Korean J. of Pharmacology
Vol. 23, No. 1, pp. 15-23, 1987

Studies of Alterations in Spleno-Hepatic Reflex in Portal Hypertensive Cats

Hwan Kyu Song, Byung Yong Rhim, Chi Dae Kim, Ki Whan Hong*

Department of Pharmacology, College of Medicine, Pusan National University, Pusan 600, Korea

ABSTRACT

To elucidate the mechanism of splanchnic hyperemia associated with chronic portal hypertension, we have investigated the alteration in visceral reflexes in conjuction with circulatory hemodynamics in portal ligated portal hypertension in cats. When capsaicin, bradykinin and vasopressin were injected via splenic artery of sham cat, respectively, they caused not only reflex excitation of systemic arterial pressure, but also elevation of splenic venous pressure with unchanged heart rates. Simultaneously, they evoked the sympathetic efferent excitation of liver (spleno-hepatic reflex) as well as of spleen (spleno-splenic reflex). Similarly, capsaicin upon pledging on the liver surface evoked a significant increase in the pressor reflex with hepatic nerve excitation (hepato-hepatic reflex). After portal ligation, the splenic venous pressure was gradually elevated in association with decrease in systemic arterial pressure. However, the excitation of pressor reflex was enhanced on the 2nd day, thereafter, being returned to the control, and the reflexly induced spleno-splenic, spleno-hepatic and hepato-hepatic sympathetic excitations were significantly diminished on the 8th day following portal vein ligation.

In conclusion, it is suggested that sympathetic reflexes to spleen and liver are specifically intervened by the same central pathways and furthermore, the diminution of these viscero-visceral reflex excitations after portal ligation may be related to the intestinal hyperemia.

Key Words: Viscero-visceral reflexes; Portal hypertension; Capsaicin; Bradykinin; Splanchnic hyperemia

INTRODUCTION

It is widely known that the portal vein stenosis in rat leads to an increase in portal venous inflow in association with an increased portal venous pressure as a typical change of circulatory hemodynamics of chronic portal hypertension (Vorobioff *et al.*, 1983; 1984; Sikuler *et al.*, 1985). These alterations are reported not only in the animal experiments with CCl_4-induced cirrhosis (Chojkier and Groszmann, 1981; Kitano *et al.*, 1982) or biliary cirrhosis (Bosch *et al.*, 1983), but also in the pathologic conditions associated with portal hypertension in human (Epstein *et al.*, 1977; Murray *et al.*, 1958). The characterizations of these circulatory hemodynamics which have been observed are: 1) An increase in blood flow to splanchnic organs including kidney, 2) An elevation of portal venous pressure with a decrease in vascular resistance, 3) An increase in cardiac output accompanying with a decrease in systemic vascular resistance (Murray *et al.*, 1958; Witte *et al.*, 1974; Witte and Witte, 1983). Recently, on the mechanisms responsible for these phenomena, an increase in plasma glucagon (Benoit *et al.*, 1984) or prostacyclin level (Hamilton *et al.*, 1982; Bruix *et al.*, 1985), a functional alteration in beta-adrenergic receptors in the splanchnic organs (Kroeger and Groszmann, 1985), and a decreased sensitivity of the splanchnic vasculature to catecholamines (Kitano *et al.*, 1982; Kiel *et al.*, 1985) have been demonstrated.

* To whom reprint requests should be addressed.

However, it remains unclarified as to whether a change in sympathetic reflex excitation is accompanied in conjunction with development of portal hypertension.

Therefore, in this study to elucidate the mechanism of the intestinal hyperemia yielded in association with chronic portal hypertension, we have investigated the alterations in the viscero-visceral reflexes in relation with circulatory hemodynamics in portal hypertensive cats following portal vein ligation.

MATERIALS AND METHODS

Animals

Male cats (weighing 2.4-2.8 kg) were housed in the individual stainless cages and allowed free access to cat-food and water ad libitum for 3 days.

Portal vein ligation

Cats were anesthetized with pentobarbital sodium (35 mg/kg, i.p.). After midline incision of the abdomen, the common portal vein was dissected free of surrounding tissues.

Under placing a blunt end needle of 11 or 12 gauge alongside the vein, the ligature was made snugly with the No. 2 silk to the vein and needle, together. After removal of the needle the abdominal wall was closed and the animal was injected with penicillin G (50,000 units/kg, i.m.). Thereafter, the cats were allowed to recover from anesthesia and to return to the vivarium. In sham-operated cats the abdomen was opened and the manipulation of portal vein was the same without ligature.

