care testing
PT	Prothrombin times
QA	Quality assurance
SD-FFP	Solvent-detergent fresh frozen plasma
SOP	Standard operating procedure
TEG	Thromboelastography
TACO	Transfusion-associated circulatory overload

Overview of ADU cases

- **Delayed transfusion n=129** (an increase from 117 in 2018)
- **Avoidable transfusions n=99** (106 in 2018)
- **Under or overtransfusion n=35** (an increase from 15 in 2018)
- **Cases related to PCC n=16** of which 11 were delays (an increase from 9 in 2018)

Some PCC cases involved delays in provision and avoidable use but have been counted and analysed separately from those related to blood components in line with the standard SHOT reporting definitions.

Death n=4

Three of these related to delay, 2 due to a delay in red cells, and 1 to failure to give PCC in a timely manner. The 4th case was related to inadequate component transfusion in major haemorrhage associated with surgery.

Major morbidity n=4

Three cases were delays reported in relation to major haemorrhage and the 4th due to delay resulting from inter-hospital transfer.

Near miss (NM) cases n=12

Seven of these were avoidable transfusions. One was a child where a diagnosis of sickle cell disease/ trait was not considered prior to surgery.

There was 1 near miss related to delay in provision of blood, 2 related to overtransfusions, and 2 related to PCC (1 delay and 1 overtransfusion).

Information technology (IT)-related ADU cases n=25

Twelve cases were avoidable transfusions; 2 related to point-of-care testing errors and there were 3 instances where patients had apparently low platelet counts due to clumps; these results should not have been reported.

Eleven cases related to delays and 2 were overtransfusion related to pump errors.

Further details of the IT-related reports can be found in the supplementary information on the SHOT website (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2019/).

11a Delayed Transfusions n=129

Definition:

Where a transfusion of 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

- Patients are put at risk when staff do not act appropriately in the event of major haemorrhage
- Isolated prolongation of the activated partial thromboplastin time (normal prothrombin time, thrombin time and fibrinogen) in a male infant indicates factor VIII or IX deficiency and warrants urgent investigation. Laboratory standard operating procedures (SOP) should reflect this and all biomedical scientists who work 'on call' should be appropriately trained to recognise this

Recommendations

- All hospitals should regularly review their major haemorrhage procedures to ensure communication lines and practice this with drills (NPSA 2010)
- Laboratory tests of haemostasis must be interpreted in the context of clinical findings as well as other laboratory test results. Appropriate timely actions will help to avoid unnecessary delays in diagnosis and enable potentially lifesaving treatment for patients with unexplained bleeding

Action: Hospital transfusion teams, consultant haematologists, laboratory managers

Introduction

The number of reported delayed transfusions has increased from 106 in 2018 to 129 in 2019. There were 83/129 (64.3%) reports where the primary error occurred in the clinical setting, 45/129 (34.9%) in the laboratory and 1/129 (0.8%) was caused by a delayed flight. In 63/129 (48.8%) reports the need for the transfusion was emergency/urgent, 36/129 (27.9%) were elective transfusions and in 30/129 (23.3%), this was not recorded. Poor communication between the clinical and laboratory settings and staff shortages were the main contributory factors in these cases. In addition, there were 11 delays in administration of PCC, and these are counted and considered in that section. Please see Chapter 11d, Incidents Related to Prothrombin Complex Concentrate (PCC) for further information.

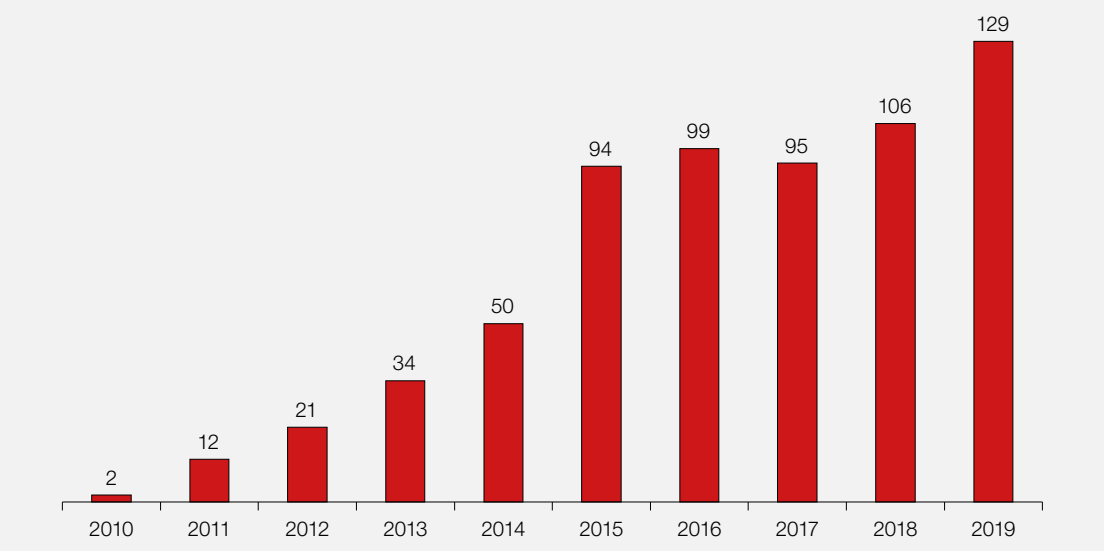

Figure 11a.1: Delayed transfusion reports by year 2010 to 2019

Death n=2

The delay was 'possibly' contributory to the patient's death in 2 cases.

A young man with bone marrow infiltration due to cancer (leucoerythroblastic blood picture) had a reported haemoglobin (Hb) 47g/L and was scheduled for a four-unit transfusion. He died two days later, not having received the planned transfusion. His Hb, prior to his death, was recorded on a point-of-care machine as 26g/L. The investigation noted that his life-expectancy was very poor, and it was unlikely that the transfusion would have made a difference.

A case that was not recognised by the reporter as a death related to delayed transfusion involved an elderly man with gastrointestinal bleeding with delayed diagnosis of a large duodenal ulcer. Clinical reviews and transfusions were repeatedly delayed with poor recognition of ongoing bleeding and transfers between departments. His Hb remained less than 60g/L over a prolonged period (17 hours) resulting in a cardiac arrest. At the inquest the coroner concluded that the recorded cause of death at 1b on the death certificate was 'haemorrhagic cardiac arrest'.

