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ORIGINAL RESEARCH

The efficacy of prehospital IV fluid management in severely injured adult trauma patients: a systematic review and meta-analysis

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Abstract

Purpose The most widely used prehospital strategy for the management of hemorrhagic shock or trauma accompanied by hypotension is fluid resuscitation. Though current guidelines suggest early and aggressive fluid resuscitation, contemporary literature suggests a more restrictive approach. Our objective was to evaluate the effectiveness of low/ no IV fluids in comparison to standard resuscitation in reducing mortality for trauma patients in the prehospital setting.

Methods *Population*—adults with blunt or penetrating trauma in the prehospital setting with severe injury (defined as SBP < 90 mm Hg and/or a shock index > (1). *Intervention*—low-dose/no IV fluids. *Comparison*—standard resuscitation. *Outcome*—mortality. A librarian-assisted search of five databases (Medline, Embase, Web of Science, and CINAHL, Cochrane trials) was completed in June 2021 (updated in November 2022). ROBINS-1 and ROB-2 tools were used to assess risk of bias in observational and randomized studies, respectively. An inverse variance method and random-effects model of statistical analysis were utilized, with data reported as risk ratios with related 95% confidence intervals. Heterogeneity of studies was assessed through analysis of the I^2

Results Seven studies (six observational and one randomized trial) were included, with three thousand and fifty study participants included for analysis. Four studies compared high- to low-dose fluids, and three compared fluids to no fluids. We found no difference in mortality when comparing standard resuscitation to restricted resuscitation (RR 0.99, 95% CI [0.80–1.22], $I^2 = 54\%$).

Conclusion Weak, primarily observational evidence suggests that standard fluid resuscitation has no significant mortality benefit over restricting/withholding IV fluids in severe/hypotensive trauma. This review adds evidence to questioning the requirement for IV fluids in trauma given the lack of mortality benefit, in addition to demonstrating the need for more randomized studies in this area.

Keywords IV fluid · Resuscitation · Trauma · Systematic review

Presentations: an abstract of this paper titled "Does a restrictive fluids resuscitation strategy pre hospital reduce mortality in severely injured trauma patients?" was presented at the Canadian Association of Emergency Physicians conference in Quebec City on June 1st, 2022.

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Résumé

Objectif La stratégie préhospitalière la plus utilisée pour la prise en charge du choc hémorragique ou du traumatisme accompagné d'hypotension est la réanimation liquidienne. Bien que les directives actuelles suggèrent une réanimation liquidienne précoce et agressive, la littérature contemporaine suggère une approche plus restrictive. Notre objectif était d'évaluer l'efficacité des liquides intraveineux faibles ou inexistants par rapport à la réanimation standard pour réduire la mortalité des patients traumatisés en milieu préhospitalier.

Méthodes Population - adultes ayant subi un traumatisme contondant ou pénétrant en milieu préhospitalier et présentant des lésions graves (définies par une PAS < 90 mm Hg et/ou un indice de choc > 1). Intervention - faible dose/absence de fluides IV. Comparaison - réanimation standard. Résultat - Mortalité. Une recherche assistée par un bibliothécaire dans 5 bases de données (Medline, Embase, Web of Science et CINAHL, essais Cochrane) a été effectuée en juin 2021 (mise à jour en novembre 2022). Les outils ROBINS-1 et ROB-2 ont été utilisés pour évaluer le risque de biais dans les études observationnelles et randomisées respectivement. Une méthode de variance inverse et un modèle d'analyse statistique à effets aléatoires ont été utilisés, les données étant présentées sous forme de rapports de risque avec les intervalles de confiance à 95 % correspondants. L'hétérogénéité des études a été évaluée par l'analyse de l'I^2.

Résultats Sept études (six études d'observation et un essai randomisé) ont été incluses, avec 3050 participants à l'analyse. Quatre études ont comparé des fluides à forte dose à des fluides à faible dose, et trois ont comparé des fluides à l'absence de fluides. Nous n'avons trouvé aucune différence dans la mortalité en comparant la réanimation standard à la réanimation restreinte (RR 0,99, IC à 95 % [0,80–1,22], I2 = 54 %).

