

study also supports the results of Broner et al.,¹⁶ showing that DA is not able to ameliorate or accentuate hypotension occurring in septic shock.

A pivotal moment in sepsis occurs with the development of life-threatening hypotension unresponsive to conventional therapies, indicating that vascular hyporeactivity to vasoconstrictor agents is a detrimental factor. As our results show in this study, pre-treatment or post-treatment of endotoxemic animals with DA did not reverse the vascular hyporeactivity to NE. Thus, it is not surprising to observe DA-refractory shock in rats with *E. coli* endotoxin-induced sepsis. By contrast, DA further enhanced tachycardia and hypotension in the current model of sepsis. Moreover, we also observed that DA increased the mortality of rats with endotoxemia for 4 h. The detrimental effect of DA in the current model may result from the enhancement of tachycardia which could accelerate the cardiac failure seen in septic shock since DA has no effect on the development of decreased PaO₂ or metabolic acidosis.^{17,18} It has been shown that acidosis is associated with an increase of HR or cardiac failure.^{19,20} Thus, this increment of HR by DA in animals with endotoxemia may result in lethality. Indeed, our present study shows that the administration of endotoxemic rats with DA caused a higher mortality.

In conclusion, although the application of DA in patients with shock has been suggested, the outcomes of these patients are not well reported. Herein, we show that administration of DA to endotoxemic rats does not ameliorate the circulatory failure but further increases the mortality in these animals. The findings provide some implications of which clinicians should be aware when treating patients with septic shock.

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