Review of Prothrombinex Use

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Overview

> SAAS MedSTAR
> Prothrombinex
> The Audit
> Results
  • Usage
  • Time
  • Effectiveness
> Comparison to Other Australian Data
> Limitations
> Conclusions
SAAS MedSTAR

> Medical retrieval directorate of SA Ambulance

> Cover large geographic area
  • Fixed wing
  • Rotary wing
  • Rapid response vehicles

> Based at airport
  • Response times improved
  • Remote from hospital resources, including blood bank
Prothrombinex

> The 3 factor prothrombin complex concentrate available in Australia
> Prepared from pooled human donor plasma
> Contains
  • factors II, IX and X; and
  • low levels of factors V and VI
> Relatively easy to store
  • 6 month shelf life at room temperature
> Relatively low bulk
Prothrombinex continued

- Packaged as powder with water for reconstitution
- Each package contains 500iu
- Dose 15-50iu/kg
Prothrombinex

> Indications
  • Treatment or prophylaxis of bleeding in acquired deficiency of prothrombin complex factors, such as deficiency caused by treatment with vitamin K antagonists.
  • Treatment or prophylaxis of bleeding in patients with single or multiple congenital deficiency of factor IX, II or X when purified specific coagulation factor product is not available.

> Other uses
  • Some evidence suggesting efficacy in other bleeding with prolonged INR.
Prothrombinex governance

- Stored in drug fridge on base
- Total of 6 ampules 3000iu total
- Decision to take made by the tasking retrieval consultant
- Removed into esky if required
- Once removed from fridge marked with 6 month expiry date and stored in air conditioned room
- Option to rotate back to a hospital if approaching expiry
The Audit

- Ethics approval was obtained from the Southern Adelaide Clinical Human Research Ethics Committee.
- Cases where Prothrombinex was administered by the retrieval team were identified from the retrieval service patient database.
- The paper case cards of the identified patients were then manually reviewed.
- Finally, the data matched to patients in the state-wide electronic laboratory record.
Results

- Between 1 January 2010 and 31 November 2013 thirty-eight cases were identified.
- Over the same period there were 4402 adult retrievals
- Paired INR’s were available for 33 or the 38 patients
Usage

> 28/38 (74%) on warfarin
> 10/38 (26%) not on warfarin
The median time saved was 120 minutes (range 40 - 285 mins)
Dose given

> The median dose of Prothrombinex administered was 26.5 iu/kg (range 13.3 – 54.5 iu/kg)
Effectiveness

> 33/38 Had both pre and post INR’s available
  - 5 no pre INR available
  - Died
  - Unable to be data matched

> Effectiveness defined as receiving INR ≤1.5
Effectiveness

> There was no significant difference between starting and destination INR’s in the non warfarin group

> There was a significant difference between starting and destination INR’s in the warfarin group (p<0.005 Related samples wilcoxon signed rank test)
## Effectiveness

<table>
<thead>
<tr>
<th></th>
<th>Reversal</th>
<th>Not reversal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>23</td>
<td>4</td>
</tr>
<tr>
<td>Not warfarin</td>
<td>2</td>
<td>7</td>
</tr>
</tbody>
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P <0.001 Fisher’s Exact Test
Confounders

There was no significant difference between starting INR and dose given between the warfarin and no-warfarin groups (Mann-Whitney U test)
Comparison to other data

> Our usage is similar to Royal Perth hospital usage:
  • 35/47 uses were for warfarin reversal
  • Mean dose given 18 iu/kg
  • Was most effective in correcting INR in the warfarin group

Prothrombinex-VF use in warfarin reversal and other indications

Prothrombinex-VF powder for injection (PTX-VF); CSL Biotherapies, Melbourne, Vic) is a prothrombin complex concentrate (PCC). Each vial contains 500 IU factor II, 500 IU factor IX, 500 IU factor X, 25 IU antithrombin III, 192 IU heparin sodium and < 500 mg human plasma proteins. PTX-VF is indicated in the treatment and perioperative prophylaxis of bleeding in acquired deficiency of coagulation factors caused by vitamin K antagonists (ie, warfarin), and the treatment and prophylaxis of bleeding in patients with congenital coagulation factor deficiency. However, clinical data on the efficacy of PTX-VF are limited and the optimal dose is yet to be determined.1,2 Locally, the Australasian Society of Thrombois and Haematostasis recommends the use of 25-50 IU/kg of PTX-VF for warfarin reversal. However, the bleeding in patients with congenital coagulation factor deficiency is yet to be determined.

Abstract

Objective: To assess the use of Prothrombinex-VF powder for injection (PTX-VF) at Royal Perth Hospital and analyse the efficacy and safety profile of PTX-VF.

Design, setting and patients: A prospective observational audit of PTX-VF use, conducted by reviewing medical records and laboratory and imaging results for all patients prescribed PTX-VF from 1 November 2009 to 1 May 2010.

Main outcome measures: Data on indication, diagnosis, comorbidities, dose of PTX-VF, fresh frozen plasma (FFP) and vitamin K, coagulation parameters before and after PTX-VF administration, and adverse effects.

Results: 334 vials of PTX-VF were administered to 84 patients over 107 prescriptions. Indications were warfarin reversal, intraoperative bleeding and coagulopathy (56, 20 and 21 prescriptions, respectively). PTX-VF with FFP was compared with PTX-VF alone for warfarin reversal. In the International Normalised Ratio (INR) that was independent of group (P < 0.001). Lower doses of PTX-VF (< 25 IU/kg) were compared with higher doses (25-50 IU/kg). PTX-VF without FFP was effective, PTX-VF was used in intraoperative bleeding and non-warfarin coagulopathy. No adverse events were associated with PTX-VF.
Limitations

> Retrospective audit
  • Potential to have missed cases
  • Some data not available

> Guidelines changed

> NOAC

> Can this be extrapolated to other products?
Conclusions

> With a robust, but relatively simple, governance process prothrombinex can be managed remotely from a hospital blood bank.
> Usage pattern was similar to other hospital case series
> 25iu/kg represents a reasonable balance of effectiveness vs bulk
> Effectiveness in non-warfarin related bleeding is less clear