

The Pathogenesis of the Postoperative Ascites Accumulation after Transthoracic Esophageal Transection for Esophageal Varices, Especially the Relationship between the Vagus Nerve and Ascites Accumulation

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Introduction

MURAKAMI et al.^{18,27)} in our surgical division noticed that in neurotomy cases of the hepatic branches of the vagus nerve when either the esophageal transection or the proximal gastrectomy was performed for esophageal varices, postoperative ascites flow was increased more than in non-neurotomy cases. But there was no difference of postoperative liver function between the neurotomy and the non-neurotomy groups.

HABERICH^{3,13,14,15)} demonstrated the presence of osmoreceptor in the hepatic portal circulation innervated by way of the hepatic branch of the vagus nerve.

Consistent with this hypothesis are the experimental results of NIJIMA¹⁾ which demonstrated an increase in the discharge rate of afferent fibers in the hepatic branch of the vagus in response to portal infusions of hyperosmolar solutions.

SCHNIDER et al.³⁵⁾ however were unable to confirm the presence of the osmoreceptor mechanism in the liver of a dog.

But in clinical cases, the group with denervation of hepatic branch of the vagus showed abundant postoperative ascites formation. It suggested that the hepatic branch of the vagus and liver osmoreceptor influenced ascites accumulation.

The present study in rats was undertaken to elucidate the presence of osmoreceptor, to evaluate the participation of hepatic branch of the vagus in this ascites accumulation, to investigate these changes after the production of cirrhosis of the liver, and to study the difference of ascites formation between the neurotomy and non-neurotomy groups after experimental production of liver cirrhosis.

Key words: Transthoracic esophageal transection, Hepatic branch of the vagus nerve, Experimental liver cirrhosis, Experimental ascites, Hepatic osmoreceptor.

索引語: 経胸の食道縦断術, 迷走神経肝枝, 実験肝硬変, 実験腹水, 肝浸透圧受容器.

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Methods

EXP. 1 The production of cirrhosis of the liver in rats by simultaneous administration of carbon tetroxide and pentobarbital sodium.

Male and female rats weighing 150–200 g were used. Pentobarbital sodium was dissolved in distilled water at a concentration of 0.5 g/l. This was the only drinking water available to the rats 1 week prior to the first inhalation and throughout.

Each wide mesh metal cage in which the rats were housed was placed in a wooden box, with a glass top (50×40×20 cm, i.e. 40 l. capacity). Twice a week compressed air was passed at the rate of 800 ml/min, bubbling through a bottle containing CCl₄, and into the box. CCl₄ was blown in for about 7–10 minutes. The rats were lightly anesthetized by the CCl₄, and then left in the box for a further 10 minutes. Then they were taken out. CCl₄ dosage was stopped after 8 weeks.

EXP. 2 Change of osmolality of carotid blood, after 1 ml of water was infused over 10 minutes into the portal vein.

Experiments were performed on female rats, weighing 200–250 g. Under intraperitoneal pentobarbital sodium anesthesia (0.01 ml/dose) an upper midline incision was made. The portal and superior mesenteric veins were exposed, an indwelling catheter for epidural anesthesia (Acoma) with a sharp edged shaped end was directly inserted through the superior mesenteric vein into the portal vein, and fixed to the mesenterium. By means of this improved method, indwelling catheters were inserted easily into the portal vein without bleeding, and an indwelling tube for epidural anesthesia was inserted into the common carotid artery in the same manner as usual venotomy technique³².

One ml of distilled water was infused into the portal vein for 10 minutes by means of continuous infusion pump. Blood samples for plasma osmolality were obtained from the carotid catheter during the control period, immediately after completion of the infusions and at 10 minute intervals until 50 minutes had passed. Blood samples were taken three times per rat, and statistical analysis was performed. Plasma osmolality was measured with a Fiske OR Osmometer.

EXP. 3 The relationship between the hepatic osmoreceptor and vagus nerve, and its change after experimental production of liver cirrhosis.

Experiments were performed on female rats, weighing 150–250 g. These rats were divided into the four groups: normal liver with non-vagotomy, normal liver with vagotomy, cirrhosis of the liver with non-vagotomy and cirrhosis of the liver with vagotomy.

Vagotomy group; Under ether anesthesia, a midline incision was made, surgical denervation of the liver was performed by transecting the hepatic branches of the vagus nerve below the diaphragm. This was done by cutting the lesser omentum containing vagus fibers traveling toward the porta hepatis. Still more truncal vagotomy and pyloroplasty were performed.

Non-vagotomy group; Only laparotomy was performed.

Cirrhosis of the liver; Experimental liver cirrhosis was made with the same method as the

Exp. 1, in the non-vagotomy and vagotomy groups. Two weeks, after rest, under ether anesthesia, a midline incision was made, an indwelling catheter was placed into the portal vein via the superior mesenteric vein, with the same method of Exp. 2, and passed subcutaneously to the dorsum of the neck and this was exposed and fixed to the skin.

