# Fixed dose prothrombin complex concentrate for direct oral anticoagulant and warfarin reversal: a rapid and effective solution

Davies, J., Sansom, V., Ferguson, B, Piper, J, Ngu, L. and Kerr, P.

Royal Devon and Exeter NHS Foundation Trust, Exeter, UK.

## Background

In life threatening bleeding or emergency surgery rapid reversal of anticoagulation is required.

Pro-thrombin complex concentrate (PCC) is licenced for reversal of warfarin, with dosing based on body weight (kg) and INR value (standard dosing).

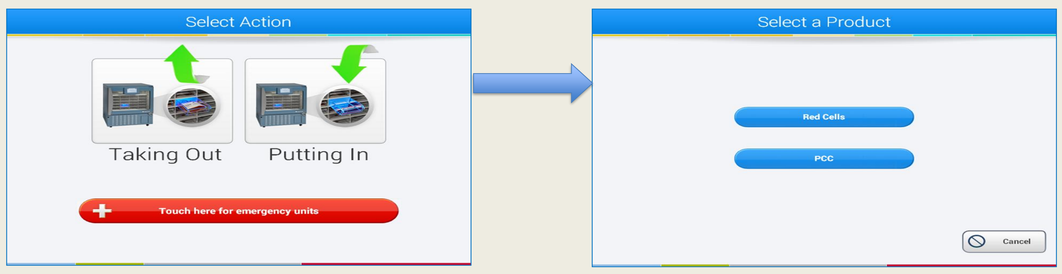
Evidence is available supporting the use of fixed lower dose of PCC for warfarin reversal in these situations. PCC is also used for reversal of direct oral anticoagulants (DOAC) at a maximum dose of 50 iu/kg, but with sparse evidence.

A protocol for fixed dose PCC (FD-PCC) at 1000iu was implemented in our hospital for all indications and anticoagulants, except dabigatran where a specific antagonist is stocked.

The Haemonetics BloodTrack system and laboratory computer system (Integrated Pathology System, DXC) were configured to support "Emergency PCC" enabling removal of 1000iu PCC from the blood fridge by clinicians without laboratory staff involvement (figure 1).

The BloodTrack system, used to administer blood products ensures electronic traceability for emergency PCC. Further doses of 500iu PCC can be requested from laboratory if indicated (figure 2).

Figure 1: BloodTrack® Courier process for accessing emergency PCC; first screen allows access to emergency products via the red bar, the required product is then selected on the following screen. The product is then scanned out using the PCC unique identification code with prompts on subsequent screens.



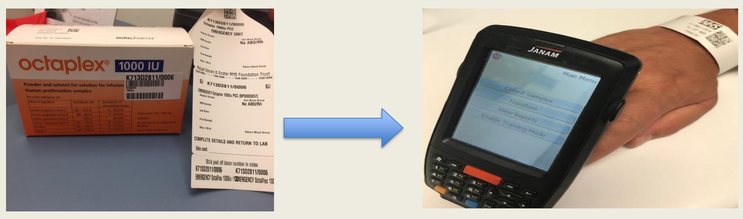




Figure 2: The unique product barcodes on the PCC, with the compatibility label are scanned against the patient ID band using BloodTrack Tx for traceability purposes.

## Aims

- To review the clinical efficacy of fixed dose PCC for DOAC and warfarin reversal
- To review the cost effectiveness of a fixed dose PCC regime

## Methods

Data were gathered from the pathology computer system, BloodTrack and patient clinical notes pre- and post-implementation of fixed dosing for:

- indication for reversal
- Anticoagulant type
- time (request to administration)
- total dose
- blood component usage
- patient survival

Data for variable dosing was obtained from patients treated between April 2015-May 2017 and data for fixed dose between July 2017 – September 2019.

Statistical comparisons were performed using the t-test for continuous data and Fisher's exact for categorical data.

## Results

Warfarin reversal:

136 patients received FD-PCC for warfarin reversal; 46 bleeding, 52 intracranial haemorrhage (ICH) and 38 prior to surgical procedures.

For standard dose PCC (SD-PCC) 21 patient records were available, 6 bleeding, 5 ICH and 10 prior to procedure.

No significant difference (p=0.5656) was found in pre-PCC INR values (FD-PCC mean 3.7, SD-PCC mean 3.4).

