Effects of carbon dioxide pneumoperitoneum on hemodynamics in cirrhotic rats

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Abstract

Background: The aim of our study was to investigate the effect of carbon dioxide pneumoperitoneum on systemic and splanchnic hemodynamics in cirrhotic rats. Methods: Sprague–Dawley rats (n = 80) were used in this study. Liver cirrhosis was induced by thioacetamide administration intraperitoneally (200 mg/kg body weight, twice a week for 16 weeks). The radioactive microsphere method was used to measure systemic and regional hemodynamic parameters before, 1 h after the start, and 1 h after the release of pneumoperitoneum. Results: Splanchnic blood flow and cardiac index were significantly depressed during pneumoperitoneum in liver cirrhosis and control groups, but no significant differences were seen between the two groups. In both groups, portal venous inflow decreased and hepatic arterial blood flow increased significantly during pneumoperitoneum. However, during pneumoperitoneum, total hepatic blood flow as a percentage of its value before pneumoperitoneum was lower in cirrhotic rats (71.0%) than in control rats (91.9%) (p < 0.05, Mann–Whitney U-test). Conclusions: Carbon dioxide pneumoperitoneum markedly decreases total hepatic blood flow in cirrhotic rats due to the impaired hepatic arterial buffer response. Liver function should be carefully controlled in cirrhotic patients after laparoscopic surgery with pneumoperitoneum.

Key words: Carbon dioxide — Hemodynamics — Liver cirrhosis — Pneumoperitoneum — Radioactive microsphere

Laparoscopic surgery is usually performed with the use of pneumoperitoneum (PP) for the visualization of the abdominal cavity. PP impairs systemic and splanchnic hemodynamics, leading to decreases in cardiac output, splanchnic blood flow, and portal venous blood flow [8, 10, 11, 19–21, 23, 25]. The alterations in hemodynamics and liver blood flow in cirrhosis are well-known [15, 24]. Therefore, liver cirrhosis (LC) is considered as a relative contraindication to laparoscopic surgery [18]. Recently, it has been shown that laparoscopic cholecystectomy may be performed in cirrhotic patients without severe complications [12, 17]. Thus, the use of laparoscopic surgery has gradually expanded for cirrhotic patients. However, the effect of PP on hemodynamics and liver function in cirrhotic patients remains unclear. In the current study, the radioactive microsphere method was used to investigate the effects of carbon dioxide (CO2) PP on hemodynamics in rats with thioacetamide (TAA)-induced liver cirrhosis.

Materials and methods

Animal model

Adult male Sprague–Dawley rats (450–500 g) were used. The study was approved by the Animal Studies Committee of Oita Medical University. The rats were randomly divided into two groups: control group and LC group. Cirrhosis was produced by intraperitoneal injections of TAA (200 mg/kg body weight) in saline twice a week for 16 weeks, starting when the rats were 4 weeks old. Control rats received intraperitoneal injections of the same volume of saline for the same period starting at the same age [6]. Hemodynamic studies were conducted 2 weeks after the last injection. All rats were fasted with free access to water 14–16 h before the start of hemodynamic evaluation.

Protocol 1: hemodynamics

Each animal was anesthetized with pentobarbital sodium (Nembutal, Abbott Laboratories, North Chicago, IL, USA) at an initial dose of 70 mg/kg intraperitoneally (IP). Polyethylene catheters (PE-50, Becton Dickinson, Parsippany, NJ, USA) filled with heparinized saline were inserted into the left ventricle via the right carotid artery and into the left femoral artery (approximately 1 cm above the femoral bifurcation). Catheter position in the left ventricle was assessed by waves detected by pressure transducers attached to a blood pressure amplifier (Model TP-400T, Nihon Kohden, Tokyo) and a digital storage oscilloscope (RM-6000, Nihon Kohden). Then, a catheter (PE-50) filled
with heparinized saline was inserted into the left femoral artery for the mean arterial pressure (MAP) and heart rate (HR) measurements. Rectal temperature was maintained between 36 and 38°C by a heat lamp, and a tracheostomy was performed. After muscle relaxation had been achieved by intramuscular injection of 2 mg/kg pancuronium bromide, animals were mechanically ventilated as described previously [4] using a rodent ventilator (Model 7025, UGO Basile, Comerio-Varese, Italy). At the end of the surgery 30 mg/kg pentobarbital sodium was added IP, and rats were ventilated for 1 h for stabilization. CO₂ was insufflated at an intraabdominal pressure of 8 mmHg using an Electronic CO₂ Surgiflator 9100 insufflator (Nisso, Tokyo).