Next, a cut down tube (Japan Medical Supply, C₂ or C₃ type) was placed in the bladder for the collection of urine. Ureteral catheterization was difficult for male rats but was comparatively easy for female rats. Because urine was easily discharged, and there was little residual urine, the bladder was tensioned temperately by the catheter. After the incision was closed, rats were confined in an exclusive cage.

In a non anesthetized state, after a relatively constant urine flow had been established, distilled water or 0.9% NaCl was infused into the portal vein at the rate of 0.1 ml/min or 0.2 ml/min, for 10 minutes. Urine flow was measured in an infinitesimal flowmeter which was developed for bioassay of ADH (Tokai Rikagaku Company).

EXP. 4 Experimental liver cirrhosis

Histologic examinations of four groups (normal liver with non-vagotomy, normal liver with vagotomy, liver cirrhosis with non-vagotomy, liver cirrhosis with vagotomy) were compared. A small midline incision was made and all the ascites was removed and measured.

EXP. 5 Measurement of hepatic blood flow by the hydrogen clearance tissue blood flowmeter, biochemical examination of blood and ascites, and histologic examination of the liver.

After the rats, which had cirrhosis of the liver by Exp. 4. were anesthetized with pentobarbital sodium (Nembutal), hepatic blood flow was measured by the hydrogen clearance tissue blood flowmeter³⁸⁾.

Blood samples were collected by cardiac puncture and total protein, albumin, globulin, A/G, cholinesterase, γ -GTP, al-phos, total cholesterol, GOT, GPT, LDH, and LAP of either blood or ascites were measured.

Sections of the liver were cut and stained with hematoxylin and eosin. Histologic examination of four groups (normal liver with non-vagotomy, normal liver with vagotomy, liver cirrhosis with non-vagotomy, liver cirrhosis with vagotomy) were compared.

Results

1) Experimental liver cirrhosis

Rats had grossly nodular and yellowish livers on naked eye inspection. The histological picture showed moderate to severe liver cirrhosis with generalized fibrosis, periportal chronic inflammation, bile duct proliferation and destruction of normal liver architecture with the formation of regenerated nodules (Fig. 1).

2) Change of osmolality of carotid blood after 1 ml of water was infused for 10 minutes into the portal vein.

Fig. 2 showed that osmolality of carotid blood had not dropped statistically immediately after portal infusion until a latent period of 10-30 minutes, but dropped after 30 minutes ($p < 0.05$),

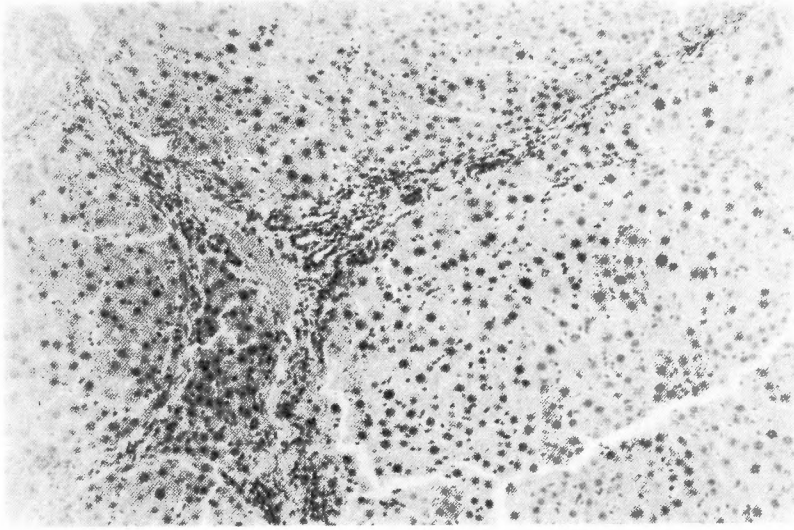


Fig. 1. Experimental liver cirrhosis in the rat. The histological picture showed moderate to severe liver cirrhosis with generalized fibrosis, periportal chronic inflammation, bile duct proliferation and destruction of normal liver architecture with the formation of regenerated nodules.

to 40 minutes ($p < 0.01$). And it recovered rapidly after 50 minutes. This result supports research that the liver is useful for the storage of minerals and fluid (*Haberich*)^{12,13,14}.

Consequently for 10 minutes after infusion starts, change of urine flow is scarcely influenced by the drop of osmolality of body fluid. So in the following experiments for hepatic osmoreceptor, the simple method was used where distilled water or 0.9% NaCl was infused into the portal vein.