No significant difference (p=0.0591) was noted in INR post PCC administration (FD-PCC mean 1.4 and SD-PCC mean 1.3). 8 patients (5.9%) given FD-PCC required additional PCC (figure 3).

Time from request to PCC administration (mins) was significantly reduced (p=0.0001) in FD-PCC (mean 48) compared to SD-PCC (mean 128). Emergency FD-PCC significantly reduced time to administration (p=0.0001) compared to laboratory issue (figure 4).

For bleeding patients, there was no significant difference in red cell (p=0.7650), or fresh frozen plasma (p=1.000) requirements between the two groups.

No significant difference was noted in survival at 24hours (p=0.2649) or 30 day (p=0.5138) between the groups.

DOAC reversal:

47 patients were given PCC for DOAC reversal; 37 FD-PCC and 10 SD-PCC. 13 required FD-PCC for bleeding, 13 for ICH and 11 prior to procedure. 3 patients were given SD-PCC for bleeding, 6 for ICH and 1 prior to procedure.

FD-PCC led to a significant reduction (p=0.0001) in time (mins) from request to administration (FD-PCC mean 32, SD-PCC mean 82).

Time to administration (mins) was significantly faster (P=0.0007) using emergency PCC (mean 23) compared to laboratory issue FD-PCC (mean 42) (figure 4).

For bleeding patients, there was no significant difference in red cell (p=0.8926) or fresh frozen plasma (p=0.9403) requirement between the two groups.

No significant difference was noted in 24 hour survival (p=1.000) or 30 day survival (p=0.4884).

Dose of PCC per patient fell from average 2714iu to 1040iu (figure 5).

Figure 3: Reduction in INR value is comparable following standard dose or fixed dose PPC.

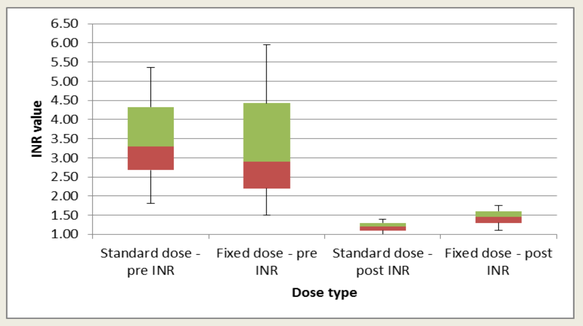



Figure 4: Fixed dose PCC reduces the time to administration compared to standard dosing for warfarin and DOAC reversal. Time to administrations is further reduced by emergency release at the blood fridge.

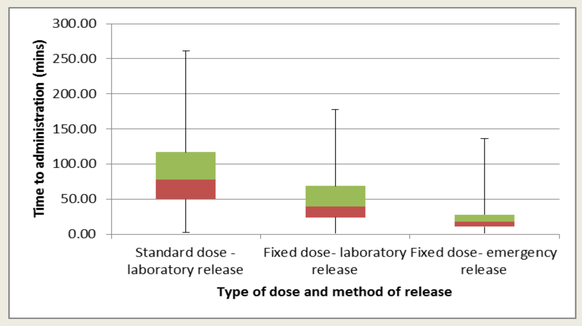
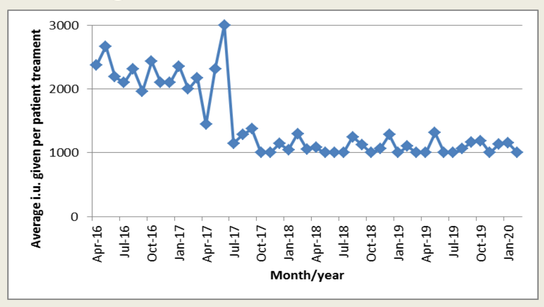



Figure 5: Fixed dose PCC reduces the amount of product used per patient, reducing stock levels and cost




## Discussion

This small study suggests that FD-PCC (1000iu) is as effective as SD-PCC for reversal of warfarin and DOAC.

FD-PCC is simpler to use, reduces time to administration and leads to cost savings.

Use of emergency rather than laboratory issued FD-PCC offers further advantage in time to administration.

No inappropriate use of Emergency PCC has been found

Website http://www.exeterlaboratory.com
Contact jennifer.davies10@nhs.net

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