

Value and impact of massive blood transfusion protocols in the management of trauma patients

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Abstract

Trauma-related injuries are the second leading cause of death and disability in South Africa. The traditional approach to surgery and resuscitation of severely injured patients has undergone change over the past 10 years. New concepts like damage control surgery and damage control resuscitation radically changed the practice of conventional resuscitation. Bleeding trauma patients die as a consequence of the so-called lethal triad or bloody vicious cycle: acidosis, coagulopathy and hypothermia. Effective initial management of trauma patients can help to improve outcomes.

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Introduction

Trauma-related injuries are the second leading cause of death and disability in South Africa, after human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS).

South Africa had 59 935 deaths due to injury in the year 2000 (157.8 per 100 000 population), caused by interpersonal violence, injuries from traffic accidents, fires and falls, in that order.¹ According to a national survey implemented by the South African Medical Research Council, the Institute for Social and Health Sciences and the World Health Organization Violence and Injury Prevention Program, approximately one million annual trauma cases were reported from 356 state hospitals, where violence accounted for more than half of the caseload. The province with the highest incidence of cases was Gauteng with an average of 11 023 cases per year, or 30.2 patients per day.^{2,3}

Bleeding trauma patients die as a consequence of the so-called lethal triad or bloody vicious cycle: acidosis, coagulopathy and hypothermia. It has been demonstrated that massive transfusion protocols may mitigate the effects of the lethal triad in the acutely bleeding patient. With this knowledge in mind, it becomes apparent that effective initial management of trauma patients is necessary to improve outcomes.

The lethal triad: hypothermia, acidosis and coagulopathy

Significant bleeding can overcome the normal compensatory mechanisms, compromise oxygenation and tissue perfusion, and lead to haemorrhagic shock.

Acute haemorrhage brings on pathophysiological responses involving the cardiovascular, respiratory, renal, endocrine and haematological organ systems. Activation of the “fight or flight response” causes increased sympathetic outflow and catecholamines in order to compensate for the acute decrease in preload, and to maintain critical organ perfusion. However, persistent haemorrhage will ultimately overwhelm the capacity of the systemic compensatory mechanisms and, in the absence of prompt and adequate intervention, may eventually lead to decompensation and death.

Surgical control of all sources of bleeding and rapid infusion of fluid and blood are the cornerstones of initial treatment of patients with haemorrhagic traumatic shock.⁴

Hypothermia

Trauma patients are particularly susceptible to hypothermia, and any further loss of temperature is detrimental to survival. Hypothermia in trauma is considered to be a core temperature below 36°C, and severe hypothermia a core temperature below 32°C.⁵ There is a near-linear relationship between mortality and the degree of hypothermia, with a significant impairment of coagulation mechanisms

occurring at temperatures below 35 °C, and complete failure at temperatures lower than 32°C.

The “coagulation cascade” is based on temperature-dependent enzymatic systems that become ineffective during extreme hypothermia.⁶

Coagulopathy

Fluid resuscitation leads to further heat loss and dilution of coagulation factors and platelets. Traditionally, the initial management of bleeding patients has been based on the use of isotonic sodium chloride-containing solutions (0.9% saline, Ringer’s lactate), the so-called crystalloids, with or without the addition of natural or synthetic high-molecular-weight substances (colloids).

From accumulated experience and a growing body of evidence we now know that crystalloids, despite having an acceptable role in early plasma expansion, are responsible (among other issues) for dilutional coagulopathy, generalised interstitial tissue oedema and activation of inflammatory proteins and mediators (proinflammatory action), leading to prolonged intensive care and hospital stay, increased septic complications and mortality in trauma patients.

