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# Intravenous glucose tolerance test in gestational diabetes and pregnancy: 'manual' versus computerized assessment

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## Summary

In order to assess the reliability of 'manual' versus computerized interpretation of the intravenous glucose tolerance test (IVGTT), fifty-five women, aged 19 to 41, underwent an IVGTT. Fifteen subjects had overt diabetes mellitus, sixteen were evaluated for gestational diabetes and twenty-four were healthy controls, fourteen of whom were pregnant. Each IVGTT was analysed by two trained physicians independently and by a simple computerized program, and the  $k'$  values obtained were compared, using the Student  $t$ -test for paired data. Significant difference ( $p < 0.005$ ) was found comparing either the 'manual' assessments or the 'manual' versus computer calculations. It is concluded that the IVGTT test must be interpreted using a simple computerized program, especially in borderline cases of pregnancy where the traditional 'manual' analysis might result in misclassification or misdiagnosis of the patient.

Intravenous glucose tolerance test; Gestational diabetes; Pregnancy; Computer

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## Introduction

The problem of identifying women with impaired carbohydrate metabolism remains controversial. Both the oral glucose tolerance test (OGTT) and the intravenous glucose tolerance test (IVGTT) use a series of measurements following a glucose load. While the OGTT is interpreted according to criteria for the individual glucose values at each point in time, with great variance among the proposed criteria

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[1–3], the IVGTT is interpreted according to the rate of glucose disappearance. The two tests were compared by several investigators, who reached different conclusions concerning their relative reliability in gestational diabetes and pregnancy [4–8]. The IVGTT is preferred in physiological (e.g. pregnancy) and pathological conditions when altered gastro-intestinal function might effect glucose absorption. The routine interpretation of the IVGTT is based on a ‘manual’ analysis of the rate of glucose disappearances, obtained by a straight line drawn through a logarithmic plot of the glucose measurements. Drawn by a ruler according to the ‘best judgement’ of the human eye, it is open to human variability and error. On the other hand, the computer fits the best line that describes the test data, using a mathematical method which minimizes the square of the error.

In our study, we compared the results of human estimation to computer calculation, in order to see if use of the computer can improve the reliability and accuracy of the IVGTT.

## Materials and methods

The IVGTT is based on the assumption that glucose concentration decreases exponentially with time following the loading dose. A loading dose of 25 g glucose (50 ml of 50% glucose solution) was given intravenously over 2–4 min. Capillary whole blood samples were obtained from the contralateral hand at 10-min intervals for 60 min for glucose measurements, using glucose oxidase reagent strips read by Glucometer. As all subjects were within +10% of their ideal body weight, a fixed glucose load dose was used. The logarithms of the glucose values from all six points (10 min to 60 min) were plotted on semilog graph paper against linear time. The half-time ( $t_{1/2}$ ) required for blood glucose to fall from a given level was determined. A straight line that according to the ‘best judgement’ of the investigator best fitted the six plotted points was drawn. Its intersection with the  $t = 0$  axis was considered as ‘glucose concentration at time 0’ ( $c_0$ ) and the value of  $t$  at  $c_0/2$  was obtained. By substituting this for  $t_{1/2}$  in the formula  $k = 69.3/t_{1/2}$  the  $k$  constant was calculated and is referred to as the  $k$  value.

The computer program fits a regression line to the natural logarithm ( $\ln$ ) glucose versus time for all six points, whose slope is the computerized  $k$  value. If the deviation of a measured glucose value from the regression line, expressed as percentage of  $c_0$ , was more than +5%, the measured value was rejected and a new regression was computed for the remaining five points. If more than one such point existed, the point with the largest deviation was rejected. The resulting  $k$  value, whether for five or six points, was then taken as characterizing the test ( $k_c$ ).

All IVGTT studies were performed between 08.00 to 10.00 in the morning. All subjects were non-obese and weighed within  $\pm 10\%$  of their ideal body weight. All studies were performed after an overnight fast, at the Out-Patient Clinic or at the Diabetes Day-Care Center. No symptoms or side-effects were observed in response to the IVGTT. Subjects were divided to three groups as follows.

Group I: Fifteen diabetic women (7 non-insulin-dependent and 8 with insulin-dependent diabetes) aged 21 to 36.

Group II: Sixteen pregnant women, aged 19 to 32, in the third trimester of their

pregnancy, with one or more of the following: past history of a large baby ( $> 4500$  g), perinatal death, diabetes in the family (parent or sibling), large fetus on ultrasound, glycosuria, toxemia, hypertension, hydramnion.

