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ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/ipec20

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To cite this article: Ross E. Orpet, Whitney J. Barrett, Kevin A. Kaucher, Christopher B. Colwell & John W. Lyng (18 Dec 2024): Prehospital Trauma Compendium: Vasopressors in Trauma – a Position Statement and Resource Document of NAEMSP, Prehospital Emergency Care, DOI: 10.1080/10903127.2024.2437656

To link to this article: https://doi.org/10.1080/10903127.2024.2437656

PREHOSPITAL EMERGENCY CARE
https://doi.org/10.1080/10903127.2024.2437656

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Prehospital Trauma Compendium: Vasopressors in Trauma – a Position Statement and Resource Document of NAEMSP

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ABSTRACT

Acutely injured trauma patients may develop shock from several potential mechanisms, including hypovolemic shock from hemorrhage, neurogenic shock from traumatic brain injury (TBI) or spinal cord injury, obstructive shock from tension pneumothorax or pericardial tamponade, or a mix of several of these mechanisms. Regardless of the cause, restoration of adequate perfusion is of critical importance to reduce the morbidity and mortality of trauma patients with shock. Multiple interventions including hemorrhage control, volume resuscitation with intravenous fluids or blood products, and pleural decompression procedures are used to address some of these issues and are discussed elsewhere in the trauma compendium. The prehospital use of vasopressors to augment organ perfusion pressures seems theoretically appealing for settings where trauma patients have hemorrhagic shock that is refractory to volume resuscitation strategies alone, where blood products are not available, in cases of hypoperfusion caused by neurogenic shock, or to address mean arterial pressure (MAP) goals in severe spinal cord injury. The National Association of Emergency Medical Services Physicians (NAEMSP) reviewed the available evidence surrounding the prehospital use of vasopressors in shock related to trauma to develop the following recommendations as supported by the evidence summarized in the subsequent resource document.

NAEMSP RECOMMENDS

- Current evidence does not support the routine use of vasopressors by EMS clinicians for traumatic hemorrhagic shock and suggests the possibility of harm.
- Current evidence does not address the use of vasopressors by EMS clinicians in the treatment of patients with severe spinal cord injury presenting with neurogenic shock or to achieve specific mean arterial pressure goals in spine injured patients in the prehospital setting.
- Prehospital hypotension has been shown to be harmful to patients with TBI; however, there is currently no evidence to support or refute the use of vasopressors by EMS clinicians in the setting of TBI.

ARTICLE HISTORY
Received 24 July 2024
Revised 22 November 2024
Accepted 25 November 2024

Introduction

Acutely injured trauma patients may develop shock from several potential mechanisms, including hypovolemic shock from hemorrhage, neurogenic shock from spinal cord injury, obstructive shock from tension pneumothorax or pericardial tamponade, or a mix of several of these mechanisms. In addition, some research suggests that certain traumatic injuries might benefit from blood pressures (BP) higher than those usually targeted in the field for the routine polytrauma patient (1–4).

Traumatic hemorrhagic shock, characterized by loss of blood volume leading to insufficient tissue perfusion, requires prompt intervention to maintain organ perfusion to prevent multiorgan dysfunction. Blood product transfusion and intravenous crystalloid infusion remain the mainstay of treatment (5, 6). However, in the prehospital setting where blood products may not be readily available and where large-volume crystalloid infusions may exacerbate traumatic coagulopathy, the use of vasopressors has been proposed as a potential solution to address hemodynamic instability (5, 7, 8).

Severe spinal cord injury with or without shock, possess distinct challenges to the prehospital clinician due to the differences in etiology from hemorrhagic shock. Current guideline recommendations by The American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons' (CNS) for the Management of Acute Cervical Spine and Spinal Cord Injuries recommend the maintenance of mean arterial blood pressure (MAP) at 85–90 mmHg in the acute setting, using vasopressor support if needed to prevent progression of neurologic injury (9).

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Supplemental data for this article is available online at https://doi.org/10.1080/10903127.2024.2437656.