Circulatory hemodynamic study

Cats were free from a diet except water for 24

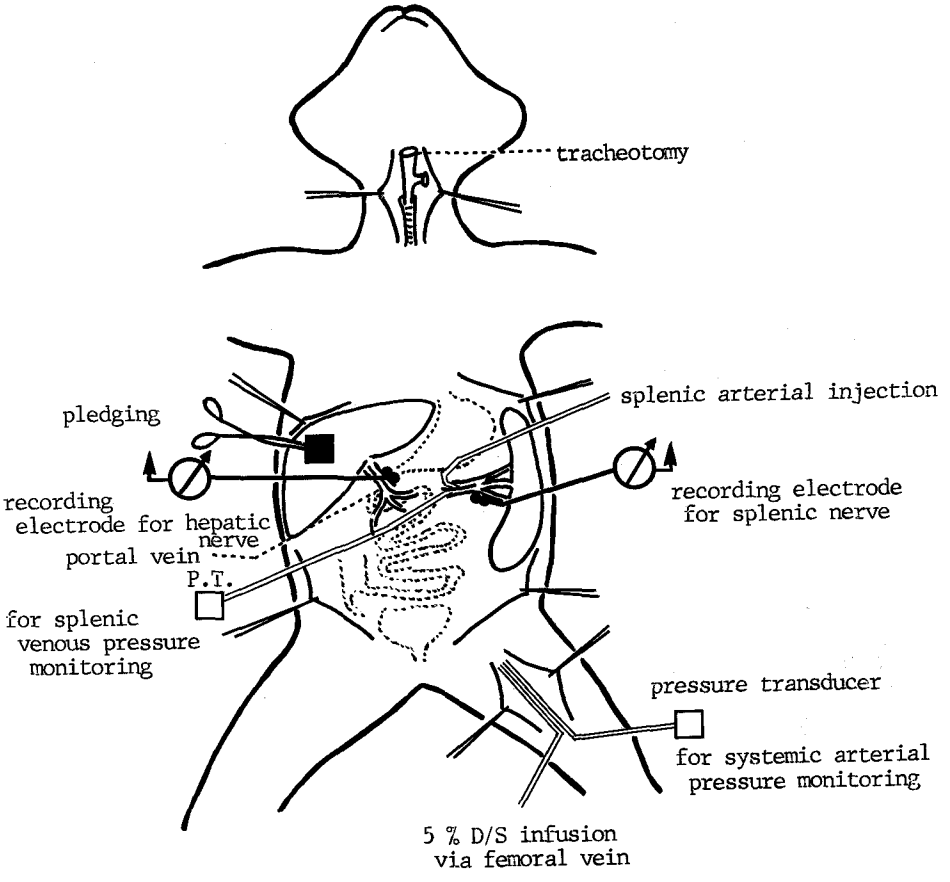

Fig. 1. Diagram of preparation for administering chemicals and recording nerve discharges from visceral sympathetic efferent fibers.

hours before experiment. They were anesthetized with ethyl carbamate (urethane, 1.0 g/kg, i.p.). After intubation, the vagus nerves were cut bilaterally. A polyethylene catheter was inserted into the femoral vein for infusion of 5% dextrose-saline. A second catheter was inserted into the femoral artery for the measurement of arterial blood pressure by using Statham pressure transducer (Model P23ID). Arterial blood was sampled throughout the experiment. The pH was maintained at 7.4 ± 0.5 by infusing sodium bicarbonate (1.5%), intravenously. Body temperature was monitored and maintained at 37 ± 0.5°C with heating pad and lamp.

Viscero-visceral reflexes

After exposing the spleen, all the branches of splenic vasculature were ligated and sectioned except that the main splenic artery and vein were left. The splenic artery was cannulated via left gastric artery or gastroepiploic artery for injection of drugs into the spleen and the splenic vein cannulated through a gastroepiploic vein to monitor splenic venous pressure (Fig. 1).

