Fluid Therapy in Trauma

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Abstract

Advances in shock resuscitation have occurred as a result of various military conflicts. Primary objective of trauma care is to minimize or reverse shock, avoiding the lethal triad of hypothermia, acidosis, and coagulopathy. The concept of Damage Control Resuscitation has evolved along with "damage control surgery" which includes hypotensive and haemostatic resuscitation, where small aliquots of fluid are infused, with hypovolaemia and hypotension tolerated as a necessary evil until definitive haemorrhage control can be achieved. In the initial stages of trauma resuscitation the precise fluid, crystalloid or colloid, used is probably not important as long as an appropriate volume is given. Haemostatic resuscitation includes early use of fresh frozen plasma in a 1:1 ratio with packed red cells with emphasis on whole blood, frequent cryo precipitates and platelets and the use of recombinant Factor VII for control of bleeding.

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Introduction

Trauma is a multi-phasic, heterogeneous mixture of blunt or penetrating injuries with different severity. The commonality among all types of traumatic injuries is that not only is the onset time precisely known, but also that there is the propensity of severe bleeding and subsequent hypovolaemia occurring, which if severe and untreated, can lead to hypovolaemic shock [1].

Civilian trauma centers usually have limited experience in managing severely injured casualties as civilian trauma patients requiring transfusion of >10 units of packed red blood cells (pRBCs) in the first 24 hours, constitutes only 1-2% of the patient population. This makes it difficult to develop and test new resuscitation concepts [2]. In combat zones 7% of combat casualties require massive transfusion. War casualities however, face the problem of logistics [2,3]. Countries like USA, UK have *immediate* access to PRBCs and thawed AB/A plasma and *rapid* access to apheresis platelets, pre-pooled cryoprecipitate, fresh whole blood, and rFVIIa in most war-zones. As a result of the opportunity to formally evaluate the immediate and long-term effects of different treatment regimens in different traumatic injuries, new resuscitation strategies have emerged from the combat hospitals of Iraq and Afghanistan [4, 5].

Fluid Space Dynamics

Total body water (TBW) is distributed between three dynamic spaces: intravascular space (IVS); interstitial space (ISS); and the intracellular space (ICS). The ISS and IVS are sometimes labelled together as the extracellular space (ECS) but both have very different functions and constituents [6].

Fluid movement from the IVS to ISS occurs at the capillary level where a capillary "membrane", separates the spaces. This "membrane" has different degrees of permeability for different substances, called the Reflection coefficient (σ). This is zero for water, 1 for albumin to which the endothelium is essentially impermeable and an intermediate range for small molecular weight particles such as ions, glucose, acetate, lactate, gluconate and bicarbonate [7].

Intravascular Space: The 3-5 L of plasma water (4.5% of TBW) moves in and out of this space. The total volume and blood pressure generates a ***capillary hydrostatic pressure*** (CHP; P_C) which forces the fluid out. The varying percentage of other molecules with a high σ, of which albumin constitutes the main bulk, generate a ***colloid oncotic pressure*** (COP, π_C), which encourages fluid movement into the IVS from the ISS. Usually these forces balance each other across the span of the capillaries (Fig. 1) [6,8].

Interstitial Space: The ISS contains about 12 L of water (12% of TBW) which facilitates transport between the cells of the interstitium and the IVS. The fluid content exerts a pressure, ***tissue hydrostatic pressure*** (THP; P_T) opposing the movement of fluid from the IVS. The large molecules, leaked out from the IVS in turn, exert

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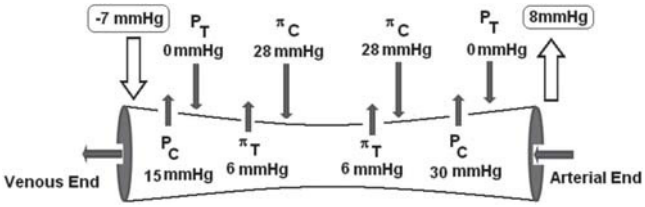

Fig. 1: Net driving force

an ***interstitial oncotic pressure*** (π_T), the value depending upon the s of the capillary barrier [8].

