

What Vasopressors Should Be Used to Treat Shock?

EBEM Commentator Contact

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SYSTEMATIC REVIEW SOURCE

This is a systematic review abstract, a regular feature of the *Annals'* Evidence-Based Emergency Medicine (EBEM) series. Each features an abstract of a systematic review from the Cochrane Database of Systematic Reviews and a commentary by an emergency physician knowledgeable in the subject area.

The source for this systematic review abstract is: Mullner M, Urbanek B, Losert H, Waechter F, Gamper G. Vasopressors for shock (Cochrane review). In: *The Cochrane Library*. Issue 3, 2004. Chichester, UK: John Wiley and Sons, Ltd. Art. No.: CD003709.pub2. DOI: 10.1002/14651858.CD003709.pub2.

The *Annals'* EBEM editors prepared the abstract of this Cochrane systematic review, as well as the Evidence-Based Medicine Teaching Points.

OBJECTIVE

To examine whether particular vasopressors are effective at reducing mortality (in the ICU, in the hospital, and 1 year) or influencing patient-oriented morbidity outcomes (ICU length of stay, hospital length of stay, duration of vasopressors, duration of mechanical ventilation, renal failure, and quality of life) in various forms of shock.

DATA SOURCES

The authors searched MEDLINE (up to November 2003), the Cochrane Central Register of Controlled Trials (Cochrane Library, Issue 1, 2004), EMBASE (November 2003), PASCAL Biomed (November 2003), CINAHL (November 2003), BIOSIS (November 2003), PsychINFO (November 2003), meta-registries of ongoing clinical trials (<http://www.controlled-trials.com>, <http://www.clinicaltrials.gov>, <http://www.centerwatch.com>), reference lists of articles, and reference lists of textbooks and contacted experts in the field.

STUDY SELECTION

Studies were blinded and unblinded, parallel-group, randomized, controlled trials with patient-oriented outcomes that compared various vasopressors, vasopressors with placebo, or vasopressors with intravenous fluids for the treatment of any form of shock.

DATA EXTRACTION AND ANALYSIS

Two reviewers abstracted data independently to a predefined collection instrument. After comparison of results, disagreements were resolved by discussion and consensus among 3 reviewers.

MAIN RESULTS

Eight studies met inclusion criteria, 7 concerning the treatment of septic shock and 1 concerning the treatment of refractory hypotension in patients after general anesthesia. Unfortunately, none of the 8 studies were designed to assess patient-oriented outcome endpoints; rather, all evaluated clinical measures such as hemodynamic characteristics.

CONCLUSIONS

The current available evidence is not satisfactory to determine whether a particular vasopressor is superior to other agents in the treatment of shock states.

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COMMENTARY: CLINICAL IMPLICATION

Shock is the result of an impaired balance between oxygen supply and demand, resulting in widespread failure of the circulatory system to provide oxygen and nutrients needed by the cells. Although the epidemiology of shock in the emergency department (ED) is largely speculative, recent evidence has suggested that septic shock is the most common form of nontraumatic shock encountered.¹ Regardless of the cause of shock, reported mortality rates consistently exceed 20%.^{2,3} Estimates indicate that sepsis occurs at an incidence of 3.0 cases per 1,000 persons per year, resulting in approximately 750,000 affected persons annually in the United States. Moreover, approximately half of these patients will gain entry to the hospital through the ED.^{4,5}

The treatment of shock involves early recognition, fluid resuscitation, and specific therapies (eg, antibiotics for sepsis) as indicated. The importance of identifying sepsis for emergency physicians is highlighted by a recent trial of goal-directed

resuscitation (a protocol aimed at early cardiovascular resuscitation and support) which reported an absolute mortality reduction of 16% when patients with severe sepsis or septic shock are treated with the protocol on recognition of the condition.⁶ One of the goals of the aforementioned protocol is circulatory support with vasopressors for arterial pressure measurements that remain abnormally low despite volume expansion. Thus, the evidence about the optimal vasopressor for use in shock states is valuable information for emergency physicians.

This Cochrane review has addressed the topic of which vasopressor should be used in shock states to affect outcome. When a comprehensive search strategy to avoid publication bias and an independent assessment process that avoids selection bias were used, only 8 trials were identified. Moreover, of the studies identified all were described as methodologically poor, providing small samples, and failed to investigate patient-oriented outcomes. When analyzed by category of shock, 7 studies were pertinent to emergency medicine as they concerned the treatment of septic shock:

- Two studies compared norepinephrine with dobutamine versus epinephrine, resulting in a relative risk (RR) of death of 0.98 (95% confidence interval [CI] 0.57 to 1.67).
- Three studies compared norepinephrine with dopamine, slightly favoring norepinephrine; RR of death of 0.88 (95% CI 0.57 to 1.36).
- Two studies compared vasopressin with placebo, slightly favoring placebo; RR of death of 1.04 (95% CI 0.06 to 19.33).

Given these wide CIs including important potential benefits or harms, these results cannot claim equivalence and were insufficient for sensitivity or subgroup analysis.

The authors do mention ongoing trials and expect to add additional relevant studies to this review in the coming years. It is hoped that these studies will result in more definitive conclusions about which vasopressor should be used in shock. Until such time, clinicians are left with a wide range of options (eg, norepinephrine, phenylephrine, dopamine, epinephrine, vasopressin, and dobutamine) and should rely on experience and local standard of care to determine the most appropriate agent to administer.

TAKE HOME MESSAGE

The primary intervention in the treatment of shock is to identify shock early, correct volume imbalances, and treat the cause of shock. Although vasopressors remain a component in the armamentarium, especially in sepsis, from the current available evidence it is unclear which vasopressor is superior for the cardiovascular support of patients in shock.

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EBEM TEACHING POINT

Clinical trials registries. Clinical research is possible only because of patients who volunteer to participate. These subjects enter into a contract with researchers, granting their trust that the project will be conducted and reported fully and honestly. Evidence-based medicine and changes in medical practice must be based on *all* available data, whether positive or negative, inferior or noninferior, equivalent or nonequivalent. Researchers, sponsors, and journals are most enthusiastic about publishing “positive” trials, and thus many trials that put various competing interests (academic, financial) at risk often remain unpublished, their results not publicly accessible. Thus, it is important to have a central repository (registry) for all clinical trials that is managed by an unbiased agency, containing valid data, publicly accessible and searchable, and which contains detailed information about the trial. In 2004, the International Committee of Medical Journal Editors mandated clinical trial registration as a condition of consideration for publication in its member journals. This requirement pertains to any trial that prospectively assigns humans to intervention and comparison groups to determine a cause-effect relationship between the intervention and outcome. This mandate is clearly a necessary step toward full transparency and disclosure for the clinical research community. Clinical trial registration is a key step toward ensuring the availability of knowledge necessary to inform health care practice and decisionmaking.⁷

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