After idenification fo splenic and hepatic nerves, they were sectioned for recording the respective efferent nerve activity from the central end. Multifiber activities of splenic and hepatic nerves were recorded by using sleeve electrodes (Narco Bio-Systems, 710-0005) connected to High gain coupler (Narco Bio-Systems, type 7310), and they were integrated at 10-second interval by Integrator (Narco Bio-Systems GPA 10) and expressed as spikes per second. The percent changes of discharge rates in response to algogenic drugs were calculated as a function of 60-second control rates.

For examination of hepato-hepatic reflex we applied small pledgets (1.5 × 1.5 cm in width of gauze) soaked with capsaicin (10 μg/ml) on the liver surface. In this case the final concentration of capsaicin applied was 0.2 μg in 1.0 ml volume.

After pledging with capsaicin, the pledgets were removed and the abdominal cavity was washed out with warmed normal saline to eliminate the residual drug effect. No response was evoked by the vehicle itself in which capsaicin was dissolved.

Drugs

Capsaicin (8-methyl-N-vanillyl-6-nonenamide, Sigma), bradykinin triacetate (Sigma), vasopressin (lysine vasopressin, Sigma) and atropine sulfate (Sigma) were used in this experiment. Capsaicin was dissolved in the solution of 10% tween 80, 10% ethanol and saline. Capsaicin, bradykinin and vasopressin were injected in volumes of 0.2 ml and flushed with 0.1 ml of saline. Injection time required was 3-5 sec.

Statistical analysis

All values are expressed as the mean ± S.E. of mean. Results within groups were compared with Student's t-test. Values of $p<0.05$ were judged to be significant.

RESULTS

I. Viscero-visceral reflex in sham-operated cats

1) Spleno-hepatic reflex: To evoke the spleno-hepatic reflex, the algogenic substances, capsaicin (1-2 μg) and bradykinin (0.5 μg), and the vasoactive substance, vasopressin (0.2 unit) were injected through the splenic artery. All these drugs caused not only the reflex excitations of systemic arterial pressure, but also of splenic venous pressure without any change of heart rates as shown in Fig. 2 and Table 1. Simultaneously, the enhanced efferent reflex activity (increased approximately by 16-26%) to liver (spleno-hepatic reflex) as well as that to spleen (spleno-splenic reflex) was occurred.

However, when bradykinin or vasopressin was administered via superior mesenteric or hepatic artery, the sympathetic efferent reflex activity to spleen was less in degree than that occurred when capsaicin was injected via the same routes (mesentero-splenic and hepato-splenic reflexes) as illustrated in Table 2.

Nevertheless, the injection of these drugs via common carotid artery or femoral vein did not evoke the reflex excitations of sympathetic nerve and cardiovascular system.

2) Hepato-hepatic reflex: In this study the reflexly induced hepatic nerve excitation in response to capsaicin was studied and the data are shown in Table 3. Application of capsaicin (2.0 μg) on the liver surface caused a significant increase in the pressor reflex (16.7 ± 4.4 mmHg, $p<0.05$) in association with an increase in hepatic nerve reflex activation (20.9 ± 2.1%, $p<0.01$). However, the reflex changes in heart rates and splenic venous pressure were trivial.

II. Portal hypertensive cats

1) Time-course changes in basal hemodynamics: In this experiment the circulatory hemodynamic excitation was observed according to varying time-courses of portal vein ligation as shown in Table 4.

Table 1. Hepatic nerve activities in association with hemodynamic responses to algogenic and vasoactive substances which were injected via splenic artery in sham-operated cats

	Mean arterial pressure (Δ mmHg)	Heart rate (Δbeats/min)	Splenic venous pressure (Δ mmHg)	Hepatic nerve activity (Δ% of control)
Capsaicin 1.0 μg	16.3±1.7**	−7.7±11.2	4.4±0.7*	25.7±3.1**
Capsaicin 2.0 μg	26.1±4.0**	0.7±9.3	6.2±1.3**	33.6±3.2**
Bradykinin 0.5 μg	19.7±1.7**	−3.3±5.2	5.6±1.2**	30.9±1.7**
Vasopressin 0.2 unit	24.4±5.7*	−18.3±5.2	4.5±0.4**	29.5±3.7**

Each data represents the mean ± S.E.M. of 5-7 experiments.
Δ represent the changes of increase or decrease (−).
Asterisks denote the significant difference from the control value (*, $p<0.05$; **, $p<0.01$).