Fluid moves into the interstitial space when CHP is increased over COP, membrane pore size increases, or intravascular COP becomes lower than interstitial COP. Normally, P_T is near zero. In some tissues it is slightly subatmospheric, whereas in others it is slightly positive. In a "typical" tissue, π_T is ~5 mmHg (i.e., much lower than π_C) [9]. Therefore, the net driving force (NDF) for movement of fluids in a capillary bed can be represented as:

$NDF = (P_C - P_T) - \sigma(\pi_C - \pi_t)$

Where:

P_C = Capillary Hydrostatic Pressure

P_T = Tissue Hydrostatic Pressure

π_C = Capillary Osmotic pressure

π_t = Tissue Osmotic pressure

σ = Reflection coefficient

Intracellular Space: The ICS is the largest space (25 L; 36% of TBW) and has potassium (K^+) as its major cation.

Apart from water, the ECS contain electrolytes, with the predominate cation being sodium (Na^+) in the same concentration as the IVS. The comparison of Na^+ content of a solution with that of the plasma is called the tonicity. Solutions can be either isotonic (*Na^+* content of 140-160 mEq/L), hypertonic (Na^+ content >160 mEq/L) or hypotonic (Na^+ content of < 140 mEq/L). Since intracellular Na^+ concentration is ~12 mEq/L, fluids containing Na^+ are not distributed to the ICS. The relative distribution within the ECS is also dependant on the relative proportion of Na^+ in the solution. Osmotically active substances (charged or uncharged) are present in all compartments of the body; solutions iso-osmolar with plasma (270-285 mOsm/L) are therefore distributed in proportion to the TBW distribution [6,10].

Changes in Fluid Space in Trauma

Under neuro-endocrinal influence, the initial response to hypovolaemia is an increase in vascular tone in the venous capacitance vessels which ensures adequate venous return. After this is exhausted, fluid from ISS is shifted to the IVS (auto-transfusion or trans-capillary refill) due to which, both P_C *per se* as well as the P_C to π_C gradient decreases [11]. Conversely, inflammatory mediators released at the site of traumatic injury decreases $\sigma$with movement of larger colloidal molecules into the ISS. This increase π_T forms a reverse pressure gradient, drawing water from the IVS back into ISS. As the lymphatic removal of these larger molecules is slow, the reverse pressure gradient lasts longer, overriding the trans-capillary refill [9,11].

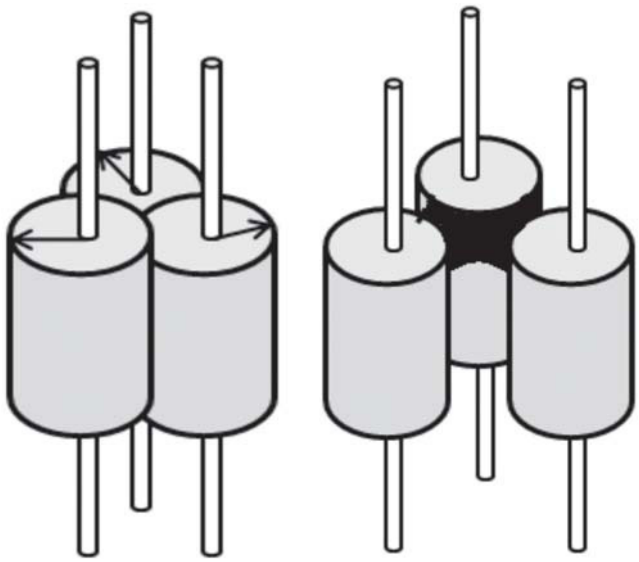

Fig. 2: Diagrammatic Presentation of Krogh's Model of Tissue Perfusion. Cylindrical area of supply around each capillary normally overlaps. Tissue oedema separates the cylinders, causing hypoperfusion in the intervening area (black).

