Exocrine Pancreatic Function in Diabetic Dogs

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Exocrine pancreatic insufficiency is frequently observed in human with diabetes mellitus, especially with insulin dependent diabetes [2, 3, 15]. The exocrine pancreatic function (EPF) has been evaluated for long term control of diabetic patients since the exocrine dysfunction is closely related to the duration of diabetic states [4, 5] and to the control in blood glucose levels [9]. EPF in diabetic dogs, however, remains obscurity. For the examination of EPF, N-benzoi-L-tyrosyl-p-aminobenzoic acid (BT-PABA) has been developed [1, 8]. This unabsorbable synthetic peptide is hydrolyzed by pancreatic chymotrypsin and releases absorbable p-aminobenzoic acid (PABA). The PABA levels in blood or urine after oral administration of BT-PABA reflects the EPF. This study was designed to evaluate the EPF in diabetic dogs using the BT-PABA test.

Eight diabetic dogs (5 females and 3 males) with no complications such as severe infections and/or renal failure, were examined (Table 1). The mean age of patient was 10.8 years, ranging from 8 to 14 years old. The patient dogs without histories of acute or chronic pancreatitis revealed persistent hyperglycemia (319–525 mg/100mL), glycosuria and/or ketonuria. The diagnosis of diabetes mellitus was based on the insulin response during the glucose tolerance test (400mg/kg i.v.) [11]. Glucose disappearance rate remarkably prolonged in all cases [T1/2: 103–525 min, fractional clearance k (%/min): 0.13–0.67]. Plasma insulin levels were determined by radioimmunoassay [10]. Fasting plasma immunoreactive insulin (IRI) levels were low or undetectable in these dogs, except case No. 6 which possessed insulin antibody resulted from long term insulin therapy. Hypo- or no-response of plasma IRI to glucose load were revealed in all cases. The changes in plasma PABA concentrations were examined instead of PABA recovery rate of 6 hours urine excretion because of the difficulty of urine collection in dogs.

After overnight-fasting, BT-PABA (PFD®, Eisai Ltd., Tokyo) was administered to these diabetic dogs at a dose of 15mg/kg body weight as a 5mg/ml solution in water. Blood samples were taken before the examination and at intervals of 15–60 min over 6 hours. The plasma PABA concentration was measured by the Bratton-Marshall method as modified by Smith [14].

Fluctuations of plasma PABA concentrations in diabetic dogs were shown in Fig. 1. In control dogs (2 female, 2 male beagle dogs), plasma PABA levels rose to a maximal value (about 10 mg/l) at 1 hour after BT-PABA administration, and then gradually decreased. In diabetic dogs, maximal plasma PABA concentrations (2.0–8.2 mg/l) were lower than that of the control dogs and the time lag to maximal value (15–240 min) were varied. As the maximal plasma PABA concentrations may be influenced by the PABA absorption and excretion rate, integrated plasma PABA concentration (ΣPABA=the area of under the curve) were estimated. ΣPABA in diabetic dogs were lower (5.6–29.6) than that of control dogs (36.0±7.1), though the index revealed no relationships to k value and insulin requirement in therapy (U/kg/day).

The reduction in EPF capacity occurs in 80% of the patients with insulin dependent diabetes [5]. This phenomenon may be explained by the result of insulin deficit in blood flow into acinar cells since insulin has a trophic action to the acinar cells [12]. The insulin rich blood flow from islet to acinar cell is supported by the insulino-vascular portal system in the pancreas [6, 13]. In diabetic dogs insulin hyposecretion may lead to the acinar cell dysfunction. The progressive deterioration of the EPF was also shown along the course of disease [9]. The re-evaluation of EPF test at 12 months after the first examination indicated that the ΣPABA in 2nd examination were reduced in 5 of the 8 cases comparing with the results of the first examination (Fig. 2). These EPF reduction obtained at the 12 months interval might be resulted from the development of
Table 1. Clinical data on diabetic dogs at the first admission

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Breed</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Fasting plasma glucose levels (mg/dl)</th>
<th>$k$ value$^a$</th>
<th>Insulin$^b$ requirement (U/kg/day)</th>
<th>ΣPABA$^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Miniature pinscher</td>
<td>14</td>
<td>Female</td>
<td>529</td>
<td>0.42</td>
<td>1.2</td>
<td>24.4</td>
</tr>
<tr>
<td>2</td>
<td>Toy poodle</td>
<td>10</td>
<td>Female</td>
<td>524</td>
<td>0.13</td>
<td>1.0</td>
<td>18.3</td>
</tr>
<tr>
<td>3</td>
<td>Yorkshire terrier</td>
<td>12</td>
<td>Female</td>
<td>518</td>
<td>0.33</td>
<td>1.4</td>
<td>11.7</td>
</tr>
<tr>
<td>4</td>
<td>Toy poodle</td>
<td>11</td>
<td>Male</td>
<td>399</td>
<td>0.44</td>
<td>1.5</td>
<td>29.6</td>
</tr>
<tr>
<td>5</td>
<td>Maltese</td>
<td>10</td>
<td>Female</td>
<td>399</td>
<td>0.34</td>
<td>0.6</td>
<td>7.4</td>
</tr>
<tr>
<td>6</td>
<td>Maltese</td>
<td>8</td>
<td>Male</td>
<td>394</td>
<td>0.19</td>
<td>1.9</td>
<td>14.4</td>
</tr>
<tr>
<td>7</td>
<td>Toy poodle</td>
<td>10</td>
<td>Female</td>
<td>332</td>
<td>0.37</td>
<td>1.4</td>
<td>5.9</td>
</tr>
<tr>
<td>8</td>
<td>Mixed</td>
<td>11</td>
<td>Female</td>
<td>319</td>
<td>0.67</td>
<td>1.3</td>
<td>5.6</td>
</tr>
</tbody>
</table>

a) $k = -\frac{\ln 2}{T_{1/2}}$ (%/min).
b) Insulin Novo Lente MC®.
c) The area under the curve of plasma PABA concentration.

Fig. 1. Changes in plasma PABA concentrations in diabetic dogs in BT-PABA test. The shaded area shows the control dogs (mean±SD).

Histological changes in the duration of disease since the sclerosis of the vessels and fibrosis as well as atrophy of acinar cells were observed in human diabetic pancreas [7].

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REFERENCES


要約
自然発症糖尿病犬の膵外分泌機能について：安田和雄・小野憲一郎1）・長谷川篤彦1）・友田 勇1）（東京大学農学部附属家畜病院、1）家畜内科学教室）——8例の自然発症糖尿病犬についてn-benzoil-1-tyrosyl-p-aminobezoic acidを用いて膵外分泌機能（EPF）を検討したところ、その程度はさまざまであったが、機能低下が全例に観察された。しかしながら、EPFの低下と耐糖能やインスリン要求量との間には特に関連を認めることはできなかった。1年後に行行った再検査の結果、5例ではEPFがさらに低下していた。