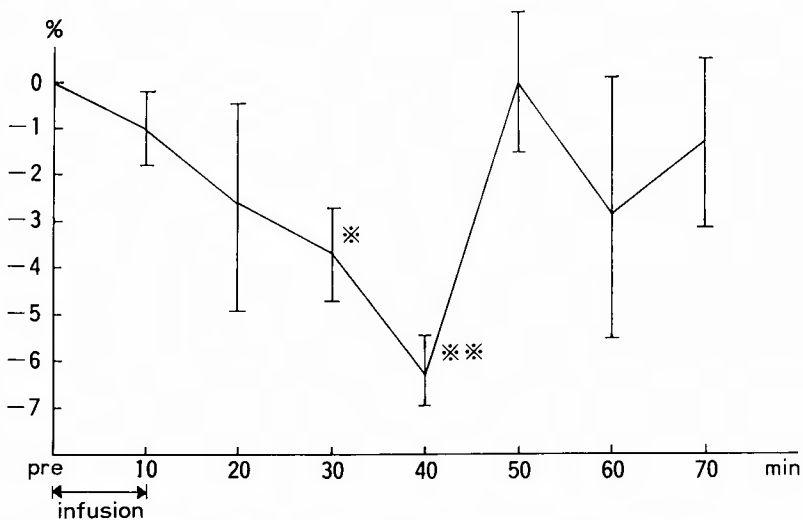


Fig. 2. Change of osmolality of carotid blood after 1 ml of water has been infused from 10 minutes into the portal vein. Female rats, under Pentobarbital anesthesia. Ordinates: decrease rate of osmolality in %. Abscissae: time in minutes. In the course of the infusion period of 10 minutes, 1 ml of water was infused into the portal vein. pre: preinfusion osmolality. Significance of differences compared with preinfusion rate. * $p < 0.05$, ** $p < 0.01$.

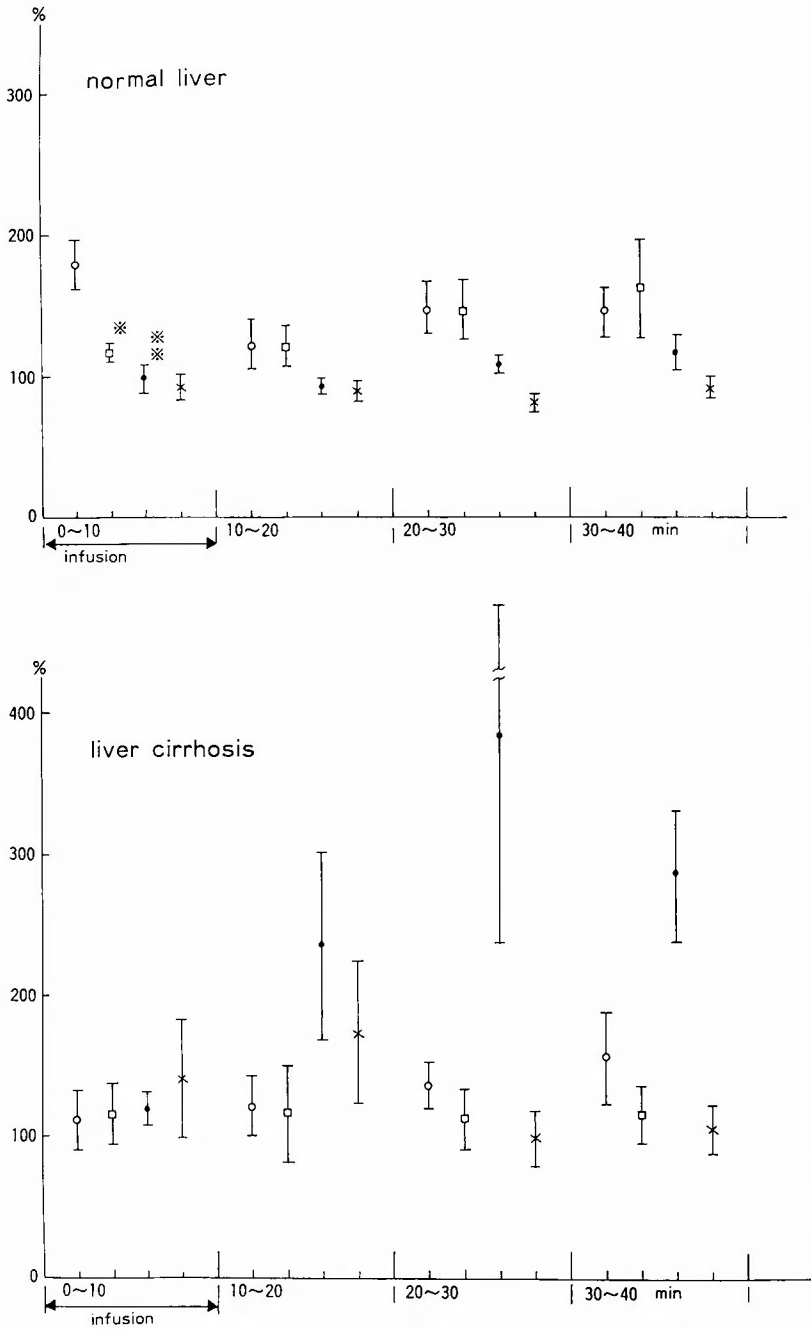


Fig. 3. The effect of diuresis on intraportal infusion of either water or 0.9% NaCl at the rate of 1 ml/min for 10 minutes. On female rats with normal liver and with experimental cirrhosis of the liver respectively with or without vagotomy. Ordinates: mean values and the bars show the standard errors. Initial diuresis has been taken as 100%. Abscissae: time in minutes. In the course of infusion period of 10 minutes, 1 ml of distilled water or 0.9% NaCl was infused into the portal vein. Significance of diuresis between distilled water and 0.9% NaCl (* $p < 0.01$), between with nonvagotomy and vagotomy (** $p < 0.05$).

