RESEARCH REVIEW

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Permissive Hypotension and Trauma: Can Fluid Restriction Reduce the Incidence of ARDS?

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ABSTRACT

Emergency care, including the resuscitation of patients involved in traumatic events, has evolved over the years. A prior practice of utilizing large volumes of crystalloids has been found to contribute to complications such as coagulopathy, fluid overload, and adult respiratory distress syndrome (ARDS). In contrast, permissive hypotension is a method of fluid restriction that allows for low blood pressure and mean arterial pressure during the resuscitation period. When permissive hypotension occurs and fluids are restricted in trauma patients, the incidence of ARDS can be reduced significantly with improvement in patient outcomes. Using evidence, nurse practitioners in the emergency department have an important role in evaluating and updating protocols such as permissive hypotension.

Key Words

ARDS, Permissive hypotension, Trauma resuscitation

Trauma care has been around since the beginning of medicine and has evolved over the years. Current practices for multisystem trauma patients include large-volume fluid resuscitation with crystalloids and blood products. Blood pressure and mean arterial pressure (MAP) frequently drive the end point of the resuscitation (Cherkas, 2011). Patients may experience complications related to volume resuscitation including clotting disorders, fluid overload, third spacing, and adult respiratory distress syndrome (ARDS). Large-volume resuscitation in trauma patients often results in fluid movement into the interstitial spaces, including those in the lungs. Acute respiratory distress syndrome is a complication causing serious ventilation and perfusion deficits, decreased oxygenation, and even death. What if trauma protocols decreased the amount of fluids administered during the resuscitation? If the MAP was allowed to be lower in the presence of adequate tissue oxygenation, could the incidence of ARDS be decreased? This review of literature examines the relationship between fluid resuscitation and the incidence of ARDS.

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Author Contributions: Melissa Kolarik is the primary author and former graduate student and Eric Roberts is the content advisor and Associate Professor.

The authors declare no conflicts of interest.

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DOI: 10.1097/JTN.0000000000000257

PATHOPHYSIOLOGY AND FLUID RESUSCITATION

Fluid resuscitation has been the key treatment option since the inception of trauma care. The end goal of fluid resuscitation is to minimize organ failure related to hypoperfusion (Coppola, Froio, & Chiumello, 2014). Trauma patients with massive bleeding can quickly become volume depleted. The decrease in circulating blood volume can have detrimental effects on the body. Hemorrhagic shock is the inadequate delivery of oxygen to vital organs (Chatrath, Khetarpal, & Ahuja, 2015). Treatment of trauma patients has been aimed at decreasing the risk of hemorrhagic shock and increasing intravascular volume. Fluid resuscitation is aimed at rapid delivery of large amounts of fluid to hypotensive patients to rapidly increase intravascular volume and blood pressure with a goal to maintain organ perfusion (Chatrath et al., 2015).

HISTORY OF TRAUMA RESUSCITATION

Traumatic injuries are very prominent in the health care system. In the United States, trauma is the fifth cause of death among people of all ages, 38% cause of surgical burden, and the leading cause of death in those younger than 44 years (Kaafarani & Velmahos, 2014). Although injury prevention is the key to decreasing death due to trauma, trauma resuscitation is vital to patient outcomes. Crystalloid resuscitation was first introduced for the treatment of hemorrhagic shock in the 1950s and 1960s (Neal et al., 2012). Crystalloids are fluids that contain salts and other minerals that are considered similar to the concentration found in the body.

The Vietnam War brought an increase in the understanding of fluid resuscitation and emergency medicine. After the war, large-volume crystalloid resuscitation became popular after Fogelman and Wilson revealed that extracellular volume loss was greater than blood loss and those crystalloids needed to be replaced (Cherkas,

2011). The war also helped increase the understanding of emergency medical services (EMS) and the use of helicopters to get hospital care out of the hospital. The start of EMS systems in the 1960s revolutionized trauma care to include the rapid assessment, intravenous access, and fluid resuscitation with crystalloids to elevate the blood pressure (Mattox, 2015).

