Letter to the editor: Damage control resuscitation

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"CLINICAL REVIEW

Damage control resuscitation for patients with major trauma

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Military conflict has always driven innovation and technical advances in medicine and surgery. Accepted concepts of trauma resuscitation and surgery have been challenged in the wars in lraq and Afghanistan, and novel approaches have been developed to address the current complexity and severity of military trauma.[1]
The aim of this article is to provide an overview of a new approach to managing major trauma known as "damage control resuscitation", which is applicable to trauma casualties most at risk of traumatic coagulopathy and death, and aims to address all aspects of the "lethal triad" immediately on receiving the injured patient.[2]

What is the "lethal triad"?

The term "lethal triad" is used to describe the mutually perpetuating combination of acute coagulopathy, hypothermia, and acidosis seen in exsanguinating trauma patients (fig 1). Hypoperfusion leads to decreased oxygen delivery, a switch to anaerobic metabolism, lactate production, and metabolic acidosis. ...
Large, well conducted retrospective studies have shown that a core temperature of less than 35°C on admission is an independent predictor of mortality after major trauma.[3w2]
Several observational studies have shown that around a quarter of trauma patients have an established, early coagulopathy on arrival in the emergency department, a finding associated with a four fold increase in mortality.[4-6]
Coagulopathy was classically considered to be the product of procoagulant protease losses (a result of consumption and bleeding), dilution (due to fluid resuscitation), and dysfunction (related to acidosis and hypothermia). Recent research, however, has shown that the pathophysiology of coagulopathy is

more complex.[7-9] ...

What are the new strategies in trauma resuscitation?

Damage control resuscitation combines two seemingly diverse strategies—permissive hypotension and haemostatic resuscitation—with damage control surgery (fig 2).[2 w3 w4] The foundation for this approach is set in the pre-hospital environment, where intravenous fluid administration is restricted to a volume sufficient to maintain a radial pulse.[w3] The term "haemostatic resuscitation" describes the very early use of blood and blood products as primary resuscitation fluids, to treat intrinsic acute traumatic coagulopathy and to prevent the development of dilutional coagulopathy.[2] Tranexamic acid, recombinant factor VIIa, and short term administration of tris(hydroxymethyl)aminomethane can also be used to "buy time". ...

What is permissive hypotension?

... The recognition that fluid resuscitation might interfere with haemostatic mechanisms, ultimately exacerbating blood loss, led to a re-evaluation of this accepted approach. Permissive hypotension—also known as "hypotensive" or "balanced" resuscitation—is a strategy of deferring or restricting fluid administration until haemorrhage is controlled, while accepting a limited period of suboptimum end-organ perfusion. ...
It is conceivable that permissive hypotension is more applicable to the management of penetrating trauma, which is often characterised by the presence of major vascular injuries, than to blunt injuries. ...

What is haemostatic resuscitatlon and why perform it?

Although aggressive and simultaneous management of all three aspects of the "lethal triad" is important, rapid and proactive treatment of the coagulopathy associated with major injury is now recognised as central to improving outcome.[13 14] Strategies include: administration of fresh frozen plasma and platelets; use of recombinant factor VIIa, cryoprecipitate and tranexamic acid; and calcium replacement. ...

How much fresh frozen plasma should I give?

In patients predicted to require massive transfusion, current US and British military practice is to administer fresh frozen plasma and packed red blood cells in a 1:1 ratio.[2 14] The aggressive and early administration of fresh frozen plasma to attenuate the acute coagulopathy of trauma shock was pioneered by military surgeons during the recent conflict in Iraq.[15] A small but well conducted retrospective analysis of military casualties who needed massive transfusion showed a statistically significant absolute reduction in mortality (46%) for those who bad been resuscitated with fresh frozen plasma and packed red blood cells in a 1:1 ratio compared with a more conventional 1:8

ratio.[15] Similar subsequent civilian studies from the US and Germany, which incorporated both patients with penetrating trauma and those with blunt trauma, have produced broadly confirmatory results.[16-20] All these studies were, however, retrospective. ...

Is there a role for factor Vlla?

... In view of the substantial cost of the product, further studies, in particular economic analyses, are needed. The widespread application of haemostatic resuscitation principles—in particular the early and targeted use of fresh frozen plasma and platelets—might lead to a decrease in the use of recombinant factor VIIa. ...

Is there a place for tranexamic acid?