Tissue oedema aggravates tissue hypoperfusion (Fig. 2) caused by hypovolaemia [12]. Hypoperfusion with decreased oxygen delivery causes uncoupling of normal metabolic pathways with lactate production, and metabolic acidosis [13].

Anaerobic metabolism is energy inefficient, causes ATP depletion with lactic acidosis and hypothermia. Roughly, a fall of 4.6°C/h occurs in hypoperfused patients. This drop can be exacerbated in the prehospital setting by environmental factors, prolonged extrication or scene time, intoxication, and convective heat losses (for example, open helicopter door during flight) as well as injudicious administration of cold resuscitation fluids and blood [4,14].

Acidosis initially facilitates the unloading of oxygen to the tissues but compounds the cascading effects of hypothermia [12]. Both contribute to the third angle of the Critical Triad - coagulopathy (Fig. 3).

The historic view that coagulopathy associated with severe injury was largely dilutional is being replaced by epidemiologic and molecular evidence for a distinct syndrome of trauma-associated coagulopathy, the causes of which are multi-factorial (Table 1) [15]. Systemic

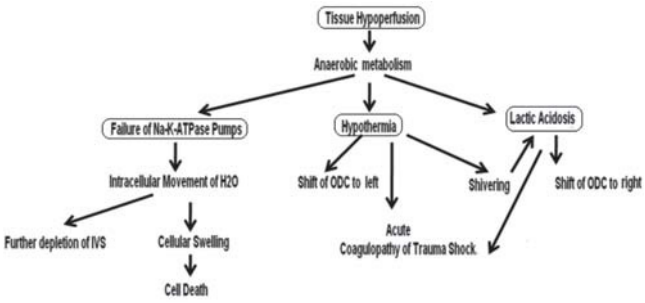

Fig. 3: Effects of tissue hypoperfusion

Table 1

Causes of acute coagulopathy of trauma-shock

Causes	Effects
Tissue trauma	Exposing the subendothelial matrix with platelet activation Liberation of Factor VII and thrombin
Fibrinolysis	Tissue thromboplastin increases in the resence of thrombin
Shock	Mechanism unknown; related to depletion of Protein C
Hypothermia	Inhibits coagulation serinases. Decreases platelet function
Haemodilution	Dilution of clotting factors. Incorporation of colloids into clot.
Acidosis	Reduction of Xa-Va prothrombinase complex activity Platelet form spheres which are devoid of aggregating tendency
Inflamation	Activated by neutrophils with platelet dysfunction Monocyte adherence to platelets
Hypocalcaemia	Due to citrate in blood and blood components

inflammatory response (SIR) is activated by ischemia/reperfusion which initiates neutrophil activation resulting in cellular injury and proliferation of both pro-inflammatory and counter-inflammatory mechanisms. Rapid resuscitation is seen to limit activation of the mediator systems and aborts the microcirculatory changes that result from haemorrhagic shock and neutrophil activation [3,4].

The net effect of the neuro-endocrinal response and the increased vascular permeability to plasma proteins, especially albumin, is water sequestration in the ISS. There is obligatory movement of sodium and chloride along with water. Large volumes of sodium-containing fluids given for resuscitation aggravate the retention [2]. Excessive fluid and electrolyte retention and interstitial oedema are an independent risk factor for SIR syndrome and multiple organ dysfunction, and failure [13]. Results of randomized controlled prospective clinical studies suggest that limiting the sodium and chloride input and optimal use of colloids, which are well retained in the vascular space, can reduce the inflammatory response to injury and improve organ function [4,5,14].

Table 2

Advanced Trauma Life Support (ATLS) guidelines 2004

- Aggressive fluid resuscitation with 2L of crystalloid solution in patients who are significantly injured or appear to be going into shock.
- Continuing this replacement until clinical signs return to normal.
- Packed red cells to be given in the following situations
  - Patients remaining in shock.
  - Patients recovering initially, but subsequently go back into shock.
  - Active ongoing bleeding >100 mL/ minute.
- Plasma and cryoprecipitate to be infused after 6-10 units of PRCs are given

Selection of Fluids (Crystalloids Vs. Colloids)

The Advanced Trauma Life Support (ATLS) Guidelines 2004 (Table 2) were based on the recognition that prolonged shock frequently led to renal failure that could be prevented by volume resuscitation and that many injured patients, who had hypotension, did not need blood at all [16].

