ABSTRACT

The leading cause of death in young adults in India is trauma and acute blood loss contributes to a large portion of mortality in the early post-trauma period. Massive transfusion [MT] is used for the treatment of uncontrolled haemorrhage. Damage control strategy concept utilised in trauma management is due to the recognition of lethal triad of coagulopathy, hypothermia and acidosis occurring in trauma. Recent experience with managing polytrauma victims from the Iraq and Afghanistan wars has led to a few significant changes in clinical practice. Simultaneously, transfusion practices in the civilian settings have also been extensively studied retrospectively and prospectively in the last decade. Haemostatic resuscitation has evolved with increased use of plasma and platelet transfusions in an attempt to maintain coagulation, antifibrinolytic drugs like tranexamic acid, recombinant factor VIIa as an adjunct to the treatment of dilutional and consumptive coagulopathy, and a reduction in the use of isotonic crystalloid resuscitation. Early definitive control of life-threatening haemorrhage has significantly improved patient outcomes.

MT protocols have been developed to simplify and standardize transfusion practices at foreign countries but unfortunately there is no systematic predefined protocol followed at many centres in India to address this situation today. The authors of recent studies have advocated a 1:1:1 ratio of packed RBCs to fresh frozen plasma to platelet transfusions in patients requiring massive transfusion, and this has been associated with decreased mortality in recent reports from combat and civilian trauma.

The Vinayaka Mission Hospital [VMH] multispecialty team has collaboratively formulated the multiple transfusion protocol [MTP] for exsanguinating trauma victims with the objective as to how to create this protocol, to identify which group of patients this type of protocol should be applied and describe the extensive coordination required to implement this multispecialty MTP.

Keywords: Coagulopathy, Haemorrhage, Multiple transfusion, Trauma.

INTRODUCTION

Trauma is the leading cause of death in all ages from 1 to 44 years (1). The World Health Organization [WHO] estimates that the burden of disease related to injuries, particularly road traffic injuries is expected to rise dramatically by the year 2020 (2). An estimated 5 million people worldwide died from injuries in 2000 - a mortality rate of 83.7 per 100,000 populations. Hemorrhagic shock and exsanguination are responsible for a large number of these deaths, accounting for up to 40% death among polytrauma patients (3). Besides surgical control of haemorrhage, adequate volume resuscitation with blood products and fluids is crucial for the survival of these victims. This article, we review the trends in transfusion practices in trauma patients.

Early identification of the patient who may require MT is critically important, particularly in areas with limited blood product availability. 3% - 5% trauma patients at admission will require massive transfusion. Massive transfusion [MT] is defined as 10 or more units of PRBC transfused in the first 24 hours (4, 5, 6). This group of patients consume majority of blood products transfused
at trauma centres (7). Several authors demonstrated improved outcomes by using predefined ratios of blood products early in care of severely injured patients (5, 8, 9, 10, 11, 12, 13, 14). Significant planning, prior coordination and dedicated blood bank are required to ensure delivery of large amount of blood products in a short period and sustained fashion.

Previous description of coagulopathy was thought not to be found in the first few hours of trauma and was associated with dilution due to fluid resuscitation. However, recent studies show at least 25% of trauma patients arrive already coagulopathic and are at higher risk of mortality (12, 15, 16). Trauma associated coagulopathy is characterized by nonsurgical bleeding that can occur with or without appropriate concentration of coagulation factors (17). Therefore, strategies to address trauma induced coagulopathy early are of paramount importance.

In acute hemorrhagic shock resuscitation, the first priority is to stop haemorrhage and the second is blood transfusion. Resuscitation is based on rapid and effective restoration of an adequate blood volume to maximize tissue oxygen delivery. Furthermore, the goal of transfusion of blood and blood products is to maintain the patient's blood composition within safe limits with regard to haemostasis, oxygen-carrying capacity, oncotic pressure, and biochemistry. Therefore, the additional administration of other blood components [in addition to PRBCs] is necessary for the prevention of dilutional coagulopathy and dilutional thrombocytopenia (18).