Learning point

- Gastrointestinal bleeding can be difficult to assess. Prompt recognition and timely management is imperative. Delays can contribute to patient death. Every second counts

A male infant in whom a diagnosis of haemophilia was delayed died from intracranial haemorrhage. This was due to an arteriovenous (AV) malformation and the clinicians did not think that an earlier diagnosis would have made a difference.

In a further case of delay, a woman in her 90s had delayed administration of PCC in relation to an intracranial bleed (this case is counted and described in Chapter 11d, Incidents Related to Prothrombin Complex Concentrate (PCC)).

Major morbidity n=4

Three cases were reported in relation to major haemorrhage.

A young man was admitted with major haemorrhage caused by a stabbing injury to his carotid artery. Red cells were rapidly available but the provision of fresh frozen plasma (FFP) was delayed (slow thaw) and platelets were not ordered urgently. The biomedical scientist (BMS) was lone working covering two departments leading to communication problems. The patient suffered a stroke which was attributed in part to delay in receiving plasma and platelets. A complete overhaul of the major haemorrhage policy and education of medical staff were undertaken.

An elderly man had severe gastrointestinal bleeding. There was delay in provision of blood components due to constraints in contacting the porter because of industrial action. Delay in correction of his coagulopathy resulted in admission to the intensive care unit (ICU).

A man in middle age was admitted as an emergency with serious gastrointestinal bleeding. There was delay in obtaining blood components for 1.5 hours after the major haemorrhage call due to lack of porters. This delay contributed to his deterioration requiring admission to the ICU with renal failure.

Case 11a.1: Inappropriate interhospital transfer in a patient with a falling Hb

An elderly woman was admitted after a fall (no fracture) 2 weeks from discharge following hip surgery (Hb 90g/L). She was found to have a popliteal vein thrombosis and was anticoagulated. Eight days later she was considered fit for transfer. However, her Hb had been falling and on the day of transfer was 58g/L. She was transferred at 12:00 before the blood results were reviewed. The hospital was experiencing winter pressure and the need to free up beds. Her condition deteriorated during transfer (National Early Warning Score (NEWS), 10), despite five hours at the second hospital, where electronic issue blood was available for the patient, she was returned to the emergency department at the first hospital for transfusion. After a delay of 45 minutes in the ambulance she was admitted at 18:00 (Hb now 46g/L). At this point the patient was showing signs of hypovolaemic shock. The first request form for crossmatched blood was sent to the laboratory without the required sample which further delayed the transfusion. When a second request for crossmatched blood was sent the laboratory staff were not informed of the urgency of the situation. The patient was transferred to a ward at 19:00; a blood transfusion had not been administered up to this point. The patient had a cardiac arrest at 22:00 and it was not until this point that she received a unit of emergency group O D-negative blood. Three additional crossmatched units were later made available and transfused. The patient survived and was eventually discharged home.

The internal review noted that 'the root cause of the incident was the most recent blood results for the patient were not reviewed prior to the patient transfer. A breakdown in communication, undefined control and command by the various teams involved in the patient's care led to fragmented management of the patient's clinical care'. A review of the transfer criteria/checklist for patients who are to be transferred between hospital sites was carried out to ensure patients are clinically fit and now includes a review of a patient's most recent bloods. At the time of the incident not all staff were aware of the major haemorrhage protocol, this highlighted learning and training needs. Staff are now aware of the major haemorrhage protocol and how it should be triggered. Staff training has been carried out for the administration of electronic issue blood. Provision of a 24/7 patient safety team including operational bed manager and critical care outreach team now provides organisational wide command and control for such unpredictable patient deterioration. The pressure on bed availability was a systems issue which contributed to the need for transfer.

Delayed transfusion associated with major haemorrhage n=16

Sixteen cases of major haemorrhage were associated with delay. One was not associated with activation of the major haemorrhage protocol (MHP), but 15 were. Six cases reported delay due to porter access, 2 due to pager failure. Overall, 6 reports cited issues with logistics and provision of components and 6 cited communication issues between the clinical area and the laboratory, but review of the cases showed several problems with communications affecting 15/16 cases. These are the same issues as identified in 2018. Eleven were emergency transfusions, 3 urgent and in 2 cases not specified. Six cases were in the emergency department or medical admissions unit, 4 in wards, 5 in theatre, recovery or ICU and 1 in obstetrics.

There was poor understanding of MHP; staff had not been trained and did not know what number to call. In 8 cases FFP provision was delayed. Further education about the time required to thaw FFP is required for clinical teams.

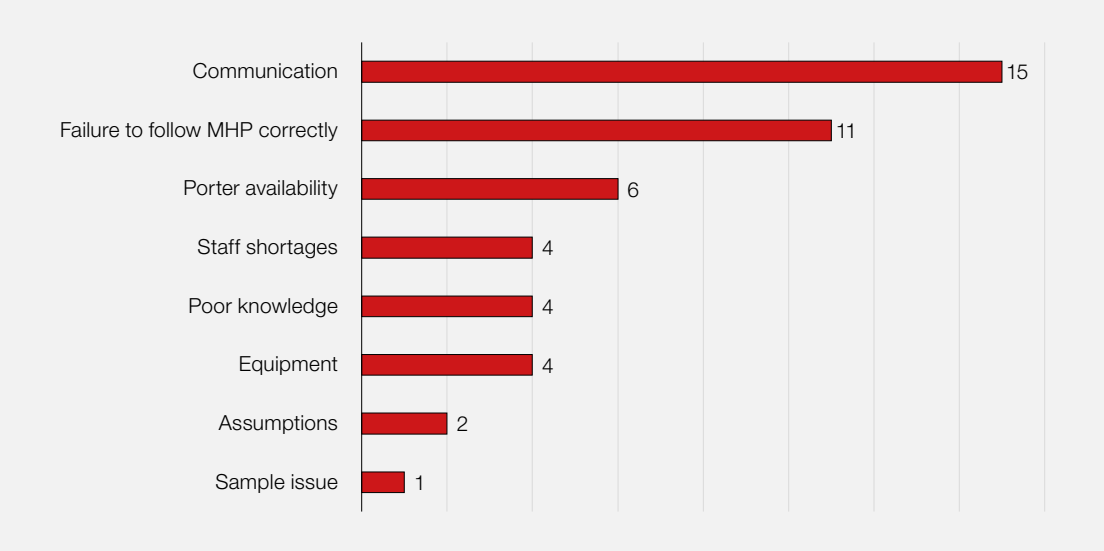

Figure 11a.2: Factors contributing to delayed transfusion in 16 cases

MHP=major haemorrhage protocol

There were delays in transportation of components between a hub with a transfusion laboratory and a specialist hospital with a surgical unit. A young man bled during elective surgery for malignant disease requiring platelets and plasma which took 1.5 hours to arrive (a distance of about 2 miles, usual transport time less than 10 minutes). The courier was delayed and could not be contacted. This patient received eight units of red cells, eight of FFP and two of platelets.

