Arkansas Trauma System Evidence-Based Guidelines for Use of Vasopressin in Shock

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Introduction-

Hemorrhage is common in all forms of trauma, and once the blood lost reaches a critical amount, the patient then develops shock as a result of loss of blood and perfusion to tissues. Traumatic hemorrhage is the most common cause of mortality in the first hour of arrival to a trauma center, and the combination of exsanguination from hemorrhage and coagulopathy account for almost half of the deaths in the first 24 hours following an injury. Too often, we forget the lethal triad of trauma: **hypotension, coagulopathy, and acidosis** and become distracted with other, less important issues. Blood will not efficiently clot when the patient is cold, or the blood pH is acidotic. Coagulopathy develops early in these trauma patients with incidence on arrival of between 25-40% complicating the treatment of hemorrhage. [1]

Rapid detection and treatment of shock continues to be one of the key goals of pre-hospital and trauma center treatment for the trauma patient. Much has been learned about treatment of hemorrhagic shock on the battlefields of Afghanistan and Iraq, and in the major trauma centers of the world. [2] Treatments that were once considered standard-of-care, such as use of large volumes of normal saline, are now known to be unhelpful and in some instances, potentially deadly. Newer research and advances have significantly changed the modern treatment of patients in hemorrhagic shock; however, those lessons have not filtered down into actions taken on the ground and in the ED. [3] Thus, it is critical that all providers in our trauma system understand and identify shock as well as how to treat shock with the most modern tools and techniques available. As a trauma system, we are continuously incorporating **evidence-based science** into our guidelines.

The following is a summary of what is now known as well as recommended and not recommended uses of vasopressin, as an adjunct to treatment of hemorrhagic shock:

Before we start- three important questions:

First: How can we easily identify trauma patients with shock or impending shock, and what should be the initial priorities for these patients?

Evaluation of the patient for hemorrhagic shock: Always assure the ABC's of trauma: airway, breathing, and circulation with a rapid, but careful primary assessment.[4]

Questions to ask:

1. **What is the blood pressure and pulse? What is the Shock Index? Is the patient in shock &/or not perfusing adequately?**
2. **If the patient is in shock: does the patient have a patent and adequate airway?**
3. **If there is a good airway, is the patient breathing and ventilating adequately?**
4. **Are there any many signs of obvious external bleeding? Are there penetrating wounds that could be causing shock? Have we applied tourniquets and direct pressure to control bleeding?**
5. **Assess and reassess for the presence of shock with the Shock Index**: The best indicator of hemorrhagic shock is the **shock index = pulse / systolic blood pressure**. [5] Patients not in shock should have a shock index of < 1. As the patient begins to bleed, the pulse rate will increase as one compensatory mechanism. When shock compensation fails, the systolic pressure will fall. Thus, as the patient worsens, the shock index will go from 0.6 to > 1.0, indicating that the patient is getting into trouble that must be quickly treated.

Shock Index Examples		
Pulse	Systolic Blood Pressure	Shock Index
80	120	0.67
100	120	0.83
120	100	1.20
130	100	1.30
140	80	1.75

6. **EMS: Reporting the vital signs, including the shock index, enroute and on a regular basis will help the receiving Trauma Center appropriately respond and prepare for the patient's arrival**.
7. **Trauma Center: Use of the shock index in the ED will help quickly identify those patients needing massive transfusion and surgical intervention, and also detect patients who were initially stable but then are starting to progress into shock.** [6, 7]

Second: Don't Forget the Principles of Damage Control Resuscitation [8] [9]

Damage control resuscitation combines 1) permissive hypotension, 2) restriction of IV crystalloid solutions with 3) quick transport to the operating room to 4) achieve control of hemorrhage, while avoiding 5) hypothermia and acidosis to avoid worsening coagulation disorders and increased bleeding. [1, 5, 10]

