Effect of Food on Liver Circulation in Conscious Dog

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ABSTRACT. Hepatic hemodynamics and the liver oxygen supply-uptake relationship, in response to eating, were investigated in a chronically catheterized conscious dog method. Portal venous pressure was significantly increased after eating, however was within the normal range reported previously. Hepatic venous pressure correlated well with portal venous pressure throughout the experiment, therefore, the pressure gradient of the portal system was unchanged. Hepatic venous oxygen content, correlated well with liver oxygen extraction, was unchanged after eating. Therefore, it is possible to assume that liver oxygen supply-uptake relationship is well maintained during digestion of food. ---KEY WORDS: conscious canine, food, liver oxygen supply-uptake relationship, portal hypertension, pressure gradient of portal system.


Food intake effects liver functions such as carbohydrate, protein, and fat metabolism, formation and excretion of bile, detoxification, phagocytosis, immunoreactions, and synthesis of blood coagulation factors [9, 10, 19, 22, 23, 26, 27]. These functions are also closely related to liver oxygenation. For example, a decrease in liver oxygen supply results in centrilobular necrosis which contributes to a disruption of these liver functions.

Over the last several decades, the effects of food intake on liver hemodynamics have been reported using direct and indirect methods [1, 6, 30, 35]. Postprandial hyperemia in mesenteric region caused by increased mesenteric blood flow is well documented [1, 6, 9]. However, this postprandial hyperemia effect on the portal venous pressure has never been examined.

A large number of studies have been made on liver oxygen supply-uptake relationship under anesthesia [11, 20, 21, 29, 31-33]. However, few attempts have been made to understand how food intake affects liver oxygenation in the conscious condition. Recently, in veterinary medicine, nutritional therapy has been recommended for patients with liver disease such as hepatic fibrosis, hepatitis, fatty liver, and portosystemic shunt. A thorough understanding of liver oxygenation in response to eating is essential.

The purpose of the present study was to investigate 1) whether or not portal hypertension occurred, and 2) the oxygen supply-uptake relationship in response to eating. In this preparation, an original chronically catheterized dog model was utilized.

MATERIALS AND METHODS

Animals and surgical preparation: Five healthy adult mongrel dogs with negative microfilaria tests, weighing 7.3±1.4 kg, fasted for 24 hr were used. Acepromazine maleate (0.05 mg/kg, SC) was administered before induction, and anesthesia induction was induced with ketamine (10 mg/kg, IV). During surgery, anesthesia was maintained with 1.0–1.5% halothane. The animals were intubated, and ventilated using a quantitative respirator (KVI-1+1, Kimura Medical Instruments). A 16G heparin coated catheter (Anthron Catheter, Toure Medical Corporation) was inserted into the left carotid artery and passed distally for the determination of arterial pressure (AP) and for blood sample collection. Another 16G heparin coated catheter was inserted into the left jugular vein and passed distally into thoracic cava for measurement of central venous pressure (CVP) and blood sample collection. A lateral thoracotomy was performed at the 7th/8th intercostal space. The muscular part of the diaphragm was incised and a 16G heparin coated catheter was inserted into the vena cava and passed into the hepatic vein for determination of hepatic venous pressure (HVP) and blood collection. After closure of the diaphragm and thoracic incision, a midline laparotomy was performed and a 16G heparin coated catheter was inserted into the portal vein to measure portal venous pressure (PVP) and to collect blood. The abdominal incision was closed. Hepatic and portal venous catheters were brought through the abdominal wall and placed in the interscapular area with other catheters. The experimental dog allowed to recover anesthesia. Three way stopcocks were attached to all catheters and were flushed with heparinized saline twice a day. Ampicillin (25 mg/kg, BID) was administered throughout the experiment.

