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REVIEW

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Vasopressin for treatment of vasodilatory shock: an ESICM systematic review and meta-analysis

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Abstract *Objective:* To examine the benefits and risks of vasopressin or its analog terlipressin for patients with vasodilatory shock. *Data source:* We searched the CENTRAL, MEDLINE, EMBASE, and LILACS databases (up to March 2011) as well as reference lists of articles and proceedings of major meetings; we also contacted trial authors. We considered randomized and quasirandomized trials of vasopressin or terlipressin versus placebo or supportive treatment in adult and pediatric patients with vasodilatory shock. The primary outcome for this review was short-term all-cause mortality. *Study selection:* We identified 10 randomized trials (1,134 patients). Six studies were considered for the main analysis on mortality in adults. *Data extraction and synthesis:* The crude short-term mortality was 206 of 512 (40.2%) in vasopressin/terlipressin-treated patients and 198 of 461 (42.9%) in controls [six trials, risk ratio (RR) = 0.91; 95% confidence interval (CI) 0.79–1.05; $P = 0.21$; $I^2 = 0\%$]. There were 49 of 463 (10.6%) patients with serious adverse events in the vasopressin/terlipressin arm and 51 of 431 (11.8%) in the control arm (four trials, RR = 0.90; 95% CI 0.49–1.67; $P = 0.75$; $I^2 = 26\%$). Metaregression analysis showed negative correlation between vasopressin dose and norepinephrine dose ($P = 0.03$). *Conclusions:* Overall, use of vasopressin or terlipressin did not produce any survival benefit in the short term in patients with vasodilatory shock. Physicians may value the sparing effects of vasopressin/terlipressin on norepinephrine requirement given its apparent safe profile.

Keywords Vasopressin · Terlipressin · Vasodilatory shock

Introduction

Vasodilatory shock is a life-threatening condition with short-term mortality ranging from 40% to 60% [1, 2]. Early mortality is usually associated with refractory hypotension. Hemodynamic management of patients with septic shock consists of fluid administration and use of vasopressors with dopamine or norepinephrine as first-line agents [3, 4]. However, a substantial number of patients remain refractory to this strategy, with worsening of organ dysfunction to death. Vasopressin, an endogenous stress hormone, has been proposed in management of such patients [5, 6]. Indeed, patients with vasodilatory shock may have circulating vasopressin concentrations

inappropriately low in comparison with their level of systolic blood pressure, particularly in the late phase of shock [5, 7]. In addition, although vasopressin infusion has little if any effect on blood pressure in normal subjects, low-dose infusion of vasopressin can restore vascular tone in patients with vasodilatory shock [5, 8–11]. On the other hand, vasopressin may have important side-effects including arrhythmias [10] and myocardial, skin, and gut ischemia [12–14]. While findings from randomized controlled trials consistently show that vasopressin infusion improves hemodynamic status in patients with vasodilatory shock [13], its effect on mortality remains controversial [15].

We performed a systematic review of the effects of vasopressin or its analog terlipressin on mortality and morbidity in patients with vasodilatory shock.

Methods

This meta-analysis was performed in accordance with preferred reporting items for systematic reviews and meta-analyses (PRISMA) recommendations [16].

Search strategy

We attempted to identify all relevant studies regardless of language or publication status (published, unpublished, in press, or in progress).

Electronic searches

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) published in the Cochrane Library (issue 1, 2011) using the search term "vasopressin" or "terlipressin" and "shock". We also searched the following electronic databases: (1) MEDLINE (1966 to March 2011) using the search term "vasopressin" or "terlipressin" and "shock", (2) EMBASE (1974 to March 2011) using "vasopressin, terlipressin, shock", and (3) LILACS (http://www.bireme.br; accessed March 2011) using "vasopressin, terlipressin, shock".

Other sources

We checked the reference lists of all trials identified by the above methods, and contacted authors to find additional unpublished data. We also searched the proceedings of the annual meeting of major critical care medicine symposia, i.e., Society of Critical Care Medicine, American Thoracic Society, the International Symposium on Intensive Care and Emergency Medicine, the American College of Chest Physicians, and the European Society of Intensive Care Medicine, for the years 1998–2010 (inclusive).

Finally we searched for ongoing randomized controlled trials, the metaregister of controlled trials, using the search terms "vasopressin", "terlipressin", "septic shock"; "sepsis" (http://www.controlled-trials.com/mrct/active, accessed March 2011).

