The intravenous glucose tolerance and postprandial glucose tests may present different responses in the evaluation of obese dogs

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Abstract
The present study compared the intravenous glucose tolerance test (IVGTT) and the glucose postprandial response (GPPR) test for the evaluation of glucose metabolism in obese dogs. A total of ten owned obese dogs (body condition score (BCS) of 9; fat mass, 45.7 (SEM 1.51)%) were used. These dogs had their weight reduced by 20% (BCS, 8; fat mass, 33.5 (SEM 1.92)%; P, 0.001), designated as weight-reduced (WR) group. A control group of ten Beagle dogs was also included (BCS, 4.5; fat mass, 18.3 (SEM 1.38)%; P, 0.01). Glucose tolerance was measured by two methods: IVGTT (infusion of 0.5 g of glucose/kg body weight) and GPPR (consumption of cooked rice to achieve 6 g of starch/kg body weight). When using the IVGTT, the area under the curve (AUC) for glucose and maximum glycaemia were higher for obese dogs compared with controls (P, 0.05), with intermediate results for the WR group (P, 0.05). Basal insulin, insulin response peak, insulinogenic index and the AUC for insulin increment from 0 to 15 min and from 60 to 120 min were higher for the obese group (P, 0.05), while the WR group and control dogs showed similar results (P, 0.05). When using the GPPR test, the AUC for insulin increment from 0 to 120 min was higher for the obese group compared with the control group (P, 0.05) and intermediate for the WR group (P, 0.05). However, the AUC for insulin increment from 120 to 360 min was similar between the obese and WR groups (P, 0.05), while it was lower for the control group (P, 0.05). The IVGTT showed that the loss of 20% body weight resulted in an improvement of glucose control with reduced insulin secretion, and these same WR dogs showed higher insulin secretion with values similar to those of obese dogs when the GPPR test was used.

Key words: Glycaemia: Insulin: Obesity

Recent studies have suggested mechanisms for the relationship between excessive body fat and many degenerative diseases. It has been found that adipose tissue, once considered to be physiologically inert, is an active producer of hormones, such as leptin and resistin, and numerous cytokines(1). The persistent low-grade inflammation secondary to obesity is thought to play a causal role in chronic problems, including orthopaedic disease, insulin resistance, diabetes mellitus in cats, abnormalities in circulating lipid profiles, cardiorespiratory disease, urinary disorders, reproductive disorders and others(2).

An important aspect of the negative effects of obesity may be due to glucose intolerance and insulin resistance(3). Both conditions can be experimentally induced in dogs by dietary manipulation causing obesity. Furthermore, lifelong dietary energy restriction has been shown to improve insulin sensitivity and glucose tolerance of dogs and has been associated with reduced disease conditions and greater longevity(3). However, few studies have examined this condition in naturally owned obese dogs, as most studies were conducted under laboratory conditions. Further studies are required to clarify the relationship between insulin resistance in naturally occurring canine obesity and the occurrence of degenerative diseases. Insulin resistance is characterised by elevated plasma insulin and exacerbated insulin responses to intravenous glucose infusion. The gold standard method to study this condition has been the hyperinsulinaemic, isoglycaemic
Materials and methods
The assay was conducted at the Laboratory of Research on Nutrition and Nutritional Diseases of Dogs and Cats, UNESP, Jaboticabal, Brazil. All procedures were approved by the Ethics and Animal Welfare Committee (Protocol no. 017665-07). All clinical procedures performed were for the direct benefit of the dogs used in the study, and the owners of all participating animals gave written informed consent.

Animals
The study included three groups. The first group was composed of ten owned obese dogs (three Labrador retrievers, one Beagle, one Rotweiller, one Dachshund and four mixed breeds; two dogs were male and eight were female; all dogs were neutered) with a median age of 83 months (minimum–maximum 19–166), a body condition score (BCS) of 9, a mean fat mass of 45·7 (SEM 1·51) % and a mean lean mass, 66·5 (SEM 1·92) % (P<0·001); no changes in lean mass (in kg) (P>0·05)). A control group of ten Beagle dogs was also included (5·0 (SEM 0·75) years old; BCS, 4·5; fat mass, 18·3 (SEM 3·38) % and lean mass, 81·7 % (P<0·01)).

Weight-loss protocol
A BCS was assigned to each dog using a 9-integer system, as described previously (5), and body composition was determined by the 2H isotope dilution technique (6). The dogs were fed restricted amounts, which corresponded to 60 % of their initial body weight; this group was designated as weight-reduced (WR) group (BCS, 8; fat mass, 33·5 (SEM 1·92) % and lean mass, 66·5 (SEM 1·92) % (P<0·001); no changes in lean mass (in kg) (P>0·05)). A control group of ten Beagle dogs was also included (5·0 (SEM 0·75) years old; BCS, 4·5; fat mass, 18·3 (SEM 3·38) % and lean mass, 81·7 % (P<0·01)).