Group III: twenty-four non-diabetic females (14 pregnant, 10 non-pregnant), aged 20 to 41, comprising a control group.

The non-diabetic subjects, whether pregnant or not, were combined in one control group as we did not find a significant difference comparing their  $k$  values. All 55 subjects underwent an IVGTT as previously described. Each test was analysed 'manually' by two trained investigators independently, and the  $k$  value was obtained. The  $k_c$  value was obtained using the computerized program. The  $k$  values obtained in each way were paired and analysed using the Student  $t$ -test for paired data.

## Results

Since the computer interpretation of the  $k$  value was based on a mathematical correlation to the measured data points, we used it as a reference. Table I shows the two individual 'manual' interpretations of the  $k$  values ( $k_A$  and  $k_B$ ) compared to the computerized  $k$  value ( $k_c$ ). A significant difference ( $p < 0.005$ ) was noted among two out of three groups, comparing investigator B  $k$  values ( $k_B$ ) to either investigator A  $k$  values ( $k_A$ ) or to the computer's  $k_c$ . On the other hand, no significant difference was found comparing investigator A  $k_A$  values to the computer's  $k_c$ .

On our calculations for  $k_c$ , we defined a deviant glucose value as one that is displaced from the initial regression line by more than 5% of the intercept value ( $c_0$ ). In a given IVGTT, more than one such point may be present. In such an event we rejected the one with maximal deviation and calculated the  $k_c$  for the remaining 5 points. In 29 of the 55 tests performed (53%) such excessive deviation occurred. Altogether the computer had rejected 7 points in group I, 10 points from group II and 12 in group III. Most points with excessive deviation from the regression line occurred at the 10-min time. The preponderance of  $t_{10}$  as the reject point was significant according to the  $\chi^2$  test ( $p < 0.001$ ).

TABLE I

'Manual' versus computer  $k$  value

	No.	Mean $k_c^a$	Mean $k_A^b$	Mean $k_B^c$	Paired $t$ -test		
					$m(k_c - k_A)$	$m(k_c - k_B)$	$m(k_A - k_B)$
Group I	15	0.78	0.74	0.85	0.037	0.085 *	0.106 *
Group II	16	1.63	1.71	1.72	0.076	0.090 *	0.016
Group III	24	2.18	2.21	2.11	0.030	0.065 *	0.115 *
Total	55	1.64	1.66	1.65	0.025	0.021	0.017

<sup>a</sup>  $k$  value by computer program.

<sup>b</sup>  $k$  value by investigator A.

<sup>c</sup>  $k$  value by investigator B.

\*  $p < 0.005$ .

## Discussion

Maternal glucose metabolism is increased during pregnancy. While parameters such as the glucose disappearance coefficient seem to be unchanged, the glucose distribution space and glucose transfer are increased [9]. The glucose disappearance rate after an intravenous load is a function of both endogenously secreted insulin and glucose itself [10]. Several protocols were suggested for the IVGTT interpretation and performance [4–8,11]. However, some difficulties were described with regard to the techniques and the interpretation of the results [10]. For the obstetrician seeking maximal separation of gestational diabetics from either overt diabetics or normals, the  $k$  value seems to be a much sharper index, especially during the third trimester when glucose absorption is impaired.

Our results suggest that there might be a significant difference between the 'manual' and the computer interpretation of the IVGTT. Comparison of the 'manual' interpretations of two trained investigators revealed significant individual differences. Thus, the reliability of manually performed IVGTT is highly questionable. Comparing the mean  $k$  values obtained by each method (Table I), there is sharp distinction of  $k$  values between diabetics, gestational diabetics and normal controls, either pregnant or not. The diabetics also had fewer points rejected (with excessive deviation of  $\pm 5\%$ ). The  $t = 10$  min points seem to deviate the most. Similar observations were previously described [12], and it was suggested that the 10-min point should be disregarded if it deviates by more than 50 mg/dl from its predicted value. We believe that if the concept of rejection of a deviated point is accepted, all the data points must be examined and only then should a decision upon the criteria for rejection be made. This decision-making is made easy by a simple computer program, using the ratio between the absolute deviation and the glucose concentration at time 0 as a criterion.

In order to avoid errors in the evaluation of impaired glucose tolerance (IGT) in pregnancy, computerized evaluation is a must. Although we have used a large computer in this study, the 'computerized'  $k$  values can easily be obtained using a small personal computer or even a programmable calculator capable of performing linear regression analysis.

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