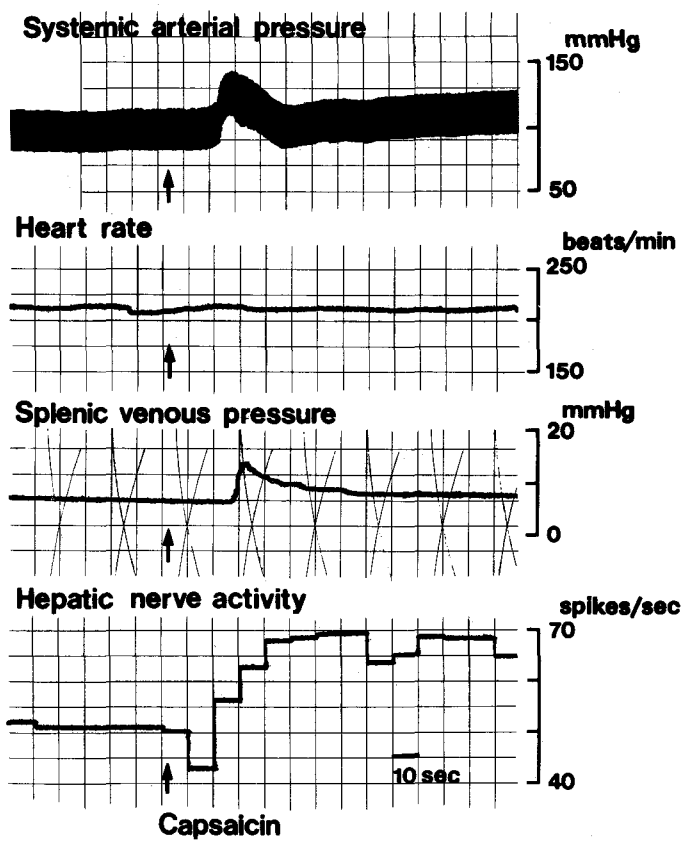

Fig. 2. Typical tracing of the cardiovascular hemodynamics and hepatic efferent nerve activity induced by capsaicin (2.0 μg) injected via splenic artery.

Table. 2. Spleno-visceral and viscero-splenic reflexes in response to capsaicin, bradykinin and vasopressin, respectively, in sham-operated cats

	Capsaicin 1.0 μg	Bradykinin 0.5 μg	Vasopressin 0.2 unit
	Efferent nerve activity, Δ% of control		
Spleno-visceral reflex			
Spleno-splenic	16.9±3.1*	20.6±4.8*	24.1±4.3**
Spleno-hepatic	19.9±4.1*	26.5±4.4**	27.2±6.6*
Viscero-splenic reflex			
Mesentero-splenic	21.3±5.3*	10.4±3.3	6.1±3.5
Hepato-splenic	23.4±4.8**	6.3±3.7	2.4±1.9

Spleno-visceral reflexes were evoked by injection of drugs through splenic artery and the sympathetic nerve activity was determined at splenic and hepatic nerve, respectively. In the case of viscero-splenic reflexes, drugs were injected through splenic and superior mesenteric artery, respectively and sympathetic nerve activity was determined at splenic nerve. See other legends in Table 1.

Table. 3. Cardiovascular and hepatic nerve responses to capsaicin pledged on the liver surface in sham-operated cats

Mean arterial pressure (Δ mmHg)	Heart rate (Δ beats/min)	Splenic venous pressure (Δ mmHg)	Hepatic nerve activity (Δ% of control)
16.7±4.4*	4.1±2.8	1.9±0.5	20.9±2.1**

Hepatic pledging was conducted to estimate hepato-hepatic reflex.
Each data represents the mean ± S.E.M. of 5 experiments.
*, $p<0.05$; **, $p<0.01$; Compared to control value. See others in Table 1.

Table 4. Actual levels of the circulatroy hemodynamics and hepatic nerve activities in sham-operated and portal vein-ligated cats

	Sham-operated	Days after portal vein ligation		
		2	4	8
Mean arterial pressure, mmHg	95.1±2.6	86.7±4.4	78.3±3.3**	86.0±3.3*
Heart rate, beats/min	187.3±18.1	192.3±8.4	209.5±10.9	182.3±2.6
Splenic venous pressure, mmHg	6.4±0.8	11.1±0.7**	15.1±1.3**	20.3±0.5**
Hepatic nerve activity, spikes/sec	46.2±3.5	45.4±7.0	45.1±3.5	47.9±4.5
Splenic nerve activity, spikes/sec	51.7±7.2	48.3±5.8	52.3±8.3	49.9±6.4

Each data represents the mean±S.E.M. of 5-7 experiments.
Asterisks denote the significant difference from the corresponding level of sham-operated group (*, $p<0.05$; **, $p<0.01$).

