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Indrani Ghosh¹ and Rudrashish Haldar^{2*}

¹Senior Resident, Department of Maternal and Reproductive Health, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

²Assistant Professor, Department of Anaesthesiology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

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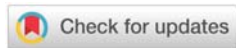
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***Corresponding authors:** Rudrashish Haldar, MD, DNB, PDCC, Assistant Professor, Department of Anaesthesiology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, Tel: 8004904620; E-mail: rudrashish@yahoo.com

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Keymessage: Stored blood at low temperature when transfused to patients of trauma can cause hypothermia leading to derangement of various systems and increased mortality. Therefore adequate warming of blood using different available techniques and equipments is essential prior to transfusion

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Introduction

Blood and blood products (except platelets) are stored at low temperatures to prevent haemolysis, maintenance of sterility and the functional integrity of blood components [1], delay metabolic deterioration and growth of accidentally introduced pathogens. Red blood cells (RBC's) and whole blood are stored at 1°C to 6°C, plasma and cryoprecipitate is frozen and platelets are kept at room temperature. Trauma victims who form a major share of the admissions in Operation Theatres (OT's), Post Anaesthesia Care Units (PACU's), Resuscitation Bays and Intensive Care Units (ICU's) often require large volumes of RBC's and occasionally whole blood along with other resuscitative measures for their management. Since RBC's and whole blood units are stored at low temperatures rapid infusion in these patients can result in significant drop of their core body temperatures. Trauma in itself is a cause of altered thermoregulation leading to thermal stress and altered thermal homeostasis. Up to 66% of trauma victims are hypothermic at admission [2]. Anaesthesia administration disturbs the temperature homeostasis and causes redistribution of heat. Autonomic responses are altered under anaesthesia and thermoregulatory defense mechanisms are not activated. There is impairment of thermoregulation and vasoconstriction

Review Article

Blood warming in trauma related transfusions-Precepts and practices

Abstract

Trauma patients often have a high incidence of hypothermia which is secondary to prolonged exposures, surgery and anaesthesia induced alteration of thermal homeostasis and infusion of cold fluids during resuscitation. Transfusion of red blood cells and blood products (except platelets) which are stored at low temperatures compound the situation by causing a further decrement in the core body temperatures. The resultant hypothermia is detrimental as it involves majority of the organ systems and causes numerous deleterious effects like wound infection, platelet dysfunction and arrhythmias, which complicates the clinical scenario. To avoid hypothermia and the resultant undesirable physiological consequences, it is imperative to warm the blood and blood products prior to transfusion. This article highlights the adverse effects of blood transfusion associated hypothermia and briefly discusses the available practices of warming of blood and blood products along with their merits and demerits.

and reduction in metabolic rate [3]. Neuraxial anaesthesia blocks thermal input, reduces vasoconstriction and shivering thresholds. Surgical interventions further contribute to temperature drop due to exposure, lower OT temperature and cold irrigation fluids. Administration of cold or inadequately warmed blood and products in such patients can accentuate hypothermia who are already susceptible to substantial drop in core temperatures.

Physiological consequences of transfusing cold blood

Infusing insufficiently warmed blood and blood products reduces the core temperature and contributes to the development of hypothermia. Hypothermia inherently exposes these patients to a multitude of adverse effects influencing the cardiovascular, gastrointestinal, endocrinological, immune and coagulation systems as elucidated.

Cardiovascular system: Decreased cardiac output, decreased blood pressure, increased systemic vascular resistance, dysrhythmias (atrial flutter/fibrillation, bradycardia, asystole), cardiac events (ischaemia, angina, myocardial infarction) [4].

Gastrointestinal system: Gastric erosion, ileus, bowel wall oedema [5].

Endocrinological system: Decreased insulin secretion, increased insulin resistance, hyperglycaemia [6].

Immunological system: Decreased WBC count, inhibition of neutrophil and macrophage functions [4].



Coagulation system: Decrease in platelet numbers (clumping) and functions, hypothermic coagulopathy, decreased coagulation kinetics [4].

Moreover, acidosis may develop in patients infused with cold blood and products owing to respiratory depression, lactic acid build-up and reduced hepatic clearance of acid. The resulting metabolic acidosis reduces the binding of ionotropes to their receptors thereby adversely affecting their actions. This hampers stabilization of haemodynamics which is an essential component of resuscitation of trauma victims [7].

Culmination of all these factors can significantly raise the morbidity and mortality following resuscitation with cold blood and products [2]. The perils of hypothermia with concurrent acidosis and coagulopathy constitute the “lethal triad” in trauma patients. Core temperature below 32°C is almost always lethal in trauma patients. Thus, the undesirable consequences of intravenously administered cold blood cannot be underestimated.