Illustrative cases

It is important that there are clear lines of investigation and accountability where multifactorial errors occur. One elective transfusion was delayed by several hours following a need for samples to be taken four times. After the first sample was sent the ward was told no request for blood had been made by the doctor. The second and third samples were rejected by the laboratory staff as the sample forms were not completed correctly. A fourth sample was sent, tested and blood was made available. The original request form was eventually found in the laboratory, meaning the first sample could have been tested after all. This caused a delay of 9 hours. There was no case review and no transfusion team input as the hospital had contracted out to a private laboratory provider. The fundamental reason for the delay in this case was the misplaced blood request form in the laboratory. A junior doctor involved with the inaccurate request form completions received training due to the subsequent sample errors.

Treatment with solvent-detergent treated FFP was delayed for a woman with acute myeloid leukaemia because the BMS did not know how to issue it – this case is discussed in Chapter 14, Laboratory Errors, Case 14.2.

Case 11a.2: Delayed treatment of gastrointestinal haemorrhage

A man in his 60s was admitted with chest symptoms and possible gastrointestinal bleeding. His Hb fell over 2 days from 115g/L to 96g/L on day 2, and 50g/L early the following morning when he had a cardiac arrest. Although the laboratory staff provided all components promptly there were misunderstandings with the medical staff who had not received adequate training, and communication was confused. The review considered that transfusion could have occurred earlier as the Hb was clearly falling.

Case 11a.3: Delayed treatment of severe anaemia

An elderly woman was admitted with anaemia, possibly due to bleeding. Her Hb was 45g/L and she was not adequately transfused over the next 6 hours and had a cardiac arrest. The patient was located in a busy and overflowing department and was moved several times during her stay which contributed to the delay. As a result of this incident changes to clinical practice have been implemented regarding the group-check sample rule (i.e. that in an emergency, O D-negative units can be obtained).

Case 11a.4: Missed diagnosis and delay in treatment of a child with haemophilia and intracranial bleeding

A male infant <6 months of age presented to hospital A with a history of falling down the stairs while in his mother's arms. The child was seen by a consultant and was noted to be unharmed, and there were no safeguarding concerns.

Six days later the infant re-presented at hospital A with an acute collapse. The computerised tomography (CT) scan showed an extensive intracranial bleed with mid-line shift. Two coagulation screens showed an un-clottable activated partial thromboplastin time (APTT) with normal prothrombin time (PT). No further investigations such as coagulation factor assays were performed. The infant had vitamin K administered before transfer to a tertiary centre, hospital B. He was transferred as a time critical transfer, details of the discharge summary and communication between hospitals was not available.

At hospital B the infant was electively intubated. Coagulation samples were sent to the laboratory ~8 hours following admission. His APTT was 101 seconds with normal PT and thrombin time. The BMS noted in the report that these were abnormal and requested a repeat, but the abnormal results were not discussed with a haematologist by either the laboratory or clinical teams. Solvent-detergent fresh frozen plasma (SD-FFP) was requested, and 3 units of SD-FFP were issued and transfused. This resulted in partial improvement in APTT to 47s but not full correction. After the third plasma transfusion, the results were discussed with a haematologist over 24 hours after admission to hospital B. A diagnosis of haemophilia A was made following specific blood tests for clotting factors (factor VIII found to be 7IU/dL). Factor VIII concentrate was administered 48 hours after admission, and 36 hours post APTT of 101s. The child also had a pulmonary haemorrhage and subsequently died from the intracerebral bleed. The case review noted that an intracranial arteriovenous malformation was the cause of bleeding. RCA identified lone BMS working overnight covering haematology/ blood transfusion with unclear SOP combined with lack of recognition of importance of isolated prolongation of APTT by clinical and laboratory staff as key factors and corrective and preventive action to address these were instituted.

There are several learning points from the case to help improve patient safety and care given in similar situations in the future with learning applicable to both clinical and laboratory teams. Essentially the diagnosis of haemophilia was delayed resulting in delayed institution of the right treatment.

An isolated prolonged APTT in a male infant (with normal PT and TT) is characteristic of severe haemophilia A (factor VIII) or B (factor IX deficiency). This requires urgent investigation, even outside core hours, as the correct replacement therapy can be lifesaving. This was missed in both the hospitals involved. At each hospital, no contact was made by either the clinical or the laboratory staff to immediately alert the haematology medical staff to seek advice or arrange factor assays. Intracranial haemorrhage is a recognised presentation of severe haemophilia at this age and although this child had an AV malformation, the previous history of a fall down the stairs 6 days prior has added significance. If the haemophilia had been known the child would have received prophylactic factor cover. Vitamin K is not indicated for treatment of an isolated prolonged APTT.

The BMS in the second hospital was under pressure, lone working on night shift covering haematology, coagulation and blood transfusion. Whilst coagulation results are often abnormal in patients in ICU, medical staff also failed to recognise the significance of isolated prolongation of APTT in a male infant with intracranial bleeding. The standard operating procedures (SOP) have been revised appropriately to clarify laboratory action when there is an isolated prolonged APTT and procedures for authorising FFP. Laboratory staffing has been reviewed with a plan to ensure that there are two qualified BMS at night with clear policy for escalation. The UK Transfusion Laboratory Collaborative standards (2014, being updated currently) set out the minimum standards for staff qualifications, training, competency and the use of information technology in hospital transfusion laboratories and compliance with these are accepted by both the United Kingdom Accreditation Service (UKAS)/Clinical Pathology Accreditation (UK) Ltd (CPA) and the Medicines and Healthcare products Regulatory Agency (MHRA) as evidence to support their inspection programmes for laboratories.

This case also demonstrates the importance of a comprehensive, full handover of complex patients between hospitals to ensure no relevant history or test results are overlooked. Education of clinical staff as well to be able to recognise red flags in interpreting basic haemostatic tests and the importance of timely management is vital.

