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Journal club critique

Could dopamine be a silent killer?

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Expanded Abstract

Citation

Sakr Y, Reinhart K, Vincent JL, Sprung CL, Moreno R, Ranieri VM, De Backer D, Payen D: Does dopamine administration in shock influence outcome? Results of the Sepsis Occurrence in Acutely Ill Patients (SOAP) Study. Crit Care Med 2006, 34:589-597 [1].

Background

The optimal adrenergic support in shock is controversial. We investigated whether dopamine administration influences the outcome from shock.

Methods

Design and setting: Multicenter observational cohort study in 198 European ICUs in 24 countries from May 1–15, 2002.

Subjects: 1058 adults with ICU stay ≥24h and circulatory shock, 462 of which had septic shock.

Intervention: None.

Measurements: Shock was defined as hemodynamic compromise necessitating the administration of vasopressor catecholamines and septic shock the presence of shock plus infection. Patients were followed until death, hospital discharge, or for 60 days, whichever came first. Differences in ICU, hospital, and 30d mortality were determined dependent on whether a subject received dopamine, with secondary analysis by dobutamine, epinephrine, or norepinephrine use.

Results: The intensive care unit mortality rate for shock was 38.3% and 47.4% for septic shock. Of patients in shock, 375 (35.4%) received dopamine (dopamine group) and 683 (64.6%) never received dopamine. Age, gender, Simplified Acute Physiology Score II, and Sequential Organ Failure Assessment score were comparable between the two groups. The dopamine group had higher intensive care unit (42.9% vs. 35.7%, p=.02) and hospital (49.9% vs. 41.7%, p=.01) mortality rates. A Kaplan-Meier survival curve showed diminished 30 day-survival in the dopamine group (log rank=4.6, p=.032). In a multivariate analysis with intensive care unit outcome as the dependent factor, age, cancer, medical admissions, higher mean Sequential Organ Failure Assessment score, higher mean fluid balance, and dopamine administration were independent risk factors for intensive care unit mortality in patients with shock.

Conclusion

This observational study suggests that dopamine administration may be associated with increased mortality rates in shock. There is a need for a prospective study comparing dopamine with other catecholamines in the management of circulatory shock.

Commentary

Norepinephrine was the first vasopressors introduced into clinical practice [2]. In early use, norepineprhine was often used to treat shock without adequate volume resuscitation. Not surprisingly, many patients with shock manifested signs of worsened tissue perfusion following treatment with norepinephrine in the absence of adequate intravascular volume loading. Thus, when dopamine was introduced as a less potent vasopressor with greater inotropic activity, it was widely accepted and became the vasopressor of choice. Now, in the face of more rational resuscitation strategies, the relative merits of dopamine, norepinephrine, and other vasopressors deserve reconsideration.

In the current study, Sakr and colleagues [1] examined mortality differences among ICU patients with shock stratified according to whether they received dopamine or not. In secondary analyses, patients were also stratified on the basis of treatment with dobutamine, epinephrine, or norepinephrine. The study included patients with a variety of causes of shock; 44% had septic shock and the remainder had forms of shock not associated with infection. In univariate analyses, the authors found that dopamine use was associated with greater ICU, hospital, and 30-day mortality. After adjusting for baseline characteristics and illness severity, dopamine use remained an independent predictor of ICU mortality regardless of whether shock was due to sepsis or other causes. Interestingly, epinephrine was also associated with greater 30-day mortality, yet norepinephrine and dobutamine were not. The authors concluded that dopamine administration may be associated

with increased mortality in shock and called for prospective randomized trials of dopamine and other catecholamines for the management of circulatory shock.

This was a very well done study involving a large, well-described cohort cared for in a variety of settings in approximately 25% of European ICUs. As is the case with most observational pharmacoepidemiology studies, there are a number of limitations that deserve consideration. Being observational in nature, this study cannot prove a cause and effect relationship and is intended to be hypothesis-generating rather than hypothesis-testing. This point was carefully noted by the authors. Information about the use of activated protein C, corticosteroids, and early goal-directed resuscitation were not collected, so the authors could not account for these therapeutic modalities in their analyses. Indication bias in this type of study is notoriously difficult to address. Simply put, in non-randomized studies, subjects receive specific drugs for specific indications. These indications are often inextricably linked to outcome, and can therefore bias associations of drug use with outcome. Statistical methods used to account for this source of bias include multivariable modeling and propensity scores; the latter can be used to adjust for the likelihood of having received the drug of interest [3]. While the authors did use multivariable modeling, they did not include a propensity-based analysis. Doing so would have increased the robustness of their findings. It also would have been helpful if the authors considered clustering effects in their models. Patients in one hospital experience common treatment protocols delivered by shared clinicians, meaning that observations within a hospital are often correlated [4]. Failure to account for this correlation, or clustering, can lead to overstated statistical significance [5].

If we assume for the moment that administration of dopamine does worsen the risk for a bad outcome, then we must ask the question: what is the reason for this deleterious effect? Multiple factors could be involved, among them: tachyarrhythmias, gut mucosal effects, neuro-endocrine axis suppression [6,7], and immunosuppression [8].

Recommendation

Dr. Sakr and colleagues have provided very intriguing data, suggesting that patients in shock treated with dopamine are more likely to have a poor outcome than are patients treated with other vasopressors. These data add further support to findings obtained in earlier studies by Martin and colleagues [9,10], who showed that survival is better for patients with septic shock when norepinephrine rather than dopamine is the vasopressor employed to support blood pressure. Given the observational nature of the present data, results from a randomized, controlled trial will be needed before the findings can be applied to routine patient care. Such a study is currently underway [11]. It is expected that this trial will be completed in December 2010. We, like many others, anxiously await the results.

Competing interests

The authors declare no competing interests.

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