Once trauma resuscitation and EMS became more prominent in medicine, researchers started to look at the benefits of resuscitation and started developing protocols. Multiple studies have revealed that intravenous fluid could be rapidly distributed through the body and recommended that three times more crystalloids were needed to replace blood loss, resulting in the 3:1 rule of administering 3 L of crystalloids to 1 L of estimated unit of blood loss (Carrico, Canizaro, & Shires, 1976). Practitioners began using this method of fluid administration as a protocol for trauma resuscitation without sufficient evidence. This theory was never tested on animals or humans before it found its way into common practice and resulted in large-volume crystalloid administration leading to an increase in ARDS (Mattox, 2015).

Early trauma resuscitation strategies recognized the need to replace blood volume loss with crystalloids and blood products. The first massive transfusion protocols (MTPs) were started in the 1970s and resulted in unintentional hemodilution related to large volumes of crystalloids administered prior to the blood products (Ramakrishnan & Cattamanchi, 2014). Crystalloids were infused to increase circulating volume in large quantities while awaiting blood products. The massive transfusion order set is designed to bring non-type-specific packed red blood cells (PRBCs) in large quantities as well as blood products such as platelets, fresh frozen plasma, and cryoprecipitate.

MODERN TRAUMA RESUSCITATION PROTOCOLS

Trauma resuscitation has changed over the last few decades, and new thoughts related to protocols have been formed. Many protocols address the amount of crystalloids to be administered during the resuscitation phase of trauma care. Advance Trauma Life Support recommends 1–2 L of crystalloids while waiting for whole blood to be available (Feinman, Cotton, & Haut, 2014).

The MTP is also a treatment option in multisystem trauma patients. Only 25% of trauma patients need blood transfusions, and only 2%–3% of those require an MTP (Ramakrishnan & Cattamanchi, 2014). The purpose of the new transfusion protocol was to get blood products to patients sooner, decreasing the amount of crystalloids infused. Blood products better expand volume without fluid shifts into the interstitial space. This protocol can be defined as the transfusion of 10 or more units of PRBCs in the first 24 hr (Kaafarani & Velmahos, 2014). Institutions may vary on the exact content in the MTP. A ratio of 1:1:1 of PRBCs, plasma, and platelets is the suggested protocol for transfusion (Feinman et al., 2014; Ramakrishnan & Cattamanchi, 2014).

Hemostatic resuscitation is an emerging trend. This is the use of a chemical or medication to cease the bleeding in a trauma patient. There are many products on the market including topical dressings, sprays, polymers, glues, and other agents to control bleeding, but none have proven to be more effective than another and only provide temporary abatement until definitive treatment is available (Mattox, 2015). Another product available to practitioners is tranexamic acid (TXA). This is an antifibrinolytic that prevents clot breakdown by inhibiting plasminogen activation and plasmin activity (Cap et al., 2011). Administration of TXA is a bolus, followed by a continuous infusion. Tranexamic acid was studied in the randomized, double-blind CRASH-2 study of 20,211 patients and found that TXA can significantly reduce the risk of mortality and is a viable option in controlling bleeding, relative risk (RR) = 0.91, 95% CI [0.85, 0.97], $p = .0035$ (CRASH-2 Collaborators et al., 2011). Aprotinin and aminocaproic acid are other antifibrinolytics that can be used (Kaafarani & Velmahos, 2014).

Another concept emerging in trauma resuscitation is the use of volume expanders such as hypertonic solutions or colloids. A volume expander restores circulating intravascular volume while utilizing less fluid (Duchesne, Kaplan, Balogh, & Malbrain, 2015). Hypertonic saline is given in smaller volumes because it remains in the intravascular spaces longer than crystalloids (Feinman et al., 2014).

Damage control resuscitation is a concept that stems from damage control surgery (DCS), which quickly controls the hemorrhage in trauma patients with the intent to return to the operating room later to completely fix the damage. The collection of interventions that are aimed at reducing or preventing the metabolic complications of trauma is referred to as damage control resuscitation to include permissive hypotension, restriction of crystalloids, and blood production administration given in ratios to mirror whole blood (Bogert, Harvin, & Cotton, 2016). This is coupled with limited surgical intervention to control bleeding, allowing for resuscitation to take place, and definitive surgical repair is performed at a later date (Quinn & Frith, 2015).

