CRITICAL CARE

COMMENTARY

Fibrinogen depletion in trauma: early, easy to estimate and central to trauma-induced coagulopathy

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See related research by Schlimp et al., http://ccforum.com/content/17/4/R137

Abstract

Fibrinogen is fundamental to hemostasis and falls rapidly in trauma hemorrhage, although levels are not routinely measured in the acute bleeding episode. Prompt identification of critically low levels of fibrinogen and early supplementation has the potential to correct trauma-induced coagulation and improve outcomes. Early estimation of hypofibrinogenemia is possible using surrogate markers of shock and hemorrhage; for example, hemoglobin and base excess. Rapid replacement with fibrinogen concentrate or cryoprecipitate should be considered a clinical priority in major trauma hemorrhage.

Fibrinogen is the primary substrate of the coagulation system and is fundamental to hemostasis. Fibrinogen falls to critical levels soon after the onset of major trauma hemorrhage but is not considered part of routine clotting assays. To maintain the integrity of coagulation function it is recommended that fibrinogen is replaced when it falls below 150 to 200 mg/dl. Early recognition and replacement has the potential to rapidly reverse trauma-induced coagulopathy, arrest hemorrhage and improve outcomes. Schlimp and colleagues have demonstrated that it is possible to estimate fibrinogen in the emergency department using widely available point-of-care assays [1].

The literature contains numerous reports of improved outcomes when early high-dose plasma is administered as part of a massive hemorrhage protocol. Fibrinogen supplementation with either cryoprecipitate (the UK or USA) or fibrinogen concentrate (Europe) is often delayed or considered second line in the empiric delivery of hemostatic coagulation therapy. The therapeutic mechanism by which plasma controls hemorrhage or corrects coagulopathy remains unknown. Early fibrinogen supplementation is commonplace in postpartum hemorrhage and cardiac surgery, with only limited data indicating a potential therapeutic benefit in trauma [2]. Each unit of plasma contains approximately 500 mg fibrinogen, and therefore the efficacy of large-volume plasma transfusions in massive hemorrhage protocols may in part be due to restoration of fibrinogen levels. For this reason, early fibrinogen replacement is the subject of two pilot randomized controlled trials in the UK (CRYOSTAT) [3] and Austria (FiTIC) [4] due to report later this year.

Fibrinogen falls early [5], rapidly reaches critical threshold values relative to other coagulation factors [6] and is associated with higher transfusion requirements and increased mortality. Schlimp and colleagues have confirmed that hypofibrinogenemia is common in major trauma and is an almost universal problem in those patients presenting with hemoglobin <8 g/dl [1]. The identification of early hypofibrinogenemia requires a laboratory assay; for example, the Clauss method. Fibrinogen levels are rarely available to the trauma physician in a clinically relevant timeframe and thus fibrinogen supplementation (for example, cryoprecipitate) is often delayed.

Rotational thromboelastometry and thromboelastography provide a more rapid and global assessment of coagulation and can provide an estimate of the contribution of functional fibrinogen to clot strength [7]. These tests are expensive, however, and although available at point of care they require further modification, simplification and validation before this technology has global appeal for the trauma community. This study has shown it is possible to risk stratify patients for low or critical fibrinogen levels, using

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hemoglobin and base excess that are rapidly available in emergency trauma care. However, even with the addition of the Injury Severity Score, which is not available within the first few hours of care, the regression model only accounted for 51% of the variation in fibrinogen. Other important, iatrogenic and patient factors therefore contribute significantly to the depletion of fibrinogen in trauma hemorrhage.

The mechanism by which fibrinogen loss occurs in trauma continues to be the subject of ongoing debate and research. There is limited evidence to support a consumptive process such as disseminated intravascular coagulation [8,9], although clearly fibrinogen will be utilized because the coagulation system is activated following hemorrhage. Acidosis and hypothermia compound trauma-induced coagulopathy and have profound effects on fibrinogen breakdown and synthesis [10], which is supported by the findings of the current study that demonstrated critical and low levels of fibrinogen in 81% and 63% of shocked patients, respectively [1]. Finally, resuscitation with gelatins and hydroxyethyl starch solution reduce the concentration of fibrinogen through dilution and interfere with fibrin polymerization [11]. Fibrinogen is thought to only contribute approximately one-third of viscoelastic strength to the overall clot, with platelets being the major determinant of clot firmness in rotational thromboelastometry/thromboelastography. Estimation of fibrinogen deficit alone risks missing the global derangement of hemostasis typified by trauma-induced coagulopathy.

The estimation of fibrinogen levels by Schlimp and colleagues reminds us that fibrinogen loss is not only rapid and significant in trauma but is detectable in the emergency department. Metabolic acidosis, injury severity and hemorrhage reduce fibrinogen, but other endogenous and iatrogenic factors contribute to the depletion of this primary substrate of coagulation. Rapid identification of hypofibrinogenemia should be routine in all injured patients and a priority in major trauma hemorrhage, either through estimation or functional assessment with rotational thromboelastometry/thromboelastography. Understanding the mechanism by which fibrinogen is lost and the efficacy of early fibrinogen replacement are research imperatives, and are likely to yield significant therapeutic benefit.

Competing interests
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