Additionally, the Emergency Neurological Life Support: Traumatic Spine Injury guidelines recommend volume resuscitation first followed by vasopressors if MAP goals cannot be met (10). Neurogenic shock, a form of distributive shock from unmitigated vasodilation in those with neurologic injury from spinal cord injury (SCI) usually above the level of T4, is not mentioned in current societal guidelines or recommendations but should be considered by the Emergency Medical Services (EMS) clinician. Neurogenic shock often presents with hemodynamic instability, thus necessitating volume resuscitation or vasopressor support. Considering the etiology of spinal cord injury, and more specifically neurogenic shock compared to hemorrhagic shock, it might be reasonable to consider different management options if isolated spinal cord injury is suspected. While the mentioned guidelines establish goals primarily for in-hospital use, the treatment concepts to prevent secondary SCI and future neurologic deficits are often applied in prehospital treatments.

A final potential application of vasopressors in the prehospital setting may include injury patterns where hypotension has demonstrated deleterious effects, such as hypotension associated with traumatic brain injury (TBI). Several reports highlight the impact that even brief episodes of prehospital hypotension are associated with increased risk of mortality (3, 11). These findings underscore the critical role of early BP management in TBI and SCI patients to optimize cerebral and spinal cord perfusion and potentially improve neurologic outcomes.

To investigate the role of vasopressors in the prehospital setting specifically in the resuscitation of injured patients with different forms of traumatic shock, we reviewed the literature to develop recommendations and identify gaps in the evidence that could be a focus of future research.

Methods

Content Areas

In collaboration with the compendium editorial board, our author team identified several content areas of interest regarding the role of prehospital administration of vasopressors for traumatic shock. Our literature search and evidence review are organized to inform the following content areas:

1. Use of prehospital vasopressors in the management of hemorrhagic shock.
2. Use of prehospital vasopressors in the management of neurogenic shock and SCI.
3. Use of prehospital vasopressors in the management of TBI.

Search Strategy

We performed a structured search of the literature using guidance developed for the National Association of EMS Physicians (NAEMSP) Trauma Compendium (12). The search strategy identified literature relevant to EMS, trauma, and vasopressors and is summarized in the Supplemental File. We searched PubMed on December 23, 2022 for articles published from inception through that date.

Screening of Publications

Titles and abstracts of all citations identified in our initial search were independently reviewed by two authors (WJB and REO) to determine each paper's relevance to the pre-established content focuses. Bibliography searches of retained articles were also performed to identify additional relevant articles. Papers were excluded if they were not relevant to our predefined content focus areas. Disagreements between these two authors were adjudicated by advancing the paper to full text review. These and all other papers that were assessed to be possibly relevant underwent full text review by a single author (REO) and retained articles were categorized according to relevance to content focus areas.

Additional manuscripts pertaining to other clinical environments outside of the prehospital setting were identified through our initial review of the literature as background for this work, as well as a review of the papers and bibliographies found in the described search strategy, and through non-structured PubMed search strategies. Importantly, these additional manuscripts were not used in the development of the recommendations, as they did not directly address the prehospital use of vasopressors but were used to inform the discussion of these topics.

Evidence Evaluation

A single author (REO) abstracted the data from the articles retained after full text review using a structured data abstraction form. Abstracted information was collated by content area.

Development of Recommendations

The primary writing group (REO, KAK, WJB) individually reviewed the data abstraction form and then met to develop recommendations based on the evidence gleaned from our literature review. The bullets and summary of the literature were secondarily reviewed and revised by authors CBC and JWL. The recommendations were ultimately reviewed by the NAESMP Standards and Practice Committee and approved by the NAEMSP Board of Directors.

Results

Literature Review

Of the initial 116 articles identified in our search, only three were retained following the screening process outlined in Figure 1. Bibliography review did not harvest any additional articles specific to prehospital use of vasopressors.