Conclusion Des preuves faibles, essentiellement observationnelles, suggèrent que la réanimation liquidienne standard ne présente aucun avantage significatif en termes de mortalité par rapport à la restriction/rétention des liquides IV dans les cas de traumatismes graves/hypotensifs. Cette revue ajoute des preuves à la remise en question de la nécessité des fluides IV en traumatologie, étant donné l'absence de bénéfice en termes de mortalité, en plus de démontrer le besoin de plus d'études randomisées dans ce domaine.

Mots-clés Liquide IV · Réanimation · Traumatisme · Revue systématique

Clinician's capsule

What is known about the topic?
Though current guidelines suggest early and aggressive fluid resuscitation in trauma, contemporary literature suggests a more restrictive approach.

What did this study ask?
What is the effect of restricted versus standard fluid resuscitation on mortality for trauma patients in the prehospital setting?

What did this study find?
There was no difference between strategies

Why does this study matter to clinicians?
This review allows emergency clinicians to incorporate contemporary evidence of fluid resuscitation into their practice.

Introduction

For several decades, trauma has been a major cause of fatality in Canada [1] and globally. In 2020, unintentional injury and trauma was the fifth leading cause of death among all ages, and the leading cause of death among those under age 25 [2]. Despite advances in trauma systems, the mortality rate of major trauma remains up to 14% across Canada [2]. Severe trauma is often accompanied by hemorrhage, shock, and subsequent patient deterioration. Perhaps the most widely accepted strategy for the management of hemorrhagic shock or trauma accompanied by hypotension is through fluid resuscitation. By far, isotonic fluids such as crystalloids and colloids are the most commonly used fluid in resuscitation. As compared to blood and blood products, these fluids are more readily accessible, more easily managed, more cost effective, and less prone to leading to adverse reactions [3]. Despite the relative simplicity of these fluids, preferred dosage of fluid in the context of trauma remains unclear.

In the management of severe trauma and hypotension, some studies suggest that restrictive fluid resuscitation may reduce mortality [4, 5], while others find no association between the two [6, 7]. Some studies found benefits in mortality when comparing administering to withholding fluids [9] while others did not [10, 11]. The administration of IV fluids also carries some level of risk, including coagulopathy, compartment syndrome, electrolyte disturbances, and artificial inflation of the systolic blood pressure [3]. The controversy surrounding fluid resuscitation is further exacerbated by mounting evidence that increasing prehospital time to begin fluid resuscitation may drastically reduce positive

outcomes and increase mortality [12–14]. Thus, clear evidence of the most appropriate resuscitation strategy in the context of trauma is warranted, especially in the prehospital context where fluid resuscitation most often takes place.

The objective of this review was to evaluate the effectiveness of non-blood product IV fluids (i.e., crystalloid/ isotonic fluids or colloids) in reducing mortality for severely injured adult trauma patients in the prehospital setting.

Methods

Eligibility criteria

This review sought to include randomized trials, non-randomized trials, and observational studies. Trauma was defined as any cause of blunt or penetrating injury and severity quantified to a corresponding prehospital systolic blood pressure (sBP) of 90 mm Hg or lower, or a shock index (SI) greater than 1. Certain patient populations including pregnancy, isolated head or spinal cord injury, burns, cardiac arrest, and non-hemorrhagic causes of shock were excluded to maximize homogeneity of results. The ideal primary intervention of interest was the complete withholding of any non-blood product IV fluid, although studies comparing high volume to low volume parenteral fluid administration were also considered. The primary outcome of interest was 30-day all-cause mortality. Any study with an outcome measure of all-cause mortality, regardless of timing or setting, was also included. Studies not reporting mortality as an outcome measure were excluded.

