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Title: SPLANCHNIC CIRCULATORY RESPONSE TO KETAMINE IN STRESSED AND UNSTRESSED DOGS

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Introduction. The influence of ketamine on the systemic circulation has been extensively investigated, but changes in hepatic cirulation are still unknown. The purpose of this study was to measure the changes in hepatic circulation induced by ketamine in acute experiments ("stressed" dogs) and chronic experiments ("unstressed" animals).

Methods. This study was performed using two groups of mongrel dogs; eight animals (Group I) were used in acute experiments and five animals (Group II) in chronic experiments.

Anesthesia for the surgical procedure in all animals consisted of alpha-chloralose (100 mg/kg i.v.) and controlled ventilation. A Swan-Ganz thermister tipped catheter was placed in the pulmonary artery. A catheter was placed in the distal aorta via a branch of femoral artery. Another catheter was inserted through a branch of the femoral vein into the posterior caval vein at its junction with the hepatic veins. Following laparotomy, a catheter was introduced into the portal vein via a branch of the superior mesenteric vein, and electromagnetic flowmeter probes were placed around both the portal vein and hepatic artery. Hepatic venous catheter was placed in Group I animals only.

In Group I, hemodynamic variables, arterial and venous blood gases and pH were determined thirty minutes after completion of the surgical preparation ("asleep baseline values"), then ketamine (8 mg/kg) was administered i.v. All flows and pressures were recorded continuously; cardiac output was measured at five minute intervals; blood gases and pH were determined at 10-20 minute intervals. The data observed twenty minutes after the injections of ketamine were stable and steady and, therefore, used for analysis.

Following the above surgical preparation in Group II dogs, the abdominal cavities were closed, and the catheters and wires externalized through subcutaneous tunnels and placed into a specially designed pocket. The animals were allowed to recover. During the 3 recovery days, all catheters were intermittently flushed, and measurements were recorded. On the 4th day, after the dogs were accustomed to the environment, the "awake baseline values" were measured and the response to ketamine, 8 mg/kg, was determined as in the Group I animals.

Results. The circulatory changes observed are presented in Table 1. Arterial, portal and hepatic vein (Group I only) blood gases and pH were not significantly altered in either group.

Discussion. Ketamine administered in acute experiments (Group I) led to a decrease in MAP and CI without significant changes in liver circulation.

A comparison of the "awake and asleep baseline" values from the two groups shows that the complex which consisted of surgical preparation, controlled ventilation and chloralose anesthesia, resulted in a significant decrease in CI by 34% and PBF by 42%, an increase in PVR by 50% and in HABF/THBF ratio by 24%, when compared to awake values. The effect of ketamine on splanchnic circulation in trained dogs (Group II) consisted of a significant increase in MAP, CI, HABF, PP, PVR, and HABF/THBF ratio ($p < 0.05$). An increase in PP without concomitant change in PBF led to a significant increase in calculated PVR, and suggests portal venular vasoconstriction. Since hepatic vein oxygen content did not decrease, liver hypoxia probably did not occur.

The data suggest that the alterations in the variables caused by the complex of "chloralose anesthesia - controlled ventilation-surgical stress" in acute experiments obscured the effects of ketamine on hepatic circulation which were clearly revealed in trained dogs.

Table 1. Main circulatory variables (mean ± S.E.) during ketamine anesthesia. φ

Group / Variable	I, acute experiments B/L	I, acute experiments K	II, trained dogs B/L	II, trained dogs K
MAP	142±9.7	132±8.9°	97±6.3*	120±5.6°
CI	2.87±0.39	2.39±0.28°	4.34±0.45*	5.38±0.31°
HABF	22±3.0	20±2.8	29±5.4	33±5.2°
PBF	68±8.9	72±10.4	118±14.6*	118±16.4
PP	11±1.6	10±1.9	10±0.9	12±0.9°
PVR	15.9±1.9	13.0±1.4	7.9±0.9*	10.2±1.1°
HABF/THBF	0.25±0.03	0.22±0.3	0.19±0.02	0.22±0.03

φ B/L = Baseline values; K = Ketamine 8 mg/kg; MAP = Mean Arterial Pressure in torr; CI = Cardiac Index in L/min/m^2; HABF, PBF, and THBF = Hepatic Artery, Portal and Total Hepatic Blood Flow in ml/min/100g liver, respectively; PP = Portal Pressure in torr; PVR = Portal Venular Resistance in 10^2 x dyn. x sec. x cm^{-5}.

* = $p < 0.05$ compared with B/L values of Group I according to paired t-test.

° = $p < 0.05$ compared with B/L values of Group II according to student t-test.

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