Delay in requesting appropriate tests was a significant factor in this case. Clinical teams need to ensure that appropriate samples are sent based on clinical profile with correct tests requested, results followed up and actioned. Safe patient care is only possible when all staff involved work collaboratively with a shared responsibility. Coagulation screening is frequently performed in unwell patients, often inappropriately, and results are often misunderstood (Amukele et al. 2011, Samkova et al. 2012). Consultant and trainee haematologists will be able to assist in interpreting the results and taking appropriate actions. Figures 11a.3 and 11a.4 summarise the basic coagulation tests and their interpretation.

Learning points

- Severe abnormalities of coagulation in a bleeding patient require urgent discussion with a haematologist
- Severe bleeding disorders can present in neonates and early childhood in the absence of family history
- In the neonatal period and up to 6 months of life the interpretation of coagulation results can be complex and normal ranges appropriate for age and gestation should be used, thus underlining the need for early specialist input
- Laboratory coagulation standard operating procedures should state what action to take when there is an unexpected isolated prolonged APTT. There should be urgent discussion with a haematologist. Factor VIII and IX assays should be performed as an emergency so that the missing factor can be replaced. Fresh frozen plasma does not contain a sufficient concentration of the missing factor to correct haemophilia A or B and treat bleeding in this setting
- Communication between hospitals during patient transfer must be comprehensive and include all laboratory information including any pending results
- Clinicians must provide laboratory staff with relevant clinical information so that they provide appropriate interpretation of results and be open to challenge by laboratory staff
- A holistic systems approach to incident investigation, reviewing timelines and mapping events throughout the patient journey would help to identify missed learning opportunities

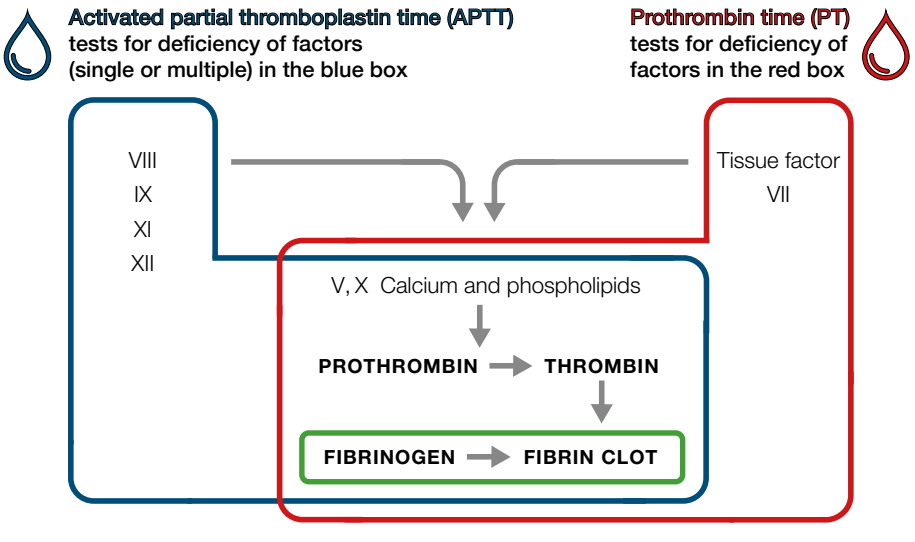

Figure 11a.3: Mechanisms of the coagulation screen to show which coagulation factors affect the standard tests

Figure 11a.4: Interpretation of the coagulation screen

Prothrombin time	Activated partial thromboplastin time	Thrombin time	Interpretation
Abnormal	Normal	Normal	Factor VII deficiency
Normal	**Abnormal**	Normal	Deficiency of FXII, XI, **IX, VIII** (single or multiple)
Abnormal	Abnormal	Normal	Deficiency in the common pathway, isolated V or X deficiency. Multiple factors e.g. liver disease, warfarin therapy

Notes: *many sick patients have disturbances of coagulation tests that* ***do not predict bleeding (and in some cases are associated with a thrombotic risk)****. These tests were introduced in the 1960s to screen for congenital factor deficiencies. The PT is very sensitive to FVII deficiency and is used for warfarin monitoring but note that the APTT will also be prolonged (because FIX is reduced) but to a lesser extent. The sample must be taken carefully (good venepuncture, free flow) to avoid activation and in the correct volume (as it is taken into a specific volume of anticoagulant citrate) to avoid erroneous and misleading results.*

Isolated prolongation of the APTT can be due to haemophilia A (FVIII deficiency) or B (FIX deficiency,) where the need for diagnosis and treatment is urgent. It is also prolonged in FXII deficiency (common but of no clinical significance) and factor XI deficiency (uncommon and usually not associated with serious bleeding). The thrombin time does not depend on other coagulation factors as thrombin is added to the test system. Many laboratories measure the amount of fibrinogen rather than the thrombin time. (Prolongation of standard coagulation tests can also be caused by inhibitors).

Vitamin K results in increased synthesis of factors II, VII, IX and X so will correct the PT but not FVIII, FXI, V or X deficiency. Normal ranges are different in childhood and any hospital with paediatric patients must use an age-appropriate normal range to avoid unnecessary investigation and treatment.

Near miss delays n=1

A major haemorrhage call was initiated for a patient with an obstetric bleed. Emergency group O D-negative red cells were not available from the two satellite refrigerators due to the need for temperature calibration but were rapidly released from the main laboratory. Laboratory staff had not informed clinical staff that no emergency units would be available from the satellite refrigerators.

Conclusion

The cases reported and described above are of extreme concern and demonstrate systemic shortcomings that should be urgently addressed. These include review of the porter services and emergency back-up arrangements. Where the use of refrigerators has to be suspended temporarily (or longer) for maintenance there must be clear communication of alternative procedures for emergencies.

The management of major haemorrhage continues to require improvement in many hospitals with attention to streamlining communication, training and drills.

References

Amukele TK, Baird GS and Chandler WL. (2011) Reducing the use of coagulation test panels. *Blood Coagul Fibrinolysis* 2011;**22(8)**:688-695.

NPSA (2010) NPSA Rapid Response Report: The transfusion of blood and blood components in an emergency' 21 October 2010. https://www.transfusionguidelines.org/document-library/documents/npsa-rapid-response-report-the-transfusion-of-blood-and-blood-components-in-an-emergency-21-october-2010-pdf-100kb [accessed 08 June 2020].

Samkova A, Blatny J, Fiamoli V, et al. (2012) Significance and causes of abnormal preoperative coagulation test results in children. *Haemophilia* 2012;**18(3)**:e297-301.