Information sources and search strategy

Between June 24 and June 28th, 2021, a systematic search of the electronic databases Ovid MEDLINE, Embase, CINAHL, and Web of Science was performed. The search strategy was developed in collaboration with an experienced health services librarian on the team, who completed each database search. A second health services librarian also peer-reviewed the search. For full search histories, please see Supplemental Digital Content 1. The search was repeated on November 9th 2022 in preparation for publication. The updated search included the original four databases identified above, in addition to a search of the Cochrane Database and Register of Clinical Trials.

Selection process

The literature search completed by the academic librarian was uploaded to RAYYAN [15], an online systematic review study screening and selection program, for review. Authors 1 and 2 reviewed the titles and abstracts of studies identified in the electronic search. A standardized form was used to determine eligibility of studies. Data extracted from all included studies can be found in Table 1.

Data collection process and data items

Data were extracted into an Excel spreadsheet, and reviewed independently by Authors 1 and 2. Included data items sought for retrieval can be found in Table 1. Raw and calculated numerical data included for meta-analysis were subsequently uploaded to Review Manager 5.4 [16].

Study risk of bias assessment

This review utilized two risk of bias assessment tools suggested by the Cochrane Database of Systematic Reviews; the ROB-2 [17] tool for randomized studies and the ROBINS-I [18] tool for non-randomized studies.

Effect measures

Extracted elements were uploaded into RevMan [16], where dichotomous mortality outcome data were expressed as risk ratios (RR) with related 95% confidence intervals (CI).

Synthesis methods

This review undertook the meta-analysis techniques outlined by the Cochrane Handbook for Systematic Reviews of Interventions, Version 6.2 [19]. An inverse variance method was utilized in accordance with the Cochrane Handbook [19]. Mortality data were uploaded into RevMan [16], where calculated risk ratios with related 95% CI were reported in a forest plot. A specified set of subgroup analyses were identified prior to study inclusion with the intention of being implemented if significant heterogeneity was present. The primary characteristic of interest for subgroup analysis was fluid dosage. After completion of data collection and synthesis, a subgroup analysis of blunt vs. penetrating trauma was also considered if significant heterogeneity was identified.

Reporting bias assessment

Reporting bias was assessed by visual inspection of the funnel plot of compiled risk ratio data, with a plan for analysis as to possible causes of asymmetry other than reporting bias if marked funnel plot asymmetry was observed.

Certainty assessment

Certainty of the evidence was assessed utilizing the BMJ GRADE [20] system.

Table 1 Characteristics of included studies

First author (year)	Methodology	N	Mean age (% male)	Age range	Mean ISS
Bickell (1994) [4]	Prospective (NR)	598	31 (90%)	>16	26
Brown (2013)	Prospective (NR)	1216	40 (In—66%, Cr—76%)	>18, <90	41
Dula (2002)	Case–control (NR)	150	In—43, Cr—47 (In—52%, Cr—60%)	U	17
Kaweski (1990)	Retrospective (NR)	6855	31 (75%)	U	25— > 50
Schreiber (2015)	Pilot trial (R)	192	42 (73%)	>15	>15
Yaghoubian (2007)	Retrospective (NR)	194	26 (U)	U	In—17, Cr—16
Zitek (2021)	Retrospective (NR)	878	In—39, Cr—38 (In—77%, Cr—69%)	>18	In—17, Cr—10

Transport time (min)	Inclusion criteria	Injury type (% blunt/ % penetrating)	Type of IV fluid
12 (+/− 6) min	SBP < 90 mm Hg	Penetrating (0%/100%)	CR
U	SBP < 90 mm Hg, base deficit > 6 meq/L, transfusion in first 24 hrs, or AIS > 2	Blunt (100%/0%)	CR
In—18 min Cr—14 min	SBP < 90 mm Hg	Blunt (100%/0%)	U
36 min	SBP (<90 or >90 mm Hg) ISS (<25, 25–50, or >50)	Blunt + penetrating (83%/17%)	U
<15 min	SBP <90 mm Hg and a GCS > 8	Blunt + penetrating (67%/33%)	CR + CO
U	SBP < 90 mm Hg	Penetrating (0%/100%)	U
U	SBP < 90 mm Hg or HR > 100	Blunt + penetrating (70%/30%)	CR

