EDUCATIONAL COMMENTARY – MASSIVE TRANSFUSION PROTOCOL

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Learning Objectives

On completion of this exercise, the participant should be able to

- define massive transfusion;
- discuss the benefits of implementing a massive transfusion protocol (MTP);
- state the clinical situations in which an MTP might be activated; and
- describe the components included in an MTP “pack” and the ratio of those components.

Introduction

As a recently graduated medical technologist in the 1980s, I quickly learned that the emergency department physicians and surgeons in the hospital where I was employed had a “formula” when transfusing large quantities of blood: ten red blood cell (RBC) units followed by four units of thawed fresh frozen plasma (FFP) and ten platelet concentrates, pooled. Repeat that pattern until bleeding was under control. That formula seemed to hold true in my next few positions with the only change being a switch from ten platelet concentrates to one apheresis platelet. Today, that formula has changed, with many hospitals, especially those with active trauma centers, implementing massive transfusion protocols (MTP).

Outcomes witnessed when transfusing whole blood to critically wounded soldiers in combat suggested that a ratio of one RBC unit to one plasma unit provided better outcomes in patients with hemorrhagic shock. According to the American College of Surgeons, hemorrhage is the leading cause of death within the first hour after arrival at a trauma center, and exsanguination or coagulopathy cause more than 80% of deaths in the operating room. Management of bleeding in these patients is now known as damage control resuscitation. The goal of transfusion in a massive transfusion setting is to maintain tissue oxygenation and hemostasis to prevent multiple organ failure. Transfusion is started immediately on patient presentation with massive bleeding, before any laboratory testing.

An MTP provides a standardized response for the rapid delivery of blood components needed to prevent exsanguination and restore oxygenation and hemostasis in patients who require damage control resuscitation. Lines of communication are established that enable rapid ordering and transport of blood components to the patient. Guidelines for laboratory testing to monitor the patient’s condition and need for additional transfusion and testing frequency may be included in the protocol. Once the protocol is developed, staff must be trained on MTP activation, with practice drills conducted to gain competency.
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Although initially focused on patients with bleeding due to traumatic injuries and/or major surgical bleeds, MTPs may be extended to other patient populations, such as those with gastrointestinal, obstetric, or vascular bleeds.

Massive Transfusion Protocols

Massive transfusion is conventionally defined as the replacement of a patient’s entire blood volume in less than 24 hours. Transfusion of ten units of RBCs within 24 hours meets this definition in the average adult. Transfusion of 50% of the patient’s blood volume within 3 hours or transfusion of four to five RBC units in 1 hour are other acceptable definitions.\(^2,3\)

Because patients who require large quantities of blood may present with little to no warning and demand an immediate response, having a well-designed massive transfusion protocol can increase the efficiency of the response for these patients. When staff involved have defined roles and expectations, it can limit the confusion and stress that can develop in these emergent cases.

There is general agreement that an MTP is appropriate in trauma cases. It is less clear whether MTP is useful when there is nontraumatic bleeding.\(^2\) Suggested indicators for MTP activation include the following:\(^1\)

- Pulse greater than 120/min
- Systolic blood pressure less than 90 mmHg
- Positive FAST (focused assessment with sonography in trauma; i.e., bedside ultrasound to detect internal bleeding)
- Penetrating wound to the torso
- Ongoing hemodynamic instability
- Bleeding that requires surgical intervention

The development of the massive transfusion protocol should include input from the transfusion service, emergency department physicians, surgeons, and anesthesiologists. Other stakeholders may be identified if the ability to activate an MTP is extended to other medical services (e.g., gastrointestinal or obstetrics service) or if delivery of blood products is assigned to another department.

Transfusion Service Support in Massive Transfusion Protocol

In an MTP, blood components are provided as a set or “pack” in a ratio meant to re-create whole blood. At this time, there is no standard concerning which blood components should be included in each pack of components or the number of each of those components within the pack. Each facility must define in their MTP the contents of each pack, which may vary between packs, and frequency of delivery.
Ratio of Blood Components

Rather than transfuse ten units of RBCs followed by four units of plasma and ten platelets as was done in the past, transfusion in an MTP case today is more often one unit of RBCs and one unit of plasma (or two RBC units with one unit of plasma). In both the Prospective Observational Multi-center Major Trauma Transfusion (PROMMTT) study in 2013 and the Pragmatic, Randomized Optimal Platelet and Plasma Ratios (PROPPR) study in 2015, patients whose transfusions consisted of a RBC to plasma ratio closer to 1:1 had better survival rates than those with more RBCs and fewer plasma units.

At Nebraska Medicine in Omaha, Nebraska, the first and second MTP packs for adults contain six leukoreduced group O Rh positive RBC units, six group A or AB thawed plasma units, and one apheresis platelet. One unit of pre-pooled cryoprecipitate (the equivalent of five individual units of cryoprecipitate) is included from the third pack onward. Each MTP pack must be requested by the physician.

