2820MED – Trauma and Environmental Conditions in Paramedic Practice – Critically Appraised Topic (CAT)

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Word count: 1511

Title: Vasopressors are important to patient outcome in haemorrhagic shock.

Clinical Scenario

Paramedics respond to a patient with lacerations to the arm and wrist after dropping a glass panel at work. Estimated blood loss > 2000mL. Post haemorrhage control and initial aggressive fluid resuscitation, the patient remains hypotensive with narrowed pulse pressure, pronounced tachycardia, delayed cap refill and increasingly altered mental state.

PICO Question

For prehospital patients with haemorrhagic shock, does treatment with vasopressors improve patient outcomes compared to standard medical therapy?

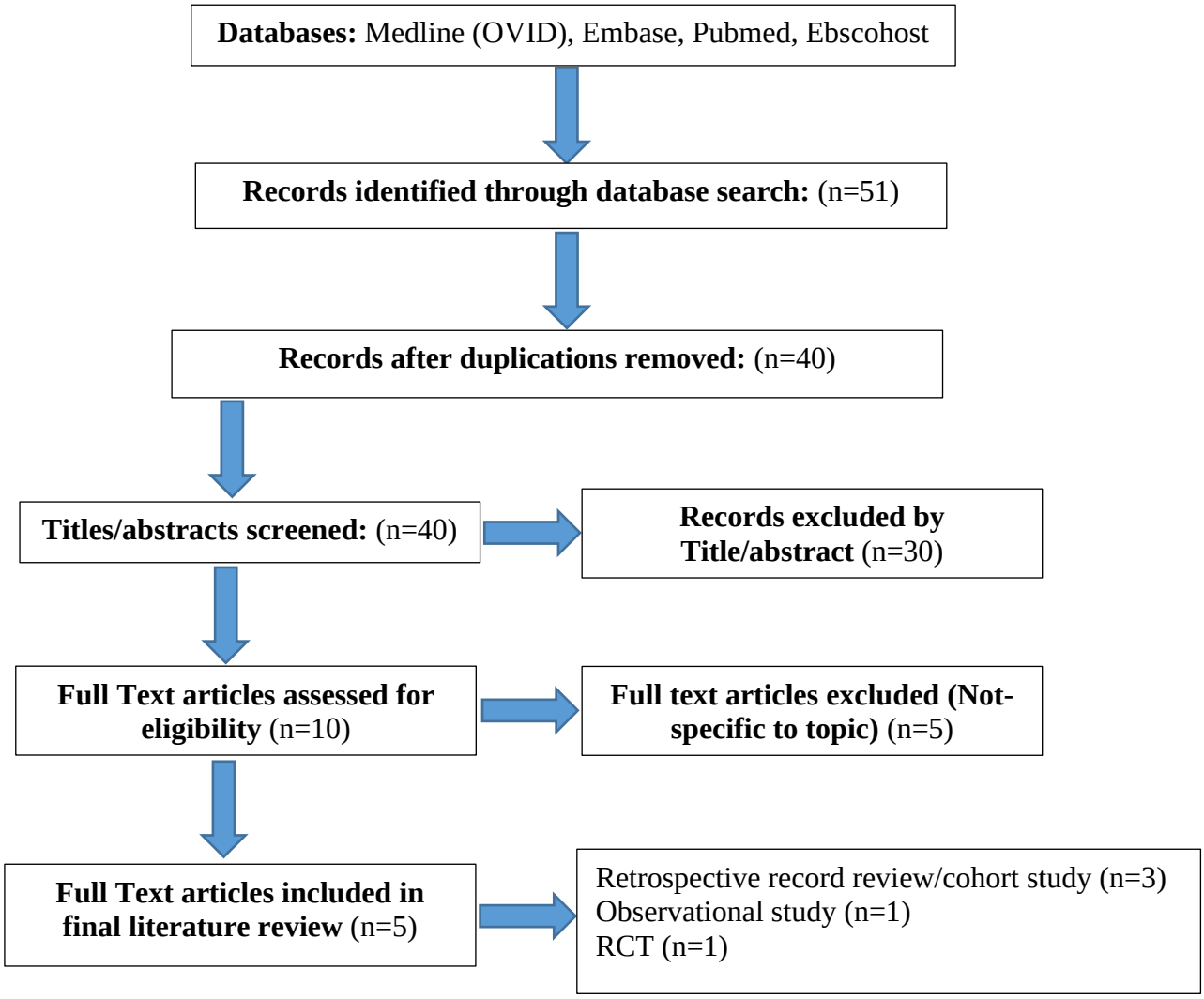
Search Rationale

The leading cause of preventable death in trauma patients is uncontrolled haemorrhage, contributing to almost 50% of deaths within 24 hours (Gupta et al., 2017). Current guidelines suggest limited use of vasopressors for patients with haemorrhagic shock although, large variations in practice continue to exist (Hylands et al., 2017). Proponents identify that vasopressors mimic initial physiological responses to blood loss; improving preload, coronary perfusion, myocardial contractility and prevention of vasodilation following exhaustion of response mechanisms (Gauss et al., 2018). This allows for maintaining minimal perfusion without exposure to large volumes of intravenous fluids which may cause hemodilution and weaken clot strength (Hylands et al., 2017 & Gupta et al., 2017). Arguments against vasopressors highlight the associated increased oxygen consumption, cardiac afterload and excessive vasoconstriction leading to regional ischemia (Gauss et al., 2018).

To date, the role of vasopressors remains controversial, with no clear guidelines and paucity of well controlled randomized trials publishing data on the use of prehospital vasopressors for haemorrhagic shock (Fisher et al., 2021 & Gupta et al., 2017). Attempting to explore this critical gap further, a search will be performed aiming to identify and evaluate contemporary literature.

Search Strategy

("Vasopressor agents" OR Vasopressor* OR pressor* OR Adrenaline OR Epinephrine OR norepinephrine OR nor-epinephrine OR Dopamine OR Catecholamine) AND (Paramedic* OR prehospital OR pre-hospital OR "out of hospital" OR "out-of-hospital" OR ambulance* OR "emergency medical services" OR EMS) AND ("Haemorrhagic shock" OR "Hemorrhagic shock") limit to (English language AND humans AND year = "01/01/2016 - 15/09/2021").



Author/ Date	**Study Design/Level of evidence (NHMRC)**	**Study Aim**	**Population (Sample characteristics)**	**Results**	**Strengths and Limitations**
