Hemodynamic and Biochemical Changes during Total Hepatic Vascular Exclusion in Dogs

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ABSTRACT. Twelve healthy Beagles were divided into 3 groups of 4 dogs each. To compare 2 methods of total hepatic vascular exclusion (THVE), we investigated the hemodynamic changes during THVE and assessed the influences on hepatic, renal and pancreatic biochemistry and the complications after THVE. In Group A, the thoracic aorta, hepatic pedicle and prehepatic and posthepatic caudal vena cava were occluded for 20 min, while in Group B, the celiac and cranial mesenteric arteries, hepatic pedicle and prehepatic and posthepatic caudal vena cava were occluded for 20 min. In Group C, a sham operation was performed. The arterial, venous and portal venous pressures and serum biochemistry parameters were measured before and during THVE and for 30 min after reperfusion. The carotid arterial pressure did not change in Group A during THVE, but decreased in Group B. The femoral and portal venous pressures in Group B increased significantly during THVE compared with those in Group C. With the exception of alanine aminotransferase, the serum biochemical profiles remained unchanged after the operation. For 7 days after the operation, no complications were observed in any of the dogs. In conclusion, occlusion of thoracic aorta, hepatic pedicle and prehepatic and posthepatic caudal vena cava is a feasible and safe method of hepatic vascular occlusion. This technique appears to be effective for canine hepatic surgery, such as removal of a large right-divisional hepatic tumor and attenuation of intrahepatic portosystemic shunt.

KEY WORDS: canine, total hepatic vascular exclusion.

Hepatic vascular occlusion during hepatic resection is effective in reducing intraoperative bleeding, and various effective techniques of vascular occlusion have been described in human medicine [2, 9, 16]. The Pringle maneuver is the oldest and simplest technique of hepatic vascular occlusion and is widely used by many surgeons. This maneuver involves temporary occlusion of inflow to the liver, i.e., of the hepatoduodenal ligament, including the portal vein, hepatic artery and common bile duct [1, 9, 16]. By using this technique, the bleeding from the portal vein and hepatic artery can be arrested, but the backflow bleeding from the hepatic veins cannot be prevented [1, 9, 16]. Total hepatic vascular exclusion (THVE) entails temporary occlusion of inflow to and outflow from the liver, i.e., of the hepatic artery, prehepatic and posthepatic caudal vena cava and portal vein [9, 16]. During THVE, inflow occlusion is achieved by the Pringle maneuver, while outflow occlusion is achieved by clamping the prehepatic and posthepatic caudal vena cava [9, 16]. Some reports on THVE in people have described that occlusion of the caudal vena cava causes marked reductions of venous return and cardiac output, consequent increases in systemic vascular resistance and heart rate and a decrease in mean arterial pressure [2, 6, 7, 11, 16]. Therefore, THVE causes major hemodynamic disturbances in people and requires complicated anesthetic management [2]. This technique is selected on the basis of the general condition of the patient, intrahepatic location of the tumor and the availability of safe operating conditions. In small animal medicine, 2 methods of THVE have been reported in dogs with hepatic arteriovenous fistulas and intrahepatic portosystemic shunts [3, 12, 21]. One method involves occlusion of the celiac artery, cranial mesenteric artery, portal vein and the prehepatic and posthepatic caudal vena cava [3, 21], while the other involves occlusion of the thoracic aorta, hepatic artery, portal vein and the prehepatic and posthepatic caudal vena cava [12]. However, the influences of these 2 methods of THVE on the cardiovascular system, liver, kidney and pancreas are still unclear, and the superior method remains to be determined. Many resection techniques for liver lobectomy, particularly that of the left-divisional lobes, can be safely performed without THVE; however, in cases of large hepatic tumors that involve the caudal vena cava and/or main portal vein in the right-divisional lobes, the THVE technique is preferable. In this study, we compared 2 methods of THVE: occlusion of the celiac and cranial mesenteric arteries with the Pringle maneuver and occlusion of the prehepatic and posthepatic caudal vena cava versus occlusion of the thoracic aorta with the Pringle maneuver and occlusion of the prehepatic and posthepatic caudal vena cava.