Recognition of the contribution of hyperfibrinolysis to the development of acute coagulopathy in trauma shock has led to renewed interest in antifibrinolytics. ...
On the basis of extrapolated evidence from studies of elective surgery, and given the lack of serious adverse effects, European guidelines for the management of bleeding after major trauma recommend tranexamic acid as an adjunct to the management of traumatic haemorrhage.[w12] ...

When should I give calcium?

lonised hypocalcaemia is common in critically ill patients and is associated with increased mortality.[w17]
A recent non-systematic review, however, extrapolated that ionised calcium concentrations of less than 0.6-0.7 mmol/l could lead to coagulation defects and recommended maintaining a concentration of at least 0.9 mmol/l.[w19]

Does the storage age of packed red blood cells matter?

... A recent large retrospective cohort study of trauma patients showed that transfusion of red cells stored for longer than two weeks was associated with significantly increased odds of death. This finding was observed despite leukoreduction, but was apparent only among patients who received at least six units of packed cells.[w22] ...

How should I prevent and treat hypothermia?

The detrimental effects of hypothermia on coagulation, platelet function, and metabolism are well recognised. ...
Prevention of hypothermia is easier than reversal, and the importance of mitigating heat loss is well appreciated. ...

How should I manage metabolic acidosis?

... Although correction of metabolic acidosis requires restoration of organ perfusion, volume replacement may need to be deferred until haemorrhage has been controlled. ...
The traditional treatment for severe lactic acidosis in critical illness is sodium bicarbonate, but little rationale for its use and no evidence of its effectiveness in general, or in the trauma setting, is available.[22]...
Tris(hydroxymethyl)aminomethane is a biologically inert amino alcohol capable of accepting hydrogen ions.[23] ...

What is damage control surgery?

... The aim of damage control surgery is to stop haemorrhage and minimise contamination. Haemorrhage is controlled by temporary clamping, packing, shunting, or ligation, and hollow viscus injuries are either closed or resected without anastomosis.[24] ...

SUMMARY POINTS

Trauma resuscitation must address all three components of the "lethal triad": coagulopathy; acidosis; and hypothermia.
Damage control resuscitation integrates permissive hypotension, haemostatic resuscitation, and damage control surgery.
Coagulopathy is common in patients with haemorrhagic shock. ...

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Letter to the Editor

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Damage control resuscitation 2009

The current article ‘management of major trauma’ [5] requires essential additional information.
Although the definition of “lethal triad” has been established and described as a combination of acute coagulopathy, hypothermia and acidosis during exsanguination of trauma patients, it is still deceptive. We define “lethal triad” differently; a better word would be *causality* and not *combination*.
Coagulopathy in exsanguinating patients is almost always caused by acidosis and hypothermia and this is well documented. Coagulation activity declines by 10% when temperature declines by 1 °C [11]. Furthermore, the activity of three clotting factors is reduced by 50% at a pH of 7.2 (base deficit 12.5 mmol/l) and doubled at pH 7.6 (base excess 16.5 mmol/l) [8].

Therefore, we suggest the following:

Major bleeding – reversing hypothermia, prevents acidosis!

The reversal and the prevention of hypothermia can be accomplished quite easily. We recommend the early application of measures to reduce heat loss, whilst warming the hypothermic patient in order to achieve and maintain normothermia [11].
In contrast, the prevention (not management and treatment) of acidosis [5] is the key to effective therapy of coagulopathy during exsanguination. Contrary to *in vitro* findings, several studies *in vivo* revealed that despite successful correction of acidosis, coagulopathy was still present up to 12-18 hrs [4, 6, 7, 9].

What causes acidosis during major haemorrhage? The facts [14]:

1. As a result of blood loss, haemorrhagic shock is associated with hypoxia, and hence metabolic acidosis with an increased base deficit (BD, negative base excess) and lactate levels.
2. Recently, volume replacement solutions augmented preexisting acidosis via additional infusion- and dilution acidosis. Ringer's lactate given during shock with consecutive lactic acidosis, causes additional calcium binding and thus leads to coagulopathy (10 mmol/l lactate levels cause a 50% decrease of ionized calcium).
3. The production and storage of packed red blood cells (RBCs) is associated with 'RBC aging'. In freshly prepared RBCs, a BD of 20 mmol/l was classed as normal, while in 21-days old RBCs a BD of 40 mmol/l was measured. In contrast, freshly frozen plasma (FFP) presented high levels of citrate [12] and has alkalescent potential.
4. 21-days old RBCs induce hypocalcaemia due to their high lactate levels of 20 mmol/l.
5. The average age of RBCs at the time of transfusion is currently 20 days world-wide (90,000 RBCs units studied in 3 trials). The transfusion of 3 RBCs (approximately 1 litre) causes a 'load' of 40 mmol of H^+-ions to the patient, while the kidney purges only 50 mmol of H^+-ions daily.
6. A massive transfusion leads to metabolic acidosis and, hence coagulopathy. Mortality is strongly associated with the number and age of transfused RBCs; the latter fact is present when more than 5 RBC units are transfused (14,500 patients from 4 trials).