Multidisciplinary approach by the Vinayaka Mission Hospital [VMH] to formulate the multiple transfusion protocol [MTP] for exsanguinating trauma victims was considered with the objective as to how this protocol should be created, to identify which group of patients this type of protocol be applied and describe the extensive coordination required to implement this MTP.

CREATION OF THE MULTIPLE TRANSFUSION PROTOCOL

Damage control haematology defines the process of aggressively delivering large amounts of blood products before any laboratory defined anaemia or coagulopathy occurs in patients with life threatening haemorrhage (8, 19, 20). This strategy based protocol provides blood products to hemodynamically unstable trauma victims in an immediate and sustained manner. In the absence of such a predefined protocol, access to the appropriate volume and ratios of blood products may be significantly delayed. Potential delay may include physical ordering of blood products, communication and decision making, sending laboratory samples and timely receiving their results.

Severity of trauma induced coagulopathy, improved survival and decrease in overall usage of blood may occur with rapid infusion of correct ratio of products.

Multidisciplinary team:-

For a successful creation and implementation of an institute based protocol requires cooperation and input of multiple specialties. Trauma victims travel through the system from the emergency room to the operating room, and if still alive to the intensive care unit and transfusion medicine must be active participants in resuscitating these massively bleeding patients. Thus experts from the emergency and critical care department and transfusion medicine department were actively involved in reviewing and formulating the MTP with assistance provided by the haematology, anaesthesiology, surgery, orthopaedics and nursing department.

Identifying the optimal ratio:-

The reversal of coagulopathy in trauma involves the normalization of body temperature, haemorrhage control, and transfusion with blood products as needed. Some authors have advocated that coagulopathy can best be avoided or reversed when severe trauma victims are transfused with at least the equivalent of whole blood (21).

There is paucity of literature available to help clinicians organize and develop data driven institutional MT protocol (6). There are no prospective data informing about the optimal ratio of blood products for exsanguinating trauma patients. Also exhaustive review of literature demonstrated no class I data describing the ideal ratio to transfuse these blood products.

Randomized, controlled trials as to how best to administer coagulation factors [FFP, platelet concentrate and cryoprecipitate] in the presence of ongoing severe traumatic haemorrhage are difficult to execute and have
not been published. Several authors have attempted to define the optimal transfusion regimen using military experiences, animal data and other such related research studies.

A pharmacokinetic model to simulate the dilutional component of coagulopathy during haemorrhage confirmed that during trauma resuscitation, the equivalent of whole blood transfusion is required to correct or prevent dilutional coagulopathy. This pharmacokinetic model documented that once excessive deficiency of factors has developed and bleeding is unabated, 1 to 1.5 units of FFP must be administered for every unit of PRBCs transfused. If FFP transfusion starts before plasma factor concentration drops below 50% of normal, an FFP/PRBC transfusion ratio of 1:1 would prevent further dilution (22).

Hirshberg et al created a computer based hemodilution model to simulate the exsanguinating patient and recommended plasma to PRBC of 2:3 and a ratio of platelets to PRBC of 8:10 (23). Ho et al developed a pharmacokinetic mathematical model to simulate coagulopathy seen in trauma patients and recommended 1:1 ratio for plasma, platelets and PRBC in trauma patients (22). The US military utilised this similar ratio for the DCR of exsanguinating victim in combat (4, 5, 24).

One other study showed a lower 30 day mortality when receiving plasma: RBC at a ratio of 2:3 or greater and apheresis platelets: RBC at a ratio of 1:5 or greater when compared to those receiving less than these ratios (11). Beekley advocates in clinical practice transfusing on a 1:1:1 ratio, essentially tries to recreate the transfusion of whole blood (24). Duchesne et al evaluated their 4 year experience of patients who required a MT at a trauma centre and found those resuscitated with plasma to RBC ratio 1:1 had distinct survival advantage over those with ratio 1:4 (9). Holcomb et al reported their finding from a multi centre, retrospective study of 466 massively transfused civilian trauma patients and the author demonstrated that patients receiving higher ratios of plasma and platelets to PRBC had decreased truncal haemorrhage and increased survival at 6 hours, 24 hours, and 30 days (25). Maegele et al in the evaluation of the German Trauma Registry, evaluated outcomes in 713 critically injured patients receiving MT and found that higher ratios of plasma to PRBC showed reduction in mortality (26). Sperry et al evaluated 415 blunt trauma patients within the "Glue Grant" database and derived that FFP: PRBC > 1:1.5 significantly lowered mortality rate in the first 48 hours (14).