Calculations and statistical analyses
Calculation procedures used for IVGTT data interpretation have been described in the literature (8). Data obtained during the GPPR test were analysed as described by Carciofi et al. (9). The integrated area under the curve (AUC) for glucose and insulin absolute values and increments were calculated by the trapezoidal method using ORIGIN software (version 6.0; Microcal Software, Inc., Northampton, MA, USA). Glucose and insulin curves were analysed by repeated-measures ANOVA. Glucose and insulin parameters and the AUC were analysed by paired (obese × WR or non-paired t tests. Variables not complying with ANOVA assumptions were analysed by the Wilcoxon test. Data were analysed using the general linear model procedure of the Statistical Analysis Systems statistical software package version 9.0 (SAS Institute, Cary, NC, USA). Results were considered to be significantly different when P<0·05.
Table 1. Results of the intravenous glucose tolerance test in obese dogs, in these same dogs after a loss of 20 % of body weight (weight-reduced (WR) dogs) and in a group of control non-obese dogs

(Medians and ranges)

<table>
<thead>
<tr>
<th></th>
<th>Obese (n = 10)</th>
<th>WR (n = 10)</th>
<th>Control (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>Minimum–maximum</td>
<td>Median</td>
</tr>
<tr>
<td>Κ (%)</td>
<td>3·6 a</td>
<td>2·49–6·69</td>
<td>2·6 a</td>
</tr>
<tr>
<td>T1/2 (min)</td>
<td>19·5 a</td>
<td>10·35–27·79</td>
<td>26·7 a</td>
</tr>
<tr>
<td>ΔIΔG</td>
<td>0·14 a</td>
<td>0·09–0·17</td>
<td>0·10 b</td>
</tr>
<tr>
<td>IRP (µU/ml)</td>
<td>71·9 a</td>
<td>56·40–108·70</td>
<td>18·0 b</td>
</tr>
<tr>
<td>IRT (min)</td>
<td>15·0 a</td>
<td>1·00–30·00</td>
<td>10·6 ab</td>
</tr>
</tbody>
</table>

K, percentage of glucose disappearance; T1/2, time for glucose concentration to reduce to half; ΔIΔG, insulinogetic index; IRP, insulin response peak; IRT, insulin response peak (in time).

a Values within a row with unlike superscript letters were significantly different by Wilcoxon’s test (P < 0·05).

Results

After their regimens, dogs lost 22·0 (SEM 1·1) % of their initial body weight in a mean rate of 0·70 (SEM 0·05) % of their body weight per week. The mean reduction in body fat mass was 27 (SEM 2·0) %, with no reduction in lean mass (in body weight per week). The mean reduction in body fat mass was 27 (SEM 2·0) %, with no reduction in lean mass (in kg) (P > 0·05).

In the IVGTT, higher glycaemia was found for obese dogs than for control dogs at times 1·0, 2·5 and 5·0 min (P < 0·05). The AUC for glucose, maximum and mean glycaemia were higher for obese dogs than for control dogs (P < 0·05) and intermediate for WR dogs (P > 0·05). Basal insulin concentration was higher for obese dogs (29·59 (SEM 7·64) pmol/l) than for WR (13·4 (SEM 7·8) pmol/l) and control (10·2 (SEM 6·8) pmol/l) dogs (P < 0·05). Insulin response peak, insulinogetic index, the AUC for insulin increment between 0 and 15 min and between 60 and 120 min were higher for obese dogs (P < 0·05) than for WR or control dogs that were not different from each other (P > 0·05). Data are presented in Table 1.

In the GPPR test, obese dogs (903 (SEM 61·0) mg/l) presented higher basal glycaemia than WR (67 (SEM 33·3) mg/l) and control (683 (SEM 33·7) mg/l) dogs (P < 0·05). Results are illustrated in Fig. 1. The AUC for glucose from 0 to 360, from 0 to 120 and from 120 to 360 was higher for obese dogs (P < 0·05) than for WR and control dogs. The AUC for insulin increment between 0 and 120 min was higher for obese dogs than for control dogs (P < 0·05) and intermediate for WR dogs (P > 0·05), although the delayed secretion (AUC for insulin increment between 120 and 360 min) was similar for obese and WR dogs (P > 0·05), with higher values than for control dogs (P < 0·05).

Discussion

Obese dogs have insulin resistance, as determined during the IVGTT by elevated fasting plasma insulin concentration, insulinogetic index, insulin response peak and delayed insulin secretion (AUC for insulin increment from 60 to 120 min). The loss of 27 % of fat mass (WR dogs) resulted in significant improvement in carbohydrate metabolism; in the IVGTT, WR dogs showed results similar to those of control dogs. Alterations in carbohydrate metabolism were also evident in obese dogs in the GPPR test, with high glucose and insulin postprandial levels. However, the induced weight loss was not enough to reverse these alterations; in the GPPR test, WR dogs still showed elevated delayed insulin secretion with values similar to those of obese dogs.
Hormones(7), using the postprandial response to evaluate intestine producing and releasing dozens of peptides and digestion and whole-body metabolism performed by the ing. Considering the complex endocrine control of food other studies were found to compare with the present find- between 120 and 360 min are very important to differentiate groups. Obese animals presented a remarkable elevation in the ideal body condition. The amount of body fat mass and possibly the time that the animals remained obese are points that need to be adequately considered in studies of obesity in dogs.

Interpreting the GPPR test, we observe that the results between 120 and 360 min are very important to differentiate obese animals presented a remarkable elevation in glucose and insulin serum concentrations in this interval. No other studies were found to compare with the present findings. Considering the complex endocrine control of food digestion and whole-body metabolism performed by the intestine producing and releasing dozens of peptides and hormones(7), using the postprandial response to evaluate carbohydrate metabolism, appears to be much more reasonable.

Conclusion

The IVGTT and GPPR test present different results, and maybe different responses. While the IVGTT showed that the loss of 20% body weight resulted in the improvement of glucose control with reduced insulin secretion, these same dogs at the GPPR test showed higher insulin secretion with values similar to those of obese dogs.

Acknowledgements

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