Trakia Journal of Sciences, Vol. 3, No. 5, pp 5-7, 2005

Available online at:
http://www.uni-sz.bg

ISSN 1312-1723

Original Contribution

DEVELOPMENT OF A MODEL OF INTRAVENOUS GLUCOSE TOLERANCE TEST IN DOGS

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ABSTRACT

Insulin resistance (IR) is a common problem in humans as well as in domestic dogs. Therefore, developing a method for defining glucose tolerance (GT) and IR is needed in veterinary medicine practice. Our aim was to adapt a model of intravenous glucose tolerance test (IVGTT) in dogs and to define parameters of GT in adult male individuals. We used 12 healthy male mongrel dogs, 4-7 years of age and weighing 13.7 kg each. Blood samples collected were analysed using the glucose-oxidase method on a Glucometer Ellite (Bayer®). Results showed that IVGTT in dogs were highly reproducible and could provide baseline parameters for GT.

Key words: insulin resistance, blood sugar, IVGTT, dogs

INTRODUCTION

Insulin resistance is an altered response to the action of insulin - both exogenous and endogenous Physiologically effective concentrations of insulin are unable to provide normal glucose uptake into peripheral tissue (1), and to suppress glucose production by the liver (2). Low insulin effectiveness stimulates pancreas to produce more insulin in order to maintain normal glucose blood levels. IR is typical of many syndromes, illnesses and metabolic disorders, such as impaired glucose tolerance, hyperinsulinaemia, dyslipidaemia, hypertension, cancer, high blood coagulation, acute and chronic infections, traumas, and most of all IR is typical of obesity and diabetes type II (1). Researches in the recent years show that these disturbances, studied in details in humans, are also typical of some pets as cats and dogs, and are due to high degree of over-nutrition or acute and chronic inflammations. So a method for estimating IR and disturbances of GT is needed in veterinary medicine practice. Insulin sensitivity can be tested in different ways, which can be applied both in humans and animals: euglycaemic-hyperinsulinaemic clamp technique, oral glucose tolerance test (OGTT), described in dogs by Kaneko (3), insulin tolerance test (ITT), and intravenous glucose tolerance test (IVGTT). The aim of this study is to develop a model of IVGTT in dogs, which can be used in veterinary practice. In this study we used the experience of several investigators- Bergman (4, 5, 6), Andrew (7), Sarov (8), Bloomgarden (9).

MATERIALS AND METHODS

We used twelve healthy male, mongrel dogs, 4-7 years of age, weighing 13.654±3.315 kg. Adapting period continued one month. For the whole period of experiment dogs were fed a standard maintenance diet (*"Jumbo dog", Gallisman S.A., Bulgaria*). Dogs were kept in individual cages and went out for walks twice a day - half an hour in the morning and another half an hour in the evening. In this way we provided conditions similar to the conditions of pet breeding. During adapting period, persons involved in the performance of IVGTT took care of the dogs. In this way we avoided stress situations while performing the test, which could influence the results.

The test started with measuring glucose blood levels twice in a ten-minute interval (-10min and 0min). Immediately after 0 min we infused into *v. cephalica* 40% glucose

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solution, 0.3 ml/kg body weight, for a period of 2 min using pumps.

Blood samples were collected from *v. cephalica* of the opposite forelimb on 3rd, 5th, 30th and 60th min after infusion. Glucose blood levels were measured at the moment of sample collection by glucose-oxidase method using Glucometer Ellite /Bayer®/.

RESULTS

After performing the test we obtained the following results - blood glucose levels on minute (– 10 and 0) did not precede normal values of 5.5 mmol/l. In this, the dynamics of the test of highest glucose blood levels were reached on the 3rd min after infusion 12.48 ± 0.62 mmol/l. In the short period between 3rd and 5th min there was a relatively quick decrease of glucose blood levels to 11.02±0.60 mmol/l, which was followed by a slow decrease to 5.05±0.17 mmol/l on 30th min (**Figure 1**). Glucose blood levels and coefficients of variance obtained from IVGTT are shown on **Table 1**. Comparing these results to results from IVGTTs performed on humans and rabbits, we found that there were significant differences between dogs and humans in blood glucose levels on 3rd, 5th , 30th and 60th min ($p<0.001$).While comparing rabbits and dogs there were significant differences only on 30th and 60th min ($p<0.001$; **Figure 1**). Glucose tolerance curves in dogs and rabbits were almost identical in the first phase of insulin secretion (**Figure 1**).

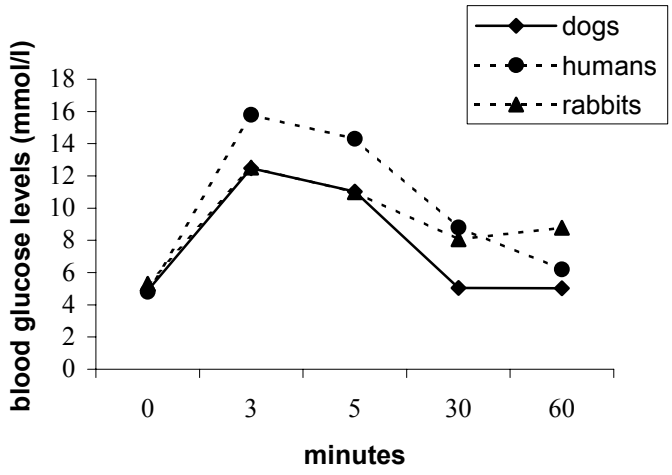

Figure 1. *Comparative analyses of glucose blood levels in dogs, humans and rabbits (IVGTT). Data about rabbits and humans were kindly offered by Sarov et al. (10).*

Table 1. *Glucose blood levels and coefficients of variance in IVGTT in mongrel dogs*

Dynamics min	*Glucose blood levels (mmol/l)*	*Coefficients of variance %*
-10	4.88±0.14	10.05
0	4.88±0.18	12.86
3	12.48±0.62	17.19
5	11.02±0.60	18.95
30	5.05±0.17	11.32
60	5.02±0.12	8.41

DISCUSSION

The results show the two-phase character of insulin secretion - a rapid increase immediately after glucose stimulation, which was followed by a slowly developing and long lasting response. The phase character of insulin secretion is due to rapid release of already produced insulin in the initial phase, while in the second phase insulin is being produced *de novo* and release is much slower.

Coefficients of variance showed that this model of IVGTT in dogs has good reproducibility. Though IVGTT was performed on mongrel dogs, values of standard deviation were low. These results and our previous studies confirmed that the

applied dose of glucose solution and the period of 60 min after infusion are appropriate for estimating the glucose tolerance and its disturbances, and even more - to suggest probable disorders in insulin sensitivity. This makes our model of IVGTT easier to perform in veterinary medicine practice, as compared to other methods that last 120-180 min or even more (2). In dogs, the second phase seemed to develop more rapidly, and on 30th min blood glucose levels decreased to its initial levels. Comparative analyses of glucose tolerance in dogs, humans and rabbits show that each species has a specific glucose dynamics, and GT in dogs is much similar to GT in rabbits, than to GT in humans.

The results obtained from our research can be used as baseline parameters of GT in adult male dogs, for this model of IVGTT. Defining the baseline parameters of GT for the different age categories of both genders will be a subject of our further investigations.

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