Table 5. Time-course changes in the circulatory hemodynamics and hepatic nerve activities in response to capsaicin pledged on the liver surface after portal vein ligation in cats

	Sham-operated	Days after portal vein ligation		
		2	4	8
Mean arterial pressure, ΔmmHg	15.4±1.4	23.4±4.6*	16.3±3.2	18.4±5.9
Heart rate, Δbeats/min	2.3±3.7	2.1±2.3	1.8±2.7	3.3±0.6
Splenic venous pressure, ΔmmHg	1.7±0.5	1.5±0.3	3.0±1.5	0.8±0.5
Hepatic nerve activity, Δ% of control	22.7±2.4	24.3±4.9	18.7±3.4	14.9±1.5*

Each data represents the mean ± S.E.M. of 5-7 experiments.
*, $p<0.05$; Compared to the value of sham-operated group.
Δ represents the chage of increase.

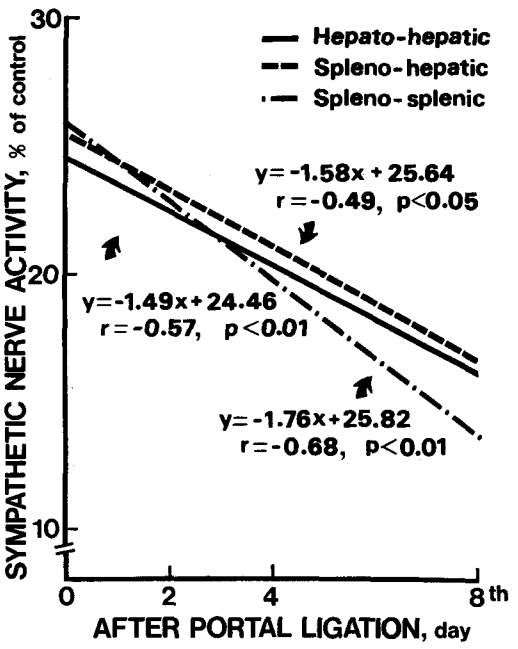

Fig. 3. Linear regression lines of the changes in sympathetic nerve excitation induced by algogenic substance, capsaicin as a function of date after portal ligation.

The splenic venous pressure was significantly elevated to 11.1 ± 0.7 mmHg ($p<0.01$) on the 2nd day and to 20.3 ± 0.5 mmHg ($p<0.01$) on the 8th day after portal ligation. In contrast, the systemic arterial pressure was decreased on the 4th day and thereafter, it was maintained at lower level without any change of heart rates. The actual nerve activity (spikes per sec) of the multifibers of hepatic or splenic nerve was, however, little changed.

2) Changes in viscero-visceral reflexes: To estimate the effect of portal ligation on the reflex excitation of spleno-hepatic and hepato-hepatic systems, capsaicin was applied as an evoker as described aforementioned at varying time-courses. As shown in Table 5, on the 2nd and 4th day after portal ligation the hepatic efferent reflex activity in response to capsaicin pledged on the liver surface (hepato-hepatic reflex) was not markedly altered when compared to that of sham-operated cat. However, on the 8th day after portal ligation, it was significantly diminished (14.9 ± 1.5 vs. 22.7 ± 2.4 % of control, $p<0.05$).

In contrast, the pressor reflex excitation evoked by capsaicin was rather accentuated on the 2nd day (23.4 ± 4.6 vs. 15.4 ± 1.4 mmHg of control, $p<0.05$) and thereafter, it returned to the control activity

To compare the time-course diminution of reflexly excited efferent activity, the precent change in the spleno-splenic, spleno-hepatic and hepato-hepatic reflexes were plotted as a function of date following portal ligation. As shown in Fig. 3, the sympathetic efferent reflex activities were inversely correlated with an increase in splenic venous pressure and three regression lines showed the similar slopes.