The objectives of this study were to investigate hemodynamic changes during THVE, assess the influences of THVE on hepatic, renal and pancreatic biochemistry and function and demonstrate the major and minor complications during and after THVE for safer hepatic surgery in dogs.
MATERIALS AND METHODS

Twelve adult female Beagles (weight, 10.3 ± 2.0 kg) were used in this study. All the dogs were confirmed to be healthy based on a complete blood cell count, serum biochemistry, thoracic and abdominal radiography and abdominal ultrasonography findings. The experimental protocol was performed in accordance with the “Guide for the Experiment of Animals” produced by the College of Bioresource Sciences, Nihon University. The dogs were fasted for 12 hr before the study, and at 30 min before induction of anesthesia, 0.2 mg/kg meloxicam was subcutaneously administered as an analgesic. General anesthesia was induced using a mixed intravenous injection of 0.2 mg/kg midazolam hydrochloride and 0.2 mg/kg butorphanol tartrate, followed by 4 mg/kg propofol. After endotracheal intubation, the dogs were mechanically ventilated with isoflurane in a mixture with pure oxygen and placed in dorsal recumbency. The carotid and femoral arteries and jugular and femoral veins on one side were catheterized for monitoring the arterial and venous blood pressures, respectively. The catheter that was inserted into the jugular vein was used to collect venous blood samples for serum biochemical analysis. During the operation, 5% glucose in acetate Ringer’s solution was infused at a rate of 10 ml/kg/hr.

Celiotomy was performed from the xiphoid process to the pubis. Furthermore, the falciform ligament and xiphoid process were removed, and caudal median sternotomy was performed. Following partial incision of the diaphragm, the thoracic caudal vena cava was exposed on the cranial side of the diaphragm. The hepaticorenal ligament was transected, and the caudal vena cava was exposed on the cranial side of the right renal vein and phrenicoabdominal vein. The thoracic aorta on the cranial side of the diaphragm (in Group A) and the celiac and cranial mesenteric arteries (in Group B) were exposed and dissected free of perivascular tissue. Umbilical tapes were placed around the thoracic aorta, celiac and cranial mesenteric arteries and prehepatic and posthepatic caudal vena cava and passed through Rummel tourniquets. Thereafter, a Rummel tourniquet was placed through the epiploic foramen and around the hepatoduodenal ligament containing the portal vein and hepatic artery. A 24-gauge over-the-needle catheter was introduced into the jejunal vein for monitoring the portal venous pressure.

The 12 dogs were divided into 3 groups of 4 dogs each. In Group A, the thoracic aorta, hepatic pedicle including hepatic artery and portal vein and prehepatic and posthepatic caudal vena cava were occluded. In Group B, the celiac and cranial mesenteric arteries, hepatic pedicle and prehepatic and posthepatic caudal vena cava were occluded. In Group C, a sham operation was performed without occlusion.

THVE was induced by tightening all tourniquets 30 min after preparation for hemodynamic stabilization. In groups A and B, THVE was continued for 20 min, which has been reported to be the maximal time of canine hepatic ischemia [15], and was followed by reperfusion. The systolic arterial pressure and venous and portal venous pressures were measured before THVE, at 10 and 20 min during THVE and at 15 and 30 min after reperfusion. The arterial and venous catheters were removed after all measurements were completed. Caudal thoracic and abdominal closures were performed routinely, following which the dogs recovered from the anesthesia. An initial bolus of 0.4 mg/kg butorphanol during recovery followed by 0.2 mg/kg butorphanol every 2–3 hr for 24 hr and 0.1 mg/kg meloxicam subcutaneously once daily for 3 days were administered for postoperative analgesia.

