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Essay Title: Plasma Use in the Traumatic Brain Injury Patient: A Critically Appraised Topic in Trauma

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Title: Prehospital plasma use in traumatic brain injury patients improves outcomes.

PICO (Population-Intervention-Comparison-Outcome) Question

In prehospital traumatic brain injury patients does plasma, in comparison to standard cares, improve patient health outcomes?

Topic Relevance and Rationale

Traumatic brain injuries (TBI) are associated with a high mortality rate, making up approximately 33% of all injury-related deaths in civilian patients (Hernandez et al., 2017). In patients that do survive a TBI, there can be long-standing neurological and functional deficits (Hernandez et al., 2017). Currently in TBI patients, prehospital guidelines focus on the use of haemodynamic maintenance as hypotension and hypoxia can significantly worsen patient outcomes (Hernandez et al., 2017). Despite this, there is a lack of effective interventions available to paramedics and other prehospital medical providers. Therefore, in order to improve current management guidelines and patient outcomes, it is crucial that this PICO question is investigated, and relevant literature is analysed.

Search Strategy

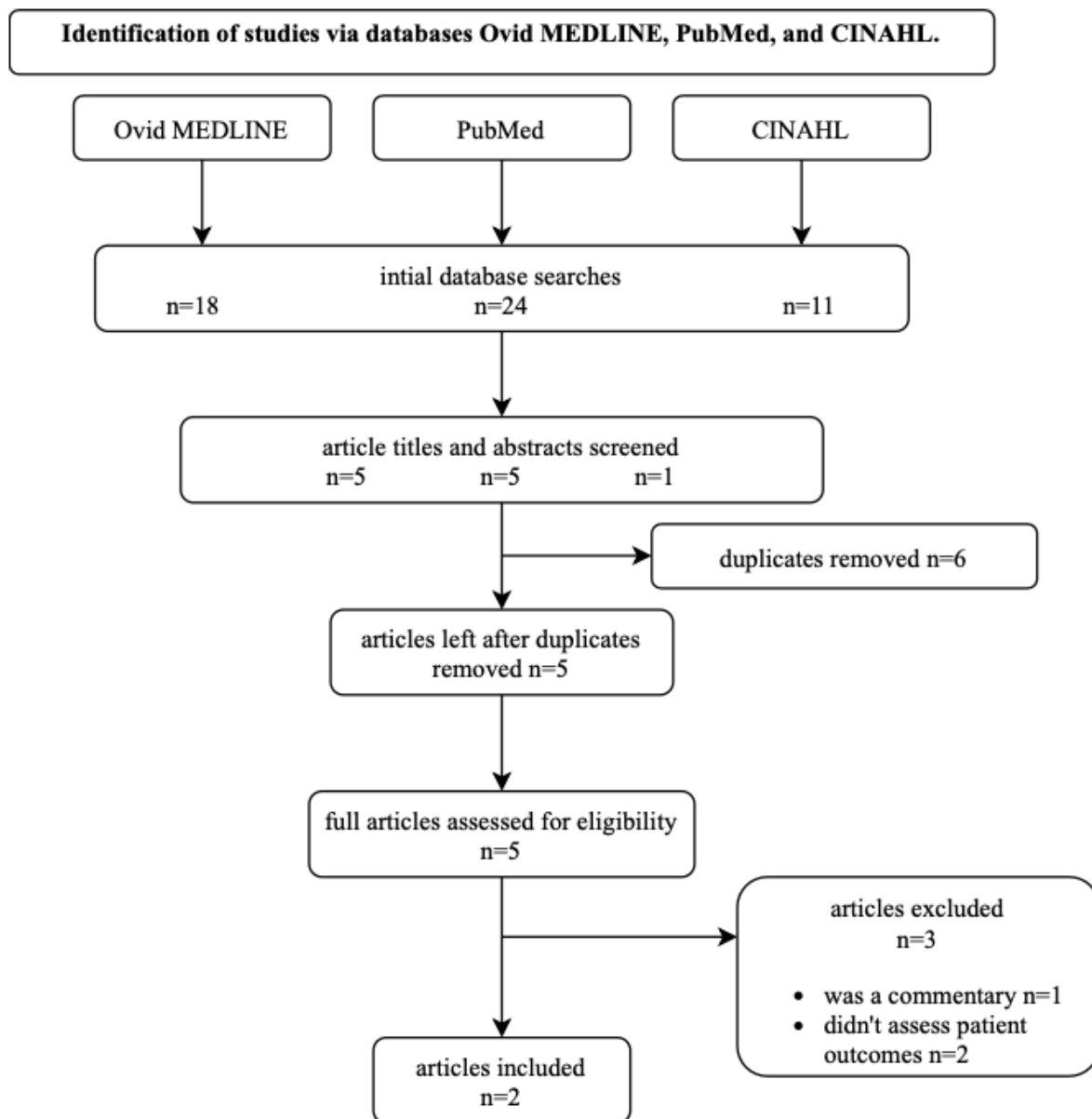
The electronic databases Ovid MEDLINE, PubMed, and CINAHL were utilised to locate relevant literature within the past five years (September 2016 – September 2021). The following MeSH headings and keywords were used:

(prehospital* OR paramed* OR pre-hospital* OR ‘out of hospital*’ OR out-of-hospital* OR ambulance* OR ‘emergency medical service*’ OR EMS) AND (‘traumatic brain injury’ OR TBI* OR ‘traumatic brain injuries’) AND (plasma* OR ‘blood plasma*’ OR ‘fresh frozen plasma*’ OR ‘frozen plasma*’ OR FFP) limit to (English language AND humans).

Articles of any study design were included if they contained information pertaining to the use of plasma for TBI patients in the prehospital setting with associated outcomes. Animal studies and reports not written in English were excluded.

Search Outcomes

The initial database search located a total of 53 articles. Through initial screening of titles and abstracts 11 were selected for further review. After duplicates were removed, 5 full-text articles were analysed. Of these, 3 were excluded and 2 were included.



Study Results and Analysis

Authors and Year	Study Design	Population	Study Aims	Results	Strengths and Limitations
Gruen et al., 2020	Cluster Randomized Clinical Trial	166 patients aged ≥ 18 years with TBI, transported by air medical services between May 2014 and October 2017.	To evaluate the relationship between prehospital plasma administration and survival in patients with TBI.	<ul style="list-style-type: none"> - Reduced 30-day mortality in plasma vs standard care group (55.4 vs 35.1%) - Reduced 24-hour mortality in plasma vs standard care group (35.9 vs 16.2%) - Reduced rate of prehospital intubations in plasma vs standard care group (78.3 vs 71.6%) - Reduced requirements for CPR in plasma vs standard care group (9.8 vs 4.1%) 	<p>Strengths:</p> <ul style="list-style-type: none"> - randomised study design allowing for a decreased risk of selection bias - recent publish year allowing for up-to-date research - adjusted for unbalanced baseline patient variables <p>Limitations:</p> <ul style="list-style-type: none"> - non-blinded study design resulting in the potential for investigator bias. - CT machine used to diagnose TBI and the

					<p>potential misdiagnosis of TBI</p> <ul style="list-style-type: none"> - only viewed air medical services and not other prehospital ambulance services. - smaller sample size
Hernandez et al., 2017	Retrospective Single Institution Study	76 trauma patients aged >15 years with head injuries undergoing prehospital transfusion at a trauma centre between January 2002 and December 2013	To determine whether patients receiving prehospital thawed plasma, in comparison to pRBC, showed differences in neurological outcomes.	<p>- Higher median GOSE at dismissal seen in patients receiving plasma compared to those receiving pRBC (7 versus 5.5).</p> <p>- Lower median DRS scores at dismissal seen in patients receiving plasma compared to pRBC (2 versus 9).</p>	<p>Strengths:</p> <ul style="list-style-type: none"> - long study period to allow for a more holistic view - excluded patients that received both pRCB and plasma to ensure proper comparison of the two interventions <p>Limitations:</p>