All hemodynamic parameters were registered at three time points: before (immediately before the induction of PP, n = 10 in each group), during (1 h after the start of PP, n = 10 in each group), and after (1 h after the release of PP, n = 10 in each group).

For measurement of blood flow ⁵¹Cr-labeled microspheres (15.5 ± 0.1 μm diameter; New England Nuclear, Boston, MA, USA) with a specific activity of 310 MBq/g were suspended in 0.02% Tween-80. The microsphere suspension was mixed thoroughly by agitation and sonication (Ultrasonic Sonicator, USC-1, Iuchi, Japan). Thereafter, 0.1 mL of microsphere suspension (approximately 50,000 microspheres) was injected into the left ventricle over a 5-s period, followed immediately by a 0.4-mL saline flush over a 20-s period. This injection was carried out with a syringe pump (210, KD Scientific, Boston, MA, USA) at a rate of 1.2 mL/min. Five seconds before the microsphere injection, blood withdrawal was begun through the femoral arterial catheter at a rate of 0.75 mL/min with a syringe pump (210, KD Scientific). The total period of blood withdrawal was 1 min for each microsphere injection. At designated time periods, animals were killed by an overdose of pentobarbital. The heart, lung, liver, stomach, spleen, pancreas, small intestine, large intestine, kidney, and mesentery were removed, blotted, and weighed. The radioactivity of each sample was analyzed using a gamma counter (ARC-361, Aloka, Tokyo).

At least 300 microspheres were trapped in both a reference sample and organs to ensure the validity of measurements. To check for adequate mixing of the microspheres, radioactivity in each kidney was also assessed. In instances in which a disparity of more than 10% existed between the right and left kidney, the data were excluded [5].

Regional blood flow was calculated according to the following formula: regional blood flow (mL/min) = organ radioactivity (cpm)/reference blood sample radioactivity (cpm) × 0.75 (mL/min). Portal venous inflow (PVI; mL/min) was calculated as the total blood flow to the stomach, spleen, pancreas, small and large intestines, and mesentery.

Cardiac output (CO) was calculated according to the following formula: cardiac output (mL/min) = radioactivity injected (cpm)/reference blood sample radioactivity (cpm) × 0.75 (mL/min). Cardiac index (CI; mL/min/kg body weight) was calculated by dividing CO by body weight (kg). Total peripheral resistance (TPR) was calculated by the ratio of CO to mean arterial pressure. Total hepatic blood flow was calculated as the sum of hepatic arterial blood flow and portal venous inflow.

Protocol 2: portal pressure

Two groups of rats (n = 10 in each group) assigned to the same group categories used in protocol 1 were studied. Each rat was anesthetized and ventilated in the manner described previously. A catheter (PE-50) filled with heparinized saline was inserted into the left femoral artery for the MAP and HR measurements. Following midline laparotomy, the ileocolic vein was cannulated with a catheter (PE-50) for the portal pressure measurements. The abdominal incision was tightly closed in two layers.

Statistics

All values were expressed as the mean ± SEM. Data were analyzed using a computer-based software system (Stat View J-4.02, Abacus Concepts, Berkeley, CA, USA). Differences between the groups were analyzed using the Mann–Whitney U-test. Differences within a group were tested by one-way analysis of variance (ANOVA). When ANOVA revealed significant differences (p < 0.05), a post hoc Fisher’s F-test was used for multiple comparisons. Differences were considered significant at p < 0.05.

Results

The livers of TAA-treated rats showed marked regenerative nodules and fibrosis, which are characteristic of the histology of human cirrhosis (Fig. 1). The mortality rate during the TAA treatment was less than 3% (1 of 40 rats died during treatment), and all rats showed histology compatible with cirrhosis.

Systemic hemodynamics

Before the induction of PP the MAP and TPR were lower in cirrhotic rats than in control rats (Table 1). In the LC group, TPR was significantly higher during PP than before PP. There were no significant differences between the two groups in HR. The CI was higher in cirrhotic rats than in control rats before the induction of PP (Fig. 2A). However, the CI decreased similarly during