Intervention	Average fluid in each arm (ml)	Outcome
High—Immediate resuscitation, mean	High—870 ml	Decreased mortality in delayed resuscitation
Low—Delayed resuscitation, mean	Low—92 ml	
High—High dose (> 500 ml) fluids	High—U	Increased mortality and coagulopathy with high dose, SBP increased with high dose
Low—Low dose (< 500 ml) fluids	Low—U	
High— >500 ml fluids	High—U	No association between fluid level and mortality
Low— <500 ml to no fluids	Low—U	
Both High + Low grouped on ISS and SBP, mean 620–1554 ml	High—1245—1554 ml Low—0 ml	No association between fluid level and mortality
High—standard resuscitation (1000 ml) + crystalloid to achieve SBP > 110 mm Hg	High—2000 ml	No association between fluid level and mortality
Low—controlled resuscitation (250 ml) if SBP < 70 mm Hg	Low—1000 ml	
High— > 100 ml	High—500 ml	No association between fluid level and mortality
Low— < 100 ml	Low— <100 ml	
High— > 1000 ml	High—500–2000 ml	No association between fluid level and mortality
Low— < 1000 ml	Low—0–1000 ml	

R randomized, *NR* non-randomized, *In* intervention group, *Cr* control group, *High* High Fluids Group, *Low* Low Fluids Group, *PT* penetrating trauma, *BT* blunt trauma, *CR* crystalloid, *CO* colloid, *U* unspecified

Results

Study selection

A total of 5,625 records were identified through the 4 primary databases searched. A summary of the results of the search can be found in the PRISMA [21] flow diagram (Fig. 1). An updated search in November 2022 included the Cochrane Database and Register of Clinical Trials, yielding an additional 221 records total and 167 duplicates from the previous search, for a result of 54 new records screened. No new studies were identified. A total of 641 new records from the primary 4 databases searched were also screened in the November 2022 update, yielding no additional studies. The final count of records included in this review was seven primary studies.

Study characteristics

A summary of the characteristics of excluded studies, including reasons for exclusion, can be found in Supplemental Digital Content 2. A summary of the characteristics of included studies can be found in the characteristics of included studies table (Table 1). Six non-randomized

