The Iothalamate Clearance in Cats with Experimentally Induced Renal Failure

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ABSTRACT. Plasma iothalamate (IOT) disappearance rates were measured after a single-injection of IOT (113.8 mg/kg, IV) in cats with experimentally induced renal failure. The disappearance rates especially fitted into the one compartment model. The mean value of plasma disappearance rates of IOT in these cats with induced renal failure (2.16 ± 0.240 × 10⁻³ μg/ml/min) was markedly lower than that of clinically healthy cats (4.10 ± 1.00 × 10⁻³ μg/ml/min). These results demonstrate that IOT clearance is available for evaluation of renal function in cats.—KEY WORDS: disappearance rate, feline, iothalamate.

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It has widely been accepted that the measurement of glomerular filtration rate (GFR) is the most sensitive and quantitative method for detection and evaluation of renal dysfunction. Inulin clearance (Cin) is a standard method for GFR measurement, however, Cin has not been constantly used in small animal clinics, especially for cats, because of a number of technical and facilities difficulties, i.e., continuous intravenous infusion, urine and blood collection, etc. [9]. Although the most widely used measure of GFR in cats has been endogenous or exogenous creatinine clearance [6, 9], creatinine is secreted from the renal tubule and is effected by some kinds of drugs, and the creatinine pool changes at the time of chronic renal failure [8, 10, 12, 13]. Furthermore, creatinine was considered to be a precursor of methylguanidine, one of the uremic toxins inducing uremic syndrome in cats [1, 5]. Recently, iothalamate (IOT) clearance was carried out and demonstrated to be closely correlated with the Cin [2]. The measurement of IOT clearance is a simple method with high performance liquid chromatography (HPLC) [3] and does not require urine samples.

This note deals with IOT clearance in clinically healthy cats and cats with experimentally induced renal failure.

Eight male cats (Ico:Fec Eur (Tl)ı) weighing 1.3 to 3.2 kg, and aged 1 to 3 years were used in this study. They were diagnosed to be healthy, based on the evaluation of physical examination, complete blood cell count, serum biochemical profile and urinalysis. They were divided into two groups, controls (4 cats) and cats with renal failure (4 cats, BUN: 29.5–50.7 mg/dl, creatinine: 1.37–2.70 mg/dl) experimentally induced by a two step procedure described previously [14]. The IOT clearance study was done after more than a month post operation. Food was withheld from each cat for 12 hr prior to the study, but access to water was not restricted. A priming volume of 113.8 mg/kg of IOT (DIP Conray, Daiichi Pharmaceutical Co., Ltd., Japan) was given through the indwelling intravenous cannula, and was followed by an injection of 3 ml of saline to ensure adequate flushing of residual IOT from the cannula. Three ml/blood samples were collected with a heparinized syringe from the jugular vein at 0, 5, 10, 20, 30, 60, 90, 120, 150, 180 and 360 min after injection of saline. Plasma was separated by centrifugation at 3,000 rpm for 20 min and stored at -20°C until assay. Plasma samples (0.2 ml) were deproteinized by adding four volumes of perchloric acid (0.7 M) and centrifuged at 3,000 rpm for 20 min. The supernatant was filtered with a microfilter (MILLIPORE=0.45 mm, Nihon Millipore Co., Ltd., Japan). An aliquot of the filtrate (5 μl) was used for the assay of IOT.

The concentration of IOT was determined by a HPLC system which consisted of Shimadzu LC-6A liquid chromatograph, Shimadzu SPD-6A UV spectrophotometric detector (Shimadzu Co., Kyoto, Japan) and a reverse-phase column ODS-2 (4.6 mm × 150 mm, Shimadzu Co., Kyoto, Japan). The mobile phase consisted of 2% acetonitrile adjusted to pH 1.9 with phosphoric acid. The flow rate of solvent was 1 ml/min. Samples were quantified by UV absorption at 254 nm relative to the external standard curve.

Two phases in the logarithmic regression curves were observed after administration of IOT in both groups. One phase was a non-linear, sharp regression lasting until 30 min after injection, and the other was a linear, gradual regression (30 to 360 min after injection) (Fig. 1). For nonmetabolizable substances excreted only by the kidney, the disappearance rate of the substance from blood is reflected in part by renal function. IOT has been

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Fig. 1. Disappearance rate of plasma iothalamate in clinically healthy cats (○) and cats with experimentally induced renal failure (●). The vertical axis is expressed with a logarithm. The regression curve after 30 min. of IOT injection in the clinically healthy cats showed y=log310-0.00216x, and that of cats with experimentally induced renal failure showed y=log285-0.00410x.
Table 1. Plasma iothalamate concentrations (μg/ml) in clinically healthy cats and cats with experimentally induced renal failure

<table>
<thead>
<tr>
<th>Time (min.) after injection</th>
<th>Control (N=4)</th>
<th>Renal failureab (N=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>post injection</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>499.8 ± 60.30</td>
<td>204.1 ± 14.76</td>
</tr>
<tr>
<td>10</td>
<td>379.4 ± 31.71</td>
<td>178.9 ± 9.49</td>
</tr>
<tr>
<td>20</td>
<td>299.5 ± 26.63</td>
<td>148.6 ± 6.73</td>
</tr>
<tr>
<td>30</td>
<td>265.7 ± 18.89</td>
<td>127.8 ± 8.92</td>
</tr>
<tr>
<td>60</td>
<td>180.1 ± 19.60</td>
<td>108.8 ± 6.58</td>
</tr>
<tr>
<td>90</td>
<td>134.2 ± 27.22</td>
<td>93.5 ± 3.64</td>
</tr>
<tr>
<td>120</td>
<td>102.3 ± 26.23</td>
<td>79.4 ± 6.03</td>
</tr>
<tr>
<td>150</td>
<td>77.6 ± 24.07</td>
<td>70.0 ± 3.10</td>
</tr>
<tr>
<td>180</td>
<td>61.7 ± 25.26</td>
<td>59.6 ± 3.51</td>
</tr>
<tr>
<td>360</td>
<td>15.3 ± 8.86</td>
<td>29.8 ± 1.65</td>
</tr>
</tbody>
</table>

a) Experimentally induced renal failure. Data are given as mean ± STD. N=number of cats tested.

...samples should be collected from at least 30 min after administration of IOT for calculating disappearance rates, and we recommend collection at least 3 times, at 60, 90, 120 min after a single injection of IOT. The single-injection of IOT should offer radiographic evaluation of the kidney in addition to this quantitative information of renal function, because IOT is one of contrast media for excretory urography. Further studies will be necessary for estimating renal functions on clinical feline cases.

REFERENCES