3) The relationship between hepatic osmoreceptors and vagus nerve, and its change after experimental production of liver cirrhosis.

Fig. 3 showed the effects of either water or 0.9% NaCl infusions, at the rate of 0.1 ml/min, into the portal vein on urine flow, in the rats which had normal livers in either the non-vagotomy or vagotomy groups. These data were studied especially for first 10 minutes. The non-vagotomy group showed diuretic action immediately following the water infusion. However 0.9% NaCl infusion failed to increase urine flow. This data indicates the existence of hepatic osmoreceptors in the rats ($p < 0.01$).

In the vagotomy group the diuretic reaction was diminished during water infusions ($p < 0.05$). This possibility is supposed by liver denervation experiments, which demonstrated that intact afferent vagal innervation is a necessary for hepatic osmolality in rats.

In Fig. 4 urine flow during the infusion at the rate of 0.02 ml/min for 10 minutes showed a similar tendency to the results in Fig. 2.

Next, rats which have experimentally produced liver cirrhosis was examined with the same method. The non-vagotomy group of water infused rats showed no diuretic action at either 1 ml or 2 ml infusions.

In the vagotomy group with liver cirrhosis, urine flow increased or decreased and a definite tendency was not recognized.

Short Summary

[1] Our results suggest the presence of an osmoreceptor located in the liver and innervated by the vagus nerve.

[2] It was suggested that the liver osmoreceptor was destroyed by liver cirrhosis.

[3] In the vagotomy group with liver cirrhosis, osmoreceptor regulation mechanism was perhaps harmed seriously.

[4] The portal vein infusions of 0.9% NaCl did not show the diuretic action compared with that of distilled water. So increase in volume had little influence on urine flow.

[5] Tests with 1 ml of 2 ml infusions produced the same results.