8. **What is the proper IV fluid for the patient—either in the field or in the ED?** Modern research tells us that use of balanced salt solutions (e.g. Plasmalyte ®) are much better for the patient than normal saline, as normal saline compounds any existing acidosis in the patient, while balanced salt solutions do not. Research going from the 1990s began to question the use of crystalloids in the initial treatment of hemorrhagic shock. [11] Continued research since that time has supported the concept that the patient with hemorrhagic shock is best treated with Hypotensive Resuscitation techniques (**Permissive Hypotension**) until they are at a trauma center that has the capability of 1) massive transfusion protocol; AND 2) capability to surgically explore the chest, abdomen, or extremities. Additionally, large doses of crystalloid solutions have been shown to increase complications and increase coagulopathy in the bleeding patient. In 2014 the Committee on Tactical Combat Casualty Care dropped normal saline from the recommended fluid list for hemorrhagic shock resuscitation.
9. **Why should we not raise the blood pressure back to normal levels?** Raising the blood pressure before the patient is at a trauma center where bleeding can actively be stopped increases the mortality of patients with hemorrhagic shock due to increased bleeding caused by raising the blood pressure without a way to stop bleeding. Thus, large volumes of IV fluids should be avoided until surgery can be performed. [12] [13] [14] [15]

   Permissive hypotension is generally defined as maintaining a systolic blood pressure of around 90 mm. If a blood pressure cannot be measured (ex- battlefield or austere environments) then a good substitute is administering enough fluids to maintain a weak radial pulse and consciousness of the patient. ***"Current tactical combat casualty care guidelines are straight forward and target a systolic blood pressure of 90 mm Hg or even lower, as long as the victim is still awake during casualty evacuation care."*** [16]
10. **What is the proper amount to administer, and when should I give it?** As noted above, avoid giving crystalloid fluids until blood, blood products are available, and patient is in a trauma center where immediate surgery is available to stop the bleeding. This means that buffered crystalloid solutions (Plasmalyte, etc.) should be used in small amounts (<500 ml) given to maintain the systolic blood pressure of ≤ 90 mmd (see above for Permissive Hypotension). Modern therapy involves using permissive hypotension,

restricting crystalloid fluids, and giving blood as soon as it is available (see below), even before giving other IV fluids, such as a balanced salt solution. Multiple studies have shown that patients have better survival and need less blood transfusions if moderate hypotension is allowed rather than raising the pressure by giving crystalloid IV solutions.[1 17 18 19]

11. **Avoid hypothermia and correct it if present.** Patients cannot clot effectively if they are cold, thus hypothermia leads to more bleedings and more shock. Measure the patient's temperature and takes steps to warm the patient and keep them warm in the ED, OR, and during transport. ***Several warm blankets placed on the patient at all times are much cheaper than a unit of blood and may keep the patient from further bleeding***.

Third: Are the patient's injuries critical enough for transport to a Trauma Center?

1. **Use the Arkansas Field Triage to determine the severity of injury.** Any patient with major trauma should be transported quickly to the most appropriate trauma center, and EMS providers should **contact ATCC for the location of the most appropriate (not closest) trauma center**:[20]
2. **The Shock Index > 1 is a good predictor that the patient is critically injured and will need blood transfusions and surgery.**
3. **It does the patient no good to waste time at a hospital that can't adequately care for them**. Death from hemorrhagic shock increases for each minute that there is a delay in reaching blood transfusion and surgical capability.[7, 10] Transport of a patient to a hospital without a blood bank and general surgeons that can quickly perform damage control surgery can be lethal to patients that are critically injured. Use ATCC to help get the patient to the closest appropriate hospital that can care for the patient.

Use of Vasopressin in Hemorrhagic Shock

It is not advised to use vasopressors (Dopamine, Epinephrine, Levophed, etc.) for treatment of hemorrhagic shock particularly BEFORE the patient has access to the operating room and blood transfusion components. [21] [22] [23]

However, recent research has shown promising benefits of using **Vasopressin** as an adjunct to Massive Transfusion Protocol blood products and prompt surgery to stop the bleeding. [24] Vasopressin acts differently than other vasopressors and is felt to help the body's compensation mechanisms for hemorrhagic and other forms of shock.