Avoidable Transfusions n=99

11b

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

- Group O D-negative units are being used when D-positive would be appropriate in more than 50% of cases
- Poor communication resulted in avoidable use of D-negative units when crossmatched or group specific units were available
- Haematinic deficiencies continue to be poorly recognised and managed inappropriately
- Take time to identify patients and label the sample correctly. This avoids the need for repeat samples

Recommendations

- Hospitals should review their use of O D-negative units and ensure that group O D-positive units are used in emergencies in older patients as advised by guidelines (NBTC 2019)
- Hospitals should promote the Choosing Wisely recommendations related to transfusion and note the NHS Commissioning for Quality and Innovation (CQUIN) safety indicators for preoperative anaemia prior to major surgery

Action: Hospital transfusion committees

Introduction

In addition to the 99 cases, there were 3 cases counted under ‘delays’ with avoidable transfusion, and 4 cases of avoidable PCC administration.

Death n=0

There were no deaths related to the transfusion in this category.

Major morbidity n=0

Avoidable transfusions

Many avoidable transfusions result from wrong results and poor communication. Hospital policies for use of O D-negative units need updating. Note that 23 patients developed transfusion-associated circulatory overload where they received excessive red cell volumes (more appropriately calculated according to weight) and they are reported in the Chaper 17b, Transfusion-Associated Circulatory Overload (TACO).

Avoidable use of group O D-negative units n=31

More than half of these patients (23/31, 74.2%) were adult men and women over 50 years of age. Twenty-two required urgent or emergency transfusion and could therefore have received group O D-positive units.

Learning point

- Group O D-negative red cells are in short supply. Hospitals should use the available toolkit, and transfusion policies should ensure that group O D-positive units are used in emergencies in older patients as advised by guidelines (NBTC 2019)

Crossmatched or group-specific units

In 10 cases crossmatched units were available, and in 5 cases group-specific units could have been given.

Learning point

- It may be useful to have a standard operating procedure for the issue of emergency blood that involves a check of previous pre-transfusion testing in all but the most dire emergencies. This may identify instances where crossmatched units were available

In 5 cases group O D-negative units were used because of delays obtaining crossmatched units due to earlier errors, particularly labelling errors leading to sample rejection and need for repeat samples. One preoperative crossmatch was missed due to failures of communication.

Case 11b.1: Panic at low haemoglobin (Hb) level results in avoidable use of group O D-negative blood

A patient in her 60s was readmitted with bleeding from arthroscopy sites. Her Hb had fallen to 67g/L from 87 four days previously. Her international normalised ratio (INR) was 7.7 (on warfarin for mitral and aortic valve replacements). She was not hypotensive or decompensated. The junior staff gave emergency O D-negative units against the advice of haematology staff. A sample was available in the laboratory and she could have received group-specific units. The INR was corrected using intravenous (IV) vitamin K.

Haematinic deficiencies n=9

Six patients (all female) with iron deficiency and 3 with vitamin B12 and/or folate deficiency received avoidable transfusions. One patient received an unnecessary unit of emergency O D-negative blood. Iron deficiency is common in pregnancy and could be detected as a result of the first blood test taken at the booking visit.

A woman with symptomatic iron deficiency, Hb 59g/L, had a delay in transfusion for several hours while the medical team tried to obtain intravenous iron from pharmacy, but this was not available out-of-hours. (This case is counted in delays). A single unit given in timely fashion would have been appropriate followed by IV iron.

Two men with anaemia and minimal symptoms were transfused inappropriately (one prescribed by a consultant) for B12 deficiency. In contrast one symptomatic woman in her 80s with B12 deficiency, Hb 32g/L, had a delay in transfusion of nearly 16 hours.

Five ‘choosing wisely’ recommendations have been published recently which promote a reduction in unnecessary transfusion (The Royal College of Pathologists 2020).

The NHS England CQUIN scheme for 2020-21 (NHS England 2020) will include a patient safety indicator focusing on the management of preoperative anaemia in patients awaiting major surgery. The overall aim is to ensure that at least 60% of patients are treated in accordance with National Institute for Health and Care Excellence (NICE) guidelines (NICE 2015). 'Major surgery' in this CQUIN includes cardiac surgery, colorectal resection, cystectomy, hysterectomy, hip and knee replacement, and open arterial surgery.

In order to qualify, there is an expectation that within 6 weeks prior to surgery patients will have:

1. Hb measurement to screen for anaemia AND
2. If anaemic, serum ferritin measurement AND
3. If iron deficiency anaemia diagnosed, appropriate oral or IV iron therapy started

Learning points

- Medical staff, particularly those working in emergency departments, need better education about anaemia, in particular how to recognise iron, B12 and folate deficiency which can often be treated with the missing vitamin alone, but when an elderly patient has severe symptoms a limited (usually single unit) transfusion may be indicated
- Primary care physicians have a responsibility to understand and manage haematinic deficiencies appropriately
- The transfusion-related 'choosing wisely' recommendations should be widely promoted, and patients should be encouraged to discuss the appropriateness of their transfusions

Platelet transfusions n=16

Five patients received inappropriate platelet transfusions after low counts were reported without film review. All had platelet clumping. Another patient received an unnecessary platelet transfusion prior to surgery as she was thought to be on clopidogrel, but this had been stopped 4 years previously.

Learning point

- Unexpected low platelet counts should prompt film review and consideration of the possible diagnosis before platelet transfusion is triggered

Prescription for avoidable red cell transfusion based on wrong Hb results n=27

A variety of causes were described. Two patients were transfused on the basis of other patients' results due to 'wrong blood in tube' errors. Erroneous results from blood gas analysers were reported in 5 cases. In 1 instance the point-of-care haemoglobin machine gave a wrong result due to faulty control material. Causes included diluted samples and malfunction of a machine which required cleaning. In 1 case the blood gas printout was wrongly read taking the result for O_2Hb instead of the total Hb. The O_2Hb of 47% was misinterpreted by medical staff as a low Hb of 47g/L. The elderly patient had haematemesis. As a result of the erroneous interpretation, the MHP was activated but stood down when it was realised that the correct Hb was 134g/L (see Annual SHOT Report 2018 page 81 for a similar report last year (Narayan et al. 2019)).

