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Distribution and Elimination of Insulin and C-peptide in a Benign Insulinoma Patient

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ABSTRACT. The distribution and elimination of insulin and C-peptide was evaluated in a case of benign insulinoma, using the method of gel chromatography. The significant differences between total Immunoreactive insulin (IRI) level and the level of Peak I plus Peak II of IRI was noticed in splenic vein. This fact suggested that intermediate and/or abnormal IRI could be released from the tumor. In order to diagnose a hypoglycemic patient with completely normal IRI and CPR level in peripheral blood, the gel chromatographic separation of IRI from splenic and/or portal blood could be useful.

Key words : Immunoreactive insulin — C-peptide immunoreactivitiy— Insulinoma — gel chromatography — Insulin analogues

There are some investigations to elucidate the insulin levels in peripheral and portal blood, obtained simultaneously[1—4]. Hed et al.[5] found higher insulin concentrations in peripheral venous blood than in portal blood after the provocation of glucose and tolubutamide, or glipizide. They suggested that these findings reflect a release of previously bound insulin from peripheral tissues.

But little is known about the distribution and elimination of insulin and C-peptide in the case of benign insulinoma patient who had a normal level of insulin in peripheral circulation and elevated insulin level in benign insulinoma tissue. On the other hand, Kakita et al.[6—8] have reported two insulin analogues and gel chromatographic separation of C-peptide and proinsulin. In this benign insulinoma case[9], the level of insulin in splenic vein was rather high and that in peripheral circulation completely normal at fasting. The level of blood glucose was always low as shown previously[9]. Our methods to separate insulin analogues and C-peptide molecules were applied to the patient to elucidate the distribution and elimination of insulin and C-peptide molecules.

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MATERIALS AND METHODS

The patient of benign insulinoma was reported previously[9]. A 53-year-old woman had complained of hypoglycemic attacks for 5 years. Before surgery, hepatic venous blood was taken percutaneous-transhepatically. During the surgery, the benign insulinoma was identified at the tail of pancreas. The catheter tube was inserted into portal and splenic vein through superior mesenteric vein. Blood samples were taken at the same time from splenic, portal and peripheral vein, respectively. After the removal of the tumor, venous blood samples were taken from the catheter at portal vein according to the time of 10, 20 and 30 minutes, serially.

Extraction, separation and radioimmunoassay of insulin immunoreactivity (IRI) and C-peptide immunoreactivity (CPR) were carried out according to the reported methods[6,8].

RESULTS AND DISCUSSION

Before surgery as shown in Table I, the IRI level of splenic venous blood was remarkably higher (0.35 pM/ml) than that of portal, hepatic and peripheral venous blood. On the contrary, Peak I and Peak II of IRI were 0.06 and 0.06 pM/ml, respectively. Some IRI could be lost on the way of extraction and/or gel chromatographic procedure. Comparing the data of normals and diabetics, which were reported by us[6], these lost IRI could be intermediate insulins and/or abnormal insulins. Because that the level of portal venous blood IRI (0.09 pM/ml) dropped remarkably from that of splenic venous IRI (0.35 pM/ml), it could be speculative that intermediate or abnormal IRI should rapidly be degraded on the way from splenic to portal vein. The level of IRI in portal and hepatic venous blood was quite normal[5]. The level of Peak II of IRI in splenic vein (0.06 pM/ml) and Peak I of IRI in portal vein (0.11 pM/ml) were remarkably high, comparing to the peripheral venous levels of normals[7]. The levels of peak I of CPR in splenic and portal vein were remarkably high, comparing to the peripheral level of normals[8], but Peak II of CPR was not elevated. In hepatic vein, the Peak I level of CPR was almost normalized. Therefore, liver might have a significant role of elimination of the CPR, which might be abnormal. After removal of the tumor as shown in Table II, Peak I of IRI had been almost normalized, but Peak I of CPR was delayed to be normalized, probably due to its half life.

From above mentioned results, the followings can be drawn : 1) The significant differences between total IRI level and the level of Peak I plus Peak II of IRI in splenic vein was noticed. This facts suggested that intermediate and/or abnormal IRI could be released from the insulinoma tissue. 2) The significant high level of Peak I of IRI in portal vein was detected in the patient who had completely normal level of total IRI and CPR in the peripheral circulation. 3) Peak II of IRI in splenic vein was elevated. 4) Peak I of CPR in splenic and portal vein was elevated significantly, but Peak II of CPR stayed

TABLE The Levels of IRI and CPR

I.

	IRI*			CPR**		
	Total	Peak I	Peak II	Total	Peak I	Peak II
Splenic vein	0.35	0.06	0.06	1.70	0.90	0.05
Portal vein	0.09	0.11	0.02	1.23	0.48	0.18
Hepatic vein	0.04	0.07	0.00	0.64	0.12	0.05
Peripheral vein	0.04	0.04	0.02	0.53	0.23	0.09

II.

Portal vein		Before Operation	After Operation 10 Min.	20 Min.	30 Min.
IRI*	Total	0.09	0.09	0.08	0.07
	Peak I	0.11	0.09	0.09	0.07
	Peak II	0.02	0.02	0.00	0.00
CPR**	Total	1.23	1.10	0.90	1.00
	Peak I	0.48	0.41	0.35	0.35
	Peak II	0.18	0.14	0.16	0.18

* The values were corrected according to the recovery rate of extraction (0.833) and gel filtration (0.647).

** The values were corrected with the recovery rate of extraction (0.607) and gel filtration (0.717).

All unit are picomole/ml.

at normal level.

In order to diagnose benign insulinoma with completely normal IRI and CPR level in peripheral blood, the gel chromatographic separation of IRI and CPR from splenic and/or portal blood could be useful for the diagnosis of benign insulin producing tumor.

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