Editorial

Vasopressin: the level of evidence is growing

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Comment on: McIntyre WF, Um KJ, Alhazzani W, *et al.* Association of Vasopressin Plus Catecholamine Vasopressors *vs.* Catecholamines Alone With Atrial Fibrillation in Patients With Distributive Shock: A Systematic Review and Meta-analysis. JAMA 2018;319:1889-900.

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Distributive shock, especially septic shock, is the most common type of shock in the critically ill patients (1). Distributive shock is characterized by a decrease in peripheral vascular resistance and vasodilation resulting in arterial hypotension. To prevent organ dysfunction, fluid resuscitation and vasopressor infusion are required.

Vasopressin is synthesized by the hypothalamus and released by the posterior pituitary gland. It stimulates V1 receptors located mainly in the smooth muscle cells, V2 receptors located in the renal collecting tubules and V3 receptors located in adenohypophysis. Stimulation of V1 receptors induces vasoconstriction by increasing the cytoplasmic concentration of ionized calcium and activating protein kinase C via a Gq protein as well as different second messengers. There is a relative deficiency of vasopressin in catecholamine-refractory septic shock (2-4). Vasopressin or its analogue terlipressin increased blood pressure in patients with hyporesponsiveness to norepinephrine (5,6). Actually, norepinephrine is recommended as the first-choice vasopressor in septic shock (7). Adrenergic overstimulation has detrimental effects (8). Vasopressin is an alternative vasopressor proposed to decrease norepinephrine dosage in septic shock (7).

In a systematic review and meta-analysis, McIntyre *et al.* aimed at determining whether the administration of vasopressin is associated with a decreased risk of atrial fibrillation compared to catecholamines in distributive shock (9).

Twenty-three randomized clinical trials were included in a qualitative and quantitative synthesis. Studies compared the administration of vasopressin (or analogues) with or without catecholamine with catecholamine alone in patients with distributive shock. Twenty-two studies evaluated patients with septic shock and two studies included patients with vasoplegia after cardiac surgery. Only five studies were multicenter and eight studies were blinded.

Atrial fibrillation was the primary outcome. Lower risk of atrial fibrillation was associated with the vasopressin with data available in 13 studies [risk ratio (RR), 0.77; 95% CI, 0.67–0.88]. In the analysis of the 7 trials at low risk of bias, this association persisted (RR, 0.77; 95% CI, 0.68–0.88]). This lower risk of atrial fibrillation with vasopressin was maintained for the subgroup of patients after cardiac surgery (RR, 0.77; 95% CI, 0.67–0.88). For the subgroup of septic patients, there was not significant difference in the risk of atrial fibrillation (RR, 0.76; 95% CI, 0.55–1.05).

Lower risk of mortality at 28 or 30 days was associated with the administration of vasopressin. However, focusing on the 2 trials at low risk of bias, there was not difference in the risk of mortality. Renal replacement therapy was lower with vasopressin in the analysis limited to the 2 trials at low risk of bias. Quality evidence was low or moderate regarding myocardial injury, ventricular arrhythmia, stroke and length of stay in hospital and intensive care unit.

McIntyre *et al.* should be commended for making a rigorous analysis using a GRADE approach. The major limitation is the variability of studies regarding the number of patients, dosage and duration of vasopressors and design of studies. Few studies are considered at low risk of bias. The authors carefully analysed the risk of bias for each

study and each variable. Hence, the reader has enlightened results. High-quality evidence was only found for atrial fibrillation.

In conclusion, the addition of vasopressin to catecholamine vasopressors compared with catecholamines alone was associated with a lower risk of atrial fibrillation in patients with distributive shock. This result was driven mainly by the study by Hajjar *et al.*, which weighted for 74.8% of the analysis (10). This study included only patients with vasoplegia after cardiac surgery. Atrial fibrillation is the most common complication in post-cardiac surgery patient. The incidence varies between 20% and 50% (11). The underlying mechanisms are multifactorial including, excessive production of catecholamines but also intraoperative factors (11). Given the weight of this study as well as the specific atrial fibrillation mechanisms after cardiac surgery, the decreased risk of atrial fibrillation associated with vasopressin cannot be generalized to all distributive shock, especially in septic shock. A recent meta-analysis confirmed a lower risk of postoperative complications in cardiac surgery patients (12).

In total, vasopressin is an interesting drug to decrease the risk of atrial fibrillation compared with catecholamines, with an apparent safe profile especially after cardiac surgery. In septic shock, potential benefit of vasopressin remains to be demonstrated.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Vincent JL, De Backer D. Circulatory shock. N Engl J Med 2013;369:1726-34.
2. Landry DW, Levin HR, Gallant EM, et al. Vasopressin deficiency contributes to the vasodilation of septic shock. Circulation 1997;95:1122-5.
3. Sharshar T, Blanchard A, Paillard M, et al. Circulating vasopressin levels in septic shock. Crit Care Med 2003;31:1752-8.
4. Lin IY, Ma HP, Lin AC, et al. Low plasma vasopressin/norepinephrine ratio predicts septic shock. Am J Emerg Med 2005;23:718-24.
5. Leone M, Albanèse J, Delmas A, et al. Terlipressin in catecholamine-resistant septic shock patients. Shock 2004;22:314-9.
6. O'Brien A, Clapp L, Singer M. Terlipressin for norepinephrine-resistant septic shock. Lancet 2002;359:1209-10.
7. Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Crit Care Med 2017;45:486-552.
8. Dünser MW, Hasibeder WR. Sympathetic overstimulation during critical illness: adverse effects of adrenergic stress. J Intensive Care Med 2009;24:293-316. Erratum in: J Intensive Care Med 2016;31:NP1.
9. McIntyre WF, Um KJ, Alhazzani W, et al. Association of Vasopressin Plus Catecholamine Vasopressors vs Catecholamines Alone With Atrial Fibrillation in Patients With Distributive Shock: A Systematic Review and Meta-analysis. JAMA 2018;319:1889-900.
10. Hajjar LA, Vincent JL, Barbosa Gomes Galas FR, et al. Vasopressin versus Norepinephrine in Patients with Vasoplegic Shock after Cardiac Surgery: The VANCS Randomized Controlled Trial. Anesthesiology 2017;126:85-93.
11. Echahidi N, Pibarot P, O'Hara G, et al. Mechanisms, prevention, and treatment of atrial fibrillation after cardiac surgery. J Am Coll Cardiol 2008;51:793-801.
12. Dünser MW, Bouvet O, Knotzer H, et al. Vasopressin in Cardiac Surgery: A Meta-analysis of Randomized Controlled Trials. J Cardiothorac Vasc Anesth 2018. [Epub ahead of print].

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