Colloid solutions, the activity of which is based on increased colloid osmotic plasma pressure and fluid shifts in favour of intravascular space, are also plagued with problems, of which the more salient are: inhibition of platelet aggregation, dilutional coagulopathy, anaphylaxis and allergic reactions, interstitial tissue deposition of heavy molecules, oedema and, to a lesser degree, activation of inflammatory proteins and mediators.⁷

Metabolic acidosis

Metabolic acidosis is the result of lactate overproduction from decreased oxygen delivery as a result of hypovolaemic/haemorrhagic shock, tissue hypoperfusion and anaerobic cellular metabolism. Acidosis is an independent predictor for disseminated intravascular coagulopathy (DIC) and increases mortality in trauma patients.⁸

To worsen the problems further, acidosis also disrupts coagulation mechanisms. Coagulation enzymatic systems do not work at pH values lower than 7.3. Certain drugs that induce and facilitate coagulation, such as human recombinant activated factor VII, are also inactive during severe metabolic acidosis.⁹⁻¹¹ Failure to control and reverse metabolic acidosis in trauma patients is an independent predictor of mortality.

Trauma mortality increases exponentially as time progresses. Patients whose acidosis is reversed within 24 hours of initial insult have a better survival than those whose acidosis persists longer than 48-72 hours after the trauma.

Damage control surgery

Damage control surgery (DCS) has been established as standard of care in severely injured patients. The concept is based on a sequence of events that comprises: abbreviated

initial operation, intensive care unit (ICU) resuscitation, return to the operating room for the definitive operation as soon as near-normal or normal physiology is attained, management of the open abdomen, and abdominal wall reconstruction, followed by physical rehabilitation.

Goals for abbreviated operation include addressing all sources of haemorrhage and gastrointestinal contamination in the quickest way possible. While blood loss kills early, gastrointestinal contamination causes problems later in the ICU. Resuscitation, continued in the ICU, will include transfusion of red blood cells (RBC), fresh frozen plasma (FFP) and platelets, inotropic support and active rewarming, until haemodynamic normality and normal or acceptable laboratory values are obtained. The patient is then returned to the operating theatre for definitive operative control and repair of injuries, usually 24-36 hours after the initial abbreviated procedure.

All of the above are based on the knowledge that persistent attempts at definitive control of the injuries at the time of initial surgery in a haemodynamically compromised patient lead to the lethal triad of acidosis, hypothermia and coagulopathy, thus minimising the chances of survival.¹²⁻¹⁷

Damage control resuscitation

The introduction of DCS forced radical change in the practice of conventional resuscitation, in the face of the newly understood challenges dictated by the need to shorten operative time and focus the effort on ICU resuscitation of the abnormal physiology and metabolism caused by tissue hypoperfusion.

Military surgeons have found that the traditional approach to resuscitation, particularly in terms of the ratio of blood products to each other and the timing of the administration of individual products, often fails to treat the coagulopathy effectively. Similar observations have also been made in civilian trauma care. Damage control resuscitation (DCR) includes the use of permissive hypotension (hypotensive resuscitation), prevention and aggressive treatment of hypothermia, DCS, reversal of acidosis with exogenous buffers, immediate use of blood products (packed RBC, FFP) in a ratio approaching 1:1, early use of platelets, early use of recombinant factor VIIa, and, when possible, the use of whole blood as the primary resuscitation fluid.

The term DCR is used to emphasise its close relationship with DCS protocols. In fact, DCS falls within DCR, as the initial aggressive management of the trauma-related coagulopathy precedes and follows the surgical intervention.^{18,19}

Massive bleeding

Massive bleeding occurs in a small subgroup of trauma patients and is defined as:²⁰

- Blood loss of nearly 100% of the blood volume within 24 hours.

- At least 50 % of the blood loss occurs within three hours.
- Fast bleeding: 150 ml/minute (1.5 ml/minute/kg over 20 minutes).

Massive blood transfusion

Massive blood transfusion is defined as the replacement of the whole blood volume within 24 hours, or 50% of the blood volume in three hours.²¹

In the past, resuscitation and transfusion protocols started with significant crystalloid and colloid infusions. The conventional approach was characterised by the indiscriminate use of crystalloids and plasma-poor RBC, which, as described above, potentiate the lethal triad.

An increasing body of evidence suggests that large volumes of crystalloid are associated with abdominal compartment syndrome as well as cardiac, pulmonary, gastrointestinal, coagulation and other complications. Crystalloids disrupt the electrolyte balance, further dilute coagulation factors and impair clot formation, resulting in greater transfusion requirements.²² Colloids such as starches, employed in doses larger than 15-20 ml/kg, are also believed to impair the coagulation mechanisms.²³

Massive transfusion protocols

A massive blood transfusion protocol (MTP) is necessary when treating the massively bleeding patient to mitigate the lethal triad of acidosis, hypothermia and coagulopathy.

