Canadian Journal of Emergency Medicine (2023) 25:946–948
https://doi.org/10.1007/s43678-023-00587-y

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Does 4-factor prothrombin concentrate (4F-PCC) reduce 24 h blood product consumption in trauma patients at risk of massive transfusion?

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Received: 30 June 2023 / Accepted: 17 August 2023 / Published online: 26 September 2023

Full Citation: Bouzat P, Charbit J, Abback PS, Huet-Garrigue D, Delhaye N, Leone M, Marcotte G, David JS, Levrat A, Asehnoune K, Pottecher J. Efficacy and Safety of Early Administration of 4-Factor Prothrombin Complex Concentrate in Patients With Trauma at Risk of Massive Transfusion: The PROCOAG Randomized Clinical Trial. JAMA. 2023 Mar 21

Article Type: Therapy

Ratings: *Methods*—4/5, *Usefulness*—3.5/5

Introduction

Background

Massive hemorrhage in trauma remains a clinical challenge and there remains uncertainty regarding the optimal resuscitation strategy for these patients.

Objectives

This study assessed the efficacy and safety of 4F-PCC administration in trauma patients at risk for massive transfusion and whether 4F-PCC reduces 24-h blood product consumption.

Methods

Design

Double-blind, randomized, placebo controlled superiority trial.

Setting

12 level I academic trauma centers in France.

Subjects

Included trauma patients ≥ 18 years admitted from scene to participating trauma centre at risk of massive transfusion.

Intervention

Compared 4F-PCC at 25 IU of factor IX per kg (1 mL/kg) and placebo (0.9% saline solution at 1 mL/kg).

Outcomes

Primary outcome was the total number of blood product units consumed in the first 24 h. Multiple secondary outcomes were assessed including arterial/venous thromboembolic events, 24 h and 28-day mortality and time to hemorrhage control.

Communicated by Ian Stiell.

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Main results

The two groups were overall well balanced. However, the 4F-PCC group received less TXA in comparison to the placebo group (76% vs. 86%) and also had higher systolic blood pressure (101 vs. 96).

This study used a modified intention-to-treat analysis, where patients were not included in the analysis if consent was withdrawn as mandated by French law. Among the 324 patients included, there was no statistically significant difference in median total 24 h blood product consumption in patients who received 4F-PCC vs. placebo. However, there were more thromboembolic events observed in the 4F-PCC group.

Outcome	4F-PCC (No. [%])	Placebo (no. [%])	Absolute difference (95% CI)	Relative risk (95% CI)	*p*-value
Total blood product consumption, median (IQR), U	12 (5 to 19)	11 (6 to 19)	0.2U (− 2.99 to 3.33)		0.72
Thromboembolic events	56 (35)	37 (24)	11 (1 to 21)	1.48 (1.04 to 2.10)	0.03

Appraisal

Strengths

- Useful question with minimal current evidence
- Pragmatic randomized control trial
- Double-blinded study design
- Low loss to follow—only patients who withdrew consent were loss to follow-up

Limitations

- The primary outcome was a surrogate endpoint rather than a true patient centered outcome.
- The trial used a combination of 4F-PCC, TXA and fibrinogen rather than 4F-PCC alone. 4F-PCC and TXA have a relative contraindication to be used together due to concern for potential interactions which may have contributed to higher rates of VTE.
- Innate differences between the pre-hospital systems in France and Canada may impact the applicability of the results, specifically with the availability of a physician on scene and the ability to give blood and TXA in the France pre-hospital system.

Context

Prior to this study, there was a lack of high-quality evidence assessing 4F-PCC in trauma. In an observation study, the combination of 4F-PCC and FFP resulted in improved survival and reduced transfusion requirements compared to FFP alone with no difference in VTE [1]. In a systematic review, compared with FFP alone, PCC and FFP demonstrated improved survival and no increased risk of VTE, however only 3 studies were included. [2]

A local trauma surgeon, Dr. Jacinthe Lampron, commented that this trauma population differs slightly from the typical urban Canadian trauma patients with long prehospital time (105 and 100 min), also, the time to get access to FFP in hospital seems long (73 and 91 min) and they had a low ratio RBC: platelet. Also, it is unclear if they had prehospital intervention or blood products administration. However, at this point in time, with the information of this study, 4F-PCC should not be systematically administered for hemorrhaging trauma patients.

Bottom line

In trauma patients at risk for massive transfusion, we should not empirically be using 4F-PCC in our transfusion strategy. The PROCOAG trial demonstrated that the administration of 4F-PCC did not result in a statistically significant reduction in transfusion requirements and was associated with higher risk of VTE, thus not supporting its routine use in trauma resuscitation.

Acknowledgements We thank Dr. Jacinthe Lampron, general surgeon and medical trauma director for the Ottawa Hospital for providing her expert opinion and contribution to this review.

Data availability The study data presented in this article was published by the Journal of the American Medical Association (JAMA) by Bouzat et al.

Declarations

Conflicts of interest No conflicts of interest to declare.

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