The AABB recently compared MTPs from four trauma centers. In one center, each MTP pack was composed of six group O RBC units, six A or AB thawed plasma units, and one apheresis platelet. In another, the MTP pack consisted of four RBC units and two fresh frozen plasma units. Additional components were requested based on thrombelastography results and ongoing bleeding. A third trauma center delivered six group O RBC units, five plasma units (three group AB and two group A) and one apheresis platelet in the first and second packs, with cryoprecipitate included in every third pack. Packs were automatically delivered every 20 to 30 minutes until the MTP was deactivated.

In a recent American Red Cross Series of Unique Creative Continuing Education Self Study (SUCCESS) webinar, Beatrice LeBeuf discussed the need to evaluate blood utilization in MTP events. When Medical City Healthcare in Texas implemented their MTP in 2011, each MTP pack contained five RBC units and two plasma units. Every other pack included one apheresis platelet, and every third pack included two pre-pooled cryoprecipitate units. When the protocol was reevaluated in 2012, the pack was modified to four RBC units and two plasma units, with an apheresis platelet in every other pack. Cryoprecipitate was dropped from the pack, as that component was frequently wasted. Further refinement in 2014 led to a pack configuration of four RBC units and four plasma units, with one apheresis platelet unit included with packs two and four. The physician must request additional platelets as needed following pack four. Packs are delivered every 15 minutes until the MTP was deactivated.

Red Blood Cells

Initially, blood components will be transfused before completion of the type and screen and/or crossmatch. A specimen for compatibility testing should be obtained and testing completed as quickly as possible. The physician should be notified immediately if any incompatibility is detected or a clinically significant antibody is identified, so that they may be alerted to a possible transfusion reaction. Red blood
cells should be group O to avoid hemolytic transfusion reactions. Ideally Rh-negative RBCs would be provided to all patients. With these being in limited supply, many institutions limit the use of Rh-negative RBCs to female patients of childbearing age.

Plasma

A key component of damage control resuscitation is the early transfusion of plasma. Because coagulation factors are consumed in the body’s attempt to stop bleeding, and plasma is lost as the patient bleeds out, inclusion of plasma in the MTP pack is critical to good patient outcomes. The most common plasma components used are thawed plasma or plasma frozen within 24 hours. Thawed plasma has diminished levels of labile coagulation factors (VIII and V) compared with fresh frozen plasma, but generally has enough stable coagulation components to restore hemostasis. With an expiration of 5 days vs 24 hours, use of thawed plasma reduces wastage. Ideally, plasma would be group AB, which lacks all ABO antibodies. But again, the limited supply of AB donors has resulted in some institutions using group A plasma instead. Group A plasma is compatible with not only group A patients, but also group O. Together these comprise approximately 85% of the population, making transfusion of group A plasma safe in the majority of cases. A study at the University of Massachusetts Memorial Medical Center looked at 385 requests for emergency release of group A plasma over 5 years. Of those cases, only 6% were for group B or AB patients, and of those, there were no reports of subsequent hemolysis or transfusion reactions.

Platelets and Cryoprecipitate

Apheresis platelets are commonly included in MTP packs, but frequency of delivery varies between institutions. While it may be desirable to transfuse group AB Rh-negative platelets to avoid ABO antibodies and potential exposure to the Rh(D) antigen (from residual RBCs in platelet components, an infrequent finding in apheresis platelets), the limited availability of these donors and the 5 day shelf life of platelets makes this difficult. With the loss of platelets due to profuse bleeding and rapid consumption in the attempt to stop that bleeding, platelets are often transfused without regard to ABO or Rh status.

Cryoprecipitate maybe transfused to deliver large amounts of fibrinogen as well as factor VIII. Containing no cellular elements and little plasma, cryoprecipitate of any ABO/Rh type can be transfused to any patient. However, the component must be thawed, and in some cases pooled, which delays delivery to the patient. With a shelf life of 4 to 6 hours, cryoprecipitate is frequently wasted and often is not included in the pack. Fibrinogen concentrate may become an acceptable alternative to cryoprecipitate.

Other Blood Components and Products

Recombinant factor VIIa has mixed results in MTP. Although patients given rFVIIA demonstrated better survival and had fewer transfusions, they were more likely to have a thromboembolic event. Tranexamic
acid is an antifibrinolytic that may be given to help stabilize clots and prevent additional bleeding. Tranexamic acid prevents plasminogen activation.

**Delivery of Blood Products**

The American College of Surgeons recommends immediate transfusion of RBCs and plasma when a patient meets MTP criteria, rather than colloid or crystalloid solutions. Storage of these components in a monitored blood bank refrigerator within the trauma center would be ideal. The MTP protocol (or associated policies) must address such items as the product inventory maintained in the trauma center, rotation of stock, delivery of additional products when the inventory is depleted, and routine maintenance and quality control of the refrigerator.