Aoki et al., 2018	Retrospective cohort study. Level: 3(II)	To evaluate the potential association of mortality with vasopressor use within 24 hours for traumatic haemorrhagic shock patients.	3551 haemorrhagic shock patients over the age of 16yo that received blood transfusion within 24 hours and presented to one of 260 emergency hospitals in Japan between 2004 and 2015. Vasopressor group (n=459). Non-Vasopressor group (n=3092).	Vasopressors was associated with increased in hospital mortality (43% vs 16%) and ED mortality (6.8% vs 2.5%). Propensity score matched patients had increased in hospital mortality but no significant difference in ED mortality.	(-) Vasopressor group had significantly worse rapid trauma scores on arrival. (-) Volume of blood transfusion differed and may be an important confounder. (+) Balanced propensity score matching. (+) Large sample size.

			Study did not include patients with TBI, Spinal injury and those requiring resuscitation. Data obtained from the Japan Trauma Data Bank.		
Fisher et al., 2021	Retrospective record review. Post-hoc analysis Level: 3(II)	To describe whether there is an association between prehospital vasopressor use in the hypotensive combat wounded patient and mortality.	Prehospital Vasopressor group (n=108). Propensity matched group (n=107). Records obtained from The Department of Defence Trauma Registry from January 2007-August 2016.	Prehospital vasopressor group were significantly less likely to survive discharge (71.3% vs 94.3%).	(-) Search strategy included all hypotensive trauma patients, not solely haemorrhagic shock. (-) Reasoning for vasopressor administration not defined. (-) Vasopressor cohort had significantly worse median injury severity score. (-) Mechanism of injury differed significantly. (-) Retrospective nature/possibility for inaccurate prehospital data. (-) Difficult to generalize to civilian community due to military nature. (+) Consistent with existing data regarding vasopressor use for haemorrhagic shock.
Gauss et al., 2018	Observational, retrospective study. Level: 3(II)	To determine the effect of early nor-adrenaline use on in hospital mortality for patients with haemorrhagic shock following major trauma.	All trauma patients with Haemorrhagic shock that received at least 4 blood transfusions within 6 hours of admission to ED. Nor-adrenaline in initial phase (n=201). No nor-adrenaline in initial phase (n=317).	Administration of nor-adrenaline did not induce a significant correction of systolic BP compared to standard group. There was no significant difference in in-hospital mortality for patients who received Nor-adrenaline in the	(-) Nor-adrenaline group presented with more severe circulatory insufficiency. (-) Observational design. (-) Necessary cohort matching reduced power of study. (+) Well-structured propensity score matching allowed for control of some