Study selection

Two reviewers (A.P. and E.P.) checked the titles and abstracts identified by the search strategy and examined in full any trial that potentially met the inclusion criteria. Any disagreement between the two authors was settled by discussion with a third author (D.A.) until consensus was reached. Agreement between the two reviewers on study inclusion was excellent ($k = 1$). The study's primary author was contacted for clarification whenever needed.

We included randomized or quasirandomized (i.e., using systematic methods, such as alternation, assignment based on date of birth, case record number, or date of presentation) controlled trials with or without blinding, with a primary focus on patients with vasodilatory shock. We considered studies on intravenous treatment with any type of vasopressin formulation (vasopressin, terlipressin). We considered that vasopressin was given as replacement therapy when it was infused at fixed dose of 0.04 UI per hour and as vasopressor therapy when it was titrated according to any hemodynamic goal (e.g., mean arterial pressure). The control group could include standard therapy (fluid replacement and/or vasopressor therapy, antibiotics, mechanical ventilation, or renal replacement therapy) or placebo.

Data collection and analysis

Data extraction

One author (A.P.) designed a data extraction form that was validated by the other authors before data abstraction. Two authors (A.P. and E.P.) independently extracted the data. Primary authors of trials were contacted to provide missing data, whenever needed. One author (A.P.) entered the data onto the computer following standard double entry procedure.

Assessment of methodological quality

Two authors (A.P. and E.P.) independently evaluated the methodological quality of studies. We documented the method of generation of allocation sequence and

allocation concealment and we described, whenever possible, whom among patients, caregivers, data collectors, outcome assessors, and data analysts remained blinded [17]. We also documented whether or not the analysis respected the intention-to-treat principle and considered loss to follow-up as adequate (≥90% of randomized patients included in the analysis), unclear (not reported), or inadequate (<90% of randomized patients included in the analysis). The methodological quality of trials was also evaluated by means of the Jadad score [18]. Any disagreement between authors was settled by discussion with one author (D.A.) until consensus was reached. We contacted the primary study author for clarification whenever needed.

Data analysis

The primary outcome measure for this meta-analysis was short-term all-cause mortality (at any time from randomization to hospital discharge). Secondary outcomes included norepinephrine dosage within the first 12–24 h of randomization, urine output, and the number of patients with serious adverse events (i.e., acute coronary syndrome, skin and gut ischemia, arrhythmias) within 28 days from randomization or up to hospital discharge depending on the follow-up design of each study. A 2×2 table with the number of patients who experienced the event and the total number of patients for each comparison group was derived from each study. The results were expressed as risk ratios (RRs) with 95% confidence intervals (CI). All statistical calculations were performed using Review Manager version 5 [19], except metaregression analyses, which were computed using the Comprehensive Meta-Analysis software package [20]. Heterogeneity between studies was assessed with χ^2 and I^2 statistics. Pooled risk estimates were calculated using a random-effect model by the method of DerSimonian and Laird with inverse-variance weighting [21]. All reported P values are two-sided. Values of $P < 0.05$ were considered statistically significant. To further explore the potential association between vasopressin dose (i.e., given as replacement therapy or vasopressor therapy), age, and the magnitude of the effect, we performed two metaregressions using vasopressin infusion rate (standardized using U/min infusion rate) and median age of the patient population as predictors. To look at a possible norepinephrine sparing effect of vasopressin, we also performed a third metaregression analysis evaluating the potential association between vasopressin dose and standard difference in norepinephrine infusion rate between treated and control patients. Potential publication bias was assessed graphically by funnel plot as well as by Begg and Mazumdar's rank correlation [22] and Egger's regression [23].

Results

Description of studies

Our search results are detailed in Fig. 1. The search strategy produced 10 trials reported as full papers, six randomized controlled trials investigating vasopressin treatment in patients with vasodilatory shock [9, 15, 24–27], and four trials investigating terlipressin [28–31] for a total number of 1,134 participants (Table 1). No studies were reported in abstract form. We have no information about ongoing trials.

Trial centers

Two studies were multicenter (i.e., >2 centers) [15, 24]. One study was conducted at two different sites [25]. The remaining trials were single-center studies.

Description of participants

Eight trials included patients with septic shock [15, 25–31]; two trials included patients with septic shock and nonseptic vasodilatory shock [9, 24]. Eight trials included adults [9, 15, 25–30]; two trials included children [24, 31]. As adults and children differ in physiology, predisposing diseases, and shock management [32], for each outcome we followed the guideline that analysis trials in adults and children be pooled separately, as suggested in the *Cochrane Handbook for Systematic Reviews of Intervention* [33]. Nonetheless, a forest plot of pediatric and adults study combined together is presented as electronic supplementary material (ESM Fig. S1).