Traditionally, there was no role defined for colloids in trauma resuscitation. Anaphylaxis and significant hypernatraemia was reported, especially with gelatins [10,17]. Gelatin-based plasma volume expanders also caused paradoxical hypotension due to release of bradykinin *in vivo* by contaminants [17]. A multitude of factors are implicated for the coagulation disturbances seen following infusion of colloids. These include coating of platelets by the colloid molecules, changes in fibrin clot formation by incorporation of the colloid molecules into the clot, with subsequent prevention of solid clot formation and due to afibrinogenemia [15,17].

Large molecular weight colloids, especially those reconstituted with NS were associated with a higher risk of conversion of pre- to renal-type of acute renal failure [18]. Apart from hyperchloraemia, hydroxyethyl starch (HES) itself was considered to be an independent risk factor.

Proponents of colloid tout the more rapid resuscitation and lower volume needed with colloid resuscitation. There is some evidence that low-molecular HES (200/0.5) and dextran may improve microcirculatory perfusion, possibly by reducing endothelial swelling or by modifying leukocyte adhesion [6,9]. These may also inhibit some components of acute inflammation but the potential impact of this on outcome remains unclear as yet [16,17].

Additionally, the liberal use of large and rapid quantities of isotonic crystalloids is increasingly being called into question.

Concept of Damage Control Resuscitation

The current ATLS guidelines (2008) stress on an

alternative strategy, aptly named "Damage Control Resuscitation" (DCR) to emphasize its pairing with Damage Control Surgical techniques [1,4,5]. Currently in use in Operations Iraqi and Enduring Freedom, it is a systemic approach to major penetrating trauma combining the 'ABC' paradigm with a series of clinical techniques from point-of-wounding to definitive treatment in order to minimize blood loss, maximize tissue oxygenation and optimize outcome [16]. It incorporates the twin concept of hypotensive resuscitation and haemostatic resuscitation [19].

Current standard treatment to achieve haemostasis for injuries on the body surface or extremities is direct pressure or a tourniquet. For suspected non-compressible bleeding, there is currently no adequate treatment [5]. If haemostasis is not assured, aggressive crystalloid resuscitation may dislodge the clot and exacerbate bleeding with cyclical hyper-resuscitation [20].

Two possible strategies can be used: *delayed resuscitation*, where the hypotensive period is deliberately prolonged by withholding fluid therapy until operative intervention achieves definitive haemostasis, or *permissive hypotension*, where fluid is given but the endpoint for resuscitation is lower than the normotensive Mean Arterial Pressure (MAP) of ~80 mmHg, aiming for MAP of 60 mmHg [21].

As per the Israeli Defense Forces Guidelines, repeated aliquots of 250 mL Ringer lactate should be infused with continuous monitoring, only if there is altered sensorium, the radial pulse cannot be palpated and systolic BP <80mmHg. Delayed resuscitation until the time of surgery will also prevent coagulopathy [22].

The role of hypotensive resuscitation is unclear in blunt trauma and head injury resuscitation strategies. The Brain Trauma Foundation, the American Association of Neurological Surgeons, and the Joint Section on Neurotrauma and Critical Care all recommend that in head or spinal injuries with haemorrhagic shock, goal of resuscitation is a systolic blood pressure (SBP) of ~100 mmHg [23].

However, small volumes of fluid may not be enough to prevent cardiac arrest secondary to hypovolaemia [4]. Also, survival may be reduced due of late complications such as multiple organ failure (MOF) and sepsis from organ damage sustained during the period of hypotensive resuscitation. ATLS recommends LR as the resuscitating fluid but NS can also be used [19].