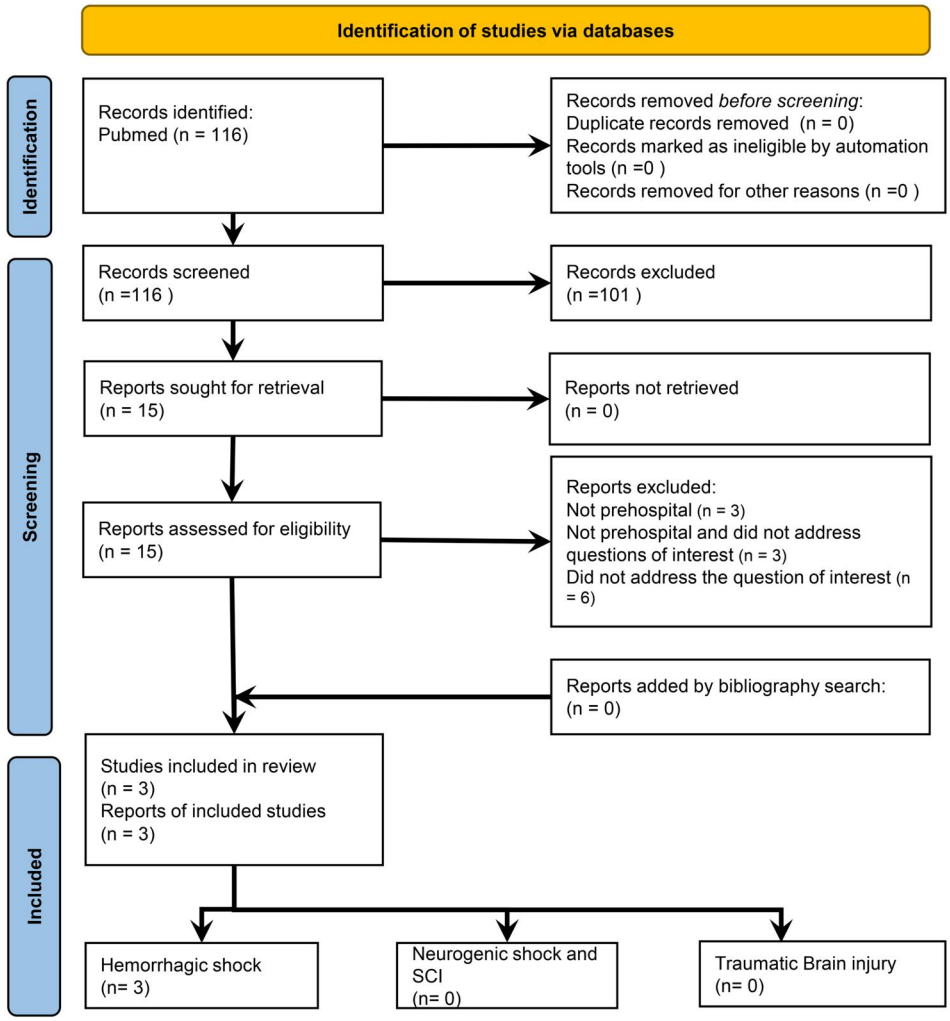

Figure 1. Literature search flow diagram. Database searched: PubMed dates: inception to December 22, 2022. See Supplemental Table for search strategy.

Evidence Synthesis

The final three articles that were used in the development of our recommendations are summarized in Table 1. There were two retrospective reviews of observational data and one prospective observational trial. None of these articles addressed the prehospital use of vasopressors for TBI or SCI. Given the limited prehospital literature, additional manuscripts pertaining to other practice settings were used to inform the discussion of vasopressor use in the prehospital setting.

Discussion

Use of Prehospital Vasopressors for the Treatment of Hemorrhagic Shock

Current Evidence Does Not Support the Routine Use of Vasopressors by EMS Clinicians for Traumatic Hemorrhagic Shock and Suggests the Possibility of Harm