Based on what is available, 1:1 for plasma: PRBC and 1:5 for apheresis platelets: PRBC seemed justifiable and was incorporated into the multiple transfusion protocol at VMH.

**Delivery of Products:**

Activation of the MTP is made by the attending emergency physician (in some cases by the anaesthesiologist or critical care physicians) based on the clinical data available in the trauma resuscitation area by phone call directly to the blood bank [BB]. However blood samples are sent to the laboratory for routine investigation at the beginning of the resuscitation of the trauma victims but activation of the protocol is not relied on the laboratory values because they are not available most of the times. A type and screen should be sent from the ED to the BB as soon as possible to convert released components over to type specific products when possible. The emergency physician provides the demographic detail of the trauma victim and the location to which the first MTP cooler box should be delivered.

The BB then executes the MTP and provides with first box containing 5 units of group specific PRBC, 5 units of FFP and 5 units of random donor platelet concentrate or a single donor platelet concentrate within an ideal time span of 45mins from the activation of the MTP to the BB. Rapid release of these products is possible by keeping several units of universal donor plasma on hand at all times. The BB begins the preparation of the second cooler box and inform the ED or the operating room that the next set is ready and release the same only when notified by the appropriate treating physician or surgeon involved in the MTP. The further preparation and release of the blood products is made only when the BB is notified to continue the same. The protocol is illustrated in Figure 1.

**Age of the blood in protocol:**

The exact role of the age of stored blood on clinical outcomes in patients with severe injuries remains
controversial. In 10 observational studies in trauma patients looking at the effects of stored blood on outcomes consistently showed an increase in organ failure, acute respiratory distress syndrome, infections and mortality (27, 28, 29, 30, 31, 32, 33, 34, 35). At VMH BB, PRBC are stored for 42 days. There is no class I data on the effects of transfusion of large amounts of old blood in patients with severe injuries. Existing observational and retrospective studies suggest that those patients receiving more than 4 units of blood will most likely benefit from transfusion of young blood [<14 days]. With lack of randomized controlled trials available and scarcity of blood products, VMH MTP does not mandate that the patients receive young blood.

Identifying patients requiring the Multiple Transfusion Protocol:

Although there are several scoring systems which are quite accurate, the majority of these scoring systems require laboratory data and injury severity assessment (36, 37, 38). The Assessment of blood consumption [ABC] score correctly identifies those individuals who will require a MT 85% of the time (39). A score of 4 predicts 100% need for MT, score of 3 predicts 45% need for MT and score of 2 predicts 38% need for MT. Given the limited access to point of care testing at our institution, the ABC score is utilized in this protocol. The ABC uses arrival tachycardia [>120 bpm] and systolic blood pressure [<90 mmHg]. In addition, positive fluid on ultrasound and penetrating mechanism of injury are used to determine the risk for MT. Our protocol modifies this score by additionally considering any evidence of massive blood loss [>1500ml]. However this scoring system must be prospectively validated.

Adjuncts:

Recombinant factor VIIa has been shown in the recent preclinical and clinical data to be safe and possibly effective in the treatment of trauma associated coagulopathy (40). Auto-transfusion devices have shown to be safe and effective. It has been proven that their use reduces the use of precious blood products of BB (41). However, due to the lack of availability of these adjuncts, they are not incorporated in the protocol.

A new analysis of the 2010 CRASH-2 study shows that tranexamic acid given as early as possible [within three hours of injury] to bleeding trauma patients is very effective in haemorrhage control. This concept is utilised and proven beneficial at our institute (42).