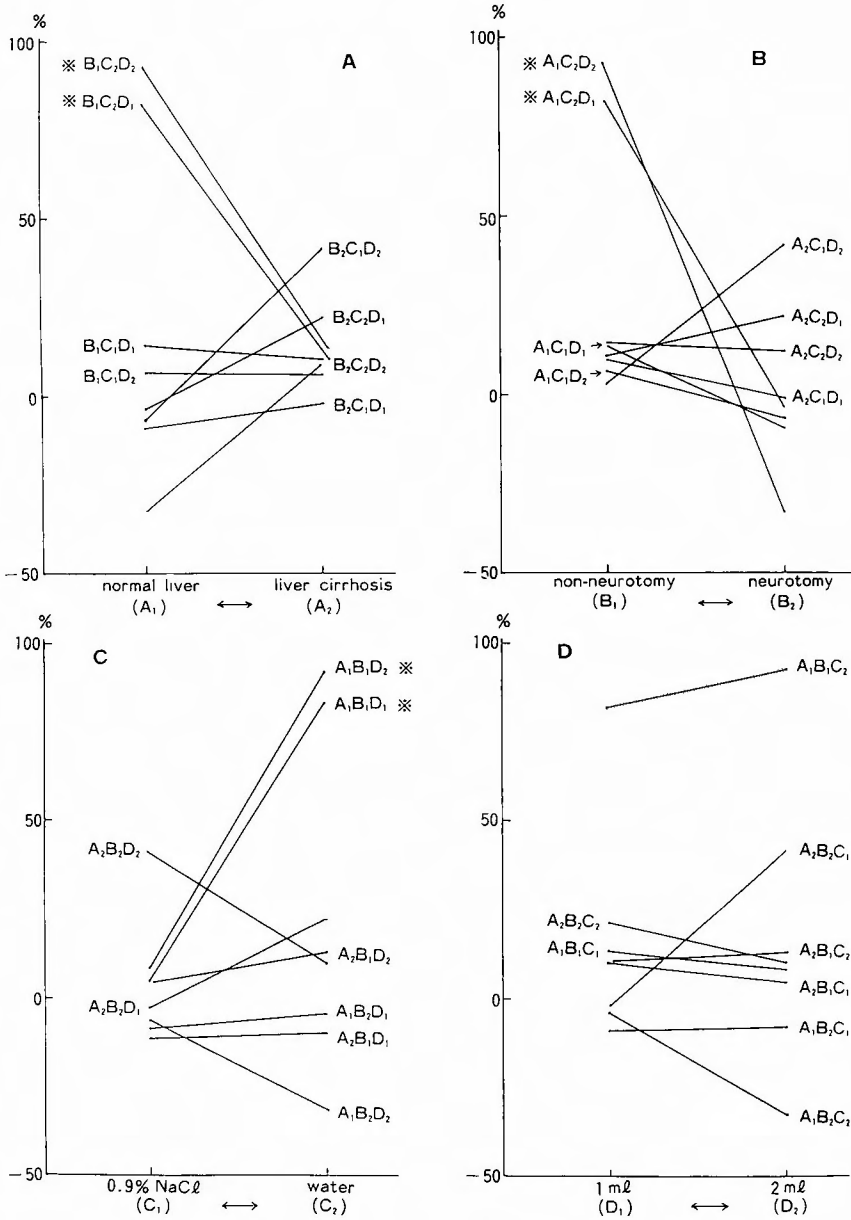
4) Experimental ascites

The volume of ascites was measured in all male rats. Vagotomy group produced abundant ascites as compared with non-vagotomy group. There was a statistically significant difference ($p = 0.003$) (Table. 1).

5) Measurement of hepatic blood flow by the hydrogen clearance tissue blood flowmeter, biochemical examination of blood and ascites, and histologic examination of the liver.

Results of hepatic blood flow by the hydrogen clearance tissue blood flowmeter were showed in Fig. 5. In normal liver rats, blood flow in vagotomy group was lower than that in non-vagotomy group. In liver cirrhosis groups, they showed lower rates than in normal liver groups, but there was no significant difference between the non-vagotomy and vagotomy groups. So it was assumed that the production of ascites was not influenced by blood flow of the liver.

In 10 kinds of biochemical examinations, a chief element analysis was used, and there were



P < 0.05

Fig. 4.

three chief elements. The first chief element was total protein, albumin, and cholesterol. The second chief element was al-phos, GOT and GPT. The third chief element was A/G and LDH. Two dimensional expression of the first chief and the second chief elements were classified in Fig. 6, but in rats with liver cirrhosis the non-vagotomy group and the vagotomy group were not classified.

Table 1. Ascites accumulation in male rats with cirrhosis of the liver.

| | Ascites (-) | Ascites (+) | Total |
|--------------|-------------|-------------|-------|
| Vagotomy (-) | 17 | 1 (5.5%) | 18 |
| Vagotomy (+) | 3 | 11 (78.6%) | 14 |

Fischer's direct probability, $p=0.0003$

As to histologic examination, histologic changes of the liver cirrhosis in vagotomy group was not detectably different from those observed in non-vagotomy group.

Discussion

VERNEY^{40,41)} proposed the existence of an osmoreceptor in the anterior hypothalamus, and that the osmoreceptor influenced the release of ADH from the posterior pituitary gland.

The studies of HENRY and PEARCE¹⁶⁾ implicated cardiac receptors in the control of vasopressin release, and VANDER and MILLER³⁹⁾ have proposed an intrarenal receptor capable of altering sodium excretion.

HABERICH et al.^{3,12,13,14)} were the first to describe diuretic or antidiuretic responses to infusions of hypo- or hypertonic fluids into the hepatic portal vein in rats, but similar systemic vein infusions were without any apparent effect. He demonstrated the presence of osmoreceptors in the hepatic circulation, and after neurotomy of the hepatic branch of the vagus nerve hepatic diuresis can no longer be triggered by intraportal infusion of water.

Moreover, he came to a conclusion that the afferents both from the peripheral volume receptors and the peripheral osmoreceptors in the portal circulation pass via the vagus nerve. The hypothalamic nuclei stand out as a control center where all the afferents from the osmoreceptors and volume receptors are integrated and coordinated. From there diuresis is regulated

| | |
|------------------------------|---------------------------------------|
| A1: normal liver | B1: non-vagotomy |
| A2: cirrhotic liver | B2: vagotomy including hepatic branch |
| C1: 0.9% NaCl infusion | D1: 1 ml/10 min infusion |
| C2: distilled water infusion | D2: 2 ml/10 min infusion |

Fig. 4. Using female rats infusion into the portal vein means of the rate of increase in urine flow during the infusion for 10 minutes.

A: normal liver (A1) ↔ cirrhotic liver (A2)

B: non-vagotomy (B1) ↔ vagotomy including hepatic branch (B2)

C: 0.9% NaCl infusion (C1) ↔ distilled water infusion (C2)

D: 1 ml/10 min infusion (D1) ↔ 2 ml/10 min infusion (D2)

Figure 3 showed changes of the rate of increase in urine flow in 16 groups assorted four items (A, B, C and D)

Fig. C showed the presence of osmoreceptor in the liver by reason of the significant difference between the 0.9% NaCl infusion and distilled water infusion groups with normal liver without vagotomy.

Fig. B showed that osmoreceptor was innervated by the vagus nerves judging from the significant difference between the non-vagotomy and vagotomy groups with normal liver when distilled water was infused.

