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# CLINICAL ARTICLE

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## Blood product utilisation during massive transfusions: audit and review of the literature

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### Abstract

Acute exsanguination is the leading cause of mortality in trauma patients.<sup>1-3</sup> Massive blood loss potentially results in the development of the 'lethal triad', comprising hypothermia, acidosis and coagulopathy.<sup>4</sup> Without prompt intervention, including the appropriate administration of blood and blood products, the majority of these patients will demise within 6 hours.<sup>2,4,5</sup> Utilisation of blood and blood products in this setting is considered a life-saving intervention. A massive transfusion can be defined as the 1) the infusion of five units or more of packed red cell concentrate (RCC) within 4 hours;<sup>6</sup> 2) infusion of more than ten units RCC within the first 24 hours;<sup>7-15</sup> or 3) infusion of six or more units RCC within 12 hours.<sup>16-18</sup> Irrespective of the formal definition, it has become evident that patients requiring six to nine units of RCC within a 24-hour period have a 2.5 times higher mortality. This mortality risk was significantly higher in patients requiring massive transfusion, than compared to patient groups requiring transfusion of less than six units of RCC.<sup>19</sup> Despite controversy with regard to the definition, the aim of these definitions remains the same: early identification of patients with life-threatening bleeds, to ensure proper resuscitation and prevention of complications associated with resuscitation.<sup>6</sup>

The use of fixed ratios of infused blood products in massive transfusion remains controversial as authors fail to reach consensus on appropriate ratios. These ratios vary from a 1:1:1 ratio for RCC:fresh frozen plasma (FFP):platelets<sup>7,12,20-24</sup> to a 6:4:1 ratio.<sup>25,26</sup> Despite this lack in consensus, it is evident that the practice of fixed ratio transfusions<sup>27,28</sup> in the form of a consistent protocol<sup>25,29</sup> has led to a significant reduction in mortality<sup>10,30</sup> from in excess of 90%<sup>31</sup> to between 30 and 70%,<sup>32</sup> although some authors refute these findings.<sup>13,17</sup>

The aim of this study was to determine local practices with regard to transfusion of blood and blood products in patients undergoing massive transfusion.

## Materials and methods

### Patient population

This study was performed as a prospective audit of all transfusion orders constituting a massive transfusion for patients admitted from February to April 2010 at the Steve Biko Academic Hospital. For the purposes of this study, massive transfusion was defined as patients receiving RCC transfusion of six units or more within 12 hours.<sup>16-18</sup> This threshold was decided upon as these patients have been shown to have a significantly higher mortality.<sup>19</sup> Patients requiring transfusion for a chronic medical condition were excluded from the study. All patients in the study population therefore required a massive transfusion for excessive haemorrhage. This included both trauma- or surgery-induced haemorrhage as well as coagulopathy induced bleeding secondary to disseminated intravascular haemorrhage (DIC), anaemia or hypothermia.<sup>33</sup> The requests spanned all departments in this tertiary hospital and were exclusively requested by medical doctors.

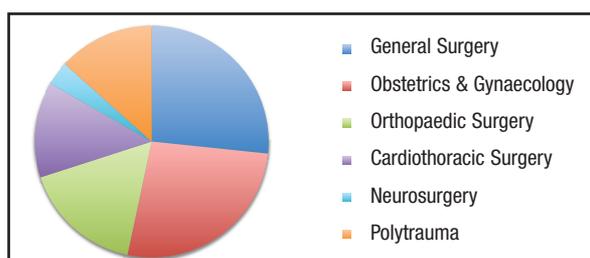
### Study parameters

The Steve Biko Academic Hospital has not implemented a formal massive transfusion protocol to date. The Department of Orthopaedic Surgery, however, did implement a protocol in January 2010 advocating a 6:4:1 ratio for RCC, FFP and platelets, as described in previous publications.<sup>25</sup> The aim of this audit was therefore two-fold: first, to evaluate ordering practices of clinicians in patients requiring a massive transfusion, including unit ratios utilised; secondly, to determine whether the implemented protocol was followed.

