Intensive Care Med (2009) 35:1310
DOI 10.1007/s00134-009-1492-6

Lavi Oud

Comment on "A comparison of epinephrine and norepinephrine in critically Ill patients"

Accepted: 28 February 2009
Published online: 15 April 2009

An author's reply to this comment is available at: doi:10.1007/s00134-009-1493-5.

Sir: Myburgh et al. have recently compared the achievement of mean arterial pressure (MAP) targets between epinephrine and norepinephrine in a heterogeneous, pressor-requiring population [1]. The authors found no difference in the hemodynamic responses between the two agents, with similar time to achievement of target MAP in all patients and in prespecified subgroups. However, interpretation of these findings and their applicability to clinical practice is limited by uncertainties about key aspects of the conduct of the study.

The authors indicate that hemodynamic management was left to the managing clinicians. However, no data are provided on the actual practice of pressor management in this study, in terms of frequency of pressor titration, range of dose increments, and maximum allowable dosing. The investigators used MAP $\geq$ 70 mmHg as default when MAP target was not specified by the patient's clinician. However, no details are reported on the alternative MAP targets. In addition, the dosing of each pressor for the whole population and the subgroups is not reported. For example, patients in septic shock often require higher pressor dosing than those with other shock categories [2, 3]. Because septic patients comprised more than half of the study population, reported Fig. 2 data on maximum daily pressor doses suggest that catecholamine doses may have been relatively low in this subgroup, especially during the first 16 h. In a recent trial comparing epinephrine and a combination of norepinephrine and dobutamine in septic-shock patients, the mean doses of both pressors were approximately 1 mcg/kg/min [3], well above those that may be inferred from Fig. 2 of this study. Finally, the authors do not include data on key confounding co-interventions (e.g., intravenous fluid volumes in subgroups, etc.).

Uneven distribution of the aforementioned factors between the drug groups and across the prespecified subgroups could have resulted in similar pressor effectiveness. It is of note that uneven practice patterns may also have resulted in better effectiveness of either agent, unrelated to their actual effect in a more strictly controlled study environment.

In addition, the time to achieve target MAP appears remarkably long. For example, the authors report that in septic-shock patients the median time to attain target MAP was 35.1 and 50.0 h for epinephrine and norepinephrine, respectively. However, in a recent study by Annane et al. [3] all patients in both epinephrine and norepinephrine groups achieved MAP $\geq$ 70 mmHg on day 1, and Martin et al. reported that 93% of their septic-shock patients responded to norepinephrine targeted to MAP $>$ 80 mmHg within 6 h of therapy [4]. The specific practice of pressor titration, other aspects of circulatory support, and use of infection control measures may have affected the time to achieve target MAP in this study.

The optimum vasopressor regimen in critically ill patients remains uncertain and is likely to vary across specific disease states. However, lack of relevant practice and confounder data hinders interpretation of Myburgh's findings of comparable pressor effectiveness and time to effect, and precludes their application in other settings.

References

1. Myburgh JA, Higgins A, Jovanovska A, Lipman J, Ramakrishnan N, Santamaria J (2008) A comparison of epinephrine and norepinephrine in critically ill patients. Intensive Care Med 34:2226–2234
2. Hollenberg SM, Ahrens TS, Annane D, Astiz ME, Chalfin DB, Dasta JF, Heard SO, Martin C, Napolitano LM, Susla GM, Totaro R, Vincent JL, Zanotti-Cavazzoni S (2004) Practice parameters for hemodynamic support of sepsis in adult patients: 2004 update. Crit Care Med 32:1928–1948
3. Annane D, Vignon P, Renault A, Bollaert PE, Charpentier C, Martin C, Troché G, Ricard JD, Nitenberg G, Papazian L, Azoulay E, Bellissant E, CATS Study Group (2007) Norepinephrine plus dobutamine versus epinephrine alone for management of septic shock: a randomized trial. Lancet 370:676−684
4. Martin C, Papazian L, Perrin G, Saux P, Gouin F (1993) Norepinephrine or dopamine for treatment of hyperdynamic septic shock. Chest 103:1826–1831

L. Oud (✉)
Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Texas Tech University School of Medicine, 701W. 5th Street, Odessa, TX, USA
e-mail: lavi.oud@ttuhsc.edu
Tel.: +1-432-3355250
Fax: +1-432-3355262