Fixed Dose Prothrombin Complex Concentrate for Direct Oral Anticoagulant and Low Molecular Weight Heparin Reversal: A Rapid and Effective Solution

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Background

Direct oral anticoagulants (DOACs) are increasingly used in place of warfarin to prevent thrombosis.

In the event of a life threatening bleed, or requirement for emergency surgery rapid reversal of anticoagulation is required. Prothrombin complex concentrate (PCC) is licenced for reversal of warfarin but is often used for reversal of DOAC in the absence of specific reversal agents.

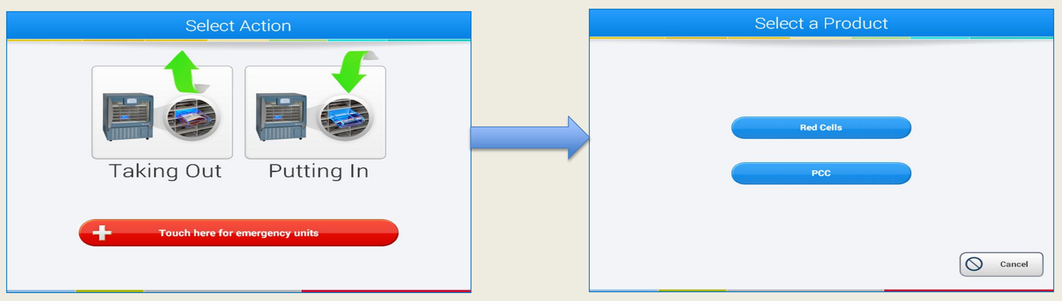
PCC for DOAC reversal is suggested at a maximum dose of 50 iu/kg, but with sparse evidence. Fixed dose PCC (1000iu) was introduced in July 2017 for all indications and all anticoagulants, with the exception of dabigitran for which a specific reversal agent is stocked.

Emergency fixed dose PCC is available electronically via the blood tracking system (BloodTrack, Haemonetics) (fig. 1) or directly from the laboratory.

Traceability is obtained via BloodTrack at administration (fig. 2).

Additional doses, on a named patient basis are available if indicated.

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.



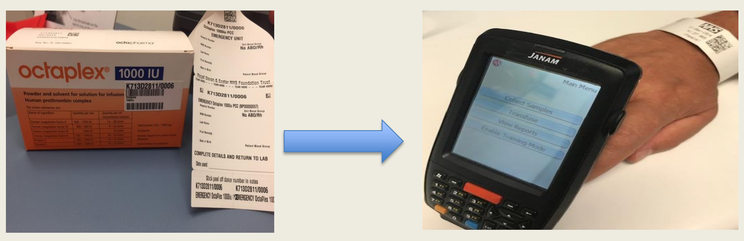


Figure 2: The unique product barcodes on the PCC, with the compatibility label are scanned against the patient ID band using BloodTrack Tx for traceability purposes.

Aims

- To review the clinical efficacy of fixed dose PCC for DOAC and LMW heparin 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
- DOAC 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 – December 2018.

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

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Results

33 cases were identified; 12 variable and 21 fixed dose.

Fourteen intracranial haemorrhage, 12 bleeding (grade 3 ACCP criteria) and 7 pre-procedure.

Rivaroxaban was most commonly used (n=24), followed by apixaban (n=6) and dalteparin (n=3).

Fixed dosing resulted in significant reduction in time (mins) to administration (n=20, mean 43, range 13-85, SD=0.015) compared to variable (n=10, mean 89, range 44-183, SD=0.50) ($p < 0.0001$) (fig. 3).

No significant difference was noted in the total dose used between the two cohorts ($p = 0.2141$).

No significant difference was noted in use of red cell transfusions using fixed compared to variable dosing (T-test p value = 0.5062), or FFP ($p = 0.5021$).

No differences were noted in 24 hour survival rate between standard dosing (11/12 survived, one transferred to another hospital with no follow up) and fixed dose (21/21 survived).

