Norepinephrine or dopamine for septic shock: systematic review of randomized clinical trials


CRD summary
The evidence showed superiority of norepinephrine over dopamine for in-hospital or 28-day mortality in critically ill populations with shock in which sepsis was the predominant etiology. With a small caveat regarding the borderline statistical significance of the findings, it appears that the authors' conclusion is reliable.

Authors' objectives
To evaluate randomised clinical trials comparing norepinephrine versus dopamine in critically ill patients with septic shock or shock predominantly secondary to sepsis.

Searching
PubMed, EMBASE, Scopus and Cochrane Central Register of Trials (CENTRAL) were searched to May 2010 without language restrictions. Search terms were reported. Bibliographies of selected articles and review articles were handsearched for further studies.

Study selection
Eligible studies were randomised controlled trials (RCTs) that compared norepinephrine with dopamine. Study populations were critically ill adults with septic shock or shock predominantly secondary to sepsis. The primary eligible outcome was 28-day or in-hospital mortality. Secondary outcomes included incidence of arrhythmia, hospital length of stay and intensive care unit length of stay.

Studies were conducted in the United States, Finland, France, India and Europe. Five out of the six included studies contained populations with septic shock. Mean participant age ranged from 42 to 67 years in norepinephrine arms and from 44 to 68 years in dopamine arms (where reported).

Three reviewers independently selected the studies for inclusion; disagreements were resolved by consensus.

Assessment of study quality
Risk of bias was assessed according to information on sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and other sources of bias. Ratings were yes (low risk), no (high risk) or unclear (unknown).

Three reviewers independently assessed risk of bias; it was unclear how any disagreements were resolved.

Data extraction
Data were extracted to calculate relative risks (RRs) with 95% confidence intervals (CIs). Authors were contacted for any missing information.

Three reviewers independently extracted data; disagreements were resolved by consensus.

Methods of synthesis
Relative risks and 95% CIs were pooled using a fixed-effect model. Statistical heterogeneity was assessed using $X^2$ and $I^2$ statistics. Sensitivity analyses were planned according to use of a random-effects model and exclusion of studies with mixed populations. A linear regression analysis was performed to investigate the presence of small-study effects.

Results of the review
Six RCTs were included in the review (2,023 patients, range 10 to 1,659) with treatment arms for norepinephrine (995 patients) or dopamine (1,028 patients). All six of the trials assessed incomplete outcome data, five were free of selective outcome reporting and four reported adequate sequence generation. Other results were more varied (reported
The risk of in-hospital or 28-day mortality was 9% lower with norepinephrine than with dopamine (RR 0.91, 95% CI 0.83 to 0.99; I²=0%; six trials); results for the fixed-effect and random-effects models were identical. A similar but statistically non-significant result was found when a study with a mixed population of shock patients was excluded (RR 0.84, 95% CI 0.68 to 1.02; I²=0%; five trials).

There was no evidence of small-study effects. Secondary outcomes were reported.

**Authors' conclusions**

The evidence showed superiority of norepinephrine over dopamine for in-hospital or 28-day mortality in critically ill populations with shock in which sepsis was the predominant etiology.

**CRD commentary**

The review question was clear and inclusion criteria were sufficiently replicable. Relevant electronic databases were accessed and attempts were made to minimise reviewer error and bias throughout the review process. Suitable quality assessment criteria were used; quality was deemed high for some domains and mixed for others.

Study details were presented and the methods of synthesis seemed appropriate. The findings were dominated by a particularly large trial with a mixed population and were of borderline statistical significance. However, sensitivity analysis revealed a similar albeit non-significant result.

With a small caveat regarding the borderline statistical significance of the findings, it appears that the authors’ conclusion is reliable.

**Implications of the review for practice and research**

The authors did not state any implications for practice and research.

**Funding**

None.

**Bibliographic details**


**PubMedID**

21436167

**DOI**

10.1177/0885066610396312

**Original Paper URL**

http://jic.sagepub.com/content/27/3/172.abstract

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Adult; Dopamine /therapeutic use; Dopamine Agents /therapeutic use; Hospital Mortality; Humans; Intensive Care Units; Length of Stay; Norepinephrine /therapeutic use; Randomized Controlled Trials as Topic; Shock, Septic /drug therapy /etiology; Vascular Resistance /drug effects; Vasoconstrictor Agents /therapeutic use

**AccessionNumber**

12012024702
Date bibliographic record published
19/07/2012

Date abstract record published
08/02/2013

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.