DISCUSSION

A circulatory state characterized by an increased splanchnic blood flow with a reduced splanchnic vascular resistance has been widely demonstrated both in the experimental and clinical portal hypertension (Murray *et al.*, 1958; Kontos *et al.*, 1964; Blanchet and Lebrec, 1982; Lebrec *et al.*, 1983; Witte and Witte, 1983; Vorobioff *et al.*, 1984).

Therefore, many studies have focused on the mechanism of the intestinal hyperemia. Recently, Benoit *et al.* (1984) have postulated the involvement of some humoral substances such as glucagon or alanine (a stimulator of release of pancreatic glucagon) in producing this hyperemia. Otherewise, the prostacyclin (Hamilton *et al.*, 1982) and prostaglandins (Bruix *et al.*, 1985) which were produced in response to increase in intraportal pressure were postulated to be responsible for the diminution of vascular resistance with increased splanchnic flow in portal hypertension or in the case of liver cirrhosis. On the other hand, Kroeger and Groszmann (1985) have examined the effect of propranolol reducing the elevated portal blood flow.

Capsaicin as a vanillylamide derivative with nonen side chain is known to have a pharmacological action producing excitation of several types of sensory neurons (nociceptive effect) when administered parenterally to experimental subject (Jessell *et al.*, 1978; Gamse *et al.*, 1980; Buck and Burks, 1983), in addition to the action to deplete substance P from primary afferent sensory neuron in the dorsal root ganglion and dorsal spinal cord (Virus and Gebhart, 1979; Burks *et al.*, 1985), and moreover, the role of substance P in the spinal cord and sympathetic outflow to the cardiovascular system have been overviewed (Pernow, 1983). Keeler *et al.* (1985) have demonstrated that intrathecal injection of substance P in anesthetized rats transmitted the excitatory information to the cardiovascular system via spinal sympathetic pathways. A tonic sympatho-excitatory role of substance P on the spinal cord is elsewhere illustrated (Gilbert *et al.*, 1982; Backman and Henry, 1984; Maurin *et al.*, 1984).

In this regard, it is assumed that capsaicin is more appropriate as an evoker of reflex rather than bradykinin or vasopressin since the latter two substances could evoke very weak splenic efferent excitation upon injection of these agents via superior mesenteric or hepatic artery.

In the present study, the reflex sympathetic excitation could be evoked in the hepatic as well as in the splenic efferent multifibers upon injection of capsaicin through splenic artery. Recently, Herman *et al.* (1982) have reported the presence of low pressure-sensitive baroreceptor in spleen, and they demonstrated that the excitation of afferent nerve ending in spleen caused reflex activation of cardiovascular system with an increase in sympathetic outflow to spleen. Thereafter, Calaresu *et al.* (1984) and Weaver *et al.* (1984) have demonstrated the role of chemosensitive baroreflex on the regulation of the cardiovascular hemodynamics. Thus, on the basis of these evidences, it was suggested that the central pathway of the sympatho-sympathetic reflex intervening between liver and spleen may be of identical one and furthermore, these visceral reflexes may be specific for spleen and liver since these viscero-visceral reflexes were not occurred when capsaicin was administered via femoral vein or common carotid artery.

Following portal vein ligation, an enhancement of reflex excitation of cardiovascular system was occurred in response to capsaicin on the 2nd day. Moreover, on the 8th day the hepatic and splenic nerve excitations were significantly diminished with little change in pressor reflex. Thus, it was presumed that under the condition of increased intraportal pressure (as reflected by splenic venous pressure) capsaicin-induced excitation of arterial pressure response could be highly sensitized in the early stage.

A question arose as to why the hepatic or splenic sympathetic nerve outflow was so markedly diminished on the 8th day without a significant reduction of pressor reflex. It is likely that the excitation of the mechano- and chemo-sensitive receptor of the sympathetic nerve ending in response to high intraportal pressure may cause to a large release of catecholamines for 7 days. Accordingly, as described by Takejasu *et al.* (1982), Wikberg *et al.* (1983) and Lurie *et al.* (1985), the concurrent down-regulation of the postsynaptic alpha-adrenoceptors caused by prolonged exposure to catecholamines leads to a reduced splanchnic vascular resistance. The mechanisms responsible for the supersensitivity of vascular beds to capsaicin on the 2nd after portal ligation can be ascribed to this early sympathetic hyperactivity. These assumptions are in good agreement with the results of Kitano *et al.* (1982) and Kiel *et al.* (1985) in which a vascular sensitivity to norepinephrine in the gastrointestinal tract has been reduced following portal hypertension or cirrhosis.

