LETTER TO EDITOR

Author Reply: Comparison of Norepinephrine and Terlipressin vs Norepinephrine Alone for Management of Septic Shock: A Randomized Control Study

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Keywords: Sepsis, Septic shock, Terlipressin.
Indian Journal of Critical Care Medicine (2023): 10.5005/jp-journals-10071-24514

Dear Editor,

We thank Dr Khera and Dr Suresh for their interest in our study and insightful comments.

In our study, drugs were delivered through central venous access as per the standard guideline in patients diagnosed with septic shock.

The guidelines for managing septic shock recommend aiming for mean arterial pressure (MAP) of 65 mm Hg.[1,2] The MAP is the driving force behind tissue perfusion, and below a certain MAP, the perfusion of tissue becomes linearly reliant on arterial pressure.[1] Hence we targeted our vasopressor therapy to keep a MAP of 65 mm Hg. LeDoux et al. found that increasing the norepinephrine dose from 65 to 75 and 85 mm Hg increased the cardiac index (from 4.7 ± 0.5 to 5.5 ± 0.6 L/min/m^2) but had no effect on arterial lactate, oxygen delivery, gastric mucosal partial pressure of carbon dioxide, red blood cells velocity, or skin capillary flow.[3] Bourgoin et al. found that aiming high MAP increased cardiac index from 4.8 (3.8–6.0) to 5.8 (4.3–6.9) L/min/m^2, and did not influence kidney function, arterial lactate, or oxygen consumption.[4] The above studies failed to show a direct correlation between cardiac index and markers of optimal tissue perfusion in patients needing vasopressors due to septic shock. Hence, cardiac index was used only to exclude patients with pre-existing cardiac dysfunction and was not measured as an outcome variable in our study.

The ProCess trial, The ARISE trial, and the ProMISe trial failed to demonstrate any mortality benefit using early goal-directed therapy (EGDT), which includes a set of "goals" including central venous oxygen saturation (ScvO2).[5–8] The latest sepsis guidelines have dropped the use of EGDT to guide fluid resuscitation and vasopressor use in septic shock.[1] Hence, ScvO2 was not included in the secondary outcomes of our study.

Our study revealed that using terlipressin and norepinephrine together reduced the total time of vasopressor administration in patients discharged from the ICU more significantly than in norepinephrine alone.[9] We observed that the occurrence of cardiac arrhythmias and the necessity for renal replacement therapy were substantially lower in the terlipressin and norepinephrine group (Group I) than in the norepinephrine alone group (Group II). Comparing the two groups, group I had more digital ischemia.[9] However, it resolved after discontinuing terlipressin, and none of the participants needed any intervention.

The sample size was calculated, keeping the alfa error of 5% with an effect size of less than 0.3 and a power of study of more than 80%.

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How to cite this article: Sahoo P, Kothari N, Sharma A, Goyal S. Author Reply: Comparison of Norepinephrine and Terlipressin vs Norepinephrine Alone for Management of Septic Shock: A Randomized Control Study. Indian J Crit Care Med 2023;27(8):603–604.

Source of support: Nil

Conflict of interest: None

The odds ratio (OR) is a standard measure of the association between exposure and outcome in the medical literature. However, individuals comprehend relative risk as a metric of association more intuitively. In a cohort study, the relative risk may be estimated directly by computing a risk ratio (RR). However, it is not valid in all situations. The odds ratio only estimates the relative risk if the outcome is a low probability. In our study, the adverse events were low probability, so we chose odd ratios. The interesting fact about the odds ratio is that it is bi-directional, which allows us to obtain the comparison required in our study. When the adverse events have a low rate in both groups, the odds ratio approximates the relative risk.

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References

1. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving sepsis campaign: International guidelines for management of sepsis and septic shock 2021. Intensive Care Med 2021;47:1181–1247. DOI: 10.1007/s00134-021-06506-y.
2. Levy MM, Evans LE, Rhodes A. The Surviving Sepsis Campaign Bundle: 2018 update. Intensive Care Med 2018;44:925–928. DOI: 10.1007/s00134-018-5085-0.

3. LeDoux D, Astiz ME, Carpati CM, Rackow EC. Effects of perfusion pressure on tissue perfusion in septic shock. Crit Care Med 2000;28:2729–2732. DOI: 10.1097/00003246-200008000-00007
4. Bourgoin A, Leone M, Delmas A, Garnier F, Albanèse J, Martin C. Increasing mean arterial pressure in patients with septic shock: Effects on oxygen variables and renal function. Crit Care Med 2005;33:780–786. DOI: 10.1097/01.ccm.0000157788.20591.23.
5. ProCESS Investigators, Yealy DM, Kellum JA, Huang DT, Barnato AE, Weissfeld LA, et al. A randomized trial of protocol-based care for early septic shock. N Engl J Med 2014;370:1683–1693. DOI: 10.1056/NEJMoa1401602.
6. ARISE Investigators, ANZICS Clinical Trials Group, Peake SL, Delaney A, Bailey M, Bellomo R, et al. Goal-directed resuscitation for patients with early septic shock. N Engl J Med 2014;371:1496–1506. DOI: 10.1056/NEJMoa1404380.
7. Mouncey PR, Osborn TM, Power GS, Harrison DA, Sadique MZ, Grieve RD, et al. Protocolised Management In Sepsis (ProMISe): A multicentre randomised controlled trial of the clinical effectiveness and cost-effectiveness of early, goal-directed, protocolised resuscitation for emerging septic shock. Health Technol Assess Winch Engl 2015;19:1–150. DOI: 10.3310/hta19970.
8. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001;345:1368–1377. DOI: 10.1056/NEJMoa010307.
9. Sahoo P, Kothari N, Goyal S, Sharma A, Bhatia PK. Comparison of Norepinephrine and Terlipressin vs. Norepinephrine Alone for Management of Septic Shock: A Randomized Control Study. Indian J Crit Care Med 2022;26:669–675. DOI: 10.5005/jp-journals-10071-24231.