Blood samples were collected from the jugular vein. The serum levels of alanine aminotransferase (ALT) and alkaline phosphatase (ALP) were measured before THVE, at 10 and 20 min during THVE and at 1, 2, 6, 12 and 24 hr and 3, 5 and 7 days after reperfusion. In addition, the serum levels of blood urea nitrogen (BUN), creatinine (Crea), amylase (Amyl) and lipase (Lip) were measured before THVE and at 12 hr and 3 days after reperfusion. After induction of anesthesia, cefazolin sodium was administered intravenously at a dosage of 20 mg/kg every 2 hr during surgery and every 8 hr postoperatively. After each dog was able to ingest food, cefalexin was administered orally at a dosage of 25 mg/kg twice daily for 7 days after the operation. The general condition of each dog was observed carefully for 7 days postoperatively.

All data were expressed as means ± standard deviation. Differences between groups were statistically analyzed using the Kruskal-Wallis test followed by a post hoc comparison (Tukey’s test). A P value of less than 0.05 was considered significant. Differences between before and during THVE and after the operation were analyzed using the Friedman test.

RESULTS

Influence on the cardiovascular system: In groups A and B, the heart rate during THVE was not significantly different than that before THVE (Fig. 1). However, in Group B, the heart rate at 15 min after reperfusion decreased to 77.8 ± 5.0 beats/min, and it was significantly lower than that before THVE (P=0.018). In Group A, the carotid arterial pressure during THVE remained unaltered (Fig. 1). However, in Group B, the carotid arterial pressure decreased markedly to 29.3 ± 9.8 mmHg at 20 min during THVE, which was significantly lower than the pressure observed in Group C (P=0.024). The carotid arterial pressure in Group B recovered to 64.5 ± 15.9 mmHg after reperfusion, but was still significantly lower than that in Group C (P=0.049). At 20 min during THVE, the femoral arterial pressure decreased to 15 ± 3.5 mmHg in Group A and 31.8 ± 7.0 mmHg in Group B (Fig. 1). The femoral arterial pressure was significantly decreased in Group A compared with Group C (P=0.007). The jugular venous pressure during and after THVE remained virtually unaltered compared with that before THVE, and the values among the 3 groups did not differ significantly (Fig. 1). The femoral venous pressure at
20 min during THVE was 10 ± 2.2 mmHg in Group A and 13.5 ± 2.4 mmHg in Group B, and it was significantly higher in Group B than in Group C ($P=0.013$). The portal venous pressure at 20 min during THVE was 14.8 ± 3.0 mmHg in Group A and 16.0 ± 5.2 mmHg in Group B, and it was significantly higher in Group B than in Group C ($P=0.024$).

**Influence on the serum biochemical profile:** In Group A, ALT remained within the normal range during THVE and after reperfusion (Fig. 2). In Group B, ALT was increased to 162.5 ± 122.5 U/L at 2 hr after reperfusion and was higher than that in Group C ($P=0.025$). ALT was within the normal reference range (10–100 U/L) in 2 dogs and increased in the remaining 2 dogs in Group B. On the other hand, ALP remained within the normal reference range (23–212 U/L) during THVE and after reperfusion, and the values in both groups did not differ significantly (Fig. 2).

The levels of BUN, Crea, Amyl and Lip before, during and after THVE were not significantly different among the 3 groups (data not shown). For 7 days after the operation, no major or minor complications were observed in any of the groups.

**DISCUSSION**

During THVE, a marked decrease in carotid arterial pressure and increases in femoral venous pressure and portal venous pressure were observed in Group B (occlusion of the celiac and cranial mesenteric arteries). Occlusion of the caudal vena cava caused congestion in the lower half of the body with an increase in femoral venous pressure. In addition, occlusion of the portal vein caused portal venous hypertension, and portal and femoral venous congestion resulted in a relative reduction in circulatory blood flow and a decrease in arterial pressure. It is likely that blood flow through alternative pathways, such as the caudal mesenteric artery, contributed to portal venous congestion after the Pringle maneuver and occlusion of the celiac and cranial mesenteric arteries in Group B. In contrast, the carotid arte-
for shorter times is considered to bring about reversible and paraplegia in dogs [14, 20]. However, aortic occlusion 60 min has been demonstrated to result in spinal cord injury hypertension and acidemia [7, 10, 18]. Aortic occlusion for 60 min has been demonstrated to result in spinal cord injury hypertension and acidemia [7, 10, 18]. Aortic occlusion for short times is considered to bring about reversible ischemic damage of the spinal cord because dogs have extensive collateral pathways from the aorta to the spinal cord [20]. In our study, none of the dogs in Group A developed paraplegia, arrhythmias or hypertension.