Based on the these evidences, it is summarized that following portal ligation the diminution of the splanchnic sympathetic efferent outflow may contribute to decreased splanchnic vascular resistance and intestinal hyperemia.

ACKNOWLEDGEMENT

We wish to thank Miss G.O. Lee for her technical assistance.

REFERENCES

Backman SB, Henry JL: *Effects of substance P and thyrotropin releasing hormone on sympathetic preganglionic neurons in upper thoracic intermediolateral nucleus of the cat. Can J Physiol Pharmacol 62:248-251, 1984*

Benoit JN, Barrowman JA, Harper SL, Kvietys PR, Granger DL: *Role of humoral factors in the intestinal hyperemia associated with chronic portal hypertension. Am J Physiol 247:G486-G493, 1984*

Blanchet L, Lebrec D: *Changes in splanchnic blood flow in portal hypertensive rats. Eur J Clin Invest 2:327-330, 1980*

Bosch J, Enriquez R, Groszmann RJ, Storer EH: *Chronic bile duct ligation in the dog: hemodynamic characterization of a hypertensive model. Hepatology 3:1002-1007, 1983*

Bruix J, Bosch J, Kravetz D, Mastai R, Rodes J: *Effects of prostaglandin inhibition on systemic and hepatic hemodynamics in patients with cirrhosis of the liver. Gastroenterology 88:430-435, 1985*

Buck SH, Burks TF: *Capsaicin: Hot new pharmacological tool. TIPS 4:83-87, 1983*

Burks TF, Buck SH, Miller MS: *Mechanism of depletion of substance P by capsaicin. Federation Proc 44:2531-2534, 1985*

Calaresu FR, Tobey JC, Heidmann SR, Weaver LC: *Splenic and renal sympathetic response to stimulation of splenic receptors in cats. Am J Physiol 247:R856-R865, 1984*

Chojkier M, Groszmann RJ: *Measurement of portal systemic shunting in rat by using γ-labeled microspheres. Am J Physiol 240:G371-G375, 1981*

Epstein M, Schneider N, Befeler B: *Relationship of systemic and intrarenal hemodynamics in cirrhosis. J Lab Clin Med 89:1175-1187, 1977*

Gamse R, Holzer P, Lembeck F: *Decrease of substance P in primary afferent neurons and impairment of neurogenic plasma extravasation by capsaicin. Br J Pharmacol 68:207-213, 1980*

Gilbert PFT, Emson PC, Hunt SP, et al.: *The effects of monoamine neurotoxins on peptides in the rat spinal cord. Neuroscience 7:69-83, 1982*

Hamilton G, Phing RCF, Hutton RA, Candon P, Hobbs KEF: *The relationship between prostacyclin activity and pressure in the portal vein. Hepatology 2:236-242, 1982*

Herman NL, Kostreva DR, Kampine JP: *Splenic afferents and some of their reflex responses. Am J Physiol 242:R247-R254, 1982*

Jessell TM, Iversen LL, Cuello AC: Capsaicin-induced depletion of substance P from primary sensory neurons. Brain Res 152:183-188, 1978

Keeler JR, Charlton CG, Heeke CJ: *Cardiovascular effects of spinal cord substance P: Studies with a stable receptor agonist. J Pharmacol Exp Ther 233:755-760, 1985*

Kiel JW, Pitts V, Benoit NJ, Granger DN, Shepherd AP: *Reduced vascular sensitivity to norepinephrine in portal hypertensive rats. Am J Physiol 248:G192-G195, 1985*

Kitano S, Koyanagi N, Sugimachi K, Kobayashi M, Inokuchi K: *Mucosal blood flow and modified vascular responses to norepinephrine in the stomach of rats with liver cirrhosis. Eur Surg Res 14:221-230, 1982*

Kontos HA, Shapiro W, Mauck HP, Patterson JLJr: *General and regional circulatory alterations in cirrhosis of the liver. Am J Med 37:526-535, 1964*

Kroeger RJ, Groszmann RJ: *Effect of selective blockade of β_2-adrenergic receptors on portal and systemic hemodynamics in a portal hypertensive rat model. Gastroenterology 88:896-900, 1985*