Measurements and calculations: A thermal recorder (WS-682G, Nihon Kohden) was used via a polygraph (RMP-6018M, Nihon Kohden) to record arterial pressure (AP), central venous pressure (CVP), hepatic venous pressure (HVP), and portal venous pressure (PVP). Mean arterial pressure (MAP) was used as hepatic arterial pressure (HAP) since the hepatic artery is a branch of the abdominal aorta. Arterial, venous, portal venous, and hepatic venous blood samples were obtained for measurements of pH/gas tensions and oxygen content and hemog-
lobin concentration (Hb) using a blood gas analyzer (GASTAT-1, Technomedica), and cytometer (MEK-5158, Nihon Kohden). The pressure gradient of the portal system (PSP) was calculated as the subtraction of the hepatic venous pressure from the portal venous pressure (PVP-HVP).

**Experimental protocol:** One week postoperatively, hemodynamic parameters and blood samples were obtained from each animal after a 24 hr fasting period (all dogs were usually fed once a day). After initial hemodynamic parameter determinations, maintenance energy requirement of a high protein diet (70 KJ/kg + 70 KJ, Prescription Diet Canine p/d, Hill’s Pet’s Products) was fed to each animal. Ninety minutes following feeding, hemodynamic parameters and blood samples were obtained; all previous estimates of mesenteric circulation have been acquired 30–90 min after feeding [1, 6]. Pressures were measured in the standing position and the zero pressure was referenced to the right atrium previously verified at surgery. All data was taken between 15:00 and 17:00 pm which was the normal feeding time. Each experimental dog was subjected to 2 to 4 measurements performed for a total of 13 periods of data collection.

**Statistics:** Data were represented by means ± standard deviation (SD). Paired Student’s t tests were used to determine significant differences from the control values. Linear regression by least squares was used to describe the relation between portal venous pressure and hepatic venous pressure. Significant difference was considered of P value was less than 0.05.

**RESULTS**

Mean arterial pressure was insignificantly changed after eating when compared to the control level. Portal venous pressure and hepatic venous pressure were significantly increased after eating (p<0.05), but the pressure gradient of the portal system, calculated as the subtraction of hepatic venous pressure from portal venous pressure, was not significantly changed throughout the experiment (Fig. 1).

Table 1 shows changes in blood gas parameters before and after eating.

| Table 1. Changes in blood gas parameter before and after meal (mean±SD) |
|------------------|------------------|------------------|------------------|------------------|------------------|
| Arterial blood   | pH | PCO₂ (mmHg) | HCO₃⁻ (mmol/L) | PO₂ (mmHg) | O₂ saturation (%) | O₂ content (ml/d) |
| Control          | 7.46±0.03 | 35.2±3.0 | 23.1±2.8 | 100.1±9.7 | 97.7±0.5 | 17.8±3.2 |
| After meal       | 7.47±0.04 | 32.2±4.4 | 23.6±4.4 | 89.6±9.9 | 97.0±1.3 | 16.8±3.2 |
| Venous blood     | Control   | 7.47±0.03 | 38.2±4.7 | 24.9±3.2 | 31.5±3.4 | 60.1±5.6 | 12.6±1.8 |
| After meal       | 7.42±0.04 | 40.8±2.6 | 26.6±3.0 | 30.1±5.0 | 57.4±8.8 | 11.7±2.2 |
| Portal venous blood | Control | 7.42±0.03 | 38.9±3.3 | 24.9±2.5 | 46.0±2.2 | 82.2±3.4 | 14.9±1.8 |
| After meal       | 7.42±0.05 | 39.2±3.4 | 25.5±2.9 | 43.0±2.1 | 78.8±2.3 | 13.4±0.8 |
| Hepatic venous blood | Control | 7.43±0.03 | 36.8±5.6 | 24.1±3.9 | 35.8±5.4 | 68.3±7.4 | 12.8±2.7 |
| After meal       | 7.42±0.05 | 39.0±4.4 | 26.1±3.3 | 35.0±6.9 | 67.0±11.0 | 11.0±1.7 |

Significant changes from control: *p<0.05.

After a meal, PO₂, oxygen saturation, and oxygen content of portal blood were significantly lowered (p<0.05), but pH, PCO₂, and HCO₃⁻ of portal blood were not significantly changed when compared to the control level. All parameters of arterial blood, venous blood, and hepatic venous blood were not changed significantly by eating.