Figure 11b.1: Example of a blood gas result illustrating the difference between total Hb (A) and O2Hb (B) (not the actual case described above)

Results

				Crit. Low	Reference Low	Reference High	Crit. High
Measured (37.0°C)							
pH		**7.37**		[7.20	7.35	7.45	7.60]
pCO_2	↑	**6.8**	kPa	[2.6	4.3	6.4	9.3]
pO_2	↓	**9.0**	kPa	[6.0	11.0	14.4	--]
Na^+	↓	**135**	mmol/L	[120	136	145	160]
K^+		**4.2**	mmol/L	[2.8	3.5	5.1	6.5]
Cl^-		**99**	mmol/L	[80	98	107	120]
Ca^{++}		**1.19**	mmol/L	[0.75	1.15	1.33	1.60]
Hct	↓	**35**	%	[18	37	50	60]
Glu	↑	**14.4**	mmol/L	[2.5	3.6	5.3	25.0]
Lac	↑	**2.3**	mmol/L	[--	0.3	2.0	4.0]
CO-Oximetry							
A tHb	↓	**110**	g/L	[70	117	174	200]
B O_2Hb		**92.5**	%	[--	90.0	95.0	--]
COHb		**1.3**	%	[--	0.0	3.0	10.0]
MetHb		**0.8**	%	[--	0.0	1.5	--]
HHb	↑	**5.4**	%	[--	1.0	5.0	--]
sO_2		**94.5**	%	[--	94.0	98.0	--]
Derived							
BE(B)	↑	**3.1**	mmol/L	[--	-2.0	3.0	--]
HCO_3^-std		**27.3**	mmol/L	[10.0	21.0	28.0	40.0]

↑↓ Outside Reference Range

Learning point

- Healthcare staff should ensure that they know how to read point-of-care test results from blood gas analysers where CO-oximetry results give several different haemoglobin (Hb) variants (e.g. methaemoglobin, carboxyhaemoglobin and reduced haemoglobin as 'HHb'). None of these are the correct or relevant Hb results. If a point-of-care result must be used the correct line is the total Hb, tHb

Plasma and cryoprecipitate transfusions n=6

Fresh frozen plasma (FFP) continues to be given inappropriately either for procedures that do not need it, or at levels of INR that do not need correction (4/6 cases). In 1 case cryoprecipitate was ordered but FFP given without prescription.

Case 11b.2: Use of the wrong haemorrhage protocol leads to inappropriate transfusion of cryoprecipitate

A woman in her 70s bled following an insertion of an intramedullary nail. Thromboelastography results were interpreted using the postpartum haemorrhage protocol and she received cryoprecipitate. The laboratory fibrinogen level was 2.2g/L. A level 2.0 to 3.0g/L would trigger replacement in postpartum bleeding but not in other non-obstetric bleeding. The transfusion was also not properly recorded.

Near miss cases n=7

Reasons included mix up of names (in 1 case the doctor was noted to be exhausted), asking for emergency O D-negative units when crossmatched units were available, failure to check Hb between units and requesting transfusion based on a diluted sample.

The most serious of these was failure to consider sickle cell disease or trait in an Afro-Caribbean child requiring surgery for a fractured femur. Staff had failed to follow their protocols, but transfusion was avoided, and a diagnosis of sickle trait made.

Conclusion

Many transfusions are unnecessary as illustrated above. All staff using point-of-care machines, particularly blood gas analysers, should ensure they understand the results.

Hospitals should follow Blood Service guidelines in relation to use of D-negative units:

The National Blood Transfusion Committee (England) recommends that 'D-negative adult males or women >50 years old with no known anti-D antibodies undergoing major haemorrhage and requiring a significant number of units (>8 units), may receive O D-positive red cells'. Also, 'hospitals should consider usage of O D-positive red cells for unknown adult male patients and women >50 years. The risk of an adverse outcome is likely to be low in this emergency setting and helps conserve O D-negative supply'. A toolkit and other resources are available (NBTC 2019; Carter-Graham et al. 2019).

SHOT
Serious Hazards of Transfusion

References

Carter-Graham S, Bolton-Maggs P, Poles D, et al. (2019) Avoidable use of a precious resource: do not use group OD-negative units when there are alternatives. *Transfus Med* 2019;**29(2)**:25-67 PO25.

Narayan S (Ed), Poles D, et al. (2019) on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2018 Annual SHOT Report. https://www.shotuk.org/shot-reports/ [accessed 08 June 2020].

NBTC (2019) National Blood Transfusion Committee Responses and Recommendations – Appropriate use of group O D negative red cells 2019. https://www.transfusionguidelines.org/uk-transfusion-committees/national-blood-transfusion-committee/responses-and-recommendations [accessed 08 June 2020].

NHS England (2020) NHS CQUIN scheme for 2020-21 https://www.england.nhs.uk/publication/commissioning-for-quality-and-innovation-cquin-guidance-for-2020-2021/ and https://www.england.nhs.uk/publication/ccg-cquin-2020-21-indicators-specifications/ [accessed 08 June 2020].

NICE (2015) Guideline NG24 Blood Transfusion. https://www.nice.org.uk/guidance/ng24 [accessed 08 June 2020].

The Royal College of Pathologists (2020) Recommendations for Transfusion Medicine. https://www.rcpath.org/profession/protecting-patient-safety/choosing-wisely/recommendations-for-transfusion-medicine.html [accessed 08 June 2020].

11c Under or Overtransfusion n=35

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 overtransfusion (if it did not lead to under/overtransfusion then it is reportable under handling and storage errors (HSE)).

Key SHOT messages

- Volume calculation of blood components in paediatric patients continues to be of concern
- Laboratory scientists should be empowered to question inappropriate requests with support from haematologists
- Point-of-care testing should be set up collaboratively with laboratory support using agreed protocols and standardisation, and hospitals should participate in national quality assurance programmes
- Correct cryoprecipitate dosing is important to avoid under or overtransfusion

Recommendation

- All medical staff, including consultants, who prescribe or authorise blood components must receive transfusion training in order to recognise components, their indications and appropriate volumes

Action: Hospital transfusion teams, hospital medical directors

Introduction

Thirty-five cases were reported in this category of which 30 were overtransfusions. Eleven of these 30 (36.7%) were in children, age range 13 days to 14 years.

Death n=1

An adult died with massive haemorrhage during surgery with inadequate component replacement. Death was considered to be 'possibly related' and is described below.

Case 11c.1: Haemorrhage during surgery with fatal outcome

A woman in her 40s with advanced rectal cancer bled during surgery. The patient started bleeding at varying rates in surgery at 14:00, until this increased at 16:00. There are conflicting reports of when the major haemorrhage protocol (MHP) was activated by the theatre team and the correct procedure was not followed. The biomedical scientist (BMS) reported that the team requested red cells and to withhold the fresh frozen plasma (FFP).