Warming of blood prior to transfusion became a common practice after the 1960's when multiple papers highlighted the dangers of cold blood transfusion [6,8], Infusion of 0.5 litre of cold blood can reduce core temperature by 0.5-1°C [9]. Infusion of 3 litres of cold blood caused a significant drop in oesophageal temperature and increased the number of cardiac arrests. However warming the blood led to a drastic decrease in the incidence of cardiac arrests when other factors were kept constant [10,11]. As raising the temperatures of blood from 4°C to 37°C requires approximately 30Kcal of energy, infusing 2.3litres of red blood cells can result in a core temperature decrease of 1-1.5°C in an anaesthetized adult trauma patient who cannot increase body heat production [12,13]. These changes in core temperatures assumes greater significance in the paediatric trauma population where thermal homeostasis has to be vigilantly maintained. Due to their reduced body surface areas, they suffer from greater decrements in core temperatures when unheated blood and blood products are transfused. As the thermal stress of infusing fluids at normothermia is essentially zero, warming devices which infuse blood at normothermia at clinically relevant flow rates allow for efficient rewarming of such patients as compared to other methods like providing external convective heat [14]. Warming of blood prior to transfusion is thus warranted to avoid iatrogenic hypothermia, raising core temperatures in hypothermic individuals and preventing coagulation abnormalities [9,15]. Therefore safe, effective and convenient means of warming blood should be readily available while treating trauma patients.

Traditional methods of warming blood

Blood can be warmed before it passes through the delivery system or when it passes through the intravenous tubings. Pretransfusion warming involves the use of warm water baths, radiant and microwave warmers. Addition of warm saline to blood (admixture) to raise its temperature was also common. Pretransfusion warming's efficacy is limited only during rapid transfusions as during transfusion, the circulating blood's temperature is inversely proportional to the rate of transfusion of the cold liquid. Therefore when the rates of infusion are

slower or if it is delayed, the temperature of the warmed blood rapidly falls toward the room temperature. Moreover with warm water baths, warming may not be uniform, local overheating may occur or the outlet port of the unit may get contaminated. Similarly technical malfunction of microwave or radiowave devices can also cause overheating, haemolysis, raised plasma potassium levels or rarely transfusion reactions. Saline admixture hastens the deterioration of blood and sterility may be compromised. Very hot fluids cause local vascular damage and cell haemolysis. The maximum safe temperature for admixture blood warming is highly dependant on the relative volume of saline and blood. Therefore it is apparent that these methods are inaccurate and associated with a host of complications. On the other hand, the advantage of these methods is their cost effectiveness as a single warmer can be used to warm multiple units of several patients or multiple intravenous lines of one patient. Thus it is evident that the concerns regarding hemolysis due to overheating [16], local vascular damage, sterility, obtaining desired temperatures and variability with different flow rates limits the universal advocacy of traditional methods of blood warming while managing trauma patients.

Inline warming is the more accepted method which consists of warming the blood while it passes through the intravenous tubings. The temperature of blood warmed through this method is inversely related to the flow rate through the tubings and directly related to the initial temperature of the warmer and the blood. Technological advances have prompted the development of specifically designed, electronically controlled commercial devices which are employed for appropriate warming of blood and blood products Advantages of this systems include (1) compatibility with RBC units (2) ability to start new units continuously once the warmer has been set up (3) since the outlet port has to be punctured prior to using the unit, it cannot be returned back after warming has commenced.

Blood warming through inline method is based on one of the following principles

(1) Immersion warming (2) Dry heat warming (3) Counter current warming. Using immersion methods, the intravenous tubings are made to pass through warm water baths. Here thinner walled tubings with greater heat transfer capacities are desirable. The long tubings which are required for adequate heat exchange however, limit the efficiency of this system during rapid transfusions. Risk of infection exists if the outlet ports come in contact with contaminated water in the baths and overheating causing haemolysis are other drawbacks of immersion heating. Dry heat warming avoids the infectious complications as the coiled tubing passes through an aluminium heating element. However current leakage and temperature control malfunction can be the rare associated complications. Counter current warming systems utilize a counter current flow of heated water around or interdigitated with the intravenous tubings. Compared to the other two methods counter current allows the rapid infusion of warm blood while resuscitating victims of haemorrhagic shock. Counter current inline warmers are relatively expensive than the other systems.



Temperature cutoff points for blood warmers

Using an approved device, temperature of cold blood can be raised to 42°C. At this upper limit of temperature, haemolysis is not apparent. This temperature point was derived from the trials conducted by Uhl et al where they had incubated red cells at 37, 40, 42, 44, 46, 48 and 50°C for 2 hours in a constant temperature waterbath. Markers of damage to red cell integrity like increased plasma haemoglobin and osmotic fragility were not evident until temperatures of 46°C [17]. Quick addition of 250ml of 0.9% warm saline at 70°C to cold blood led to a resultant temperature of 37°C without any cell damage [18,19]. A recent meta analysis however suggests that majority of the warming devices use temperatures of 43°C and even temperatures up to 45-46°C can be used while warming the blood with negligible haemolysis [20].