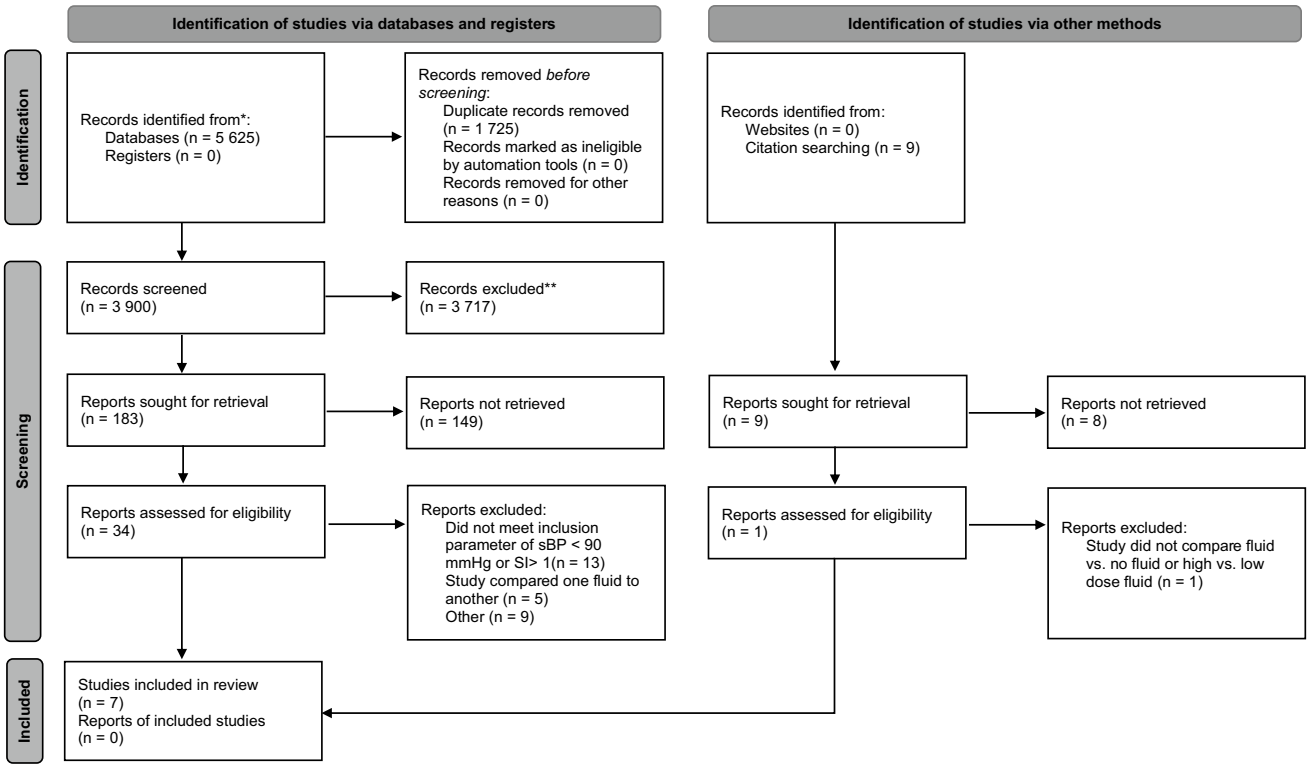

Fig. 1 PRISMA flow diagram of included studies

observational studies [5, 8, 10, 11, 22, 23] and one randomized pilot trial [7] were included. A total of 10,073 patients were included across the 7 studies, with the mean age ranging from 26 to 47. All studies included adults only, with the inclusion age ranging from > 15 to > 18. A mean Injury Severity Score (ISS) was reported in all seven studies, ranging from 10 to > 50. In terms of injury mechanism, two studies [7, 8] reported exclusively on penetrating trauma, two [22, 23] exclusively on blunt trauma, and the remaining three [7, 8, 11] on both penetrating and blunt mechanisms. The exact type of fluid utilized was noted for all studies, with three [5, 11, 22] including exclusively crystalloid, one [7] including a mixture of crystalloid and colloid, and three [8, 10, 23] studies which did not specify the fluid used. Of the seven studies, four [5, 7, 8, 22] compared high-dose fluid to low-dose fluid and three [10, 11, 23] compared receiving fluids to not receiving fluids. The exact level of fluid defined as high or low dose, as well as other defining parameters of each group, varied between studies (see Table 1). The reported outcome of interest was mortality, with the authors' conclusions of the effect of fluids on mortality reported for all seven studies. Additional relevant outcomes such as fluid level in each arm, transport time, and proportion of blunt vs. penetrating trauma, were also included in the table (see Table 1).

Risk of bias in studies

Of the seven studies included, one [7] had low risk of bias, three [4, 11, 22] had moderate risk of bias, and three [8, 10, 23] had serious risk of bias. The risk of bias of the included studies is summarized in the risk of bias of included studies table (see Table 2).

Results of individual studies, results of syntheses, and reporting biases

A funnel plot of the included studies is shown in Fig. 2. A forest plot of the included studies is shown in Fig. 3. Moderate heterogeneity of the included studies was confirmed statistically ($Chi^2 = 13.01$, $I^2 = 54\%$, $p = 0.04$). As expected, the low number of included studies limited the ability of undertaking subgroup analyses. Tests for overall effect showed no significant difference between groups (RR 0.99, 95% CI [0.80–1.22], $p = 0.90$).