What is Vasopressin?

Vasopressin is a neuropeptide or vasoactive hormone that comes from the posterior pituitary gland. It is also known as Anti-Diuretic Hormone (ADH), and Arginine Vasopressin (AVP). This is not to be confused with Desmopressin (1-deamino-8-O-arginine-vasopressin, or DDAVP) which is a synthetic analogue of arginine vasopressin, and has 10 times the antidiuretic action of vasopressin, but 1500 times less vasoconstrictor action. Desmopressin is often used to reverse platelet dysfunction in patients on Plavix ® or other anti-platelet drugs. [25]

What does Vasopressin do and why is it helpful in hemorrhagic shock?

Vasopressin is essential for maintenance of water balance and also to help maintain blood pressure and perfusion seen in various types of shock. In hemorrhagic shock, the pituitary releases 10-20% of its stores of vasopressin, but then that release tapers over time as hemorrhage continues. [26] Additionally, vasopressin that is released during shock, can be lost in the shed blood and diluted with IV fluids and transfusion products. Recent research has shown dangerous drops in the levels of Vasopressin in patients requiring at least 5 units of packed red cell transfusions.[27] Interestingly, Vasopressin does not raise the blood pressure in normotensive patients with normal blood levels of Vasopressin, or in patients with shock due congestive heart failure, in which there are already high levels of Vasopressin in the blood stream. [28]

Vasopressin depletion is important to both note and treat. It can cause catecholamine-resistant hypotension and vasodilatation, worsening the already lethal effects of hemorrhagic shock. Thus, replacement of normal levels of vasopressin will help reverse hypotension in severe hemorrhagic shock. [29] Vasopressin acts independently of catecholamines to increase vascular tone and constriction and helps stop late-stage shock vasoplegia and vasodilation due to nitric oxide and other substances released in the later stages of hemorrhage. Vasopressin also helps shunt blood away from less essential organs, delivering more blood flow to essential organs. Vasopressin is also helpful to activate platelets and thus improve coagulation in shock. [30]

What evidence is there that Vasopressin helps in treating hemorrhagic shock?

Early studies of use of vasopressin in trauma patients with hemorrhagic shock actually showed an increase in mortality with the use of vasopressin. [31], [32] However, these studies were small, retrospective, and some used multiple vasopressors, in addition to Vasopressin, or had limited blood transfusion capability despite major shock.

Other studies have noted that when vasopressors are needed by patients with severe hemorrhagic shock, mortality is higher. It is felt that vasopressors don't cause increased mortality but are markers for other factors that do cause increased mortality, including severity of injuries and amount of blood lost. [33] [34]

All of that being said, there is a recognized need for both Vasopressin and other vasopressors in the trauma patient in the OR and post-operatively, once bleeding is controlled and adequate blood transfusions are available. [35]

Now-- there are more controlled and larger studies that have been conducted and all have shown a general benefit with use of Vasopressin in traumatic shock, agreeing with the large body of evidence from animal research [36]. These studies and recent large literature reviews have shown that there is less blood usage, lower mortality, and less IV crystalloid usage with the use of Vasopressin in traumatic hemorrhage when compared to matched controls. [25, 37], [38]

Thus, vasopressin is now felt to be a valuable adjunct to the trauma patient that is hypotensive (Systolic <90) due to blood loss, and that a bolus should be given as soon as shock is identified, followed by a steady infusion of Vasopressin until normal perfusion and vital signs have returned.

How to Use of Vasopressin for Hemorrhagic Shock

Vasopressin dosage in hemorrhagic shock = 4 units arginine vasopressin IV

Followed by ≤ 0.04 u/ minute infusion, titrated to keep mean arterial pressure of 65 or greater.

Vasopressin should be given with the start of MTP and continued as a drip during surgery, resuscitation, etc. until the patient is stable.

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