## Results

### Patient population

In total, 30 patients were included in this study. The mean age was 37 years (16 to 70 years). A total of eight patients were from the Departments of General Surgery and Obstetrics and Gynaecology. Orthopaedic patients account for five of 30 massive transfusions. Polytrauma patients requiring intervention by various departments accounted for four of these patients (*Figure 1*).



**Figure 1. Department distribution of the 30 massive transfusion administered during the study period**

The most common indication for transfusion among patients from the Department of Obstetrics and Gynaecology was for post-partum haemorrhage (50% of cases). Patients from the Department of General Surgery were transfused for various trauma-related indications (gunshot abdomen etc.) and non-trauma indications (peptic ulcer disease).

### Blood product utilisation

Based on evaluation of departmental blood ordering practice as evidenced by data analysis of blood products ordered from the South African National Blood Transfusion Services, none of the clinical departments utilised a massive transfusion protocol of any kind. There was significant variation in ratios utilised (*Table I*). Polytrauma patients and patients treated by the multidisciplinary team received RCC and FFP in ratios more consistent with current practices, but did not receive nearly adequate amounts of platelets (*Table II*). Similar trends were noted with patients managed by the Department of General Surgery, where platelets were usually not included in the transfusion protocol, and a 2:1 ratio for RCC to FFP were utilised (*Table III*). The Cardiothoracic and Neurosurgery Departments were responsible for a combined number of five cases, with a very large degree of variability in blood products ordered as part of the massive transfusion (*Table IV*).

## Discussion

Use of standardised protocols for massive transfusion has been shown to lead directly to a significant reduction in patient mortality. This improvement in outcome has been largely attributed to increased use of FFP<sup>10,30</sup> instead of crystalloid intravenous fluids. The standardised approach to resuscitation as taught by the Advanced Trauma Life Support (ATLS) course for adults with significant bleeding, advocates use of 1–2 litres of isotonic crystalloids for initial volume resuscitation.<sup>24</sup> Some authors feel that this approach is only appropriate in trauma patients not requiring a massive blood transfusion.<sup>22</sup> Infusion of large amounts of crystalloids not only precipitates the dilutional coagulopathy, but also has pro-inflammatory effects<sup>34</sup> as well as increasing the risk of subsequent infection.<sup>35,36</sup> Conversely, use of smaller amounts of crystalloids and larger amounts of fresh frozen plasma in the initial resuscitation period is associated with improved 24-hour and 30-day survival.<sup>20,37,38</sup>

Unfortunately, most of the current guidelines are established through studies on euvoletic, post-operative, normothermic critically ill patients as opposed to the trauma setting, where the bulk of massive transfusions are actually performed.<sup>39</sup> This blanket transfer of data from the afore-mentioned group to the trauma setting is considered inappropriate by some authors.<sup>40,41</sup>

**Table I: Ratios of blood and blood products prescribed and administered by the Department of Obstetrics and Gynaecology**

Indication	RCC	FFP	Platelets	Cryoprecipitate
PPH	10	12	1	4
PPH	16	19	2	26
PPH	14	14	2	10
PPH	6	5	0	4
Septic incomplete abortion	7	5	0	0
Ectopic pregnancy	6	0	0	0
Ovarian ca	10	2	0	0
Unknown	10	11	2	1

PPH: Post-partum haemorrhage

**Table II: Blood and blood products administered to patients admitted to the Department of Orthopaedics and Intensive Care Units under the auspices of a multi-disciplinary team**

Indication	RCC	FFP	Platelets	Cryoprecipitate
Polytrauma	8	8	1	0
Polytrauma	7	3	0	0
Polytrauma	8	4	0	0
Polytrauma	6	4	1	0
MVA	6	6	6	0
MVA	6	6	0	0
MVA	11	12	0	0
Unknown	6	2	0	0
Unknown	7	3	1	0

MVA: Motor vehicle accident

**Table III: Blood and blood products administered to patients admitted to the Department of General Surgery**

Indication	RCC	FFP	Platelets	Cryoprecipitate
Acute abdomen	7	4	0	0
Acute abdomen	6	3	0	0
Upper GI bleed	6	4	0	0
Upper GI bleed	7	0	0	0
Gunshot abdomen	6	7	0	0
Gastrectomy	6	3	0	0
Necrotising fasciitis	6	4	2	0
Unknown	6	0	0	0