Control

Two trials compared vasopressin versus placebo [24, 26] and four trials vasopressin versus norepinephrine [9, 15, 25, 27]. One trial compared terlipressin versus vasopressin and norepinephrine [30]. Two trials compared terlipressin versus norepinephrine [28, 29]. One trial compared terlipressin versus dopamine, dobutamine, and epinephrine [31].

Vasopressin/terlipressin dose and duration

In three trials, vasopressin was infused for more than 24 h [9, 25, 26]. In two trials, vasopressin was stopped according to patient hemodynamic status, or occurrence of serious adverse event [15, 24]. In one trial, vasopressin was infused for 4 h [27]. Terlipressin was infused for less than 12 h in two trials [28, 29], and for more than 24 h in two other trials [30, 31].

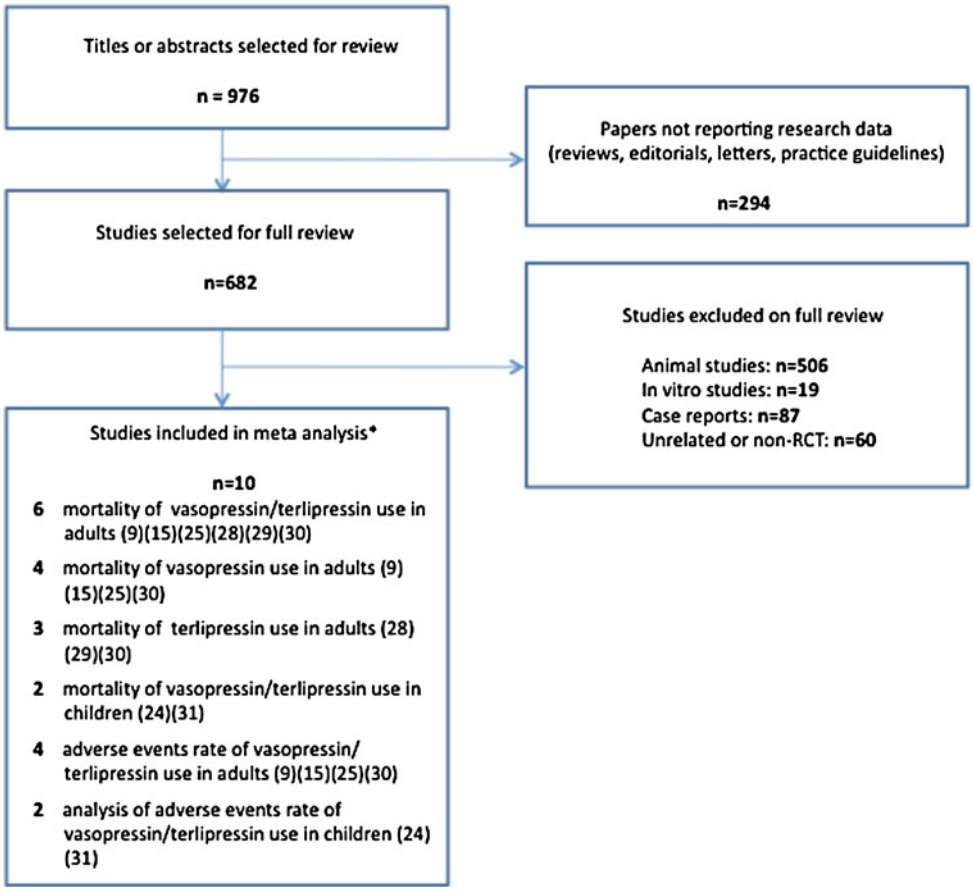

Fig. 1 Literature search and study selection. * For the analysis of mortality with vasopressin/terlipressin use in adults, vasopressin and terlipressin arms from the TERLIVAP study [30] were pooled together and compared with controls; the vasopressin and terlipressin arms of the same study contributed separately to the vasopressin and terlipressin mortality analyses in adults, respectively. Data from Malay et al. [26] were not used for main analyses but were only considered for sensitivity analysis (see text). Data from Patel et al. [27] were only used for analysis of the association between vasopressin dose and norepinephrine dose. For studies included in metaregression analyses, see Table 1