**DISCUSSION**

Previously reported portal venous pressures in the normal dog have ranged 6 to 12 mmHg [3-5, 7, 11, 12, 20, 28]. The wide range of normal portal venous pressure can be due to extraneous factors such as anesthesia and respiration. The majority of anesthetics influences both systemic and regional circulation, including the portal vasculature, with both increases and decreases of varying degrees reported [7, 31-33]. Positive pressure ventilation decreases cardiac output and increases intra-abdominal pressure that increases portal venous pressure [7, 29]. In the present study, portal venous pressure in the control state was 6.1 ± 1.3 mmHg (low normal level previously reported). There are two possible explanations. First is
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that our data was acquired in a conscious model and therefore was not affected by anesthesia or positive pressure ventilation. Secondly, low portal flow due to a 24 hr fast may decrease portal pressure. After a meal, portal venous pressure was significantly increased with the average value being 8.2 ± 0.9 mmHg. This showed that food intake can increase portal venous pressure, but within the physiological range reported. This increase in portal venous pressure may be due to an increase in portal flow after food ingestion. There are many biochemical studies which support these findings; the increase of amino acids and glucose as well as glucagon leads to an increase in portal flow [10, 24, 25, 27]. In this study, a high protein diet was fed to the experimental animals, therefore, it is assume that portal flow was increased after eating. Naturally we cannot document any indices of portal flow without measuring it directly. The use of electromagnetic flowmeters gives insight into the changes in portal venous blood flow. However, the measurement of portal venous blood flow using an electromagnetic flowmeter around the vessel has been technically difficult. The portal vascular wall has such low resilience that the electromagnetic flowmeter is difficult to place around the portal vein with the correct angle [2]. It needs further consideration that the establishment of measurement system in portal venous blood flow under conscious condition.

Heaptic venous pressure was significantly increased after eating and the increase was the same as portal venous pressure. Therefore, the pressure gradient of the portal system (that was calculated as the subtraction of heaptic venous pressure from portal venous pressure) did not change before and after eating. These findings suggest that intrahepatic portal vascular resistance must have decreased during digestion. In addition, decreases in intrahepatic portal vascular resistance may prevent development of portal hypertension after a meal. Metabolites in portal blood to the intrahepatic portal system that exhibit demonstrable vasodilator effects on the liver circulation and that may stimulate presinusoidal sphincter relaxation by actions of K+, H+, CO2, and adenosine [8, 17]. The portal blood CO2 was not significantly increased during digestion however the other parameters described above were not measured in our study.

Liver oxygen extraction ratio has been used for assessing liver oxygenation, since it reflects changes in both oxygen delivery and uptake [5, 11, 18, 29]. In addition, liver oxygen extraction ratio increases in response to a decrease in hepatic venous oxygen content [21]. Therefore, hepatic venous oxygen content would be a simple and appropriate index of liver oxygen supply-uptake relationship in case that is difficult to evaluate liver oxygen extraction ratio directly. In this study, hepatic venous oxygen content did not change throughout the experiment in spite of a large decrease in the portal venous blood oxygen content. Two hypotheses are possible to explain our findings. One is that a large increase in portal flow maintained the oxygen supply to the intrahepatic portal system within a normal range. The other is that a large increase in hepatic arterial blood compensated for the lack of portal venous oxygen supply based on the mechanism of reciprocity of total hepatic flow (RTHF) [26]. This mechanism compensates for decreased (or increased) hepatic blood flow due to a reduction (or increase) of either portal vein or hepatic arterial flow by increasing (or decreasing) blood flow in the artery or vein. In addition, this mechanism has been widely accepted and verified [3, 13-16]. Since there are no data regarding both portal venous and hepatic arterial blood flow, we can now not propose an answer to the hypotheses. In conclusion, the liver oxygen supply-uptake relationship is well maintained after a meal conducted under conscious condition in dog.

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