Technical Note

Fundamental and Clinical Evaluation of Vasoactive Intestinal Peptide (VIP) in Pancreatitis by Radioimmunoassay Kit†

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Plasma vasoactive intestinal peptide (VIP) concentrations of normal individuals and patients with pancreatitis were studied using a VIP RIA kit. The inter-assay and intra-assay variation of this kit were between 2.1 and 9.4%. The VIP levels increased in the acute phase of acute pancreatitis and patients with chronic pancreatitis. The VIP concentration increased during the first 30 min of glucose tolerance test, but this increase was much smaller than that in insulin.

These results suggest that this kit is useful for physiologic and pathologic changes in the VIP level.

Key Words: vasoactive intestinal peptide, pancreatitis, glucose tolerance test, insulin

1. Introduction

Vasoactive intestinal peptide (VIP) is a hormone extracted and purified from the porcine intestinal mucosa by Said et al. Since it is widely distributed in various human neural tissues in addition to the gastrointestinal tract, and it is considered to be a neurotransmitter. The agent is known to cause vasodilation, increase the blood flow as well as stimulate secretion of intestinal juice, pancreatic juice, bile, and more to suppress that of gastric acid. An abnormal increase in the secretion of VIP was demonstrated to be responsible for watery diarrhea-hypokalemia-acholorhydria (WDHA) syndrome, and measurement of VIP is an important factor in diagnosis of this syndrome. However, it is not certain that this hormone has any biological effect in various diseases.

In this study, the relationships between the circulating VIP level, changes in the levels of VIP and other pancreatic hormones during the glucose tolerance test were examined in patients with pancreatitis.

2. Subjects and Methods

2.1 Subjects

The study included 15 normal individuals, 10 patients with acute pancreatitis, 37 with chronic pancreatitis (20 showing irregularities or dilatation of the main pancreatic duct by retrograde pancreatography (Group I) and 17 showing regional irregularities and dilatations (Group II)), 11 with diabetes, and 7 with pancreatic cancer.

2.2 Methods of measurement

The plasma VIP concentration was determined as shown in Fig. 1, using a radioimmunoassay kit (Dainabot, USA). The values were calculated by the following formula.

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B/B_0(\%) = \frac{\text{CPM of standard or unknown sample} - \text{CPM of NSB}}{\text{CPM of 0 standard} - \text{CPM of NSB}} \times 100
\]
Blood was drawn early in the morning after an overnight fast, and the plasma was isolated in a test tube containing Trazanol® (500 KIU/ml; BMY, West Germany) and EDTA (1.2 mg/ml) at 4°C.

The glucose tolerance test was performed in 6 normal individuals, 6 patients with chronic pancreatitis, and 3 diabetic patients by oral administration of glucose (75 g).

Amylase, lipase, trypsin, and elastase-I were examined among pancreatic enzymes and insulin and glucagon among pancreatic hormones.

3. Results

3.1 Standard curve
The standard curve of the VIP concentration obtained on the basis of 5 determinations is shown in Fig. 2.

3.2 Accuracy
The inter-assay variation among determination of 3 different concentrations was 2.1–8.8%, and the intra-assay variation was 4.0–9.4%.

3.3 VIP concentrations in normal individuals and patients with pancreatic diseases
In the normal individuals, the VIP concentration was 8.7±4.6 pg/ml and showed no sexual differences. In patients with pancreatic diseases, the VIP concentration was significantly higher in those with acute pancreatitis than in the normal individuals (Fig. 3). It also increased in those with chronic pancreatitis, but was lower in Group I than in Group II. The concentration showed no differences in those with diabetes as compared with the normal individuals, but was significantly increased in those with pancreatic cancer.

3.4 Changes in VIP concentration in patients with acute pancreatitis
The VIP level in patients with acute pancreatitis increased in the acute phase associated with an increase in pancreatic enzymes such as...
Fig. 4 Time course of changes in plasma levels of VIP and serum pancreatic enzymes in patient with acute pancreatitis.

amylase, abdominal pain, and fever, but was normalized with alleviation of the symptoms (Fig. 4). However, the VIP concentration was not correlated with the amylase \((r=0.15, n=50)\) or lipase \((r=0.23, n=46)\) activity.

3.5 Changes in VIP level under glucose loading

The VIP level was increased slightly 30 min after the administration of glucose, and gradually decreased, and then returned to the pre-administration level in the normal, pancreatitis, and diabetic groups (Fig. 5). The insulin level markedly increased from 30 min after the administration of glucose in the normal and pancreatitis groups, but the response was weak and delayed in the diabetic group. The glucagon level showed no changes after the administration in any of the 3 groups. There was no significant correlation \((r=0.104, n=70)\) between the VIP and insulin levels during the glucose tolerance test.

4. Discussion

The amino acid sequence of VIP was clarified by Bodanczsky et al. and Mutt et al. This hormone is related in its amino acid sequence to secretin, glucagon, and gastric inhibitory polypeptide, and the agent is considered to be a gastrointestinal hormone belonging to the same group as secretin.

The VIP concentration has been studied by a number of investigators by RIA, and is considered by many of them to be less than 100 pg/ml in normal individuals. However, little is known about physiological fluctuations of the VIP level and its actions, such as the vasodilatation, increase the blood flow of gastrointestinal organs and so on. These actions of this agent are considered to be important factors in the clinical profile of various pancreatic diseases, especially pancreatitis, but these data have been inadequate.

Our evaluation of a high-sensitivity VIP assay kit suggested that determination is possible to about 3 pg/ml. Using this kit, we examined the relationship between the clinical picture of pancreatic diseases and the VIP level. VIP increased in the acute phase of acute pancreatitis, probably because the secretion of VIP was stimulated by tissue damage due to a rapid increase in pancreatic enzymes and hypoxia of tissues associated with shock.

In patients with chronic pancreatitis, the VIP concentration also increased with pancreatic enzyme activities, but this increase was smaller in Group I than in Group II. The increase in the VIP concentration in patients with pancreatic cancer is considered to be due to pancreatitis complicating the disease.

In our study, however, the VIP level was not related to circulating pancreatic enzyme levels and further studies are needed to clarify their
relationships. The VIP secretion increased slightly during the first 30 min of the glucose tolerance test. However, this increase was not as marked as that in insulin secretion, and was not correlated with the latter. The glucagon level also showed no marked changes during the glucose tolerance test. These data suggest that a secretory mechanism of the VIP have found no definitive relationship between this agent and other pancreatic hormones.

5. Conclusions

Physiologic changes in the plasma VIP concentration were studied using a VIP assay kit.

(1) Accuracy and sensitivity of the kit were satisfactory.

(2) The plasma VIP concentration was 8.7±4.6 pg/ml (mean±SD) in 15 normal individuals.

(3) The VIP level increased in the acute phase of acute pancreatitis and patients with chronic pancreatitis, but it appeared to be reduced in the presence of chronic damages to pancreatic tissues.

(4) The VIP concentration increased during the first 30 min of the glucose tolerance test, but this increase was much smaller than that in insulin.

These results suggest that this kit is useful for evaluation of physiologic changes in the VIP levels.

References