**Table IV: Blood and blood products administered to patients admitted to the Departments of Cardiothoracic and Neurosurgery**

Indication	RCC	FFP	Platelets	Cryoprecipitate
Stab heart	6	1	3	1
Mitral valve replacement	7	7	2	12
Aorta aneurysm bleed	12	8	1	0
Unknown	6	4	0	0
Head injury	8	8	0	0

Fresh whole blood has been suggested as the ideal resuscitation fluid for trauma patients, and has recently been widely reported within the American Armed Forces. Pre-donation screening in this population is regularly performed for HIV-1 as well as Hepatitis B and C viruses.<sup>42</sup> Blood is then obtained on demand and immediately transfused.<sup>43</sup> Data from the US Military showed improved survival in these patients,<sup>44</sup> with no significant increase in the rate of transfusion-transmitted infection.<sup>45</sup>

In settings where post-donation screening is utilised, including South Africa, it is impractical to offer whole blood as a transfusion option, as the delay associated with testing leads to loss of certain constituents, most notably coagulation factors. Fixed ratio transfusion seems to be a generally accepted practice with a ratio of 1:1:1 for RCC:FFP:platelets being the most promising considering current data.<sup>7,8,12,20,22-24</sup> It should be noted that the platelet unit referred to is a mega-unit, which may either be produced from a single donor through apheresis, or harvested from five units of blood donations.<sup>46</sup> Despite this attempt to produce 'reconstituted whole blood', by the nature of the manufacturing process of these products,<sup>47</sup> the final constitution of the three pooled units still deliver a diluted product with an estimated haematocrit of 29% and a platelet count of 88 000/ml. Administration of cryoprecipitate is not included as a routinely administered blood product in massive transfusion protocols, as FFP is thought to contain adequate amounts of fibrinogen. Cryoprecipitate should be administered once fibrinogen levels are below 100 mg/dl.<sup>26</sup> Furthermore, use of pharmacological interventions like recombinant factor VII (NovoSeven®) is currently not advocated, although initial findings are promising.<sup>12,48-51</sup>

Many protocols focus on the use of laboratory tests (PT, PTT, fibrinogen, etc.) as indicators for patient requirements and the advent of complications. These types of protocols are considered reactive by some authors who propose the use of more accessible testing parameters.<sup>52</sup>

In post-donation screening settings, it is impractical to offer whole blood as a transfusion option, as the delay associated with testing leads to loss of certain constituents

In addition, there is a lag between submitting blood for testing and receiving laboratory results so the status reflected by the laboratory data may not correspond to the clinical condition when they become available, as these patients are often highly unstable. Thromboelastography (TEG) is emerging and is a potentially useful measurement in the acute resuscitation setting as it can theoretically provide an indication of coagulation status within 10 minutes.<sup>53,54</sup> It provides a perspective on overall coagulation function, including fibrinolysis.<sup>44</sup> Point-of-care testing devices may also serve in this setting, and have been validated for venous lactate levels<sup>55,56</sup> and more recently for INR and PT.<sup>24</sup> Alternatively, implementation of fixed ratio protocols obviates use of excessive laboratory investigations in the acute phase.<sup>12</sup>

## Conclusion

Analysis of local prescription practices of blood and blood products from various clinical departments showed no consistent ratio of transfusion of the three main blood components, suggesting a lack of a protocol for this situation. The most striking feature was the frequent failure to provide adequate platelet transfusion in these patients.

The literature review suggests that a standardised protocol for massive transfusion not only improves patient outcome,<sup>12</sup> but also leads to a reduction in final volume of blood products utilised for resuscitation of heavily injured patients. This will likely be best achieved as part of a hospital-based protocol, involving all departments participating in trauma resuscitation, rather than within individual departments. Current data suggests that the best results are obtained with a 1:1:1 ratio of RCC:FFP:platelets, as this leads to administration of larger volumes of FFP in the early resuscitation. The need for administration of platelets should not be underestimated. In our clinical setting, no standardised protocol exists. It may be of significant clinical use to establish an institution-based massive transfusion protocol in order to improve patient outcome.

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