Outcomes

Mortality was reported at 24 h in one trial [26], and at 28 days [15] or at 30 days [24] in two other trials. Five trials reported ICU mortality [9, 25, 29–31], and one trial reported hospital mortality [28]. Assuming that 24-h mortality is a very different outcome from mortality assessed at longer time points such as 28 or 30 days, or at ICU or hospital discharge, data from the trial by Malay et al. [22] were only incorporated in sensitivity analysis. Then, for the primary outcome, analysis data from six adult trials ($n = 973$) and two children trials ($n = 127$) were pooled in two separate analyses. Data from Patel et al. [27] were only used for analysis of secondary outcomes (association between vasopressin dose and norepinephrine dose).

Risk of bias in included studies

An assessment of the methodological quality of individual trials is presented in Table 2.

Randomization

All trials used adequate computerized method of generation of allocation sequence.

Blinding

In six studies blinding was uncertain (unblinded/unable to ascertain) [9, 25, 28–31]. In the remaining trials, patients, physicians, nurses, investigators, pharmacists, statisticians, and sponsors remained blinded to treatment allocation.

Withdrawal

Five trials provided the number and reasons for loss to follow-up [15, 24–26, 29]. For the remaining trials, no such information could be either found in the published papers or obtained upon contacting the study authors.

Table 1 Characteristics of included studies

Source	Type of shock	Age	No. of sites	No. of participants	Interventions	Primary outcome	Secondary outcomes	Outcomes analyzed in the meta-analysis	Provision of unpublished data concerning 28-day mortality
Albanese et al. [28]	Septic shock (resistant to fluids)	>18 years	1	20	(1) Terlipressin (1 mg bolus) (2) NE (0.3 μg/kg/min)	MAP	Hospital mortality, urine flow, creat clearance	Mortality, association between age and survival benefit	No
Choong et al. [24]	Vasodilatory shock (resistant to fluids and catecholamines)	<17 years	7	69	(1) Vasopressin (0.0005–0.002 U/kg/min or 0.05 U/min); (2) Placebo	Time to vasoactive-free hemodynamic stability	30-day mortality, PELOD and MODS scores, days alive and free of organ dysfunction, adverse events	Mortality, serious adverse events, association between age and survival benefit	N/A
Dunser et al. [9]	Vasodilatory shock (w and w/o sepsis, resistant to fluids and low-dose NE)	>16 years	1	48	(1) Vasopressin (4U/h); (2) NE (0.5–2.26 μg/kg/min)	MAP	ICU mortality, changes in other single-organ function, adverse events	Mortality, serious adverse events, association between vasopressin dose and NE dose, association between age and survival benefit, association between vasopressin dosage and survival benefit	No
Lauzier et al. [25]	Septic shock (resistant to fluids)	>16 years	2	23	(1) Vasopressin (0.04–0.20 U/min); (2) NE (0.1–2.8 μg/kg/min)	MAP	HR, CI, SOFA score at the end of the experiment, mortality, adverse events	Mortality, serious adverse events, association between vasopressin dose and NE dose, association between age and survival benefit, association between vasopressin dosage and survival benefit	No
Malay et al. [26]	Septic shock (resistant to fluids and low-dose NE)	>16 years	1	10	(1) Vasopressin (0.04 U/min); (2) Placebo	MAP	NE, phenylephrine and dopamine discontinuation, mortality	Mortality	No
Morelli et al. [29]	Septic shock (resistant to fluids and catecholamines)	>18 years	1	59	(1) Terlipressin (1 mg bolus); (2) NE (0.9 μg/kg/min)	Efficacy of dobutamine in reversing SvO_2 reduction	ICU mortality, CI, HR	Mortality, association between age and survival benefit	No