COMPLICATIONS OF RESUSCITATION

Trauma resuscitation is aimed at restoring homeostasis and to maintain adequate oxygenation. Although fluid resuscitation is imperative, it is not without complications. When crystalloids are administered, only part of the fluid goes to the extravascular or intravascular spaces. The fluid not moved into either extravascular or intravascular

spaces moves into interstitial spaces, causing tissue edema and injury as seen in abdominal compartment syndrome, ARDS, or other complications (Feinman et al., 2014). Fluid that collects in the interstitial spaces cannot effectively be used by the body and causes further complications. Crystalloids can shift into the extracellular space causing an endothelial injury that increases permeability and dilution of plasma proteins causing a system inflammatory response (Coppola et al., 2014). Resuscitation of large volumes is associated with metabolic and cellular alterations that can affect cardiac, pulmonary, and coagulopathy systems (Neal et al., 2012). Fluid resuscitation with crystalloids such as normal saline or Ringer's lactate solution comes with other potential complications. These include hyperchloremic metabolic acidosis from isotonic saline or lactic acidosis as a result of Ringer's lactate solution in large quantities (Feinman et al., 2014).

A well-known complication of fluid resuscitation is called the lethal triad. The lethal triad of trauma is acidosis, hypothermia, and coagulopathy and is associated with hemorrhagic shock. This is believed to be worsened by crystalloid-based resuscitation (Bogert et al., 2016). Hemorrhage reduces the circulating volume, which leads to decreased core temperature and hypoperfusion of the tissues (Moffatt, 2013). Hypoperfusion causes the tissues to become hypoxic and revert to anaerobic metabolism. The by-product of this is lactic acid, which continues to accumulate causing more acidosis. Acidosis in combination with the hypothermia slows the clotting cascade and the body's ability to form clots to stop hemorrhage (Moffatt, 2013). The cycle continues and leads to poor outcomes. Research has shown that resuscitation to a normal blood pressure via fluid resuscitation increases hemorrhage due to dilution of clotting factors, decrease in blood viscosity, and clot disruption (Duke et al., 2012). The vicious cycle of fluid resuscitation is that hemorrhaging patients are given fluid, which causes inflammation, leading to tissue leakage, causing hypotension, so then more fluid is given (Cherkas, 2011).

ACUTE RESPIRATORY DISTRESS SYNDROME

Another complication of massive fluid administration in trauma patients is ARDS, which is a pulmonary complication that has detrimental effects on the trauma patients. Mortality rate in patients with ARDS is estimated to be 45% (Beitler, Schoenfeld, & Thompson, 2014). Pulmonary complications from trauma resuscitation have been seen since the induction of trauma protocols and continue in current practice. Acute respiratory distress syndrome can be defined as an acute and progressive condition marked by hypoxia and bilateral lung infiltrates that are seen on a chest radiograph or computed tomographic scan (Fujishima, 2014).

Acute respiratory distress syndrome is associated with inflammation and edema in the airway that produces a decrease in lung compliance. Fluid builds up in the space between the alveoli and the capillary bed, causing the interface between the alveoli and capillaries to become widened, thus decreasing gas exchange. The syndrome is characterized by profound dysfunction of gas exchange at the alveoli secondary to inflammation (Zielinski et al., 2014). It is caused by an increased permeability of microvascular barriers, thus resulting in extravascular accumulation of protein-rich edema fluid that is a cardinal characteristic of acute inflammation and a central pathophysiological mechanism of acute lung injury and ARDS (Matthay, Ware, & Zimmerman, 2012).

The frequency of patients developing ARDS is high and may be difficult to diagnose. Acute respiratory distress syndrome can be defined or diagnosed with the presence of severe hypoxemia in which the Pao_2 divided by the Fio_2 (or P/F ratio) is less than 200 mmHg, bilateral infiltrates seen on the chest radiograph, and with a normal pulmonary wedge pressure (Dushianthan, Grocott, Postle, & Cusack, 2011; Zielinski et al., 2014). Patients have varying degrees of symptoms. The syndrome is manifested in patients as tachypnea, dyspnea, and hypoxemia that lead to respiratory failure and poor lung compliance (Dushianthan et al., 2011).