Implementation:

To address the concerns over the process of rapid delivery of blood products in a uniform and predefined way, a committee was formed. This was composed of faculty from the Department of Accident and Emergency Medicine, The Department of Critical care Medicine, the Department of Transfusion Medicine and the Department of Anaesthesiology. After institutional approval, the protocol was implemented from September 2011. A comprehensive educational campaign was undertaken to instruct the individuals and groups involved in the MTP in form of formal presentations and debriefing sessions. Constant monitoring, upgrading and updating are done by the committee.

Limitations:

At our institution after initiating the MTP, we encountered problems with infusion of the products in a timely manner and unavailability of a appropriate number of blood products at the required time.

CONCLUSION

A small set of trauma victims require multiple transfusion of blood products. These patients are likely to be coagulopathic at admission. Multiple transfusion protocol is associated with improved outcome and much of this survival has been attributed to the increased plasma and platelet to PRBC ratios. Following the initiation and implementation of the protocol at our institute this improved survival rate has to be yet studied. This article mainly emphasises on team effort and damage control haematology that can improve the patient outcome and reduce the overall blood product use. Indian hospitals treating polytrauma victims must initiate their institutional based multiple transfusion protocol to have a timely supply of appropriate blood products for exsanguinating trauma victims and improve patient survival.
VMH MULTIPLE TRANSFUSION PROTOCOL FOR EXSANGUINATING TRAUMA PATIENTS

Exsanguinating trauma patient arrives to the ER

- Apply the modified VMH ABC score to identify candidates who may require MT *

Begin ABC stabilization as per ATLS protocol

- If the score is 3 or 4 — Immediately activate the MT protocol

Emergency duty physician calls BLOOD BANK (BB) to activate the protocol **

EP provides BB with patient's stat name, age, gender, ER cot no, &/or Hospital no

BB calls ER team that first round of MT box is ready

Once Box A1 received at ER, Transfuse blood products immediately

- BB sends Box A2, transfuse immediately as required

Primary stabilize the patient at ER and shift to OT/ICU as early as possible

BB releases Box B1 & B2 in similar manner only when the surgeon/anaesthetist/intensivist notifies to receive it from BB

Unless specified BB ceases preparation & release of further MT boxes

MTP discontinued & informed to BB

EP continues to resuscitate using DCR strategy***

Arrange to shift to OT if haemostasis needs to be achieved

Box A1 containing 3 units group specific PBC prepared and released within 30 mins of MTP activation

Box A2 containing group specific 2 units PRBC, 5 units FBS and 5 units platelet concentrate prepared and released within 45 mins of MTP activation****

BB receives notification & stops MTP if:
1) Hemostasis is achieved;
2) Case is completed; or
3) Patient expires

Collect blood sample for ABG, blood grouping typing and screening simultaneously and send to lab ***

Technician retrieves products and brings to ER

Send blood samples for ABG and ionized Ca2+ after transfusion

Aim Ph > 7.2 and correct electrolyte abnormalities

BB prepares next set of MT Box B

*Identifying patients who may require Multiple Transfusion:

Modified VMH Assessment of blood consumption score:

1. ER presenting SBP < 90mmHg (0: NO; 1: YES)
2. ER presenting HR >120bpm (0: NO; 1: YES)
3. Penetrating mechanism or Any definitive evidence of massive haemorrhage (>1500ml) (0: NO; 1: YES)
4. Positive fluid on abdominal ultrasound (0: NO; 1: YES)

Activate MTP if score 3 or 4

**In special situation where a patient with exsanguinating haemorrhage presents with nonrecordable BP, notify BB to send immediately uncrossed universal donor blood product in MT box A

***Collect blood samples to send lab tests for CBC, Coagulation profile, RFT and any others, but don’t wait till results arrive to activate MTP

****DCR – Damage Control Resuscitation strategy is based on allowing permissive hypotension, minimizing crystalloid and colloid based resuscitation and arranging early transfusion of blood products.

*****if single donor platelet is available, the delivery from blood bank will be within 1 hour of activation of MTP

FIGURE 1: FLOW DIAGRAM OF VMH MULTIPLE TRANSFUSION PROTOCOL ACTIVATION
REFERENCES