Table 1 continued

Source	Type of shock	Age	No. of sites	No. of participants	Interventions	Primary outcome	Secondary outcomes	Outcomes analyzed in the meta-analysis	Provision of unpublished data concerning 28-day mortality
Morelli et al. [30]	Septic shock (resistant to fluids)	>18 years	1	45	(1) Terlipressin (1.3 μg/kg/min); (2) Vasopressin 0.03 U/min (3) NE (15 μg/min)	NE requirements	ICU mortality, CI, HR, adverse events	Mortality, serious adverse events, association between vasopressin dose and NE dose, association between age and survival benefit, association between vasopressin dosage and survival benefit	No
Patel et al. [27]	Septic shock (resistant to fluids and low-dose NE)	>16 years	1	24	(1) Vasopressin (0.01–0.08 U/min); (2) NE (2–16 μg/min)	NE dose	Renal function	Association between vasopressin dose and NE dose	N/A
Russell et al. [15]	Septic shock (resistant to fluids and low-dose NE)	>16 years	27	778	(1) Vasopressin (0.01–0.03 U/min); (2) NE (5–15 μg/min)	28-day mortality	90-day mortality, days alive and free of organ dysfunction and of vasopressor use, mechanical ventilation, adverse events	Mortality, serious adverse events, association between vasopressin dose and NE dose, association between age and survival benefit, association between vasopressin dosage and survival benefit	N/A
Yildizdas et al. [31]	Septic shock (resistant to fluids and catecholamines)	<17 years	1	58	(1) Terlipressin 20 μg/kg every 6 h; (2) Dopamine (20 μg/kg/min), dobutamine (15 μg/kg/min)	MAP	HR, PaO_2/FiO_2, mortality, adverse events	Mortality, serious adverse events, association between age and survival benefit	Yes

MAP mean arterial pressure, *NE* norepinephrine, *HR* heart rate, *CI* cardiac index, *ICU* intensive care unit, *SOFA* Sequential Organ Failure Assessment, *creat* creatinine, *PELOD* paediatric logostic organ dysfunction, *MODS* multiple organ dysfunction score

N/A refers to papers that already contain 28-day mortality rate or where mortality was not reported at all

Table 2 Risk of bias in studies

Source	Sequence generation	Allocation concealment	Blinding	Incomplete outcome data addressed	ITT analyses	Jadad score
Albanese et al. [28]	Computer-generated randomization list	Unclear (not stated)	No	Loss to follow-up: not stated	Unclear (not stated)	2
Choong et al. [24]	Computer-generated randomization list	Randomization was centralized	Yes	Lost to follow-up: 5 patients	Yes	5
Dunser et al. [9]	Random number-generating scheme	Unclear (not stated)	No	Loss to follow-up: not stated	Unclear (not stated)	2
Lauzier et al. [25]	Computer-generated randomization list	Numbered, opaque sealed envelopes	No	Loss to follow-up: 1 patient	Yes	3
Malay et al. [26]	Computer-generated randomization list	Unclear (not stated)	Yes	No loss to follow-up	Yes	3
Morelli et al. [29]	Computer-generated randomization list	Unclear (not stated)	No	Loss to follow-up: not stated	Unclear (not stated)	3
Morelli et al. [30]	Computer-generated randomization list	Unclear (not stated)	No	No loss to follow-up	Unclear (not stated)	2
Patel et al. [27]	Computer-based procedure	Unclear (not stated)	Yes	Loss to follow-up: not stated	Unclear (not stated)	3
Russell et al. [15]	Computer-generated randomization list	Randomization was centralized	Yes	Lost to follow-up: 1 patient	Yes	5
Yildizdas et al. [31]	Computer-generated randomization list	Unclear (not stated)	No	Loss to follow-up: not stated	Unclear (not stated)	2

ITT intention to treat

Intention-to-treat analysis

Four trials provided information about use of intention-to-treat analysis [15, 24–26].

Effect of interventions

Primary outcome: all-cause short-term mortality

For the main analysis, we computed data from six randomized trials exploring use of vasopressin/terlipressin in adults (973 patients) [9, 15, 25, 28–30]. There were 206 of 512 (40.2%) deaths in the short term in the experimental arm and 198 of 461 (42.9%) in the control arm (RR = 0.91; 95% CI 0.79–1.05; $P = 0.21$; $\chi^2 = 1.36$, $df = 5$, $I^2 = 0\%$) (Fig. 2). Removing the only study that used hospital mortality as primary outcome [28] did not result in a significant change in risk of death (RR = 0.90; 95% CI 0.78–1.05; $P = 0.23$; $\chi^2 = 0.89$, $df = 4$, $I^2 = 0\%$). Adding the only study that used 24-h mortality as primary outcome [26] to the main analysis did not significantly alter risk of death (RR = 0.91; 95% CI 0.79–1.06; $P = 0.23$; $\chi^2 = 2.07$, $df = 6$, $I^2 = 0\%$). In subgroup analysis of five trials ($n = 925$) investigating use of vasopressin/terlipressin in adult patients with septic shock [15, 25, 28–30], mortality was 189 of 488 (38.7%) in treated versus 181 of 437 (41.4%) in control patients (RR = 0.90; 95% CI 0.77–1.04; $P = 0.17$, $\chi^2 = 1.07$, $df = 4$, $I^2 = 0\%$). In subgroup analysis of four trials of vasopressin for vasodilatory shock [9, 15, 25, 30] ($n = 879$), there were 168 of 448 (37.5%) deaths in the short term in the experimental arm and 180 of 431 (41.8%) deaths in the control arm (RR = 0.91; 95% CI 0.78–1.06; $P = 0.23$; $\chi^2 = 0.52$, $df = 3$, $I^2 = 0\%$) (Fig. 3). In subgroup analysis of three trials of terlipressin

