UAMS Journal Club Summary
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Utility of Vasopressin in Hemorrhagic Shock

Clinical Bottom Line: In hemorrhagic trauma, the use of vasopressin corresponded to a decrease in the amount of blood products administered and there was no evidence of increased complications or worsened mortality. Blood product administration should still be considered first line in hemorrhagic trauma resuscitations, but vasopressin may be considered as an adjunct especially in massive transfusions or in resource limited regions that have a limited blood products.

PICO Question:
In patients with hemorrhagic trauma, does the use of vasopressin compared to usual care, improve clinical outcomes?
P: patients with hemorrhagic trauma
I: use of vasopressin
C: compared to standard care
O: improve clinical outcomes such as total blood product administration, mortality

Background: There is significant burden of disease secondary to traumatic injury in society that results in marked morbidity and mortality. Intervention in severe traumatic injury is both time sensitive and very resource intensive. In particular, large volume hemorrhage is both common and difficult to manage both from a volume repletion and source control intervention perspective. Strategies that optimize fluid resuscitation for mortality benefits are of value. Blood products are both expensive and limited in availability especially outside major trauma centers, but the use of crystalloid is associated with increased mortality. Resuscitative strategies that can limit volume of product/fluid needed while improving morality are, again, of value to this effort. Typically, vasopressors are avoided in hemorrhagic shock as volume repletion is the main goal. However, as patients are hemorrhaging, they are depleting their stress hormones and therefore may have limited ability to have appropriate physiologic changes to shock. Vasopressin specifically has postulated benefits as not only improving blood pressure, but also by replacing the vasopressin hormone.

Trial 1:

Sims CA, Holena D, Kim P, Pascual J, Smith B, Martin N, Seamon M, Shiroff A, Raza S, Kaplan L, Grill E, Zimmerman N, Mason C, Abella B, Reilly P. Effect of Low-Dose Supplementation of Arginine Vasopressin on Need for Blood Product Transfusions in Patients With Trauma and Hemorrhagic Shock: A Randomized Clinical Trial. JAMA Surg. 2019 Nov 1;154(11):994-1003. doi: 10.1001/jamasurg.2019.2884. PMID: 31461138; PMCID: PMC6714462.

Pubmed link: https://pubmed.ncbi.nlm.nih.gov/31461138/

Validity rating: Low-moderate risk for bias.

The Basics: This is a randomized double-blind placebo-controlled trial that was performed at a single level one trauma center including 100 patients. The clinical team, research personnel, patients' families, and patients were blinded to group assignment for the duration of the trial. In both groups the patients were similar to known prognostic facts and an intention to treat and per protocol analysis was completed. Participants received either a vasopressin bolus followed by infusion or placebo bolus followed by infusion to maintain a MAP of 65mmHg.

Inclusion criteria: Adult trauma patients aged 18-65 years who had received at least 6 units of any blood product within the first 12 hours after injury

Exclusion criteria: Interhospital transfer, prehospital cardiopulmonary resuscitation, emergency department thoracotomy, recent corticosteroid use, chronic renal insufficiency, significant coronary artery disease, traumatic brain injury requiring neurosurgical intervention, pregnancy, being younger than 18 years or older than 65 years, and prisoner status.

Primary Outcome: Total volume of blood products transfused.

Secondary Outcome: Total amount of crystalloid transfused, 30 day mortality, vasopressor requirements, secondary complications.

Results: 100 patients were randomized. The vasopressin group received lower overall blood product volumes, median, 1.4L [IQR, 0.5-2.6] vs 2.9L [IQR, 1.1-4.8] ; P = .01. There were no differences in need for crystalloid, overall vasopressor use, mortality, and overall complications, although there were fewer DVTs reported in the vasopressin group.

Limitations: Single center, small sample size leading to several underpowered outcomes.
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Trial 2:

Cohn SM, McCarthy J, Stewart RM, Jonas RB, Dent DL, Michalek JE. Impact of low-dose vasopressin on trauma outcome: prospective randomized study. World J Surg. 2011 Feb;35(2):430-9. doi: 10.1007/s00268-010-0875-8. PMID: 21161222.

Pubmed link: https://pubmed.ncbi.nlm.nih.gov/21161222/

Validity Rating: Low-moderate risk of bias

The Basics:
The study design was that of a double blinded, randomized, parallel group, controlled, prospective study intending to enroll from three level 1 trauma centers in a single city in Texas. Only one center enrolled patients. Block randomization was intended to be used. Power was designed for n=165, actual n=78. Despite being underpowered for the actual n, the study still demonstrated a valid statistical evaluation. It has a generalizable population based on demographics although again would have been improved w/ multicenter and increased n.

Inclusion Criteria: Hypotensive trauma patients.

Exclusion Criteria: Admitted to the emergency department more than 6 h after sustaining the traumatic injury, had received more than 4 l of fluid since the injury, were enrolled in another shock trial, were asystolic or required cardiopulmonary resuscitation before they could be randomly assigned to one of the study groups, were pregnant by report or suspicion, were known to have DNR orders or had some visible or identifiable evidence of objection to participation (e.g., an exclusion bracelet), or had known or asserted religious objections to the administration of blood products.

Primary Efficacy Endpoint: 30-day mortality rate.

Primary Safety End-points: 24-h mortality rates, 30-day mortality rates, and the incidence of durable serious adverse events (SAEs). It is unclear what a “durable SAE” is.

Secondary efficacy endpoint: 24-h mortality, 5-day mortality, and the incidence of MODS through day 30.

Secondary Safety Outcomes: Secondary safety endpoints were the incidence of other SAEs and AEs, including abdominal compartment syndrome, extremity compartment syndrome, poor neurologic outcome (Glasgow Outcome Score B 8), number of ventilator-free days, intravenous fluid requirements, transfusion requirements (packed red blood cells, fresh frozen plasma, platelets, cryoprecipitate), and vasopressin concentrations (at baseline, after infusion, and at 12 h).

Results: The experimental (vasopressin) group required less volume of fluid over 5 days as compared to the control ($p = 0.04$). 5 day mortality was 13% in the experimental group and 25% in the control group with $p = 0.19$. The two groups had similar rates of adverse events, organ dysfunction, and 30-day mortality.

Limitations/Bias: Underpowered for actual n. Single center. Only occurred in the setting of level 1 trauma center resources. Some difference between groups, i.e.. more severe abdominal injuries in control group.