MTPs have been shown to improve survival in severely injured patients, by reducing complications such as pneumonia, pulmonary failure, need for open abdomen and abdominal compartment syndrome. Some studies have shown reduction in severe sepsis, septic shock and multi-organ failure with this practice, especially when blood products are delivered early in the resuscitation through a predefined protocol. There is also a significant reduction in the amount of blood products used during resuscitation, when MTPs are enacted.^{18,19,24-26}

In 2005, at a symposium involving professionals caring for trauma patients in the military at the United States Institute of Surgical Research, guidelines were created for massive blood transfusion, where a ratio of RBC:FFP:platelets of 1:1:1 was recommended.²⁷ Other reports in military settings showed significant reduction in mortality in massively transfused trauma patients (from 65% to 20%; p-value < 0.001) with an optimal FFP: RBC ratio of 1.4.²⁸

Currently, evidence is lacking in civilian trauma care to support the absolute use of 1:1 ratios. Randomised control trials are needed to determine the optimal ratio to use in massively transfused severely injured trauma patients.^{29,30} Recent reports on civilian trauma care suggest that ratios between 1.2 and 1.3 are also effective in reducing mortality.^{31,32} Although the optimal ratio is not yet precisely defined, the more recent literature concurs that an aggressive approach to transfusion improves survival in civilian practice.

Implementing massive transfusion protocols

An MTP is necessary when treating massive bleeding for the following reasons:³³

- To reduce the lethal triad responsible for the mortality in trauma patients.
- To optimise the logistics of delivering blood products.
- To establish active and effective communication between blood transfusion service and point of care.
- To prevent transfusion errors.
- To standardise patient care.

The goal of the protocol is early and aggressive transfusion intervention and blood component resuscitation that approaches the whole blood losses incurred.

There are multiple models for MTP, for example:

- Laboratory test result-based blood product administration (component approach).
- Predetermined blood product administration.
- Real-time transfusion service doctor involvement to oversee products administration.

MTPs should be institution based, with a clear understanding of patient needs and available resources.²⁹

Component therapy-based massive transfusion protocol

This approach requires that laboratory tests are done in a timely manner and reflect enough of the coagulation system to guide therapy. Conventional coagulation tests are not clinically relevant, as they do not reflect in vivo haemostasis. Results are also often delayed and therefore less relevant in an acute situation.

The use of the rotatory thromboelastogram (rTEG), which provides more real-time measurement during component-based therapy, facilitates appropriate use of blood products.²⁰ This protocol requires no set administration ratios of blood and related products.

Predetermined blood product administration

It is the most commonly used protocol: preset transfusion packages are utilised and delivered to the point of care. This protocol clearly defines the proportions of components to transfuse, decreasing the chances of less-than-optimal therapy.

Real-time transfusion doctor involvement

The transfusion service doctor is notified whenever a patient is massively transfused or when a severely injured patient has arrived. The doctor then determines the status of the patient and suggests the products to be administered. The transfusion clinician is primarily responsible for monitoring the patient's coagulation and other laboratory values and also to ensure that adequate amounts of products are available.

Summary

South Africa is currently experiencing very large volumes of trauma, mostly related to interpersonal violence and road traffic accidents.

The traditional approach to surgery and resuscitation of severely injured patients have changed over the last 10 years, with more emphasis on DCS and DCR characterised by early and aggressive coagulation factor therapy, limited crystalloid infusion, prevention of hypothermia and acidosis and the permissive use of moderate preoperative hypotension.

MTPs have been shown to improve survival, prevent wastage of limited resources, avoid errors and improve delivery of products in a timely fashion to the point of care.

The optimal ratios of blood components to be used are yet undetermined and, at best, controversial. Future randomised controlled trials will hopefully assist in determining the ideal ratios and most appropriate management plans for severely injured patients.

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