The patient was being monitored with thromboelastography (TEG) so samples were not sent to the laboratory for clotting. FFP was not required because the thromboelastogram was normal. Misinterpretation of Hb levels contributed and there was no documentation of blood loss during surgery. The patient became haemodynamically unstable and the first suggestion of coagulopathy was made at 3 hours from the start of surgery. A request for FFP was then made and haematology contacted for advice. In total she received 26 units of red cells, but only six of plasma, two of platelets, two pools of cryoprecipitate and fibrinogen concentrate once the coagulopathy was evident, but she unfortunately died 3 hours later during the surgery.

This hospital had not followed the recommendations of the National Patient Safety Agency Rapid Response Report (NPSA 2010). Following this case, the MHP was reviewed, and training instituted. New standard operating protocols were established for TEG, for intraoperative blood loss, and quality processes were developed for point-of-care testing.

Learning point

- Hospitals using thromboelastography (TEG) should participate in national quality assurance to increase reliability of their results (https://www.neqascoag.org/point-of-care-poc/point-of-care-programmes/rotem-teg-testing/). Three samples are sent out per year
- The results of bedside testing technologies, such as thromboelastography, should only be interpreted by those with adequate training and knowledge of the specific platform. They should be used in conjunction with patient's clinical symptoms and other testing parameters

Major morbidity n=0

No patients suffered major morbidity. One adult received more red cell units than necessary in the course of elective caesarean section for placenta accreta. A fall in blood pressure during the operation was thought to be due to occult bleeding. Her post-transfusion Hb was 171g/L and she received 10 days of low molecular weight heparin.

It is difficult to criticise transfusion in this case of surgery with a high risk of bleeding. This could be considered a reasonable clinical decision.

Illustrative cases

Paediatric cases n=11

In 11 paediatric cases of overtransfusion (2 of platelets, 9 of red cells) errors were made in calculation of volumes required or pumps were set incorrectly. In 2 instances parents of regularly transfused children (both with haemoglobinopathy) noticed that the transfusion was excessive.

In another case the need for transfusion in a child weighing 3kg was discussed at the multidisciplinary team (MDT) meeting. Although a doctor said '300mL' when the correct dose was 30mL; the rest of the team agreed. Nobody realised this was 10 times the volume required, and the electronic prescribing system had no inbuilt rules to prevent a prescription of such a large volume for a 3kg child. See Case 22.5 in Chapter 22, Paediatric Cases.

Errors in doses of blood components due to lack of knowledge

Case 11c.2: Prescription of five times the correct dose of cryoprecipitate

A young woman was admitted as an emergency with a diagnosis of myeloma with spinal cord compression. During admission she developed marked haemoptysis with evidence of deranged coagulation. Following transfusion of FFP, she was prescribed '10 units' of cryoprecipitate and received seven of these. The correct dose was two units (two pools of five). There was confusion between the locum doctor, who had no experience of prescribing cryoprecipitate, and the haematology

registrar, and this prescription was not challenged either by the laboratory or the nursing staff. It was clear that all staff groups required education about the correct dose of cryoprecipitate.

Case 11c.3: Overdose of platelets

A man in his 80s with a platelet count of 15x10^9/L received four adult therapeutic doses of platelets prescribed by a consultant, where one dose would have been appropriate. The request of 1 'mega' unit was interpreted as being 4 normal therapeutic units and all were transfused. The use of 'non-conventional' terminology by the requesting clinician was compounded by failure to clarify what was required for the patient by several people involved in this incident. The patient made a complete recovery.

Learning points

- All staff involved in transfusion must have mandatory transfusion training which should include identification of all blood components, and instruction about appropriate dosing particularly in paediatrics. The adult cryoprecipitate dose was changed from five single units to pools of five in 2006. A mobile application 'Blood Components' is available to assist blood component dosage (NHS 2018)
- Laboratory staff should be encouraged to challenge inappropriate requests with support from their clinical haematologists

Near miss cases n=2

One of these was a neonate for whom the wrong volume of red cells was prescribed but recognised before transfusion. In the 2nd case red cells were ordered and prescribed for a woman who did not need them.

Conclusion

Paediatric transfusion continues to be a cause for concern. Transfusion training should ensure that clinicians authorising transfusions understand the use of all blood components including indications, monitoring, recognising and managing adverse reactions. Point-of-care testing (POCT) equipment, such as thromboelastography, are proven, powerful technologies that can turn around accurate results in a timely manner. However, their use requires trained staff competent to carry out tests accurately, interpret results correctly and take appropriate action promptly. A quality assurance (QA) programme encompassing training, personnel, equipment, appropriateness of testing, pre-analytical, analytical and post analytical aspects of POCT from sample collection to documenting the final result, is key to the delivery of an accurate and reliable POCT programme (BSH Mooney et al. 2019). Finally, all transfusion decisions must be made after carefully assessing the risks and benefits of transfusion therapy. Clinical and laboratory staff must work collaboratively and in a co-ordinated fashion to be able to deliver individualised, holistic, patient-centred care. This was a key SHOT recommendation in 2018.

References

BSH Mooney C, Byrne M, Kapuva P, et al. (2019) Point of care testing in general haematology. *Br J Haematol* 2019;**187(3)**:296-306. https://onlinelibrary.wiley.com/doi/full/10.1111/bjh.16208#.Xqv87x5c6MI.email [accessed 08 June 2020].

NHS (2018) Blood Components. (version 1.3.0) [mobile app] [accessed 20 April 2020].

NPSA (2010) NPSA Rapid Response Report: The transfusion of blood and blood components in an emergency' 21 October 2010. https://www.transfusionguidelines.org/document-library/documents/npsa-rapid-response-report-the-transfusion-of-blood-and-blood-components-in-an-emergency-21-october-2010-pdf-100kb [accessed 08 June 2020].

Incidents Related to Prothrombin Complex Concentrates n=16

11d

Definition:

Reporters are asked to report any issues with the prescription and administration of prothrombin complex concentrate. This includes delays in administration, inappropriate prescription or problems with administration.