The current treatment of traumatic hemorrhage in the prehospital setting is volume resuscitation with crystalloids or blood product replacement. Adjunctive treatments, such as tranexamic acid and vasopressors have emerged as attractive treatment modalities with properties to combat the physiologic derangements that occur in traumatic hemorrhage (10, 13–17). Vasopressor use for the management of traumatic hemorrhage as an adjunctive treatment to blood product administration has only recently been investigated, mostly in hospital or combat settings (7, 15, 16, 18). Our review of prehospital literature identified three studies that assessed the use of prehospital vasopressors for traumatic hemorrhage. Two studies included civilian trauma patients and one study addressed vasopressor use in combat casualties (7, 15, 16). The prospective observational study by Gauss et al. compared outcomes for civilian trauma patients who received norepinephrine after receipt of at least 1 liter of crystalloid or colloid and found no difference in mortality between a propensity-matched cohort that did not receive norepinephrine in the prehospital setting (15). A later study by Gauss included data on 2,194 patients from three civilian trauma registries in both France (two registries, 1809 patients) and the United States (U.S.) (one registry, 385 patients) also found that patients that received norepinephrine (French registries) had no difference in 24-h mortality or overall mortality compared to patients that did not receive norepinephrine (U.S. registries) (16). It's important to acknowledge the differences in the prehospital systems and patient populations that limits the direct comparison of

Table 1. Evidence table.

Author/year	Content area(s)	Article type	Findings or description
Gauss 2022	Vasopressors in hemorrhagic shock	Retrospective cohort of 3 different trauma registries	No difference in 24 h mortality: TraumaBase 19% (265/1429) *vs.* TRENAU 17% (64/380) *vs.* RACSTC 16% (56/385). No difference in in-hospital mortality: TraumaBase 38% (547/1429) *vs.* TRENAU 30% (115/380) *vs.* RACSTC 30% (108/385).
Gauss 2018	Vasopressors in hemorrhagic shock	Prospective observational	After propensity score matching, no difference in mortality seen between norepinephrine and no norepinephrine—HR 0.95 (CI: 0.45–2.01, $p = 0.69$).
Fisher 2021	Vasopressors in hemorrhagic shock	Retrospective chart review	Univariable analysis found vasopressor use associated with lower odds of survival (OR 0.09, CI 0.016–0.13). After adjustment for patient category, mechanism, ISS, total blood products, prehospital HR, and SBP, the lower odds of survival persisted (OR 0.32, 0.18–0.56). After propensity matching model, using patient category, mechanism, ISS, lowest prehospital SBP ($n = 108$ in vasopressor group, $n = 107$ matched controls), the survival to discharge was lower in vasopressor group (71.3 *vs.* 94.3%, $p < 0.001$).

these two groups. Finally, a retrospective review by Fisher et al., of 120 propensity matched combat casualties from the Department of Defense trauma registry from January 2007 to August 2016, found that vasopressor-treated casualties had lower odds of survival even after adjusting for multiple variables (7). Despite their adjustments, these findings were still significantly limited by selection bias and confounding by indication as the propensity matched group had significantly higher injury severity scores.

In addition to the limited prehospital data, data on vasopressor use in-hospital and combat settings has not shown benefit or suggested harm (7, 15, 16, 18). In-hospital data regarding vasopressor use is similarly scarce. A recent small, randomized placebo-controlled pilot study in severely injured trauma patients requiring at least 6 units of blood products showed a reduced overall need for blood product administration at 48-h after admission in those who received arginine vasopressin continuous infusion (17). However, 30-day survival was not improved compared to placebo. A retrospective cohort analysis showed a higher mortality in those that received arginine vasopressin in severe hemorrhagic shock refractory to blood products and fluids (19). An additional assessment of any vasopressor use in those requiring emergent surgery for trauma (not necessarily in hemorrhagic shock) showed that vasopressors were not independently associated with mortality when excluding the use of epinephrine. This analysis suggests early vasopressor use, regardless of agent selected, was not harmful (20). A recent narrative review discussing the management complexities of traumatic hemorrhagic shock concluded that despite our desire to adopt theoretical benefits of vasopressor use in hemorrhage control, existing clinical equipoise will only be solved by adequately powered, prospective, randomized, multicenter trials (8).

Neither the available prehospital, in-hospital nor combat data address some of the unique situations encountered by EMS clinicians. For example, the current body of literature does not fully address scenarios in austere wilderness or remote rural environments where transport to definitive care is measured in hours or even days, or encounter trauma patients who are refractory to conventional or available prehospital treatments.