Fig. A showed that osmoreceptor was injured by liver cirrhosis judging from the remarkable change observed in the non-vagotomy groups when distilled water was infused, whether liver cirrhosis exists or not.

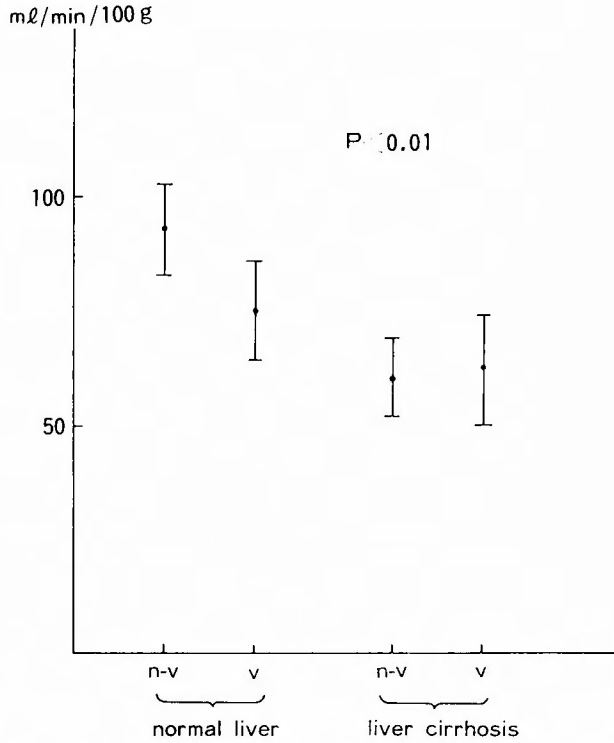


Fig. 5. Hepatic blood flow measured by the hydrogen clearance tissue blood flowmeter. Ordinates: hepatic blood flow in ml/min/100 g. Abscissae: n-v; non-vagotomy, v; vagotomy. p=Probability of the differences as determined by the t-test.

via the humoral route by way of ADH secretion and water excretion through the skin regulated by autonomic nerves with vasomotor and secretion activating function.

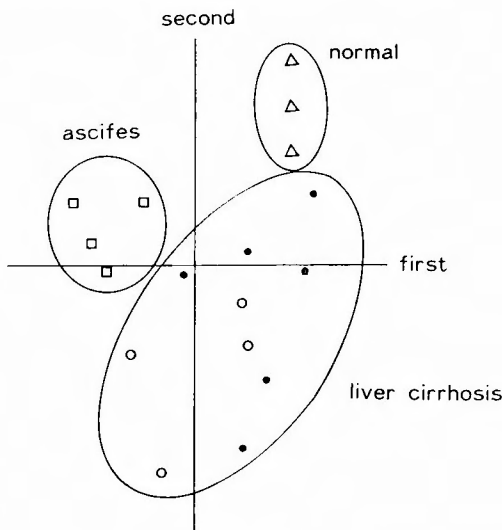


Fig. 6.

Several investigators have found that the infusion of hypertonic sodium chloride solutions into a portal vein cause a greater natriuresis than do comparable femoral infusions, they suggested that a sodium ion receptor exists in the gut or portal vein (BERGMANN⁴), CAREY⁷), CHWALBINSKA⁸), DALY⁹), LENNANE²¹), PASSO³⁰), STRANDHOY³⁷) and WILLIAM⁴²).

In contrast to these data, other investigators were unable to demonstrate any difference in diuretic response to an infusion of hypotonic fluid into a systemic compared to portal vein (GLASBY¹¹), HANSON¹⁵), KAPTEINA¹⁹) and POTKEY³¹).

The concept of neural afferent transmission of the signals perceived within the vascular bed is firmly supported by neurophysiological data. Perfusion of the liver with hypotonic or hypertonic solutions modified the discharge rate in hepatic vagal afferents in guinea pigs, rabbits and rats (ADACHI¹) and ANDREWS²). The existence of osmoreceptor in the liver, which have long been mooted and even described, has not yet been conclusively demonstrated^{5, 17, 20, 23, 26, 28, 31, 36, 42}).

MURAKAMI^{18, 27}) compared 6 cases of neurotomy of hepatic branch of vagus nerve with 12 cases of non-neurotomy concerning of postoperative liver function and postoperative ascites flow from the abdominal drainage tube. In 5 cases out of 6 cases of neurotomy, the vagus nerves were injured above the diverging point of the hepatic branch when the esophageal transection was performed for esophageal varices, and in one case they were injured when proximal gastrectomy was done. On a comparative study of postoperative ascites fluid, there was a statistically significant increase in the vagotomy group in contrast to the non-vagotomy group. But in the non-vagotomy group, two cases of serious liver damage with ICG test more than 50% and one case which had over 1000 ml of ascites while operation was performed, were found a large quantity of ascites getting out as compared with the control group. On the other hand postoperative liver functions showed statistically no significant difference between these two groups.