The best management of ARDS is to prevent its occurrence. Key treatments of ARDS are lung-protective ventilation, timely resuscitation, and antimicrobial therapy (Beitler et al., 2014). Lung-protective ventilation is mechanical ventilation that is altered from the normal trend. A low tidal volume and increased respiratory rates can lead to decreased airway pressures; this reduces the collection of edema by maintaining the integrity of the alveolar walls (Matthay et al., 2012). High tidal volumes cause a direct biomechanical injury, which, in turn, causes an increase in the inflammatory response (Beitler et al., 2014).

ARDS AND FLUID RESTRICTION

Because ARDS is a complication of fluid overload, it can be speculated that fluid restriction may decrease the incidence of ARDS. A positive fluid balance from crystalloid infusions may correlate with an increase in the incidence, severity, and mortality rate of ARDS (Ertmer, Kampmeier, Rehberg, & Lange, 2011). The concept of fluid restriction and ARDS and its benefits has recently begun to be researched. A randomized study by the ARDS network of 1,000 patients revealed that fluid restriction greatly reduced the average number of days on a ventilator by 2.5 days (14.6 ± 0.5 vs. 12.1 ± 0.5, $p < .001$; Matthay et al., 2012; National Heart, Lung, and Blood Institute ARDS Clinical Trials Network et al., 2006). Limited fluid use causes reduced production of inflammation factors, vasoactive peptides, and oxygen radicals that are contributory

in inflammation. It is also associated with an improvement in anti-lipid peroxidation, which causes reperfusion injury after an ischemic event, RR = 0.91, 95% CI [0.85, 0.97], $p = .0035$ (Duan, Li, & Liu, 2015; Li, Lin, Zhu, Li, & Liu, 2012).

A meta-analysis of published studies reviewed five trials that included 934 patients and compared limited fluid resuscitation (LFR) with regular fluid resuscitation (RFR) and found ARDS was more prominent in the RFR group, RR = 0.35, 95% Cl [0.21, 0.60], $p < .0001$ (Duan et al., 2015). A prospective observational study of 563 patients found that crystalloid administration yielded a significant risk for ARDS, especially with increased volumes at 24 and 48 hr postinjury: 24 hr $p < .001$ and 48 hr $p = .014$ (Zielinski et al., 2014). The study also found that 10 L of fluid given increased the incidence of ARDS by 10%: hazard ratio (HR) = 1.10 per 10 L, 95% CI [1.05, 1.15] (Zielinski et al., 2014). In a 5-year observational study of 1,913 trauma patients, those who had lung-protective strategies and LFR had significantly decreased pulmonary complications ($p < .01$) and lower mortality rates ($p < .01$) (Cherkas, 2011; Martin et al., 2005).

Protocols regarding a specific standard for fluid restriction have not been identified. Research has shown evidence that a decrease in the amount of crystalloids infused during trauma resuscitation can improve outcomes. Evidence also suggests that decreasing fluid resuscitation correlates with a decrease in the incidence of ARDS.

PERMISSIVE HYPOTENSION

Permissive hypotension is an emerging concept in trauma and is a resuscitation strategy that may decrease the incidence of ARDS. The past theory in fluid resuscitation was to increase the blood pressure to normal as quickly as possible. Permissive hypotension is administering fluid to an end point less than normotensive (Cherkas, 2011). By allowing the blood pressure to remain lower, less fluid is required during the resuscitation period. Patients with traumatic brain injury (TBI) are excluded from the permissive hypotension, as lower MAP in the head injury results in a reduction in cerebral perfusion, secondary injury, and poor outcomes (Kohli, Yadav, Singh, & Prabhakar, 2014).

Many benefits to restrictive fluid administration are evident in the literature. A study in 2013 revealed that prehospital resuscitation of trauma patients with restriction in fluids had lower inpatient mortality rates: HR = 0.84, 95% CI [0.72, 0.98], $p = .03$ (Feinman et al., 2014; Hampton et al., 2013). A retrospective analysis of 307 patients was performed to compare standard fluid resuscitation (SFR) with restrictive fluid resuscitation (RFR) prior to DCS and found those who received RFR had an overall lower mortality rate of 21% compared with 34% ($p = .01$) and decreased length of stay of 13 ± 15 days RFR to 18 ± 31 days for SFR ($p = .02$) (Duke et al., 2012).

