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Is phenylephrine or norepinephrine better to treat arterial hypotension?

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The classic equation P = CO x R (Pressure equals flow (Cardiac Output - CO) multiplied by arterial resistance - R) tells us that arterial hypotension can develop only if R or CO or both decreases. The first question for an anesthesiologist is to figure out what is responsible for the hypotension, vascular tone (may be reflected in values of vascular resistance R) or CO. For the purpose of this article we assume that the process of differential diagnosis led to the conclusion that the hypotension resulted from vasodilation and administration of a vasopressor in this order. What are the physiological effects of the two drugs in question?

Phenylephrine (PE) is a pure α-adrenergic agonist. Activation of these receptors (α-1 adrenoceptors) leads to vaso-constriction wherever the receptors are present. Density of α-1 adrenoceptors in the veins is much higher than in the arteries [1,2]. Therefore, it is not surprising that constriction of veins develops earlier, at smaller doses and to a greater degree than of arteries. Constriction of arterioles results in a decrease in flow through them and tissues fed by those arteries.

Constriction of veins, particularly compliant veins (i.e. splanchnic veins) squeezes blood out of the veins leading to a decrease in blood volume within the veins and the liver. This volume shifts into the systemic circulation increasing Venous Return (VR) and CO.

The α-1 adrenoceptors are also located within the hepatic veins and the liver. Constriction of that vasculature decreases flow through the splanchnic organs and tissues, and sequesters blood upstream, decreasing the VR and CO [3]. Actually, an increase in arterial pressure after injection of PE results from an increase in arterial tone by one third and by two thirds from an increase in VR [4]. Such a complexity leads to contradictions: It has been demonstrated that PE may increase or decrease CO [5].

Some patients show a decrease in CO during PE infusion. One of the likely mechanisms underlying such an effect on CO may be a decrease of venous flow through splanchnic system resulting in a decrease of VR and CO. Constriction of arterioles in the systemic circulation, particularly when PE is administered in larger doses, may be another mechanism that works in concert with the vaso-constriction within splanchnic system in decreasing VR and CO. Finally, there are α-1 adrenoceptors within the pulmonary vasculature [6,7] activation of which also may constrict the pulmonary vasculature and decrease VR and CO.

Norepinephrine (NE) has strong affinity not only to α-1 adrenergic receptors, but also to β-1 (cardiac) and β-2 (vascular) adrenoceptors. Activation of β-1 receptors affects a few cardiac functions mainly an increase in myocardial contractility. This effect is relatively minor if contractility is normal. However, the lower the baseline contractility, the more dramatic increase in contractility may be observed.

The main effect of NE on the vasculature is vaso-constriction through α-1 adrenoceptors and vasodilation via β-2 adrenoceptors. The results of α-adrenoceptors activation by NE is similar to the effects of PE. The main differences in physiologic effects between NE and PE are due to the activation of β-2 adrenoceptor that results in dilation of hepatic vasculature and facilitation of venous flow through the splanchnic system, leading to emptying of the splanchnic vasculature, shift of blood volume into systemic circulation and increase in VR and CO.

Thus, the main hemodynamic effect of β-2 agonists is a drastic shift of blood volume from splanchnic vasculature into systemic circulation leading to an increase in VR and CO. There are some experimental data that support such a notion [8,9]. Detailed description and analysis of the PE and NE is available elsewhere [5,10,11].

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