Lebrec D, Bataille C, Beucoff E, Valla D: *Hemodynamic changes in patients with portal venous obstruction. Hepatology 3:550-553, 1983*

Lurie KG, Tsujimoto G, Hoffman BB: *Desensitization of alphal adrenergic receptor-mediated vascular smooth muscle contraction. J Pharmacol Exp Ther 234:147-152, 1985*

Maurin Y, Buck SH, Wamsley JK, Burks TF, Yamamura HI: *Light microscopic autoradiographic localization of ^{3}H-substance P binding sites in rat thoracic spinal cord. Life Sci 34:1713-1716, 1984*

Murray JF, Dawson AM, Sherlock S: *Circulatory change in chronic liver disease. Am J Med 24:358-367, 1958*

Pernow B: *Substance P. Pharmacol Rev 85-141, 1983*

Sikuler E, Kravetz D, Groszmann RJ: *Evaluation of portal hypertension and mechanisms involved in its maintenance in rat model. Am J Physiol 248:G618-G625, 1985*

Takejasu K, Higuchi H, Fujita N, Uchida S, Yoshida H: *Desensistization of the alpha adrenergic receptor system in guinea pig vas deferens. Life Sci 31:89-110, 1982*

Virus RM, Gebhart GM: *Pharmacological actions of capsaicin: Apparent involvement of substance P and serotonin. Life Sci 5:1273-1284, 1979*

Vorobioff J, Bredfeldt JE, Groszmann RJ: *Hyperdynamic circulation in portal-hypertensive rat model: a primary factor for maintenance of chronic portal hypertension. Am J Physiol 244:G52-G57, 1983*

Vorobioff J, Bredfeldt JE, Groszmann RJ: *Increased blood*

flow from through the portal system in cirrhotic rat. Gastroenterology 87:1120-1126, 1984

Weaver LC, Fry HK, Meckler RL: *Differential renal and splenic nerve responses to vagal and spinal afferent inputs. Am J Physiol 246:R78-R87, 1984*

Wikberg JES, Akers M, Caron MG, Hagen P-O: *Norepinephrine-induced down regulation of alpha-1 adrenergic receptors in cultured rabbit aorta smooth muscle cells. Life Sci 33:1409-1417, 1983*

Witte CL, Witte MH: *Splanchnic circulatory and tissue fluid dynamics in portal hypertension. Federation Proc 42:1685-1689, 1983*

Witte CL, Witte MH, Bair C, Mobley WP, Morton D: *Experimental study of hyperdynamic vs. stagnant mesenteric blood flow in portal hypertension. Ann Surg 179:304-319, 1974*

=국문요약=

간문맥 고혈압 고양이에서 비-간 교감신경성 반사의 변동에 대한 연구

부산대학교 의과대학 약리학교실

송환규, 임병용, 김치대, 홍기환

만성 간문맥 고혈압에 동반하는 내장 충혈에 대한 발생 기전을 규명하기 위하여 고양이의 간문맥을 결찰하고 그 경과에 따라 비-간 교감 신경성 반사 흥분의 변동과 동시에 순환 역동학적 변동을 관찰하였다.

1. 대조 고양이(Sham 수술군)에서 비동맥을 통하여 capsaicin, bradykinin 및 vasopressin을 주사 하였을 때에는 전신 동맥압의 반사 흥분 뿐만 아니라 비정맥압의 상승을 초래하였다. 그러나 심박동수는 변화가 없었다. 동시에 비장(비-비 반사) 및 간장 (비-간 반사)에서 교감 신경의 반사 흥분을 일으켰다.
2. Capsaicin을 간 표면에 도포하였을 때는 간 신경 흥분 (간-간 반사)과 동시에 승압 반사를 유발시켰다.
3. 문맥 결찰 후에는 비정맥압은 시간 경과에 따라 증가 하였고 이에 동반하여 전신 동맥압은 감소하였다. 그러나 승압반사 항진은 제2일에 현저하게 야기되었고 그후 대조치로 회복되었다. 비-비 또는 비-간 교감 신경 반사 흥분은 제8일에 현저히 감약되었다.
4. 이상의 성적을 종합하면 비장 및 간장에 분포하는 교감 신경 반사 흥분은 동일한 중추 지배에 의하여 조절되고, 간문맥 결찰 후 내장 반사 흥분의 감소는 내장 충혈의 발생과 밀접한 관련이 있을 것으로 사료되었다.