				<p>- Higher median GOSE at follow up seen in patients receiving plasma compared to those receiving pRBC (8 versus 6).</p> <p>- Lower median DRS score at follow up seen in patients receiving plasma compared to those receiving pRBC (0 versus 4).</p>	<p>- small sample size therefore limiting the validity of the results</p> <p>- retrospective study design resulting in potential bias</p> <p>- only assessed one institution and thus may not be reflective of other centres.</p> <p>- patients were excluded if they did not survive to dismissal resulting in the potential for survival bias</p>
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Abbreviations: TBI; traumatic brain injury; CPR; cardiopulmonary resuscitation; CT; computed tomography; pRBC; packet red blood cells; GOSE; Glasgow Outcomes Score Extended; DRS; Disability Rating Scale.

Comments

The literature suggests that use of prehospital plasma in TBI patients is associated with a reduced mortality (Gruen et al., 2020). Patients that received intravenous plasma, compared with

patients receiving standard cares based on current practice guidelines, saw a significant reduction in 30-day mortality (20.3%) and 24-hour mortality (19.7%) (Gruen et al., 2020). In addition, the requirement for cardiopulmonary resuscitation was slightly reduced in the patients administered with plasma, however, was not statistically significant (Gruen et al., 2020). Furthermore, the rate of prehospital intubation was decreased in patients that received plasma however, not significantly so (Gruen et al., 2020).

In terms of neurological function and disability, patients administered with plasma saw a greater improvement in Glasgow Outcomes Score Extended (GOSE) at both hospital discharge and follow up (Hernandez et al., 2017). Additionally, plasma administered patients had a greater reduction in Disability Rating Scale (DRS) (Hernandez et al., 2017). GOSE is a measurement tool used by health practitioners to determine functional neurological outcome following a TBI whereas DRS determines an individual's level of mental impairment (Hernandez et al., 2017). Both of which are validated measures well supported by literature.

Considerations for Clinical Practice

Currently, prehospital clinical practice guidelines for TBIs aim to reduce the occurrence of a secondary brain injury by maintaining the patient's haemodynamic stability. Many different interventions have been explored to do so, specifically plasma. Evidence in the literature suggests that plasma, administered prehospitally to TBI patients, is effective in reducing mortality and long-term neurological disability. However, there is a lack of literature regarding the PICO topic and thus not enough evidence to strongly suggest the implementation of prehospital plasma into current guidelines. To advance clinical practice and provide evidence-based guidelines for paramedics and health practitioners, further research is required. Specifically, prehospital, large scale, blinded, multicentred, randomised control trials are

recommended to fill gaps in the current literature. It is suggested that future studies further investigate the effect of plasma on TBI patients, identify trends in long-term mortality, and explore the use of plasma for paediatric TBI patients.

Clinical Bottom Line

Prehospital administration of intravenous plasma acts to improve patient outcomes by reducing short-term mortality, improving neurological function, and decreasing neurological disability in patients with a TBI.

References

- Gruen, D. S., Guyette, F. X., Brown, J. B., Okonkwo, D. O., Puccio, A. M., Campwala, I. K., Tessmer, M. T., Daley, B. J., Miller, R. S., Harbrecht, B. G., Claridge, J. A., Phelan, H. A., Neal, M. D., Zuckerbraun, B. S., Yazer, M. H., Billiar, T. R., & Sperry, J. L. (2020). Association of Prehospital Plasma With Survival in Patients With Traumatic Brain Injury: A Secondary Analysis of the PAMPer Cluster Randomized Clinical Trial. *JAMA Network Open*, 3(10), e2016869. <https://doi.org/10.1001/jamanetworkopen.2020.16869>
- Hernandez, M. C., Thiels, C. A., Aho, J. M., Habermann, E. B., Zielinski, M. D., Stubbs, J. A., Jenkins, D. H., & Zietlow, S. P. (2017). Prehospital plasma resuscitation associated with improved neurologic outcomes after traumatic brain injury. *Journal of Trauma and Acute Care Surgery*, 83(3), 398–405. <https://doi.org/10.1097/TA.0000000000001581>