Tissue perfusion markers are needed to evaluate the degree and duration of hypoperfusion, oxygen debt and changes in oxygen delivery with hypotensive resuscitation. Base deficit (BD) has been shown to be a reliable measure. Elevated BD occurs before fall in blood pressure to classic "hypotension" levels and values ≥ 6 mEq/L identifies patients that require early, massive transfusion, and are at risk for adult respiratory distress syndrome(ARDS) and MOF with higher mortality [16,24].

Haemostatic resuscitation includes the prevention and treatment of hypothermia, the reversal of acidosis with bicarbonate, or trometamal, tris-hydroxymethyl amino methane (THAM) and early aggressive treatment with blood products. Patients with significant injury and/or blood loss usually present with initial derangements in coagulation, the degree of which is linearly associated with severity of injury and mortality. An initial international nominated rate (INR) ≥ 1.5 reliably predicts those casualties who will require massive blood transfusion. Thromboelastograph is a better indicator of coagulation disorder but logistic availability in war-zones may be a problem [21].

Haemostatic resuscitation concentrates on the increase use of fresh frozen plasma (FFP) with a 1:1 ratio (PRBC to FFP). Thawed plasma can and should be used as a primary resuscitative fluid since the electrolyte composition is more physiologic than crystalloids (Table 3) [3-5]. Platelets or cryoprecipitate should be transfused only if there is clinical or laboratory evidence of coagulopathy (microvascular bleeding, a prothrombin time (PT) or activated partial thromboplastin time (aPTT) > 1.5 times normal value, thrombocytopenia with a platelet count <50–100x10^9/L or fibrinogen

Table 3

Indications of rFVIIa and plasma and PRBC (1:1 ratio)

	Clinical conditions
Bleeding not controlled with tourniquets or local haemostatic dressings ('quickclot')	Truncal/axillary/neck or groin bleeding Large soft tissue injuries
Proximal amputation or mangled extremity	
Chest tube drainage	> 1000 cc blood total > 200 cc/hr for 4 consecutive hours
Physical exam findings	Decreased mental status from injury and shock Severe head injury Clinically coagulopathic
Objective physical exam or Laboratory findings	INR ≥ 1.5 BD ≥ 6 Haemoglobin - < 11g/dL in young Hypothermic from blood loss (T<96°F) Hypotensive from blood loss (SBP < 90 mmHg) or a weak/ absent radial pulse
Need for fresh whole blood transfusion	Bilateral proximal amputations Large hemoperitoneum and significant shock

INR: International normalized ratio; BD: Base deficit

concentration <1 g/L). In casualties requiring massive transfusion, early administration of rFVIIa decreases pRBC use by 23% while rFVIIa increases the level of SBP at which arterial rebleeding occurs with a tighter, stronger fibrin plug [3,25].

Fresh whole blood (FWB) must be called for early in resuscitation. One unit FWB gives a haematocrit of 29%, ~87,000 platelets with coagulation activity of 65% and 750mg fibrinogen and so is recommended as the optimal resuscitation fluid for hypotensive resuscitation for haemorrhagic shock [4,5,22].

Colloids and/or hypertonic saline have been considered as temporizing agents, and therefore might be considered second line agents, or as initial agents while preparing for the administration of blood products [17]. Hypertonic saline is at least equivalent and maybe superior in patients with traumatic brain injury [16,20,22].

Conclusion

In an attempt to further reduce mortality, a change in field practices was announced in 2007 when blood was incorporated as the primary resuscitation fluid. This apparent paradigm shift drew on an emerging body of work suggesting that management of the coagulopathy of trauma required a proactive, rather than reactive, approach.

Transfusion of plasma is, however, not without risk, including infection, transfusion-related acute lung injury, acute allergic and anaphylactic reactions, haemolysis and fluid overload. Furthermore, wide-scale adoption of 1:1 plasma to RBC ratios has important implications for the blood supply, especially in war-affected areas.

Conflicts of Interest

None identified

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