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].