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Trauma-induced coagulopathy, could cryoprecipitates improve outcomes?

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Article type
Therapy (Clinical Trial)

Rankings
Methods 4/5
Usefulness 3.5/5

Introduction

Background

Uncontrolled hemorrhages remain one of the primary causes of death in injured patients. Trauma-induced coagulopathy is associated with increased blood loss and mortality [2] and fibrinogen deficiency is a key contributor to this coagulopathy. The addition of cryoprecipitates to massive hemorrhage protocols has been previously proposed to mitigate the progression of trauma-induced coagulopathy, but the benefits associated with their use are still unclear [3].

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Objectives

To determine whether early and empirical cryoprecipitate transfusion could improve survival of trauma patients requiring a massive hemorrhage protocol.

Methods

Design

Multicenter, open-label, double-blind randomized controlled trial.

Setting

Conducted in 25 major trauma centers in the United Kingdom and 1 in the USA.

Population

Adult trauma patients (≥ 16 years old) with a severe injury, a systolic blood pressure less than 90 mmHg and an active hemorrhage requiring activation of a massive hemorrhage protocol.

Intervention

Patients in the treatment group received the blood products as specified by the local massive hemorrhage protocol with an additional three units of empirical cryoprecipitates administered as early as possible in the resuscitation bay. The control group received blood products as per their local massive hemorrhage protocol. The local regimen typically involved a balanced 1:1:1 ratio of packed red blood cells (RBCs), fresh frozen plasma (FFP) and cryoprecipitates. Notably, most massive hemorrhage protocol included units of cryoprecipitates in their second box.

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Outcomes

The primary outcome was all cause of mortality at 28 days.

Results

1604 patients were randomized into either the intervention group (799) or the control group (805). The primary outcome occurred in 23.1% of patients in the treatment group compared to 22.5% in the control group (Odds ratio (OR) 1.03; 95% CI 0.77–1.37). A pre-specified subgroup analysis revealed that 28-day mortality in the penetrating trauma was higher in the treatment group (16.2%) than in the control group (10.0%) (OR 1.74; 95% CI 1.20–2.41). No other statistically significant differences were observed among the other analyzed subgroups. In addition, there was no statistically significant difference between the two groups in terms of mortality at any time, inhospital outcomes, the number of units of blood products used in the first 24 h after the trauma, thromboembolic events or the incidence of adverse events.

Appraisal

Strengths

- Clinically relevant question
- Patient population had a high injury severity score, which could give a greater chance of seeing a treatment effect
- Robust study design with a strong internal validity

Limitations

- Convenience sampling with several patients excluded due to the unavailability of the research team
- High rates of protocol crossovers
- Fibrinogen levels were not assessed due to the empirical nature of the intervention
- Patients received an average of two liters of crystalloids, potentially exacerbating dilutional coagulopathy
- Several patients in the control group received cryoprecipitates, which could introduce bias toward the null hypothesis
- Unknown time of prehospital transport, which could increase baseline mortality in patients with longer transports
- Unblinded study design with the absence of placebo

Context

Fibrinogen deficiency can occur in trauma patients, exacerbating trauma-induced coagulopathy. A randomized controlled feasibility trial conducted in 2015 in two trauma centers based in the United Kingdom demonstrated the feasibility of administrating cryoprecipitates in less than 90 min to patients with major traumatic bleeding requiring massive hemorrhage protocol [4]. However, the CRYOSTAT-2 study showed that the empiric administration of cryoprecipitates was not associated with improved outcomes and potentially associated with increased mortality in penetrating trauma patients. Hence, no data suggest that we should give empiric cryoprecipitates to bleeding trauma patients requiring massive hemorrhage protocol. Current recommendations from well-established trauma associations recommend to administrate fibrinogen if the serum level falls below 1.5 g/L. We believe that this recommendation, despite the lack of very robust evidence to support it, should be use to guide practice.

Bottom line

Trauma is a heterogeneous and complex pathology. In accordance with the findings of the CRYOSTAT-2 study, empirically giving cryoprecipitates to all severely injured patient requiring massive hemorrhage protocol is not beneficial and associated with increased mortality in penetrating trauma patients. Based on current evidences and the expert opinion of our local trauma leaders, continuing to utilize fibrinogen levels to guide cryoprecipitates administration appears to be the preferred approach. In the near future, rapid bedside testing could be of interest as it could allow us to tailor the administration of blood products based on the specific patient's coagulation profile.

Declarations

Conflict of interest None to declare.

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