Arginine Vasopressin in Advanced Vasodilatory Shock

To the Editor:

In the article by Dünser et al on vasopressin in patients with vasodilatory shock, the authors reported that vasopressin is a pressor agent as efficient as norepinephrine but causing fewer arrhythmias. However, we feel that the conclusion that the combination of norepinephrine and vasopressin proved superior to the infusion of norepinephrine alone is not supported by the data for at least 3 reasons.

First, the vasoconstrictive effects of vasopressin on gastrointestinal perfusion are of concern. In this study, the increase in bilirubin, quite common in patients with shock, was much more pronounced in patients treated with vasopressin. In addition, the PCO₂ gap measurements may not reflect a better preservation of gastric perfusion. Indeed, PCO₂ gap increased rapidly, and unexpectedly, to its maximal level already after 1 hour in the norepinephrine group, and then remained stable over time, whereas it increased steadily in the vasopressin group so that similar values were obtained after 48 hours. One possible explanation (proposed by the authors) was that vasopressin preserved mucosal perfusion better, but then the major changes in PCO₂ gap during the first hour in the norepinephrine group cannot really be explained, as all hemodynamic indices were stable and norepinephrine dosage only mildly increased during this short period. An alternative explanation could be that the values were initially underestimated in the norepinephrine group (in view of the relative imprecision of the measurements, as reflected by a large standard deviation) and that PCO₂ gap remained constant in the norepinephrine group, implying that vasopressin worsened mucosal perfusion.

Second, the greater decrease in platelet level suggests increased platelet aggregation in the vasopressin group, a potentially deleterious effect in septic shock.² Finally, even though the survival rate was similar in both groups, the length of intensive care unit stay was somewhat (although not significantly) prolonged in the vasopressin group.

Hence, although the short-term hemodynamic effects of the combination of vasopressin and norepinephrine may be more favorable and may even provide an immediate survival benefit in experimental models,³ the impact on organ function, especially during long-term administration of vasopressin, remains to be determined. These potential limitations do not justify the authors’ conclusions on the superiority of vasopressin over norepinephrine. The results of a large and adequately powered prospective randomized controlled trial on vasopressin administration in septic shock are eagerly awaited.

Daniel De Backer, MD
Jacques Creteur, MD
Jean-Louis Vincent, MD
Department of Intensive Care
Erasmus University Hospital
Free University of Brussels
Brussels, Belgium


Response

The letter by Dr De Backer and colleagues addresses important points of our study. Their speculations about gastric tonometry–derived variables are right and must be considered. However, the fact that macrohemodynamic parameters correlate poorly with microhemodynamic measurements, and that regional gastric mucosal CO₂ partial pressure was also significantly lower in patients receiving arginine vasopressin (AVP), led us to assume that gastric perfusion was better preserved in AVP patients. A recent animal experiment found similar results.¹ After all, Dr De Backer et al are right that gastric tonometry–derived data must be interpreted with extreme caution in these patients with severe shock and multiple organ dysfunction syndrome.

The fear of possible deleterious effects of an AVP-mediated decrease in platelet count is justified and led us to conduct another prospective, still unpublished, study on the effects of a combined infusion of AVP and norepinephrine (NE) on plasmatic and cellular coagulation. Although platelets were again lower in AVP patients, no influence on global coagulation and specific coagulation parameters could be detected.

Regarding the nonsignificant difference in length of intensive care unit stay between study groups, 2 points must be considered. First, after the 48-hour study period, 6 NE patients received AVP, because NE requirements remained >0.5 µg/kg · min⁻¹. Second, this study was not planned as an outcome study. To detect a significant decrease in mortality from 66.7% to 56.7%, each study group would have to include 400 patients (Fisher exact test). In accordance with recent animal data,¹ the longer survival time in AVP patients could be an indicator for improved chances of survival in advanced vasodilatory shock treated with a combined AVP/NE infusion.

Our study aimed at examining the effects of a supplemental AVP infusion in advanced vasodilatory shock, defined as a mean arterial pressure <70 mm Hg despite NE dosages of >0.5 µg/kg · min⁻¹. There is no doubt that NE must be considered the first-line vasopressor agent in vasodilatory shock states requiring NE dosages <0.5 µg/kg · min⁻¹. However, in our opinion, the results of this study in advanced vasodilatory shock support the conclusion that a combined AVP/NE infusion is superior in stabilizing cardiocirculatory function when the benefit/risk ratio of conventional catecholamine vasopressor agents deteriorates, resulting in a higher incidence of adverse side effects, eg, tachyarrhythmias or myocardial ischemia.

Martin W. Dünser, MD
Andreas J. Mayr, MD
Hanno Ulmer, MD
Hans Knotzer, MD
Günter Sumann, MD
Werner Pajk, MD
Barbara Friesenecker, MD
Walter R. Hasibeder, MD

Division of General and Surgical Intensive Care Medicine
Department of Anesthesiology and Critical Care Medicine
University Hospital Innsbruck, Austria

Arginine Vasopressin in Advanced Vasodilatory Shock
Daniel De Backer, Jacques Creteur and Jean-Louis Vincent

_Circulation_. 2003;108:e142
doi: 10.1161/01.CIR.0000099845.53469.EA
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2003 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/108/19/e142

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/