Use of Prehospital Vasopressors for the Treatment of Neurogenic Shock and SCI

Current Evidence Does Not Address the Use of Vasopressors by EMS Clinicians in the Treatment of Patients with Severe SCI Presenting with Neurogenic Shock, or to Achieve Specific MAP Goals in Spine Injured Patients in the Prehospital Setting

Hypotension associated with SCI and neurogenic shock has been identified as an independent risk for mortality (21). Maintaining adequate monitoring and BP has been shown to be important in preventing secondary SCI and in preventing major cardiovascular complications associated with neurogenic shock. Despite the implications of these data, our literature review did not reveal any studies specifically addressing the use of prehospital vasopressors in these patient populations. This specific gap in literature prevents us from making any recommendations on their use in the prehospital setting and highlights the need for further investigation to ascertain the optimal approach to managing BP

in the SCI trauma patients during the prehospital phase of care.

Research on hospitalized spinal cord injured patients with or without the presence of neurogenic shock suggests that the optimization of MAP to ensure spinal cord perfusion is associated with improved outcomes and is recommended by two neurosurgical society guidelines (1, 2, 9, 10). A study by Hawryluk emphasized that higher MAP (i.e., >85 mm Hg) correlated with improved neurological recovery in the first 2–3 days in SCI patients (1). One prehospital study demonstrated improved preservation of neurologic function in patients with SCIs that had higher prehospital MAP; however, this study looked at recorded MAP and did not evaluate outcomes based on interventions used to attain those values (2).

Loss of autonomic tone resulting in neurogenic shock in the setting of SCI, can manifest in up to 20% of trauma patients with SCI, with the requirement of vasopressor support during hospitalization serving as an independent predictor for mortality (21). The mainstay of initial treatment as recommended by both the Emergency Neurologic Life Support (ENLS) and AANS CNS guidelines include crystalloid administration and treatment of other cardiac manifestations, such as bradycardia before initiation of vasopressors (9, 10).

Use of Prehospital Vasopressors for the Treatment TBI

Prehospital Hypotension Has Been Shown to be Harmful to Patients with TBI; However, There is Currently No Evidence to Support or Refute the Use of Vasopressors by EMS Clinicians in the Setting of TBI

Hypotension in the setting of TBI has also been linked to unfavorable outcomes similar to SCI. Several studies emphasize the significance of maintaining adequate BP in TBI patients to maintain cerebral perfusion pressures. As seen in the management of SCI, despite the argued importance of BP management in TBI, our literature review did not find any studies that specifically address the question of prehospital vasopressor use in this patient population. This specific gap in the literature prevents us from making any recommendations on the use of vasopressors in the prehospital setting and highlights the need for further investigation.

The harmful effects of hypotension in the prehospital setting in TBI patients have been demonstrated in multiple studies; however a goal BP has not been established and the use of vasopressors to achieve a specific BP have not been studied (3, 11). Chestnut et al. highlighted that even brief episodes of hypotension [systolic BP (SBP) < 90 mm Hg] in severe TBI patients were associated with a significantly increased risk of mortality (3). A study by Spaite et al. used volume expansion with crystalloids for treatment of hypotension in a multi-agency initiative to improve TBI care with a statewide TBI treatment guideline and care bundle. They found a linear association between lowest prehospital BP and mortality, suggesting treatment targets above a SBP of 90 mmHg may be warranted in this population (4, 11). It is impossible to say if the treatment effect was due to recognition and correction of hypotension or simply increased training around the protocol or other bundle elements. However, it is the only known prehospital study that included the treatment of hypotension in TBI and highlights the possible benefit of early correction of any hypotensive episodes.