These data indicated the existence of an osmoreceptive area within the hepatic portal vascular bed, and they were innervated by the hepatic branch of the vagus, and influenced by liver cirrhosis. So present experiments were performed. It was thought that if there was liver osmoreceptor the change of diuresis occurred immediately after portal infusion, so urine flow for 10 minutes immediately after portal infusion was mainly compared.

In non-anesthetized rats, it was unexpectedly difficult to keep the record of the urine flow straight. For the reason that female rats are more easily ureteral catheterized, female rats were used the same as HABERICH¹⁴). There were two distress, one is residual urine, another is an

Fig. 6. Chief elemental analysis. In 10 kinds of biochemical examination of blood and ascites. In experimental liver cirrhosis of the liver. Male rats.
 First chief element : Total protein, albumin and cholesterol.
 Second chief element: Alk-Phos, GOT and GPT.
 Third chief element : A/G and LDH.
 ^ : blood in the normal liver.
 ● : blood in the cirrhotic liver without vagotomy.
 ○ : blood in the cirrhotic liver with vagotomy.
 □ : ascites in the cirrhotic liver with vagotomy.
 Two dimensional expression of first chief element and second chief element were good classified, but in rats with liver cirrhosis between non-vagotomy and vagotomy groups were not classified.

abrupt increase of urine flow at the time of constriction of bladder while rats were slightly stimulated (indeed, in anesthetized state, the water infusion at the rate of 0.01 ml/min was so slow that rats maybe felt pain slightly). For these reasons, ureteral catheterization was performed by a as thick as possible tube, and the bladder was tensioned temporarily by the tube for little residual urine. All the cases which were doubtful of residual urine were discarded. As these experiments were enforced in all the same condition, the presence of the liver osmolality in rats was suggested.

SCHNIDER et al.³⁵⁾ found no evidence for an osmoreceptor mechanism in the liver of the dog, and they may be due to a species difference. Prior to present experiments, preliminary experiments had been performed on anesthetized dogs. Dogs of both sexes weighing from 9 to 20 kg were anesthetized with pentobarbital sodium (30 mg/kg) i.v., and polyethylene cannula was inserted into each ureter. Various osmolal fluid infusions were given into the portal or femoral vein, individually or simultaneously. And the change of urine flow was measured. On the dogs, interesting results were induced when 1.8% NaCl infusion into the portal vein had a remarkable diuretic action, but on the contrary water infusion brought about an immediately anuric state. But the data failed to provide evidence for an osmoreceptor mechanism in the liver of the dog, and only natriuresis occurred conspicuously.

It has long been known that the ascites could be produced in rats with experimental liver cirrhosis by administration of D-galactosamine, feeding on orotic acid, choline free diet, intravenous injection of egg-yolk and CCl_4 ^{6,10,25)}. CCl_4 is used by oral administration, subcutaneous injection, intramuscular injection, intraabdominal injection and by inhalation. At present intramuscular injection of CCl_4 is the popular method in Japan. McLEEN et al.²²⁾ reported that cirrhosis of the liver in rats by simultaneous administration of CCl_4 and phenobarbitone was produced in only 4 weeks. In our preliminary experiments, with intramuscular injection of CCl_4 , the production of the liver cirrhosis in rats took 4 months, but simultaneous administration of CCl_4 and phenobarbitone took half the time taken for their production in comparison with intramuscular injection of CCl_4 alone. On the other hand only one drawback is high mortality. Half the rats die of intestinal bleeding or malnutrition in summer. But this method is easy and improved one for production of the liver cirrhosis in rats.

Many factors in the development of ascites have long been known^{24,30,35)}. As to the ascites accumulation, McLEEN²²⁾ reported a great deal of ascites was produced by CCl_4 inhalation with phenobarbitone in rats. In our preliminary experiments using intramuscular injection of CCl_4 , ascites was not noted in neither male nor female rats irrespectively of vagotomy or non-vagotomy even after 4 months. With the inhalation method with pentobarbital female rats used in Exp. 2 we were unable to demonstrate any ascites.

So experimental animals for ascites production were changed from female to male rats. In the non-vagotomy group there was one case only without ascites, in contrast to the vagotomy group where abundant ascites fluid (3~30 ml) was produced in almost all the rats. Eventually if male rats were used and vagotomy including hepatic branch and CCl_4 inhalation with pentobarbital sodium were carried out, ascites was produced easily in only 2 months.

In order to clarify the origin of the difference between vagotomy and non-vagotomy groups, Exp. 5 was carried out. Measurement of hepatic blood flow by the hydrogen clearance tissue blood flowmeter, biochemical examination of the blood and histological examination of the liver showed no difference between vagotomy and non-vagotomy.

These results were in good agreement with the report by MURAKAMI^{18,27)} on clinical cases which suggested that much ascites were discharged postoperatively in the cases with transected hepatic branches of the vagus regardless of no difference of liver functions between neurotomy and non-neurotomy groups. There are many factors in the development of ascites, and in our Exp. 2, it is suggested that in the vagotomy group with liver cirrhosis the osmolality regulation mechanism was harmed seriously. So it is suspected that liver osmolality and hepatic branch of the vagus influenced ascites accumulation.