Although it is a common method in human hepatic surgery, dogs are considered to be intolerant of the Pringle maneuver in conjunction with acute occlusion of portal venous flow. Occlusion of the portal venous flow has been reported to induce portal hypertension and result in rapid cardiovascular collapse in dogs [13, 15]. Since humans and primates have a more efficient portosystemic collateral network than dogs, splanchic blood can return to the heart through this network during the Pringle maneuver [4]. In addition, it has been demonstrated that the Pringle maneuver combined with occlusion of the celiac and cranial mesenteric arteries is more effective in preventing portal hypertension in dogs than using only the Pringle maneuver alone [22]. In our study, the method involving the Pringle maneuver combined with occlusion of the thoracic aorta prevented portal hypertension and did not decrease the arterial pressure compared with the method involving the Pringle maneuver combined with occlusions of the celiac and cranial mesenteric arteries.

The significant increase in ALT in Group B was probably induced by hepatic ischemia-reperfusion injury. Since the portal venous pressure in Group B was higher than that in Group A, hepatic injury in Group B might have been a consequence of portal congestion. A previous study has demonstrated that hepatic ischemia-reperfusion injury is associated with congestion of the portal system [22]. However, contrary to our expectations, the serum levels of liver enzymes were not notably elevated.

In our study, BUN, Crea, Amyl and Lip were measured in order to evaluate the influence of THVE on other intraperitoneal organs. There were no significant changes in Groups A and B, and no major or minor complications associated with these organs were observed in any of the dogs after the operation.

We believe that occlusion of the intrathoracic aorta is technically easier than occlusions of the celiac and cranial mesenteric arteries. The intrathoracic aorta and celiac and cranial mesenteric arteries exist in the deepest region of the thoracic and abdominal cavities. So, dissection of these vessels from their perivascular tissues is time consuming and complicated by poor exposure. Moreover, isolation of celiac and cranial mesenteric arteries is more difficult than isolation of the thoracic aorta because much more fat adheres around celiac and cranial mesenteric arteries and the celiac plexus is located near these arteries.

In occlusion of the hepatic artery and portal vein in normal dogs, it has been reported that a 20-min occlusion is safe and the longest occlusion period possible without producing evidence of necrosis [15]. The theory that “the maximal time of canine hepatic ischemia is 20 min” was subsequently established, and our study was planned based on that theory. No basic studies of occlusion of inflow to and outflow from the liver in normal dogs have been conducted.

Fig. 2. The changes in the serum levels of alanine aminotransferase and alkaline phosphatase by THVE. Data are expressed as means ± standard deviation in Group A (black circles), Group B (white circles), and Group C (white squares). Pre: before THVE. Time after THVE: 10 and 20 min. Time after reperfusion: 1, 2, 6, 12 and 24 hr and 3, 5 and 7 days. * Significantly different from Group C (P<0.05).

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in veterinary medicine. In humans, 60 min of ischemia can be safely achieved under THVE or Pringle maneuver for normal livers, and an intermittent Pringle maneuver of repeated occlusion of 15 to 20 min with a reperfusion time of 5 min between each period of occlusion is generally used [16].

In conclusion, THVE for 20 min was demonstrated to be a feasible and safe method in dogs. In addition, the influence on the hemodynamic status during THVE was lesser for occlusion of the thoracic aorta and the prehepatic and posthepatic caudal vena cava using the Pringle maneuver than by occlusion of the celiac and cranial mesenteric arteries and the prehepatic and posthepatic caudal vena cava with the Pringle maneuver. Therefore, the THVE technique of temporary occlusion of the thoracic aorta and the prehepatic and posthepatic caudal vena cava using the Pringle maneuver is suggested to be of clinical value for canine hepatic surgery, including those involving the removal of a large right-divisional hepatic tumor and attenuation of intrahepatic portosystemic shunts.

REFERENCES