No significant difference (fishers exact p=1.0) was noted in 30 day survival between standard dosing (8/11 with follow up survived) and fixed dose (11/19 with follow up survived).

Use of emergency PCC accounted for 55% of all PCC issues between July 2017 – December 2018.

Access to emergency PCC significantly reduced the time to product administration ($p = <0.0001$) (fig.4).

Fixed dose PCC has led to considerable reduction in cost (fig.5) and product usage (fig. 6).

Figure 3: Fixed dose PCC enables a significant reduction in time to administration compared to standard (variable) dosing.

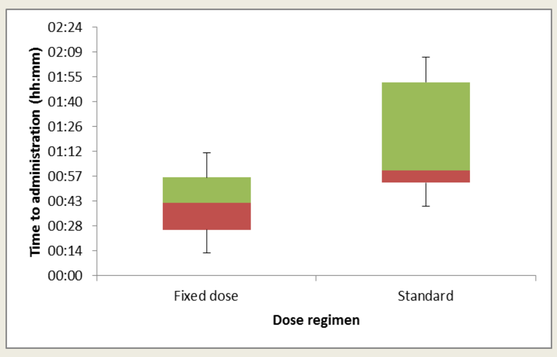
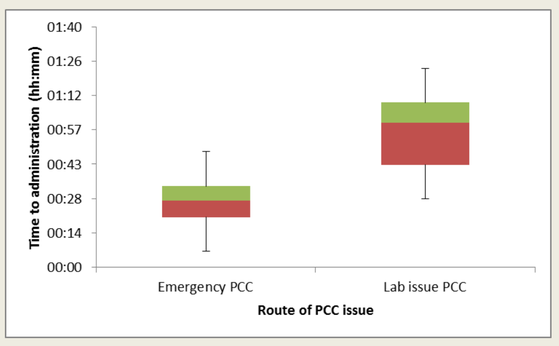
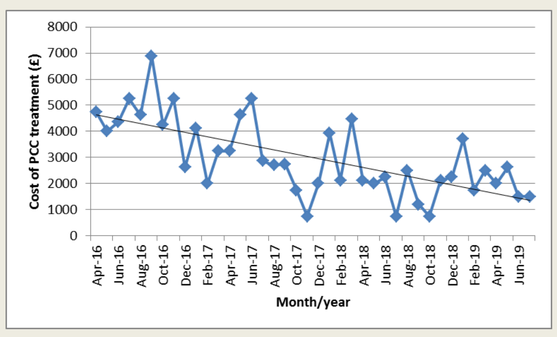


Figure 4: Administration of fixed dose PCC accessed via the emergency process is significantly faster than via the "named patient" laboratory process.





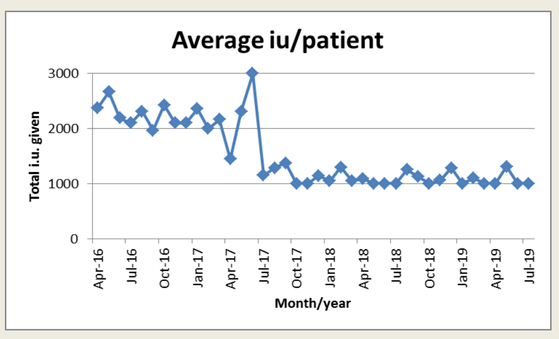


Figure 5: Provision of fixed dose PCC in July 2017 has considerably reduced cost for the Trust.

Figure 6: Fixed dose PCC reduces the amount of product used and reduces stock levels.

Discussion

This small review suggests that fixed dose PCC (1000iu) is effective (using International Society on Thrombosis and Haemostasis definitions 2016) for reversal of DOAC with no adverse effect on mortality.

Fixed dosing eliminates the requirement for ascertaining patient weight, simplifying the process for clinicians and significantly reducing the time to administration.

A fixed dosing regimen results in considerable cost savings and reduces the PCC stock requirement.

Access to emergency PCC significantly reduces time to administration and has not resulted in inappropriate use.

An additional dose of emergency PCC has now been made available in the laboratory for rapid access.