			Records obtained using multicentre trauma registry between Janurary 2010 and December 2015.	initial phase of traumatic haemorrhagic shock.	patient characteristics. (+) First large clinical cohort study to indicate no significant difference.
Sims et al., 2019	Randomized, double blind placebo-controlled trial. Level: 2	To evaluate the effect of low-dose arginine vasopressin in regards to required total volume of blood product transfusion, 30 day mortality, hospital length of stay, total vasopressor requirement and other complications.	Adult trauma patients (16-65years) who received 6 units of blood product within 12 hours of injury presenting to the trauma centre from May 2013-May 2017. Placebo group (n=51). AVP group (n=49).	Patients who received AVP required significantly less blood products (median 1.4L) and had reduced chance of DVT's. Mortality, additional vasopressor support and complications were not significantly different between the groups.	(-) Hormone Arginine vasopressin not widely utilised in prehospital setting therefore difficult to generalize results. (-) Small sample, unpowered to detect significant differences. (-) Administered dose of AVP varied depending on patients stability. (-) Use of other vasopressors not quantified. (+) Patient characteristics were balanced. (+) Controlled and blinded study.
Uchida et al., 2020	Retrospective record review. Level 3(II)	Evaluate the impact of vasopressor use in patients with severe haemorrhagic shock secondary to blunt trauma injury.	Patients >16years that received vasopressor agents with haemorrhagic shock secondary to blunt trauma. Records obtained from Osaka Critical Care Centre between April 2014 – September 2019. Non-survivor group (n=19). Survivor group (n=21).	Vasopressor use at higher dosages and/or early administration indicated a significantly higher risk of death. Early termination of vasopressors was significantly higher in the survivor group.	(-) Small sample size. (-) Lacks power for definitive. Conclusions (+) Patient characteristics not significantly different.

Comments

Addressing the PICO question was challenging due to the absence of current literature directed at prehospital administration of vasopressors and associated outcomes. Only one article included in the analysis specified prehospital vasopressor administration. This justified the use of the remaining articles which were primarily conducted in Emergency Departments

or analysed existing hospital records. Study aims were coherent across the included articles with one exception. For the most part, mortality remained the chief measure for vasopressor effectiveness, though Sims et al. (2019) primary outcome was to determine the effect on required volume of blood product transfusions. It is important to note that the included articles did reference previous studies centred around vasopressor use for haemorrhagic shock although publication dates excluded them from the review.

Overall, there was confounding discrepancies in the results. Prehospital use of vasopressors or early administration following arrival to hospital, particularly at higher dosages, was associated with increased mortality (Fisher et al., 2021; Uchida et al., 2020; Aoki et al., 2018). Contrary to this, Sims et al. (2019) & Gauss et al. (2018) found no significant difference in in-hospital mortality, instead suggesting that vasopressor use significantly reduced the amount of required blood products and risk of DVT.

The overall quality of included articles however was perplexed by retrospective study design, small sample sizes, incomplete reporting and significant differences in patient characteristics including injury severity. Propensity score matching was attempted to compensate for characteristic differences though exact methods differed between the studies.

Consider

The findings from this review add to current literature by emphasising the need for more prehospital studies. In future, large cohort randomized controlled trials are needed to detect absolute conclusions. Additionally, this will allow for a shift in protocols and potentially symmetry between different emergency service agencies. A newfound consolidation regarding optimal treatment pathways for patients with haemorrhagic shock will then progress to improved patient outcomes. Presently, no suggestions can be made regarding current practice based on the findings of this review.

Clinical Bottom Line

The quality of current prehospital data regarding vasopressor use for haemorrhagic shock is weak and requires further investigation. Recent in hospital studies have shown conflicting results regarding mortality detriment following vasopressor administration, and potential benefits regarding the amount of blood transfusions required, again highlighting the need for additional study. In the absence of current reliable literature, it is recommended that clinicians act with caution when treating haemorrhagic shock patients. Inclusive of this, is the fundamental ability to recognise the potential risks and benefits of vasopressor use in conjunction with current emergency service protocols.

References

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Appendix 1

Australian National Health and Medical Research Council levels of Evidence

Level	Intervention
1	A systematic review of level II studies
2	A randomised controlled trial
3 (I)	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)
3 (II)	A comparative study with concurrent controls: - Non-randomised experimental trial - Cohort study - Case-control study - Interrupted time series with a control group
3 (III)	A comparative study without concurrent controls; - Historical control study - Two or more single arm study - Interrupted time series without a parallel control group
4	Case series with either post-test or pre-test/post-test outcomes