What is the impact of acidosis following major haemorrhage? The facts [14]:

1. In 8,000 patients with polytrauma (4 trials) it has been shown that at the time of hospitalization, a BD of 15 mmol/l predicts a mortality rate of 50%. This number is comparable to 3,300 patients suffering from blunt trauma or gunshot wound.
2. Aside to age, injury severity score (ISS), Glasgow coma score (GCS) and pattern of injuries (head and extremity), the two most important predictive factors of mortality, i.e. BD and pro-thrombin time (PT) show a significant correlation in 4,000 poly-traumatic patients; inversely at a BD of 15 mmol/l the PT values averages to 50%.
3. Trauma patients with massive transfusion develop coagulopathy depending on the BD level. Survivors and non-survivors can be differentiated by observing their BD alone. A BD of approximately 20 mmol/l is predictive of limited survival.

So how should major haemorrhage be treated?

Do not start fluid therapy with crystalloids (only 20% remain intravascular) as previously recommended [11]; begin with balanced colloids [13] insuring that electrolytes (in particular calcium) and the acid-base state is not compromised (e.g. steady isotonic solutions such as HES 130/0.4 with BEpot of ~ 0 mmol/l). Potential BE (BEpot) describes the possible impact of a solution following infusion; this also includes anion metabolization and effects on the patient's acid-base state. Balanced fluids containing acetate are superior to lactate preparations due to faster turnover of acetate in all organs. Lactate is degraded almost uniquely in the liver (by 80%). Therefore acetate solutions are also effective during shock. Furthermore, calcium binding and functional reduction of relevant levels does not exist for acetate.
To summarize, the pattern of volume- or blood component therapy requires an urgent revision [10]: First balanced colloids, followed by plasma (volume, coagulation factors, acidosis prevention) and than fresh RBCs. We now raise the subject of "early or delayed" and, "deferring or restricting fluid administration" by "successful or less successful acidosis-prevention via an optimal volume regime".

Is there a place for haemostatic agents?

Additional attempts using clotting factors are limited: a massive transfusion limits the effectiveness of rFVIIa (NovoSeven) due to the fact that old RBCs maintain the acidosis. rFVIIa has its therapeutic window in patients with blunt or penetrating trauma, however, administration is required prior RBC transfusion and not after the 8th pack of RBCs [3]. As coagulation activity is strongly depending on the pH, one can assume that fibrinolysis as well as drugs modifying it (i.e. aprotinin, ?-aminocaproic acid, tranexamic acid) are influenced by the base deficit.

How much FFP should one give?

It seems that numerous groups have empirically approached the problem of the relation of FFP:RBC [references no. 15-20 in (5)]. The most impressive case numbers have been generated by Maegele et al. in 2008 [reference no. 20 in (5)] for massive transfusion (> 10 RBCs). The higher the ratio of FFP:RBC is inversely correlated to a fall in mortality, e.g. 24 h mortality is reduced from 33-11 %. This is of logical consequence owing to the fact that during massive transfusion (10 RBCs) with a ratio of 1:1 (FFP:RBC), the "fresh" RBC exhibit a BD of 6 mmol/l while 3 weeks "old" RBC exhibit a BD of 11 mmol/l in the patient (75 kg BW, ECFV 15 l). Lactate levels of the same patient increased by 5 mmol/l in the ECFV, which subsequently causes additional calcium binding of 0.25 mmol/l. In addition, simultaneous supply of lactate (via RBC) and citrate (via FFP) maintains the coagulopathy.

Conclusion

The key to effective treatment of haemorrhagic shock is by prevention of acidosis and hence of coagulopathy: This could be achieved by administration of first balanced acetate- and calcium-containing colloids, followed by FFPs (coagulation factors, volume substitution, alkalescent) and finally with only fresh RBCs. This subject has recently been addressed in The New England Journal, titled "New blood, old blood, or no blood?" [1].

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