Key SHOT message

- Serious bleeding in patients on warfarin puts their lives at risk. Rapid assessment is required and treatment with vitamin K and prothrombin complex concentrates (PCC) should be administered within 60 minutes and before the patient is transferred between departments or wards

Recommendations

- Hospital policies for administration of prothrombin complex concentrates (PCC) where intracranial haemorrhage is suspected or confirmed should ensure that this treatment is given within 60 minutes
- Teaching about PCC should be included in transfusion training for all staff

Action: Consultant haematologists, hospital transfusion teams

Introduction

PCC allows rapid reversal of warfarin in the context of major or life-threatening bleeding (including intracranial bleeding) usually within 10-30 minutes, but has a transient effect related to the half-life of the factors. Complete longer-term reversal of warfarin requires treatment with vitamin K in addition. Other indications for use of PCC should be discussed with a consultant haematologist and locally agreed protocols followed. It is important to note that PCC is a blood product and therefore unacceptable to some, e.g. Jehovah witnesses. This requires discussion, as some patients who refuse blood components and are bleeding may agree to receiving this.

PCC contains four coagulation factors (II, VII, IX and X). These are the factors that are lowered by warfarin therapy so infusion of these (marketed in the UK as Beriplex® and Octaplex®) results in very rapid correction of the international normalised ratio (INR) in patients on warfarin and is indicated for treatment of bleeding in these patients, particularly for intracranial haemorrhage (ICH).

Sixteen cases were reported in 2019, an increase compared with previous years (12 in 2016; 5 in 2017; 9 in 2018). These are elderly and vulnerable patients, all more than 60 years and 11 more than 80 years of age.

There were 11 cases of delayed administration, 4 in patients with ICH. PCC administration was avoidable in 4 cases; in another case a patient received fresh frozen plasma (FFP) when they should have been treated with PCC. In addition, 2 cases of near miss were reported.

Death n=1

In 1 case delay in treatment with PCC possibly contributed to death.

A woman in her 80s with a mechanical heart valve, treated with warfarin, fell at home sustaining a fractured humeral head. She also had mild anaemia but no evidence of intracranial bleed on admission. Subsequently she was hypertensive and recovering slowly but developed a reduced Glasgow coma score (GCS). An urgent brain computerised tomography (CT) scan showed spontaneous ICH. The neurosurgeons did not want to manage this surgically. They advised reversal of anticoagulation with vitamin K which was given immediately and PCC which was delayed for 5 hours. The patient died as a result of the bleed 5 days later. The delayed PCC administration resulted from confusion about prescription (electronic) and ordering (from the transfusion laboratory). The junior doctor had ordered it but not prescribed it. The system has now been changed to ensure there is no ambiguity.

Major morbidity n=0

There were no cases where major morbidity resulted from PCC errors.

Common features

Review of the cases demonstrated misunderstandings about administration such as a wrong rate and contents of vials added to normal saline. However, the instructions that come with the product are clear and should be followed. Delays were introduced by patient transfers between departments.

Delayed administration of PCC n=11

Miscommunication between the emergency department (ED) and wards to which patients were subsequently admitted resulted in delayed treatment in 5 cases with serious bleeding. These delays ranged from 2.5 to 24 hours.

A patient with ICH did not receive PCC for 10 hours although they had received intravenous vitamin K in the ED. Review of this case resulted in a change to hospital policy. Where ICH is suspected in a patient on warfarin 1000IU of PCC can be administered before the INR is known and before the head CT scan.

In another instance the hospital had insufficient stock to treat 2 patients who each required 3000IU.

Inappropriate administration of PCC n=4

In 1 case a patient had consumed rat poison and was given PCC but all coagulation tests were normal. A 2nd patient with gastric bleeding was given 500IU in preparation for surgery. This had not been prescribed and the surgery did not take place.

A patient on the coronary care unit developed gastrointestinal haemorrhage. The coagulation tests were abnormal with INR 7.4 and activated partial thromboplastin time (APTT) was ‘unrecordable’. He was not on warfarin and it is unclear why the coagulation tests were so abnormal. A discussion between the junior doctor, medical registrar and consultant haematologist resulted in administration of 3000IU PCC, this is contrary to guidance for the use of PCC (NICE 2015).

The abnormal results could have been caused by poor sampling either from a heparinised line or dilution.

Case 11d.1: An asymptomatic patient with very high INR received PCC

An elderly lady with no bleeding but a history of falls was on warfarin for atrial fibrillation. Her INR was very high, 16.2, and she received vitamin K and 3000IU of PCC as an outpatient as prophylaxis on the advice of the Patient at Home team.

This is a balance of risks. The guidelines for a high INR without bleeding recommend the following:

Asymptomatic patients with an INR of ≥ 8.0 should receive 1–5 mg of oral vitamin K (1B). The INR should be rechecked the following day in case an additional dose of vitamin K is required (Makris et al. 2012). In this instance the physician thought the risk of fall (and potential for serious harm

added to by age) was sufficient to warrant reversal, particularly as the patient was at home. Guidelines are not rules. Many hospitals would report an INR of 16 simply as >10. The management here was rational but did not follow guidelines.

Learning point

- Delayed treatment often results from transfer of patients from the emergency department to wards. If prothrombin complex concentrate (PCC) is indicated, it should be given before the patient is transferred

Near miss cases n=2

An elderly man was prescribed PCC to run over a prolonged period of several hours, but this was noted and corrected prior to infusion.

In the 2nd case (transplant surgery) the anaesthetist calculated a dose greater than required (2500IU rather than 2250IU) and then requested a further dose of 1000IU about 4 hours later. This was not appropriate as the maximum recommended dose in 24 hours for this product in these circumstances is 2500IU. The standard operating procedure for PCC was ambiguous and required revision. Medical staff are likely to be unfamiliar with the protocol which in this case was kept in the laboratory. The laboratory biomedical scientist should have challenged the request but was not up to date in competency assessment. The request for the additional dose was brought to the attention of the consultant haematologist who liaised with the medical staff and cancelled it.

Conclusion

PCC is usually required for emergency treatment of bleeding in patients on warfarin. It is usually stored in transfusion laboratories. There may be confusion about location and how to administer this resulting in delay. Patients with ICH should receive PCC within an hour of the decision being made.

SHOT is aware that this is an under-reported area. NHS Trusts and Health Boards are encouraged to regularly review use of PCC and identify areas for improvement.

References

Makris M, Van Veen J, Tait CR, et al. (2012) Guideline on the management of bleeding in patients on antithrombotic agents. *Br J Haematol* 2013;**160**:35-46. https://onlinelibrary.wiley.com/doi/full/10.1111/bjh.12107 [accessed 08 June 2020].

NICE (2015) Guideline NG 24 Blood transfusion. Prothrombin complex concentrate. Thresholds and targets. https://www.nice.org.uk/guidance/ng24/chapter/Recommendations#prothrombin-complex-concentrate-2 [accessed 08 June 2020].