Considerations for Implementation

The evidence available regarding the use of vasopressors in the field is exceedingly limited for all indications as outlined above. Some of the challenges associated with both use of vasopressors in the field and designing studies to evaluate use include (1) Lack of established BP goals for various injuries and importantly the undifferentiated trauma patient; (2) Identification of patient types based on available clinical findings rather than radiographic or specialty specific findings; and (3) Limited understanding of the role of vasopressors in hospitalized trauma patients. An EMS physician or agency considering vasopressor use for the trauma patient should carefully review the limited prehospital research, the limitations of the existing hospital-based guidelines, and the challenges of appropriate field implementation. A robust quality assurance program, likely in partnership with local trauma programs is imperative to monitor outcomes and ideally would include an intent to study outcomes. High-quality research is needed to provide better understanding of the harms or benefits of vasopressors in the trauma patient. Emergency medical services clinicians should actively participate in the development of and implementation of projects to achieve this goal.

Limitations

The greatest limitation to the development of these recommendations is the lack of evidence related to this topic. As described above within each recommendation section, there remains significant bias and limitations of the available data based on differences in practice patterns and scope, clinical settings, patient selection, and treatment outcomes. Due to the limited data available on these specific questions of interest, we included selected in-hospital data as part of the discussion related to these topics for background information only. We did not conduct a systematic review of in-hospital literature and therefore bias could have been introduced into the discussion.

Additional limitations to this guideline document are primarily related to our search strategy and review of the literature. Our search was conducted in a single database (PubMed) and limited to the English language which limit results from other geographic regions as well as types of publications. Our search results did encompass several European-based studies where practice scope is traditionally more expansive than North American EMS clinicians, potentially introducing bias and limiting external validity of the results. A single author completed the full text review of the search results so there is a risk of misclassification of the

literature. However, due to the limited number of publications on this topic, and review of study bibliographies, we suspect this limitation did not significantly impact our review or the recommendations. As described in the methods section, our author group performed the review of the selected literature and produced a set of recommendations based on the available literature, or lack thereof, but did not utilize the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology to determine quality and strength of the recommendations. This approach may have introduced bias from author opinion or expert consensus, however in choosing to not provide recommendations due to lack of evidence for two of the three questions, we do not believe this introduced any significant bias. Lastly, since this search was conducted in 2022 there is a chance that additional manuscripts have been published that would further inform some of the above topics.

Conclusions

Based on the limited available evidence suggesting no benefit or potential worse outcomes in hemorrhagic shock refractory to volume expansion, we recommend against the use of prehospital vasopressors in this trauma patient cohort. Although prehospital vasopressors may have a theoretical role in the management of SCI, neurogenic shock, or TBI patients in the prehospital setting, there is insufficient evidence to base recommendations for or against their use by EMS clinicians. Resuscitation with crystalloids or blood product transfusion remains the primary approach to address these conditions in the prehospital setting. The absence of robust evidence regarding the role of vasopressors in trauma-related shock resuscitation underscores the critical need for future research in this area to inform clinical practice and improve outcomes for critically injured patients.

Acknowledgments

None.

External Review

This document was created solely by NAEMSP and was not subject to review by external parties.

Updating Procedure

Pursuant to NAEMSP Standards & Clinical Practices Committee procedures and practices, this position statement and resource document will be reviewed and updated five years after its publication. Applicable NAEMSP review and revision practices that are current as of the time of the review will be followed. At a minimum the review process should include a search and synthesis of any new and relevant evidence that is published since the printing of this document.

Author Contributions

Ross Orpet, Kevin Kaucher, Whitney Barrett, and Christopher Colwell developed the plan for literature review and evidence extraction. All authors assume full responsibility for the collection and integrity of the data. All authors participated in the evidence extraction, data analysis, and development of the clinical practice guideline. Ross Orpet, Kevin Kaucher, and Whitney Barrett wrote the initial draft of the manuscript, all authors participated in editing. All authors assume full responsibility for the entire content of the manuscript.

Disclosure Statement

No potential conflict of interest was reported by the author(s).

Declaration of Generative AI in Scientific Writing

The authors did not use a generative artificial intelligence (AI) tool or service to assist with the preparation or editing of this work. The author(s) take full responsibility for the content of this publication.

Funding

This document was developed by NAEMSP without external funding.

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Data Availability Statement

Not applicable.

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