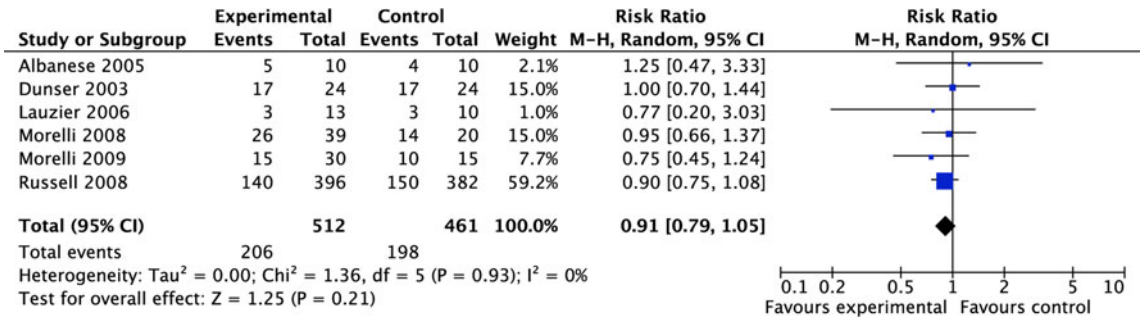

Fig. 2 Mortality in adults (CI, confidence interval)

for vasodilatory shock [28–30] ($n = 109$), there were 38 of 64 (59.4%) deaths in the experimental arm and 28 of 45 (62.2%) deaths in the control arm (RR = 0.91; 95% CI 0.68–1.24; $P = 0.56$; $\chi^2 = 1.09$, $df = 2$, $I^2 = 0\%$) (Fig. 4). Removing from the terlipressin analysis the only study using hospital mortality as primary outcome [28] did not result in a significant change in risk of death (data not shown). In subgroup analysis of two trials in children [24, 31] ($n = 127$), there were 30/65 (46.1%) deaths in the vasopressin/terlipressin arm and 25/62 (40.3%) deaths in the control arm (RR = 1.20; 95% CI 0.56–2.54; $P = 0.64$; $\chi^2 = 2.41$, $df = 1$, $I^2 = 58\%$) (Fig. 5). Metaregression analysis did not show any association between vasopressin dose ($P = 0.65$) or age ($P = 0.93$) and short-term mortality (ESM Figs. S2, S3). Funnel plot graphical analysis, Begg and Mazumdar's rank correlation, and Egger's regression did not suggest significant publication bias (Kendall's tau = 0.13, $P = 0.7$; Egger's regression intercept = 0.14, $P = 0.7$) (ESM Fig. S4)

Secondary outcomes

Norepinephrine dose

Metaregression analysis showed a significant association between vasopressin dose and norepinephrine dose ($P = 0.03$) (ESM Fig. S5).

Serious adverse events

Four trials reported data for this outcome in adults ($n = 894$) [9, 15, 25, 30]. There were 49 of 463 (10.6%) patients with at least one serious adverse event in the experimental arm and 51 of 431 (11.8%) patients in the control arm (RR = 0.90; 95% CI 0.49–1.67; $P = 0.75$; $\chi^2 = 4.07$, $df = 3$, $I^2 = 26\%$) (Fig. 6). In subgroup analysis of two trials in children [24, 31] ($n = 127$), there were 10 of 65 (15.4%) patients with at least one serious

