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Why is Epinephrine Not the Drug of Choice in Cardiogenic Shock?

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Why is Epinephrine Not the Drug of Choice in Cardiogenic Shock?

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Abstract

Through the years, epinephrine has been the drug of choice for patients with cardiogenic shock. However, epinephrine was clinically inferior to norepinephrine in comparison studies because of the negative patient outcomes, which were statistically significant. These effects include type B lactic acidosis, tachycardia, increased myocardial oxygen demand, and arrhythmias.

Keywords: cardiogenic shock, epinephrine, norepinephrine

Background

In theory, epinephrine is good for clinical use. It is a catecholamine with a high affinity for alpha-1, beta-1, and beta-2 receptors and is commonly used in ~20-40% of patients with cardiogenic shock.[1] However, it is important to note that because of the high affinity for beta-1 and beta-2 receptors, the use of epinephrine can lead to increased chronotropy and inotropy. These increases, along with vasoconstriction, cause an increase in mean arterial pressure (MAP) and coronary blood flow relative to an increased duration in diastole. Ironically, even though it is sometimes known as “high dose” norepinephrine, epinephrine in high doses can cause even stronger effects due to its alpha-receptor affinity.

The Downsides

From a hemodynamic perspective, one of the downsides of epinephrine use is increased afterload, which can cause decreased cardiac output. High-dose usage of epinephrine causes increased pulmonary vascular resistance, increasing right ventricular afterload. Epinephrine also results in an increased heart rate and stroke work, which increases myocardial oxygen demand. Unsurprisingly, this stimulation of the heart can cause arrhythmias. Other downsides include cardiac toxicity with arterial wall damage and necrosis, stimulation of myocyte apoptosis, hyperglycemia, insulin resistance, and type B lactic acidosis.

Comparison Studies

In a study of the hemodynamic effects of epinephrine, norepinephrine, and phenylephrine in rats, epinephrine use showed a significant increase in heart rate and an increase in cardiac output and myocardial oxygen demand.[2] A mechanism common with these characteristics is tachycardia.

In a randomized trial of under 300 patients, with approximately half with cardiogenic shock, epinephrine and norepinephrine had similar effects on MAP.[3] However, as seen in the rat model, there was still an increase in heart rate, lactate, and insulin dose needed.

A smaller study of 30 randomized patients with cardiogenic shock compared epinephrine to norepinephrine-dobutamine. MAP and cardiac index were similar for both

drugs, but higher lactate and heart rates were seen with epinephrine use. In addition, epinephrine appeared to cause less diuresis.[4]

Epinephrine versus Norepinephrine

Following this small trial, a larger randomized study compared epinephrine to norepinephrine and included 57 patients with acute myocardial infarction complicated by cardiogenic shock. As seen with the other studies, MAP was similar between the two groups.[5] In addition, the epinephrine groups had higher lactate, a higher incidence of tachycardia, and increased myocardial oxygen demand. The trial was stopped early because there was a statistically significant signal of harm seen with the use of epinephrine; the incidence of refractory shock was 37% vs. 7% in the epinephrine vs. the norepinephrine groups, respectively.

Conclusion

In conclusion, epinephrine use in cardiogenic shock is associated with excess lactic acid (mainly type B lactic acidosis), tachycardia, increased myocardial oxygen demand, and increased arrhythmias. In small trials, norepinephrine seems clinically superior to epinephrine for patients with cardiogenic shock, and larger observational studies have demonstrated higher mortality rates with epinephrine use. Despite this data, epinephrine is still widely used.

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