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Non-occlusive mesenteric ischaemia: just avoid norepinephrine, what else?

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In this issue of *EJCTS*, Wiesmueller *et al.* [1] present their study showing that the use of 2 or more vasopressors after cardiac surgery is a strong predictor of the extent of non-occlusive mesenteric ischaemia (NOMI). Interestingly, only epinephrine and norepinephrine were discussed. Vasopressin, probably the most effective first-line vasopressor for vasoplegic syndrome after cardiothoracic surgery, was not mentioned. We believe that this class of vascular smooth muscle tone modulators requires closer consideration, particularly in NOMI, as vasopressin is often used in refractory hypotension in addition to high-dose norepinephrine, resulting in even higher systemic vascular resistance and increasing the risk of impaired vascular macro- and microcirculation [2].

Paradoxically, vasopressin may have a beneficial effect in distal small bowel ischaemia and concomitant use of vasopressors [3]. Vasopressin at high doses is a known vasoconstrictor of intestinal blood flow; therefore, it has been successfully used in upper and lower gastrointestinal bleeding [4]. But why does not all vasopressin therapy result in mesenteric ischaemia, especially of the distal small intestine? Nussbaum *et al.* described that doses of vasopressin administered proximally to the superior mesenteric artery can increase peripheral vascular resistance and thus intestinal bleeding [4]. It is possible that vasopressin acts as a potent vasoconstrictor on the intestinal shunt vessels, thereby redistributing splanchnic blood flow in favour of the distal small intestine [3]. Another explanation could be that vasopressin induces clinically relevant ischaemia only at higher doses [5]. Vasopressin doses of 1–2 U/h do not show an increased incidence of small bowel ischaemia in clinical practice. However, ischaemia of the colon may be more common with vasopressin therapy [3]. Ischaemia of the colon is curable by resection, but extensive ischaemia of the small bowel is not curable by resection.

In experimental studies, a hypodynamic state or hypovolaemia (lack of volume loading)—in conjunction with increasing doses of vasopressin—particularly endangered intestinal blood flow [2]. In a number of clinical studies, no side effects on the splanchnic circulation were observed with the administration of vasopressin [6, 7]. In an observational cohort study in cardiac surgery patients with NOMI, vasopressin administration (mean dose 2.7 U/h) with superior mesenteric intraarterial iloprost infusion led to an improvement of the small intestinal blood flow in comparison to patients treated with norepinephrine alone [8]. The authors attributed this result to preventing alterations of endothelin-1, a potent vasoconstrictor and risk factor for NOMI and decreased small bowel blood flow, and to antioxidant effects of vasopressin. In a multicentre, randomized, double-blind trial (VASST), vasopressin versus norepinephrine was investigated in septic shock patients [9]. Although not powered to assess the incidence of acute mesenteric ischaemia, patients in the vasopressin group experienced a lower rate of this serious adverse event (3.4% vs 2.3%).

It should be noted that studies on vasopressin and mesenterial ischaemia show partly contradictory results. Well-designed and adequately powered studies are certainly needed, in which both the cohort studied and the comparator drug are judiciously selected. Current guidelines for the treatment of NOMI recommend discontinuing vasopressors whenever possible [10]. However, despite the positive association of increased incidence of NOMI and mortality with the use of vasoactive and inotropic drugs, the question remains whether the causative problem is the direct effect of the drug or the underlying condition for which the drug is being administered. In the prevention, detection and management of cardiac surgery patients at risk of or already experiencing NOMI, the goal likely remains the same: to maintain adequate cardiac output and perfusion pressure. This undoubtedly requires vasopressors. Perhaps in the near future, the role of vasopressin will be seen in a clearer and more differentiated way. In the case of NOMI, switching to other, less harmful vasopressors rather than strict discontinuation may be recommended.

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