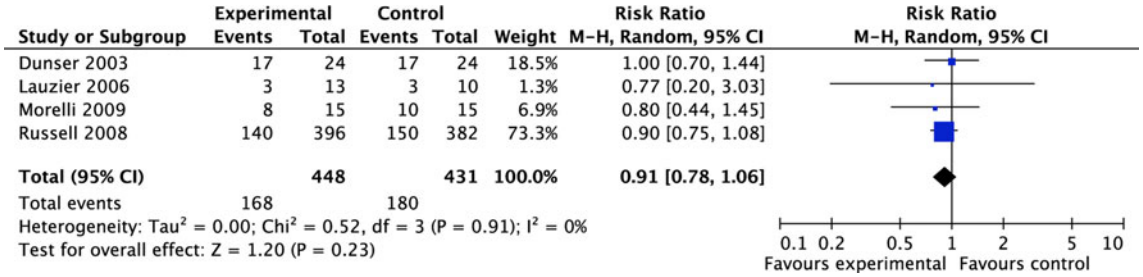

Fig. 3 Vasopressin mortality in adults (CI, confidence interval)

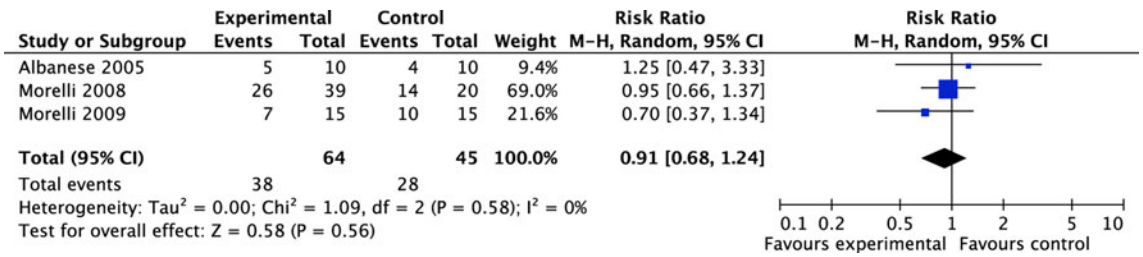

Fig. 4 Terlipressin mortality in adults (CI, confidence interval)

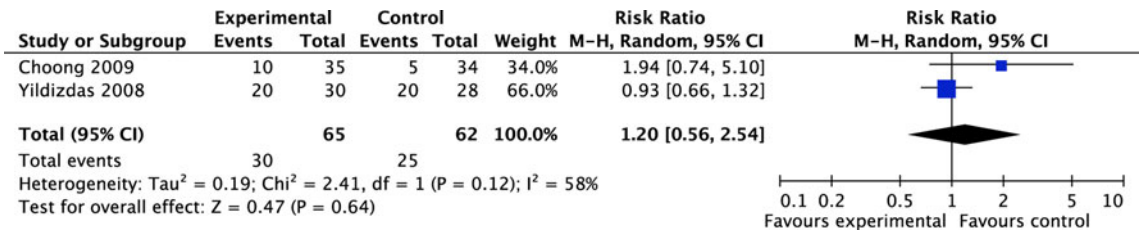

Fig. 5 Mortality in children (CI, confidence interval)

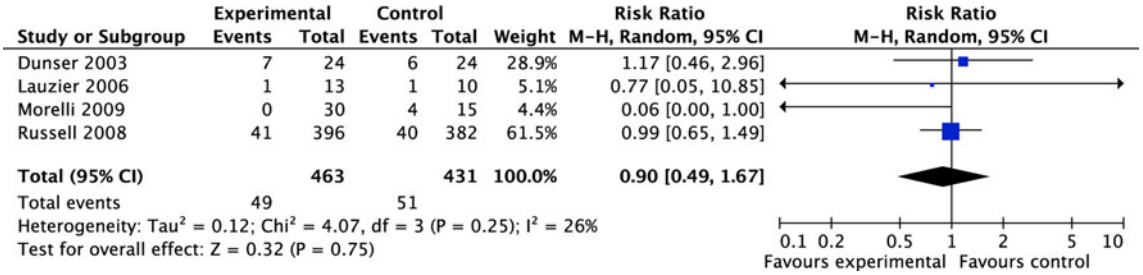

Fig. 6 Serious adverse events rate and vasopressin/terlipressin infusion in adults (CI, confidence interval)

