INTRODUCTION: It has been reported that the endogenous reduced glutathione (GSH) was reduced in endotoxin shock and the exogenously administered GSH increased the tissue GSH level. We have shown that GSH improves the depressed cardiovascular performance and impaired effects of dopamine in severe metabolic acidosis in dogs. The purpose of this study was to investigate the effects of GSH treatment on endotoxin shock in dogs.

METHODS: Eighteen adult mongrel dogs of either sex weighing 10-20 kg were anesthetized with pentobarbital sodium (25 mg/kg). After endotracheal intubation animals were ventilated mechanically with room air under full relaxation with pancuronium bromide (0.08 mg/kg). After catheterization, dogs were divided into two groups, 12 in non-treated group and 6 in GSH-treated group. Hemodynamic parameters measured were mean arterial pressure, heart rate, mean pulmonary arterial pressure, central venous pressure and cardiac output. Cardiac index, peripheral vascular resistance and stroke volume index were calculated. Arterial and mixed venous oxygen contents were measured using Lex-02-Con. Oxygen consumption and oxygen extraction ratio were calculated using standard formula. Serum B-glucuronidase and plasma lactate levels were measured by standard methods. Oxygen transport in each group was measured, each dog was intravenously injected 3 mg/kg of endotoxin. In GSH-treated group, 500 mg/kg of GSH was administered intravenously 5 minutes after endotoxin injection and in the non-treated group saline was infused instead of GSH in the same way. All parameters were determined at 1 hour interval for 5 hours after the injection of endotoxin.

RESULTS: The mortality rates of dogs after endotoxin injection were 8%, 17%, 42% and 50% at 2, 3, 4 and 5 hours respectively in the non-treated group. However, in GSH-treated group all dogs survived until 4 hours after the endotoxin injection and at 5 hour the rate was 17%.

Hemodynamic changes with the injection of endotoxin in both groups were shown in the table 1 and they were not significantly different between the two groups. Oxygen transport in both groups was lower at 1, 2 and 3 hours after endotoxin injection, but they were not statistically different from the value in the GSH-treated group. Oxygen consumptions in the non-treated group were significantly lower than those in the non-treated group at 1 and 3 hours after the endotoxin injection. Serum B-glucuronidase and plasma lactate levels in the non-treated group were significantly higher at 1, 2, and 3 hours after the endotoxin injection. (Table 2)

DISCUSSION: Although hemodynamic parameters were not significantly different between the two groups, the oxygen consumptions were significantly lower and the serum B-glucuronidase levels were significantly higher in the non-treated group at the early stage of endotoxin shock. This suggests that the oxygen utilization in the tissue was more severely impaired in the non-treated group. This was reflected in the rapid increase in mortality rate at the later stage in the non-treated group. These results suggest that the GSH is a useful drug in the treatment of endotoxin shock.

Table 1

Table 2

REFERENCES