In lieu of onsite storage, RBCs and plasma may be delivered in coolers or insulated boxes packed with wet ice. Again, policies must be developed to address who is responsible for delivery of products to the trauma center. With the trauma center staff involved in direct patient care and the transfusion service staff occupied with preparing the blood components, it may be necessary to designate staff from another area to serve as “runners.” This responsibility should be clearly defined in the MTP, as well as how the need for product delivery is communicated. Some institutions choose to deliver MTP packs on a defined schedule (e.g., every 15 to 30 minutes), whereas others only deliver on the physician’s request for an MTP pack. At Nebraska Medicine, one person in the trauma suite is designated to contact one person in the transfusion service. With communication limited to between these two individuals, there are fewer phone calls and less chance of duplicate or missed orders. The trauma suite individual is also responsible for contacting the runner to obtain the pack from the transfusion service and deliver it to the trauma center.

All transport containers must be validated before use to demonstrate maintenance of proper storage conditions and to determine the maximum length of storage allowed. Return of unused products should also be addressed. In addition to assigning responsibility for returning unused products, there must be a policy that addresses how the transfusion service determines that components are acceptable for return to general inventory (e.g., use of temperature indicators or taking the temperature of returned units).

If the MTP continues after the patient has moved out of the trauma center (i.e., operating room or intensive care unit), it is imperative that this is communicated to the transfusion service and those responsible for delivering the blood products to ensure timely delivery.

**Deactivation of the MTP**

The MTP should be discontinued when bleeding has ceased and the patient’s blood pressure and heart rate have stabilized. Once bleeding comes under control, laboratory tests that can assist in determining the need for continued transfusion with specific blood components include the following:
Review of MTP Events

At Nebraska Medicine, every MTP event is followed by a debrief attended by transfusion service leadership and the physician and patient care staff involved in the MTP. During this time, they review what worked well and where there are opportunities for improvement in the MTP protocol.

Suggested quality improvement monitors for massive transfusion protocols include the following:

- Number of patients meeting MTP activation criteria vs. number of MTP events
- Availability and timely delivery of blood products
- Inappropriate orders (e.g., physician orders for components not included in the pack [if that is not allowed per protocol]; orders of next MTP pack to obtain only one specific component)
- Blood component wastage
- Patient complications due to massive transfusion - these include, but are not limited to, the following:
  - Dilutional coagulopathy
  - Disseminated intravascular coagulation
  - Hypothermia
  - Citrate toxicity
  - Lactic acidosis

Items to Address When Designing a Massive Transfusion Protocol

When designing a massive transfusion protocol, there are several additional items to address beyond those previously discussed, for which there are no “right” answers. One must consider staffing and available resources within the institution to develop the best plan for that institution (and be willing to adjust that plan when quality monitors show opportunities for improvement).

One item to consider is how the patient will be identified. In a trauma setting, there is typically no time to register the patient in the hospital information system, at least not in the usual manner. Aliases may be temporarily assigned. Whether those are registered in the hospital information system or merely on paper should be addressed either in the MTP or related policies, because this will affect how orders are
delivered to the transfusion service and how blood components are labelled for the patient. Plans should also be made for multiple victims who are all unidentified.

Traceability of units may also be an issue. Will the units have computer generated tags/labels and be released for transfusion in the laboratory information system? That may depend on the ability of the laboratory information system to efficiently release uncrossmatched blood with minimal quality assurance flags. Alternatively, unit tags and release forms may be handwritten, with documentation in the laboratory information system occurring after the MTP is deactivated. Perhaps units will not be directly labeled with patient/unit information at all, but delivered to the MTP documented on an emergency release form. This form can then be used to document final disposition of the units as transfused, returned to the transfusion service in acceptable condition, or returned in unacceptable condition.

Inventory control is also critical. Good communication between the patient care staff and transfusion service will allow adequate time for preparing additional components, as well as ordering inventory from the blood supplier. When formulating the protocol, one may wish to consult the hospital’s blood supplier to determine if the supplier can adequately meet the need for products and deliver in a timely manner when an MTP is activated.

Summary

Massive transfusion is the replacement of the patient’s entire blood volume in 24 hours or less, typically ten units of RBCs in the adult patient. A massive transfusion protocol anticipates these events and allows for the rapid delivery of blood products to patients who need damage control resuscitation. The goal in these cases is to restore tissue oxygenation and hemostasis. To that end, the transfusion of one unit of plasma for every one to two units of RBCs has provided good patient outcomes. Blood components are delivered in predefined packs of RBC and plasma units, and may include apheresis platelets. Successful MTP activation relies on good communication between those caring for the patient, the transfusion service, those delivering the MTP packs to the bedside, and the blood supplier. Massive transfusion protocol events should be reviewed for opportunities for improvement, and the protocol should be updated to reflect those improvements.

References

1. American College of Surgeons Trauma Quality Improvement Program. Massive Transfusion in Trauma Guidelines. 


4. Massive Transfusion Protocols – A Sampling. AABB. 


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