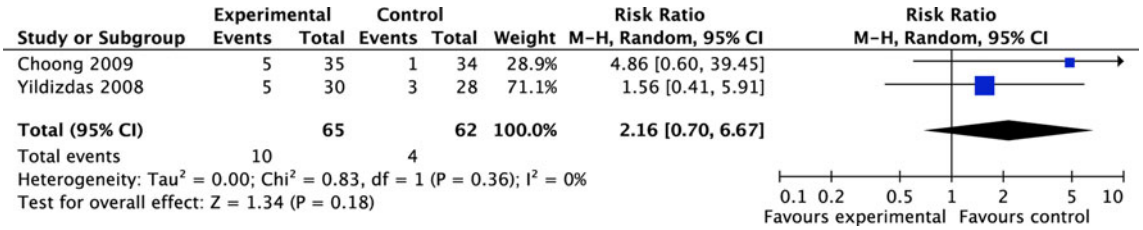

Fig. 7 Serious adverse events rate and vasopressin/terlipressin infusion in children (CI, confidence interval)

adverse event in the experimental arm and 4 of 62 (6.4%) patients in the control arm (RR = 2.16; 95% CI 0.70–6.67; $P = 0.18$; $\chi^2 = 0.83$, $df = 1$, $I^2 = 0\%$) (Fig. 7).

Discussion

For this meta-analysis, we performed a comprehensive search of the literature with no restriction on language, age, or publication status. We included only randomized clinical trials comparing vasopressin or its analog terlipressin with either norepinephrine or placebo in patients with vasodilatory shock. Low-dose vasopressin may help to restore blood pressure in patients with hypotension refractory to catecholamines, and may favor pulmonary vasodilation and increase glomerular filtration rate and plasma cortisol levels [10, 34]. The current Surviving Sepsis campaign guidelines recommend that vasopressin should not be administered as the initial vasopressor in septic shock (grade 2C), and that vasopressin at constant dosage of 0.03 units/min may be added to norepinephrine with anticipation of an effect equivalent to that of norepinephrine alone [3].

Overall this systematic review and meta-analysis did not show any evidence for survival benefit from vasopressin/terlipressin therapy. Although there was no statistically significant heterogeneity across the studies, there were important differences between the trials. First, the trials evaluated vasopressin or its analog terlipressin, which differ markedly in terms of their pharmacokinetic properties. Furthermore, the treatment doses varied between trials, with some studies evaluating continuous infusion of a fixed replacement dose [8, 9, 15, 26] and others titrating vasopressin as vasopressor therapy [24, 25, 30]. The study populations also differed between studies in terms of age or cause of shock, with some trials including only septic shock [15, 25, 27–31] while others included a mixed population [9, 24]. Finally, there was marked difference between trials in the choice of the time point for mortality assessment. We attempted to explore the influence of some of these differences on mortality by conducting metaregressions and subgroup analyses. No evidence of any influence of age, type of molecule (vasopressin or terlipressin), or dose was found. Sensitivity analysis conducted excluding the VASST trial [15] yielded very similar findings, suggesting that this large trial did not influence the direction of the point estimate (data not shown). As the numbers of patients treated with low-dose steroids and/or activated C protein were evenly distributed in the majority of trials in both treated and control groups, or not stated at all, sensitivity analyses based on these two variables were not performed.

Treatment with vasopressin significantly reduced norepinephrine requirement. Finally, this systematic review and meta-analysis did not suggest any increase in the risk of serious adverse events with vasopressin or terlipressin.

Implications for research

Future randomized clinical trials need to be adequately powered to explore (1) vasopressin effects on 28-day

mortality in adults according to the severity of shock given the results from VASST [15], the largest trial in this meta-analysis, (2) improvement in organ dysfunction in children, as actual mortality from shock in this group of patients is commonly low, (3) vasopressin benefit-to-risk ratio in nonseptic vasodilatory shock, (4) potential synergistic effects between vasopressin and corticosteroids, and (5) vasopressin effects on renal function using appropriate outcome measure such as the RIFLE criteria.

Implications for practice

Overall, use of vasopressin or terlipressin did not produce any survival benefit in the short term in patients with vasodilatory shock. Physicians may value the sparing effect of vasopressin/terlipressin on norepinephrine requirement given its apparent safe profile.

Conflict of interest None.

Appendix

The ESICM Systematic Review Group was established in 2010 to provide an international collaboration focused on critical care systematic reviews. Its primary goals are to highlight the role of systematic reviews (SR) and meta-analyses (MA) in clinical research and to facilitate access to high-quality SRs and MAs for practicing clinicians, thereby promoting use of evidence-based medicine. It is the first intensive or critical care medicine society to provide its members, patients, public health authorities, and the general public with an organized database of systematic reviews and diagnostic interventions pertaining to intensive care. The Unit Board is composed by Djillali Annane (Chair) and Mark Hamilton (Deputy).

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