Certainty of the evidence

The overall grade of evidence in this review was determined to be low in accordance with the BMJ GRADE [20] recommendations, signifying significant uncertainty of the

Table 2 ROBINS-I and ROB-2 risk of bias assessment of included studies

ROBINS-I risk of bias assessment								
First author (year)	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported results	Overall bias
Bickell (1994)	Moderate	Low	Low	Moderate	Low	Moderate	Low	Moderate
Brown (2013)	Moderate	Low	Low	Low	Low	Moderate	Low	Moderate
Dula (2002)	Serious	Low	Low	Low	Low	Moderate	Low	Serious
Kaweski (1990)	Serious	Low	Moderate	Low	Low	Moderate	Low	Serious
Yaghoubain (2007)	Serious	Low	Moderate	Low	Low	Moderate	Low	Serious
Zitec (2021)	Moderate	Low	Low	Low	Low	Moderate	Low	Moderate
ROB-2 Risk of bias assessment								
First author (year)	Bias arising from the randomization process	Bias due to deviation from intended intervention	Bias due to missing outcome data	Bias due to measurement of the outcome	Bias in selection of reported results	Overall bias		
Schreiber (2015)	Low	Low	Low	Low	Low	Low		

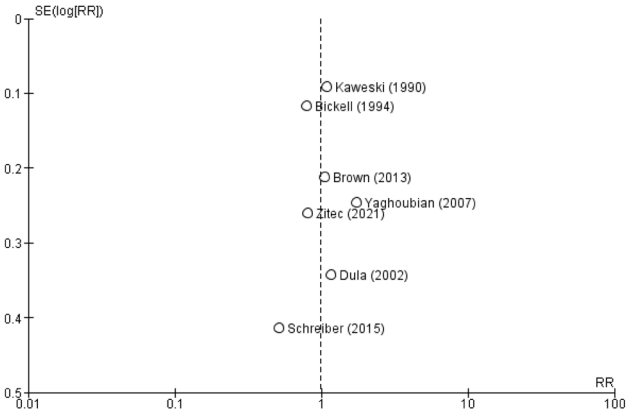

Fig. 2 Funnel plot of included studies

estimated effect size. The GRADE [20] table can be found in Supplemental Digital Content 3.

Discussion

Interpretation

The findings of this review show no significant effect of the administration of IV fluids in the prehospital setting for severely injured adult trauma patients. Five studies [7, 10, 11, 22, 23] found no significant difference between high/low and high/no fluids, one [4] found a significant decrease in mortality with delayed resuscitation, while another [8] found an increase in unadjusted mortality in the low/no fluid group. The calculated effect estimate suggests that both high and low-dose fluids have no mortality benefit for severe trauma in the prehospital context.

Previous studies

Recent evidence suggests the use of smaller doses (< 1L) of IV fluids in trauma, allowing for permissive hypotension until hospitalization or surgical intervention can take place [4–6, 12, 13, 25]. This lower level of IV fluid administration may also partly be due to evidence suggesting the overall benefit of prioritizing rapid transport as opposed to advanced life support at the scene, where the resulting decreased level of fluids was found to lead to decreased mortality [6, 12–14, 24]. Though the evidence of high versus low levels of fluid has been somewhat well established, the implications of fluids versus no fluids has not. The effect estimate in this review suggests no benefit in the reduction of mortality in administering IV fluids in the prehospital setting versus not administering fluids. Only three studies [10, 11, 23] actually measured fluids versus no fluids, though the possibility of no net benefit is

