Commentary

Arginine vasopressin versus norepinephrine: will the stronger one win the race?

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Abstract

In the current issue of *Critical Care*, Friesenecker and colleagues present a well-designed comparative study on the microvascular effects of arginine vasopressin (AVP) and norepinephrine (NE) in a physiological, unanesthetized hamster model. The authors clearly demonstrate that AVP, but not NE, has marked vasoconstrictive effects on large arterioles, whereas the impact on small arterioles is comparable for both vasopressors. However, it remains unclear if these results, *per se*, reflect a stronger vasopressive potential of AVP versus NE, as macrohemodynamic variables were not different between study groups. Since the authors did not investigate the effects of AVP and NE in vasodilatory shock states, the microcirculatory response in sepsis or systemic inflammatory response syndrome remains inconclusive. The same authors previously reported that AVP infusion in patients suffering from vasodilatory shock carries the risk for ischemic skin lesions. This in turn raises the question whether the quality of vasopressors should be judged by their potency.

In the current issue of *Critical Care*, Friesenecker and colleagues [1] present a well-designed comparative study on the microvascular effects of arginine vasopressin (AVP) and norepinephrine (NE) in awake hamsters under physiological conditions. The authors used the dorsal skinfold window chamber technique to measure vascular diameter, cross-sectional area and blood flow of five different sizes (A0 to A4) of subcutaneous arterioles. Whereas continuous infusion of both drugs resulted in similar macrohemodynamic changes, AVP led to a more pronounced reduction in vessel diameter and blood flow of the proximal, large (A0) arterioles than NE. Interestingly, both vasopressors had similar effects on the skin microvasculature in more distal, smaller (A1 to A4) arterioles. From these results the authors conclude that the strong vasoconstrictive effect of AVP on large arterioles accounts for its strong vasopressive potency and may explain its efficacy in catecholamine-refractory vasodilatory shock.

To the best of our knowledge, Friesenecker and colleagues are the first to have compared the effects of AVP and NE on different subcutaneous vessel calibers. Nevertheless, the study has to face some criticism.

First of all, the conclusion that especially the vasoconstrictive effect of AVP on large (A0) arterioles accounts for its strong vasopressor effect cannot be drawn from the presented data. In this context it is especially noteworthy that the authors observed differences in neither macrohemodynamics (i.e. mean arterial pressure (MAP)) nor microcirculatory effects on A1 to A4 arterioles between both study groups. The fact that the stronger vasoconstrictive effect of AVP on A0 arterioles was the only difference between groups suggests that the constriction of large arterioles had (almost) no impact on total peripheral resistance. This thesis is supported by Poiseuille's law implying that resistance is inversely correlated to the fourth power of the vessel radius. Accordingly, the small vessels primarily account for changes in vascular resistance rather than the large ones [2].

Using the same animal model, Gerstberger and colleagues [3] compared the effects of either 10 pmoles/kg of AVP or the same dose of angiotensin (ANG) II on the hamster subcutaneous microcirculation. These authors reported that the vasoconstrictive effects of both drugs on small (A3) arterioles were comparable, whereas ANG II, but not AVP, contributed to a marked constriction of greater (A1) arterioles. This vasoconstriction of A1 arterioles by ANG II was associated with a much greater vasopressor effect (i.e. change in MAP) than AVP. Notably, the AVP plasma levels measured in the study by Gerstberger and colleagues were about 100 pg/ml, thus representing the upper therapeutic range during AVP infusion in patients with hyperdynamic septic shock [4]. The contradictory results of Friesenecker

ANG = angiotensin; AVP = arginine vasopressin; MAP = mean arterial pressure; NE = norepinephrine.

and colleagues [1] and Gerstberger and colleagues [3] emphasize that the effects of vasoactive agents on the microcirculation are still not fully understood. Therefore, the study of Friesenecker and colleagues [1] gives another important and interesting insight into the diversity of the microvascular response to vasoconstrictor agents.

With respect to the second conclusion, the study by Friesenecker and colleagues would have certainly profited from studying groups suffering from vasodilatory shock secondary to systemic inflammation. This holds especially true, since clinical and experimental research has clearly shown that distribution abnormalities in vasodilatory shock states contribute to significant changes in microvascular hemodynamics [5]. Therefore, interventions in the physiological state may not necessarily be suitable to predict the response of the same intervention under pathological conditions, such as sepsis.

Finally, although redistribution of blood flow away from non-vital organs (e.g. the skin) to vital organs represents one of the primary therapeutic aims of vasopressor therapy (especially in septic shock patients), it should be kept in mind that this approach may result in severe hypoperfusion of non-vital organs. Whereas it is well known that AVP infusion (especially when applied in higher doses) increases the risk of gut mucosal ischemia [6], skin hypoperfusion appears to be another clinically relevant complication. In this regard, the study group of Friesenecker and Dunser recently reported on the incidence and risk factors of ischemic skin lesions in patients with catecholamine-resistant vasodilatory shock [7]. Importantly, the authors found that ischemic skin lesions are common among patients with vasodilatory shock treated with AVP and that the combination of sepsis and treatment with AVP may especially be a risk factor for the development of ischemic skin lesions.

In conclusion, Friesenecker and colleagues [1] correctly state that AVP has a stronger vasoconstrictive effect on large arterioles of the subcutaneous vasculature in healthy hamsters compared to NE. Unfortunately, the very interesting question of whether or not the stronger vasoconstrictive effect on large vessels is also maintained in vasodilatory shock remains unresolved. The fact that AVP infusion may impair gut mucosal microcirculation [6] and skin perfusion [7] suggests that the stronger one may not necessarily be the better one.

Competing interests

The authors declare that they have no competing interests.

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