TITLE : DECREASED DOPAMINE-BETA-HYDROXYLASE ACTIVITY IN SEPTIC SHOCK

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Systemic arterial tone is markedly reduced during septic shock, suggesting a much less effective catecholamine-induced vasoconstriction than in pure cardiogenic or hypovolemic shocks. Inhibitors of the last enzyme of the catecholamine synthesis chain, namely Dopamine-Beta-Hydroxylase (D.B.H.), have been isolated from Gram-negative microbial cultures (1). Such inhibitors induce inhibition of D.B.H. activity, decrease of tissue catecholamine contents and systemic arterial hypotension, when experimentally given to either animals or man (2). We thus compared plasma D.B.H. activity in patients suffering from Gram-negative septic shock, with critical ly ill patients with non septic shock, in order to determine if a decrease in D.B.H. activity could be detected in human septic shock.

PATIENTS AND METHODS

Thirty-one critically ill patients were studied and divided into three groups according to the following criteria : sepsis was demonstrated by patent septic focus (peritonitis, intraabdominal abcess, pneumonia, urinary tract infection) and/or positive blood cultures. Shock state was demonstrated by arterial hypotension (systolic arterial blood pressure below 90mm Hg) associated with oliguria and acute mental signs of distress. The three groups of patients were :

1) Control : 9 critically ill patients without sepsis or shock.
2) Non septic shock : 11 patients with cardiogenic (myocardial infarction) or hypovolemic shock (hemorrhage or dehydration).
3) Septic shock : 11 patients with severe septic shock, due to Gram-negative infection.

Patients were not given catecholamine at the time of the study. Blood was always withdrawn through previously inserted central venous or pulmonary artery catheter, and immediately centrifuged. The removed plasma was stored at -20°C.

Plasma D.B.H. activity was determined according to the photometric method described by Nagatsu and Udenfriend (2). One unit per liter (U/L) represents one micromole of octopamine formed.

RESULTS (Table I)

Plasma D.B.H. activity was within normal limits in control patients, i.e. without sepsis or shock.

In patients with non septic shock, D.B.H. activity was significantly higher than in the control group.

In patients with septic shock, plasma D.B.H. activity was markedly and significantly lower than in either critically ill patients without shock or patients with a non septic shock.

DISCUSSION

Plasma D.B.H. activity was found to be very low in any of the investigated patients with septic shock. Such a decrease in D.B.H. activity is not likely to be due to the metabolic consequences of the shock itself, as D.B.H. activity was increased in the other types of shock.

The above data suggest a marked decrease in D.B.H. activity during human septic shock. It is likely to be related to the present of large amounts of D.B.H. inhibitors of microbial origin in such severely septic patients. Such an inhibition could account, at least in part, for the decrease arterial systemic resistances usually demonstrated in septic shock, by altering the increase of catecholamine synthesis in response to shock.

TABLE I

PLASMA D.B.H. ACTIVITY

	D.B.H. (U/L)	Difference from control
CONTROL	21.3 ± 5.2	—
NON SEPTIC SHOCK	29.1 ± 9.3	$p < 0.05$
SEPTIC SHOCK	7.4 ± 3.4	$p < 0.001$

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