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Effects of Dopamine on Circulatory Failure and Survival in Rats with Endotoxemia

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ABSTRACT

Dopamine (DA, 3,4-dihydroxyphenylethylamine), a dopaminergic and β_1-adrenergic receptor agonist, had been suggested to treat patients with hypotension and shock. However, the beneficial effect of DA on cardiovascular function is transient, and the development of metabolic acidosis is not improved. This study evaluated the circulatory effects of DA in rats with endotoxic shock. DA (3 or 10 $\mu g\ kg^{-1}\ min^{-1}$) was administered to anesthetized rats at 30 min prior to or after injection of *Escherichia coli* endotoxin (lipopolysaccharide, LPS; 10 mg kg^{-1}, i. v.). A group of sham-operated time-control rats was used as a control. The injection of LPS caused a biphasic decrease of blood pressure, i.e., an early-acute hypotension (within 15 min) and delayed hypotension (at 2-4 h), and significant tachycardia during the experimental period. Endotoxemia for 4 h was associated with severe vasuclar hyporeactivity to norepinephrine (NE; 1 $\mu g\ kg^{-1}$, i.v.) and a survival rate of about 80%. The pre- or post-treatment of LPS rats with DA further enhanced the delayed hypotension, tachycardia, and lethality, whereas it had no significant effect on vascular hyporeactivity to NE. Our results suggest that DA is not a suitable therapeutic agent in rats, and may be humans with endotoxic shock. (N. Taipei J. Med. 2000; 3:207-214)

INTRODUCTION

Severe sepsis induced by endotoxin, the lipopolysaccharide (LPS) component of the cell wall of Gram-negative organisms, is associated with hypotension, vascular hyporeactivity to vasoconstrictor agents, myocardial dysfunction, and maldistribution of organ blood flow, and may eventually lead to disseminated intravascular coagulation or even septic shock.[1,2] LPS is also a potent cellular activator which results in elaboration of a variety of vasoactive substances when administered into the blood stream.[3,4] The shock state in the animal model that follows LPS administration is usually associated with decreased cardiac output and increased systemic vascular resistance which may be a compensatory effect to raise the blood pressure.[5-8] This hemodynamic response, however, differs from the high cardiac output and peripheral vasodilatation seen in the early phase of human septic shock.[9] Since such a short period of observation time after endotoxin administration in animals may not be well matched with the clinical development of septic shock, it is likely

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