Conclusion

The increase of ascites flow was observed in clinical cases who had undergone transthoracic esophageal transection or proximal gastrectomy for esophageal varices accompanying the division of the hepatic branches of the vagus nerve. Taking into consideration these facts experimental liver cirrhosis was produced in the rats and relationship between the vagus nerve and ascites accumulation were investigated.

- 1) The rats had osmoreceptor in the liver, and it was innervated by the vagus nerve.
- 2) Osmoreceptor in the liver was harmed by experimental liver cirrhosis.
- 3) In rats with experimental liver cirrhosis with additional neurotomy of hepatic branch of the vagus, osmoregulation was further injured.
- 4) Liver cirrhosis was produced by simultaneously CCl_4 inhalation and administration of pentobarbital sodium for only two months. Female rat and male rat with intact vagus nerve had no ascites formation but male rat with neurotomy almost all had ascites accumulation.
- 5) As to hepatic blood flow, biochemical examination of blood and histologic examination of the liver there were no detectable difference between the neurotomy and non-neurotomy groups.

These results suggested that ascites accumulation in rats with liver cirrhosis was influenced by the vagus nerve, especially hepatic branch, and osmoreceptor in the liver.

And it was demonstrated that in clinical cases when hepatic branch of the vagus nerve was injured during the operation for esophageal varices more ascites formation was produced postoperatively. Consequently during these operations we have to take notice of preservation of the hepatic branch of the vagus.

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和文抄録

食道静脈瘤に対する経胸的食道離断術後の腹水貯留と
迷走神経肝枝切離との関連

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教室で食道静脈瘤の患者に経胸的食道離断術を施行した際、肝枝が分岐するより中枢側で迷走神経が損傷されたと思われる肝枝切離群と非切離群について術後の腹水流出現状態を比較したところ、切離群において有意差をもって腹水の増加が認められたが、肝機能は両者のあいだに差は認められなかった。

最近肝臓あるいは門脈系に種々の受容器が存在し、それが内部環境の恒常性維持に役割を演じているとする報告がみられる。そこでラットに肝硬変を作成し、迷走神経と肝の浸透圧受容器との関係、および腹水貯留の状態を検討した。

1) 肝硬変作成法としては、雌のラットを用いて、非迷切群と、肝枝切離を含む全幹迷切およびドレナージ群の両群について、ペントバルビタールナトリウムを 50 mg/100 ml に溶解し飲水させた。1週間後より密閉した容器にラットをいれ、四塩化炭素を10分間吸入させ、さらに10分間放置する吸入法を週2回、2か月間行ったところ、肝に偽小葉を形成する乙型肝炎硬変が作成された。

2) 雌のラットを用いて、門脈内にカテーテルを挿入、体外に導き、導尿を行ったのち、麻酔より覚醒させ非麻酔の状態、門脈より、蒸留水または生食水を 1 ml または 2 ml/10分間注入したのち、主として注入後10分間の尿量を、正常肝群と肝硬変群にわけて計測し、比較検討したところ、次の結果をえた。

a) 正常肝ラットで蒸留水を注入した群では、注入と同時に著明な尿量の増加があり、肝に浸透圧受容器があることを推定せしめた。

b) 正常肝ラットで迷切を行った群では、逆に尿量の減少がみられ、迷走神経切離は、肝の浸透圧受容器に影響を及ぼすことが推定された。

c) 肝硬変を作成し蒸留水を注入した群では、注入後も尿量の増加はなく、肝硬変によって肝浸透圧受容器が損傷された可能性が示唆された。

d) 肝硬変を作成し迷切を行った群では、逆に尿量の増加、減少と変動がはげしく、肝浸透圧調節機構に重大な損傷をきたしたものと思われた。

e) 生食水注入群では、どの群においても尿量の増加は軽度であった。

f) 生食水、蒸留水のいずれも 1 ml または 2 ml/10分間注入群のあいだの差は認められなかった。

3) 雌のラットでは肝硬変を作成しても、まったく腹水の貯留は認められなかったので、雄のラットにかえて、同様に肝硬変を作成したところ、迷切群では18例中1例のみに腹水が認められたのみであったが、迷切群では、14例中11例に、3~30 ml に達する腹水の貯留をみた ($p=0.0003$)。

4) 上述の差がどこにあるかを、水素クリアランス法による肝の組織血流量、血液生化学的検査成績、肝の組織像について検討を加えたが、いずれについても迷切群と非迷切群のあいだに差は認めえなかった。

以上の諸成績より、ラットにおいて肝硬変症の際の腹水貯留には、迷走神経および肝の浸透圧受容器が関与していることが考えられた。また臨床的にも、食道静脈瘤手術の際には、迷走神経肝枝の保存に留意すべきであることを強調したい。