Commentary

The International Sepsis Forum's controversies in sepsis: my initial vasopressor agent in septic shock is dopamine rather than norepinephrine

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Abstract

Norepinephrine (noradrenaline) and dopamine are commonly used first-line vasopressor agents in the treatment of patients with septic shock. Recently increasing interest has focused on whether one or other of these agents is superior in terms of improving outcome. Studies have looked particularly at the possible local effects of the vasopressors on splanchnic circulation, because evidence suggests that this area is important in the development and maintenance of septic shock. However, the many studies performed have yielded conflicting data and there is, as yet, little evidence to support one drug over the other in terms of their splanchnic effects. Overall, though, dopamine has many assets that make it a good first-line drug when compared with norepinephrine, and these are highlighted in the present, brief commentary.

Keywords outcome, splanchnic blood flow, vasopressors

Septic shock is associated with profound cardiovascular alterations that frequently necessitate administration of vasopressor agents in order to maintain arterial pressure. Norepinephrine and dopamine are the two adrenergic agents that are commonly used in the treatment of septic shock that persists despite adequate fluid therapy. Dopamine has stronger β-adrenergic properties than does norepinephrine, and additional dopaminergic effects that can selectively increase splanchnic and renal blood flow. Over the years studies have investigated the effects of vasopressor agents on various aspects of the septic shock response, including systemic haemodynamics and oxygenation, and more recently regional blood flows and oxygenation, with the ultimate aim of determining which vasopressor, if any, has the superior profile and which vasopressor improves outcome the most. However, although there is a plethora of animal studies, there are few good clinical studies comparing the available agents, and recent expert panels have been unable to recommend one drug over another [1]. The debate, therefore, continues as to which catecholamine, if any, is to be preferred in the patient with septic shock.

In the present issue of *Critical Care*, Sharma and Dellinger [2] raise a number of arguments that favour norepinephrine over dopamine. However, we feel that their case lacks potency for the reasons discussed below, taking each of their sections in turn.

Norepinephrine produces less tachycardia

This is indeed true, although because dobutamine is often administered with norepinephrine to provide cardiac support, and dobutamine increases heart rate, clinically this factor is of little relevance. In addition, is tachycardia really a problem? The normal response to a severe infection is an increase in cardiac output secondary to increases in both stroke volume and heart rate. It may even be an advantage to have some degree of tachycardia in these conditions. Moreover, this tachycardia is usually well tolerated; it is rare to see the development of myocardial ischaemia secondary to septic shock. Admittedly, in some cases, in which the heart rate is very fast, preference could be given to norepinephrine, but these are exceptional cases.

Norepinephrine increases cardiac index

This is an advantage of dopamine and actually a major advantage. Although some studies have demonstrated an increased cardiac index with norepinephrine, generally norepinephrine raises blood pressure via its vasoconstrictive effects, with little effect on cardiac index. Hence, norepinephrine carries a risk for decreasing blood flow to the tissues, and additional dobutamine is usually required to improve cardiac function and balance these effects.

Norepinephrine has no deleterious effect on cerebral perfusion pressure

This is true. Of course, a vasopressor will result in a higher mean arterial pressure and, therefore, a higher cerebral perfusion pressure. However, is this really a problem in septic shock? When septic shock resolves, the patient usually has no neurological sequelae.

Norepinephrine has no effect on the hypothalamic–pituitary axis

This is indeed true, because dopamine administration can reduce the release of a number of hormones from the anterior pituitary gland, including prolactin [3,4]. However, if dopamine is used only for limited periods of time (as in shock resuscitation), then the deleterious effects of this action have not been demonstrated.

More effective and better outcome with norepinephrine compared with dopamine

Although the study quoted by Sharma and Dellinger, that by Martin and coworkers [5], does show improved outcome for the patients treated with norepinephrine, that study was a nonrandomized observational study, and the results must therefore be treated with caution. As Drs Sharma and Dellinger show elsewhere in their commentary, there is, as yet, no good clinical study indicating that one catecholamine is superior to another.

Norepinephrine ameliorates splanchnic hypoperfusion

Indeed, this is rather an argument in favour of dopamine. As Dellinger and Sharma state, Ruokonen and coworkers [6] measured splanchnic oxygen consumption in septic shock patients receiving either norepinephrine (0.07–0.23 μg/kg per min) or dopamine (7.6–33.8 μg/kg per min) and found no changes in splanchnic blood flow or oxygen consumption with norepinephrine, whereas dopamine consistently increased splanchnic blood flow. A recent study compared dopamine, norepinephrine and epinephrine in 20 patients with septic shock [7]. Although there were no differences in splanchnic blood flow or partial carbon dioxide tension gap between norepinephrine and dopamine, dopamine was associated with a lower mixed venous–hepatic venous oxygen saturation gradient than was norepinephrine.

Norepinephrine increases glomerular filtration pressure

It is true that norepinephrine can sometimes restore urinary output by raising renal perfusion pressure, but this is of interest only in those patients with profound hypotension. Otherwise, dopamine has a better effect on renal perfusion. However, this does not necessarily indicate that routine administration of dopamine is necessary to 'protect the kidneys', and indeed the use of renal doses of dopamine has recently been challenged [8] and can no longer be recommended.

Norepinephrine decreases serum lactate concentrations

This is an unimpressive and unsubstantiated statement. Although lactate levels tend to increase with epinephrine administration, there is no evidence that this is a problem with dopamine administration. Indeed, animal data [9] have even reported that norepinephrine, but not dopamine, increases portal lactate levels in sheep.

Additional points

A number of additional points are worthy of mention. First, dopamine has been shown in rats to increase the clearance of pulmonary oedema by upregulating sodium–potassium adenosine triphosphatase function in alveolar epithelial cells [10]. If this is also the case in humans, then it could represent an important additional benefit of dopamine in critically ill patients, many of whom will be receiving mechanical ventilation. Second, dopamine has also been shown to improve diaphragmatic function, probably by increasing oxygen supply to that region [11], which is another function that may be important in the critically ill population. Third. dopamine has been shown to improve protein synthesis in the postischaemic liver [12]. Finally, norepinephrine promotes bacterial growth [13] by improving iron uptake by bacteria, and may impair bacterial clearance [14].

Conclusion

We believe there is no evidence that dopamine should be replaced by norepinephrine in the treatment of patients with septic shock. On the contrary, although dopamine is a less effective vasopressor than norepinephrine, it preserves oxygen supply to the organs better. It can therefore be the initial drug of choice in circulatory shock, although in many cases norepinephrine may need to be added later if maximum doses of dopamine fail to restore perfusion pressure. Well designed randomized, controlled clinical trials are needed to compare dopamine with norepinephrine as first-line agents in the resuscitation of acutely ill patients with septic shock that is unresponsive to fluid administration.

Competing interests

None declared.

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