

Haemorrhage Control in the German Army – Lessons Learned

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ABSTRACT

Modern warfare causes severe injuries, and despite rapid transportation to theatre regional trauma centres, casualties frequently arrive coagulopathic and in shock. Conventional resuscitation beginning with crystalloid fluids to treat shock causes further dilutional coagulopathy and increased hemorrhagic loss of platelets and coagulation factors. It is a recommendation of the transfusion medicine council (TMC) of the federal armed forces of Germany that the administration of rFVIIa combined with hypotensive resuscitation can increase survival time of combat casualties. The TMC further encourages the use of fibrinogen for combat casualties with massive haemorrhage and also the transfusion of fresh whole blood (FWB) for trauma induced coagulopathy as well.

1.0 INTRODUCTION

In the current conflict in Afghanistan and Kosovo soldiers with severe injuries caused by high-velocity weapons and explosive devices presented in significant numbers to military hospitals. As a result, military physicians are seeing combat casualties who require massive transfusion at four to five times the frequency seen in civilian practice. Haemorrhage is the most frequent cause of potentially preventable deaths in the field hospitals. Potentially preventable hemorrhagic deaths occur when patients arrive at field hospitals with potentially surgically correctable injuries but bleed to death before control of bleeding is achieved or is effective. Such combat casualties need better haemostatic and circulatory support to keep them alive and to stop their bleeding. In this paper the author represents the recommendations of the TMC of the Federal Armed Forces of Germany concerning haemorrhage control.

2.0 USE OF RECOMBINANT FACTOR VII A IN THE DEPLOYED MILITARY SETTING

2.1 Factor VIIa (Novo Seven)

Factor VIIa occurs naturally in the body and combines with exposed Tissue Factor in the wall of injured blood vessels and possibly on platelets to activate the clotting cascade. Factor VIIa is also involved in the activation of clotting factors on the surface of platelets (1). Recombinant Factor VIIa (rFVIIa) is a manufactured version of Factor VIIa for intravenous administration (2). rFVIIa is licensed for treatment of bleeding episodes in patients with haemophilia A or B and patients with deficiencies of certain clotting factors (inhibitors of Factors VIII and IX, congenital factor VII deficiency) (3). It is also approved for prevention of bleeding in surgical interventions or invasive procedures in these patients (4). Use of rFVIIa in trauma is currently an “off label” use.

2.2 Human Evidence for rFVIIa in Trauma

rFVII was first used in an Israeli trauma patient in 1999 (5) and there are multiple additional anecdotal reports and some limited case series (6). A five year retrospective cohort study at a Canadian Level 1 trauma centre has concluded that rFVIIa may improve early survival of massively bleeding trauma patients, although surgical control of haemorrhage remains the principal therapeutic aim (7).

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The joint Australian and New Zealand Haemostatis Registry represents a large series of rFVIIa use in trauma outside a randomized controlled trial (108 trauma cases) (8). rFVIIa was found to be effective in controlling haemorrhage in 59% of cases.

US military experience of rFVIIa has been extensive and includes multiple combat casualties with blunt, blast, burn and penetrating trauma, injured by Improvised Explosive Devices (IED) attacks (9).

A recently published article (10) represents the results of two parallel randomized, placebo-controlled double blind clinical trials in thirty –two hospitals including Germany. Among 301 patients randomized, 143 blunt trauma patients and 134 penetrating trauma patients were eligible for analysis. rFVIIa resulted in a significant reduction in RBC transfusions in severe blunt trauma and similar trends were observed in penetrating trauma. Questions regarding minimal effective dose, number and frequency of doses and the indicated patient population creates a field ripe for further exploration.

2.3 Current Recommendation of the Federal Armed Forces Transfusion Medicine Council (TMC)

- rFVIIa is currently authorized for consultant use only in life-threatening haemorrhage where conventional resuscitation and/or surgical techniques have failed.
- rFVIIa should be considered if there is evidence of continued bleeding after 6-8 units of packed red blood cells and correction of coagulopathy with cryoprecipitated plasma failed
- rFVIIa 100mcg/kg IV Bolus (with a second bolus of 100mcg/kg after 60min if required) is advocated as an adjunct in controlling haemorrhage following blunt and penetrating trauma

Contraindications to rFVIIa use as an adjunct to traumatic haemorrhage are:

- Combat Casualty is expected to be unsalvageable despite rFVIIa

3.0 USE OF FIBRINOGEN IN THE DEPLOYED MILITARY SETTING

3.1 Fibrinogen (Haemocomplettan)

As the precursor of clot formation, fibrinogen plays an important role in coagulation function. Fibrinogen deficiency is associated with uncontrolled bleeding and compromised survival (11). Thus regulation of fibrinogen availability is critical to survival in combat casualties. As an acute phase protein, fibrinogen is synthesized in the liver and released into the circulation. It is catabolized through normal protein degradation, the coagulation process, and other unknown pathways. In acute injured trauma patients, fibrinogen levels were observed to be the first coagulation proteins and factors to drop to pathophysiological levels (12). Haemorrhage, hypothermia and acidosis results in a deficit in fibrinogen availability (13-15).