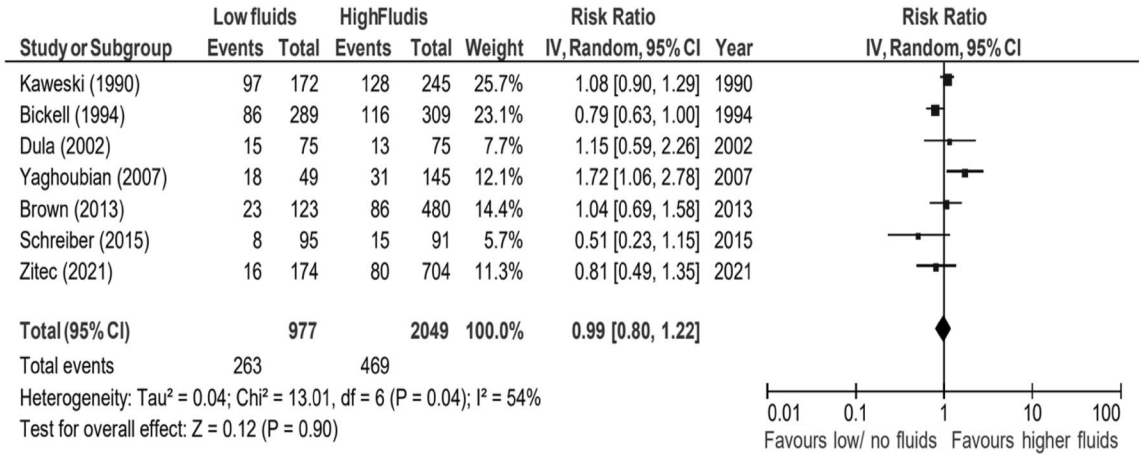

Fig. 3 Forest plot of included studies

supported by the overall effect estimate showing no significant benefit in fluid administration. To the knowledge of the authors, virtually no consensus has ever declared that the complete withholding of fluids would be the best approach in terms of fluid resuscitation for severely injured trauma patients.

Strengths and limitations

This review has various strengths. First, internal validity was a high priority. Various sources of evidence in systematic review methodology were utilized, including the Cochrane [19], PRISMA [21], and GRADE [20]. Further, the involvement of two experienced health system librarians strengthens the quality of the literature search of this review, with a high likelihood that all potentially relevant studies were identified. This review also has certain limitations. First, though a preemptive protocol was developed by the authors, this review was not registered. Further, the small number of included studies limited the ability for a more robust meta-analysis and reduced confidence in the estimated effect size. This small number of studies also limited the ability to perform a subgroup analysis, which may have found a difference in outcome if performed (for example, analysis of blunt vs. penetrating trauma). In addition, the observational nature and high risk of bias of the included studies limited the strength of the evidence. Lastly, combination of randomized and observational data may further limit accuracy of the effect estimate.

Clinical implications

This review holds important implications for practice. As mentioned, the effect estimate of this review suggests that both high- and low-dose fluids have no mortality benefit for severely injured adult trauma patients in the prehospital setting. IV fluid administration also carries the potential inherent risks of coagulopathy, electrolyte disturbance, and artificial sBP inflation [3]. Though these findings may appear somewhat significant at face value, clinicians should be reminded of the low quality of currently available evidence, with only one randomized trial and several poor to moderate quality observational studies to guide practice.

At best, this review adds evidence to questioning the requirement for IV fluids in trauma given the lack of mortality benefit, and certainly demonstrates the need for more randomized studies in this area.

Research implications

This review holds important implications for research by identifying the need for randomized trials evaluating the effect of prehospital IV fluids in trauma patients. If undertaken, these trials should compare the prehospital administration of standard dose IV fluids to administering no fluid in patients with severe trauma (similarly to this review, defined as a SI > 1 or sBP < 90 mmHg).

Conclusion

Weak, primarily observational evidence suggests that standard fluid resuscitation has no significant mortality benefit over restricting/withholding IV fluids in the context of severe/hypotensive trauma. This review adds evidence to questioning the requirement for IV fluids in trauma given the lack of mortality benefit, in addition to demonstrating the need for more randomized studies in this area.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s43678-023-00447-9.

Declarations

Conflict of interest SH reports no conflict of interest, financial or otherwise. EK reports no conflict of interest, financial or otherwise. AC reports no conflict of interest, financial or otherwise. RO reports no conflict of interest, financial or otherwise.

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