The manner in which practitioners measure the end point of resuscitation changes with the idea of permissive hypotension. The end point of permissive hypotension can be measured by mental status, heart rate, blood pressure, and palpable pulses, as well as laboratory values such as base deficit and lactate levels (Cherkas, 2011). Another tool to guide resuscitation is the thromboelastography (TEG) study. The TEG studies can be used as they provide real-time coagulopathy data that look at various aspects of coagulation to tailor MTP and fluid resuscitation to the individual patient (Kaafarani & Velmahos, 2014).

The blood pressure end points for permissive hypotension have been discussed and studied. A prospective, randomized, controlled study placed 90 patients into groups based on MAP targets of 50 and 65 mmHg (Morrison et al., 2011). The small study concluded that an intraoperative MAP of 50 mmHg did not significantly decrease 30-day hospital survival rates: $p = .58$, 95% CI [0.96, 1.07] (Morrison et al., 2011). In another randomized study, 110 subjects were randomized into groups to study systolic blood pressure (SBP) of greater than 100 mmHg versus 70 mmHg and found that the average blood pressure during a rebleeding incident after the resuscitation period was 100 mmHg and survival rates were similar between the two blood pressure groups ($p < .001$) (Dutton, Mackenzie, & Scalea, 2002). In an experimental study of pigs to determine the blood pressure at which the pigs rebleed after trauma revealed that rebleeding occurred at the average SBP of 94 ± 3 mmHg and MAP of 64 ± 2 mmHg (Sondeen, Coppes, & Holcomb, 2003). In patients with hemorrhage and no TBI, SBP of 70–90 mmHg should be the goal of resuscitation or palpable peripheral pulses and normal mentation (Cherkas, 2011).

IMPLICATIONS FOR PRACTITIONERS

Trauma care has evolved over the decades, with nurses and nurse practitioners leading the change. As evidence emerges regarding fluid restriction, nurse practitioners can be on the forefront of that change. Change in health care and trauma resuscitation is inevitable.

Nurses and nurse practitioners need to evaluate and update the current protocols in their institution as evidence emerges. Fluid restriction should be considered in patients who are at risk for ARDS or other complications. Therapies other than the use of massive fluid exist for resuscitation. The massive blood transfusion protocol allows for blood products to be given as a volume expander and should be given in a true to whole blood ratio. The transfusion of blood early can greatly reduce the need for crystalloids and reduce complications. Other options for controlling bleeding and volume expanders may be utilized in the stabilization of multisystem trauma patients.

Monitoring patients for complications and response to therapy is important. Along with vital signs, laboratory

values such as base excess/deficit and lactate levels have been helpful in determining resuscitation status. Thromboelastography has increased in use for the treatment of trauma patients to evaluate clotting properties of whole blood and patients' coagulation status (Feinman et al., 2014).

New protocols regarding fluid restriction and ARDS need to be developed. In order for this to be achieved, more research is necessary in areas such as resuscitation end points related to blood pressure and other monitoring parameters, minimum isotonic volumes needed for resuscitation that limits ARDS as a complication, and usefulness of other volume expanders in place of large fluid volumes to reduce fluid shifts into interstitial spaces. Nurses and nurse practitioners can help develop and implement research studies to supply evidence related to ARDS in trauma care.

CONCLUSION

Trauma care has progressed over the years. Recent research reveals the need for limited crystalloid administration in trauma resuscitation. Permissive hypotension of patients can yield lower volumes of crystalloid administration and prevent fluid overload. Evidence shows that early blood product administration in place of large-volume resuscitation for an end point of permissive hypotension has the greatest positive impact on trauma patients. Complications related to large fluid administration have been identified, including ARDS. Allowing for lower blood pressure and limiting the amount of crystalloids given to multisystem patients can greatly decrease the incidence of ARDS. More research is needed specifically regarding permissive hypotension and decreasing the incidence of ARDS.

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