3.2 Human Evidence for Fibrinogen in Trauma

Fibrinogen deficiency develops earlier than deficiency of any other clotting factor during resuscitation with packed red blood cells (16) and the concentrations of clotting factors in Cryoplasma is relatively low. Consequently the use of fibrinogen may be the way forward, especially if sufficient amounts of plasma are not available within a reasonable time. A number of experts in the field suggests that the use of fibrinogen may be the next major advance in the treatment of acquired coagulopathy associated with trauma and that the use of fibrinogen may allow compensation for thrombocytopenia in the injured casualty (17). Interesting parallels have been drawn from patients with normally higher fibrinogen levels who suffer less blood loss during surgical interventions than those patients with lower fibrinogen levels (18).

3.3 Current Recommendation of the Federal Armed Forces Transfusion Medicine Council (TMC)

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- Fibrinogen should be considered if there is evidence of continued bleeding after 6-8 units of packed red blood cells and correction of coagulopathy with cryoprecipitate plasma failed.
- 1-2 g IV bolus Fibrinogen (Haemocomplettan) should be administered initially and cumulated amounts of 4-8 g IV bolus if required.

4.0 USE OF FRESH WHOLE BLOOD (FWB) IN THE DEPLOYED MILITARY SETTING

4.1 Fresh Whole Blood

Fresh whole blood (FWB) transfusion for traumatic haemorrhage and coagulopathy is not recommended in civilian German hospitals. Compared with blood components that can be processed, tested, freeze-dried, packaged, stored, shipped and reconstituted, FWB was considered to be logistically impractical, wasteful and unsafe. However as military physicians we should be aware of the benefits of whole blood. Military surgical teams in the past history utilize FWB by relying on a “walking blood bank” of soldier donors when blood requirements outpace supplies and when coagulopathic combat casualties require blood products unavailable at their current echelon of care – two conditions that often coincide.

4.2 Human Evidence for Fresh Whole Blood

During the first Gulf War, FWB was used to treat several coagulopathic combat casualties when platelet supplies run short (19). It became the major blood product used in Somalia when the supply of tested packed red blood cells was exhausted (20) and it was used to treat profoundly coagulopathic casualties in Bosnia and Kosovo, accounting for 12% and 13% respectively of all blood cells used (21). More recently, FWB was used in 13% of all transfused combat casualties in Operation Iraqi Freedom (OIF)(22). Current U.S. Army clinical practice guidelines state that FWB is appropriate for combat related casualties if there is life-threatening injury and if any blood component (RBC’s, plasma, platelets) is indicated for treatment and not available, or if transfusion of available blood components in a 1:1:1 ratio with adequate surgical control does not effectively reduce life-threatening bleeding (23).

4.3 Current Recommendation of the Federal Armed Forces Transfusion Medicine Council (TMC)

- FWB transfusions in military trauma fills avoid left by the unpredictable nature of combat casualty care and military logistics
- FWB is a convenient, safe and effective treatment for many patients who otherwise might die
- FWB transfusion is a ultima ratio procedure
- FWB is indicated for treatment if any blood component, which is indicated for treatment (RBC’s, Plasma, Platelets) are not available
- A predeployment roster of pre-screened donors ABO and Rh should be provided
- Onsite ABO typing should be performed
- Direct cross match should be performed if possible

5.0 CONCLUSION

There is clear evidence that a significant proportion of severely injured casualties are coagulopathic on admission to hospital and that there is a need to proactively treat the condition. The most relevant supporting evidence needs to be derived from observation on combat casualties and hopefully sufficient data will soon be available to assess the full benefits of damage control resuscitation in the relevant population of critically injured casualties. It is unrealistic to expect a prospective randomised clinical trial in these circumstances and further specific questions may need to be addressed in animal models. FWB transfusions in a combat theatre should be a part of an integrated approach to preventing and interrupting the vicious cycle of traumatic coagulopathy. Novel haemostatic agents, the prevention and treatment of hypothermia, and effective resuscitation with awareness of the potential of rebleeding with overly aggressive fluid resuscitation should augment the administration of rFVIIa, Fibrinogen and FWB.