Established norms for blood warming devices

These blood warming devices should stringently conform to the following instructions:

1. The devices used for warming should be licensed for use with blood and blood products.
2. Temperature of blood should not be allowed to rise beyond 42°C.
3. The devices should have an alarm system and a visible thermometer.
4. Temperature rise should be uniform without affecting the RBC morphology and rapidly to accommodate the maximum expected flow rates.
5. These devices should be maintained and validated regularly by the Biomedical Engineering Department.
6. These devices should be operated by personnel's who are trained to do so.
7. The use of blood warmers and the temperatures of the warmers during transfusion should be recorded in the patients charts.

Depending upon the clinical situation, warmers can either be pressure driven or gravity driven. The higher flow rates (220-600ml/min) obtained when warmers are pressure driven makes effective in cases of severely exanguinated patients of trauma with severe circulatory shock. Gravity dependant flows (90-200ml/min) are useful in situations where the bleeding is not so severe and moderately fast infusions are required to maintain normovolemia and haemodynamic stability [14,21].

Hazards of rapid infusion devices

Perioperative air embolism can be a catastrophic complication of rapid infusion of blood when used along with pressurized devices. Extreme caution should be exercised while administering large volume of warmed blood intravenously so that air entrainment and subsequent embolisation does not occur. The reported incidence of fatal air embolism after pressurized infusion cell saver blood was 1 in 31,300 [22]. To

prevent this mishap an air detector coupled with automatic shut off should be incorporated along with rapid infusion devices. Pressurized infusion of cell saver blood should also be avoided as these bags contain considerable amounts of air which is difficult to vent out.

Blood warmers for specific situations

- Paediatric patients:** Conventional fluid warmers may not be able to adequately heat at low flow rates used during resuscitation of paediatric trauma patients. Specially designed warmers like the Hotline and the Buddy warmers are appropriate in these situations. These devices provide warming at the distal end of intravenous line thereby minimizing heat loss prior to venous entry of the blood and can be used with low flows [23,24]. The Buddy system has microporous membranes for air venting during fluid resuscitation however air venting during blood infusion is not possible. The bulk, volume and large priming volume of hotline system makes it a bit inconvenient for use in neonates.
- Trauma on site resuscitation:** Newer devices with the advantages of portability makes it convenient to provide concurrent heating and transfusing making them of immense values for trauma site, emergency departments or operation theatre resuscitation. Screw blood warmer (1390/08/25-72397) and split blood warmer (1390/08/25-72396) are two devices which use metal contact heating to warm blood. Similar equipments include Blood Warming Apparatus (4167663) and Intravenous Fluid Warming Cassette with Stiffening Member and Integral Handle (US 2007/0173759 A1) [25].
- Aeromedical evacuations:** Evacuation of trauma victims through the air route is a faster means to transport them to centres which are well equipped to deal with such emergencies. However with every rise of 1000 feet (305 metres) at the level of troposphere, a temperature drop of 2°C occurs. Compact, durable and lightweight warmers are of immense benefit while transportation of such patients and they allow simultaneous resuscitation with blood and fluids. The General Electric (GE) enFlow® is one such device which weighs less than 4 pounds, provides flow rates up to 200cc/min and maintains the temperature of infusate to 40°C +/- 2°C. Its tested to be shock and vibration proof and capable of delivering performance up to an altitude of 15,000 feet [26]. Stand alone battery option as well as adaptable power sourcing with air ambulances makes it a valuable tool to minimize the adverse effects of unheated blood during air evacuation.

Apart from trauma resuscitation, certain other clinical situations also mandate warming of blood namely:

- Adult patient receiving 50ml/kg/h of blood
- Paediatric patient requiring 15ml/kg/h of blood
- Exchange therapy in neonates



- Patient with active cold agglutinin
- Severe forms of paroxysmal nocturnal haemoglobinuria
- Blood transfusion through central veins [10,15].

Conclusion

Deliberate intraoperative hypothermia is used as an established therapeutic modality in certain surgeries like neurosurgery where it is employed to prevent cerebral ischaemia and cognitive defects [27,28]. Major trauma and the subsequent haemorrhagic shock can often be complicated by administration of cold blood for resuscitation in form of hypothermia, acidosis and coagulopathy. This complicates the clinical physiology, course and management of these patients and drastically increases the associated mortality and morbidity. To diminish the effects of administration of large volumes of cold blood and maintenance of near normothermia, it is desirable to warm RBC's and blood products to a sufficiently higher temperatures and improve the clinical outcome of such patients. Techniques and devices for blood warming has seen vast improvements over the past few years which permits the synchronized warming as well as transfusion for resuscitation thereby reducing thermal stress and preserving thermal homeostasis. Considerations related to blood warmers include their cost, safety, effectiveness, ability to function at high flow rates and universal usage.

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