Prediction of the need for insulin therapy in pregnant women with impaired gestational glucose tolerance (IGGT)

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Summary: Objective. Our aim was identify pregnant women with impaired gestational glucose tolerance (IGGT) at risk for more severe gluco-metabolic alterations who could require subsequent insulin therapy during pregnancy.
Methods. We studied 78 pregnant women with IGGT after a 100 g glucose oral tolerance test. Patients were divided into two groups based on a cut-off value of a 15% reduction from normal values of the glucose load. Sixty-three patients had at least one value above this cutoff point, while 15 had all residual values below the cut off. All patients were put on a diet and glycemia reassessed: those who showed pre-prandial blood glucose higher than or equal to 90 mg/dl and/or 2-h post-prandial higher than or equal to 120 mg/dl underwent insulin therapy.
We matched the presence of at least one residual value in the oral glucose tolerance test above the limit used with the subsequent need for insulin treatment.
Results. The presence of at least one residual value above the "–15%" cutoff in the glucose tolerance test was associated with high risk (positive predictive value 79%), whereas normality of the residual values indicated low risk (negative predictive value 80%), of insulin need during the rest of pregnancy.
Conclusions. Pregnant women with IGGT definitely do not have a normal metabolic condition, sometimes even requiring diet and insulin treatment. From our results, the need for more accurate monitoring and insulin treatment may be predicted by simply looking at the residual values in the glucose tolerance test.

Key words: Gestational diabetes mellitus pregnancy.

INTRODUCTION

Pregnancy is associated with a temporary change in maternal glucose metabolism involving a decrease in insulin sensitivity, reaching values similar to those see in Type II Diabetes ([1]). A pregnant woman needs a two-to threefold increase in her post-prandial insulin secretion in order to maintain normal glucose tolerance. Glucose intolerance develops in women that are unable to compensate for such metabolic modifications. The most documented and used diagnostic criteria for gestational gluco-metabolic alterations are those of O'Sullivan and Mahan, modified for plasma values by the US National Diabetes Data Group (1979), and

Received 10-8-1995 from the
Department of Obstetrics and Gynecology
University of Ancona, Italy
Revised manuscript accepted for publication 20-11-1995.

adopted later by two International Workshops ([2]).

Diagnosis of gestational diabetes (GDM) requires at least two abnormal values in an oral glucose tolerance test, while impaired gestational glucose tolerance (IGGT) is defined as the abnormality of only one value in the glucose tolerance test. Although diagnostic criteria for IGGT are well standardized, the same cannot be said for the clinical significance of IGGT. There are controversies concerning IGGT's influence on negative perinatal outcome ([2-7]), the need for intensive blood glucose monitoring and/or insulin treatment ([8-11]).

The aim of this study was to seek additional criteria for the oral glucose tolerance test; criteria able to differentiate IGGT patients at risk for severe glucometabolic alterations who could require insulin therapy during pregnancy.

MATERIALS AND METHODS

The study group consisted of 78 IGGT patients who were admitted to the Department of Gynecology and Obstetrics at the University of Ancona Faculty of Medicine from January 1st, 1991 to December 31st, 1993. The diagnosis of IGGT was made based on a standardized oral glucose tolerance test. The patient, after an overnight fast of 12 hours and a controlled diet consisting of at least 150 g of carbohydrates daily for three days before the test, ingested a 100 g glucose load on the morning of the examination. Four venous blood samples were made: fasting, 1, 2 and 3 hours after glucose load. Abnormal values were defined: $\geq$105 mg/dl in a fasting state, $\geq$190 mg/dl after 1 hour, $\geq$165 mg/dl after 2 hours and $\geq$145 mg/dl after 3 hours. All patients suffering from IGGT followed a diet having a low content of olygosaccharides. These same patients later underwent a glucose profile test; such a test consisted a six venous blood samples, drawn before and two hours after each major meal (breakfast, lunch, dinner). Pre-prandial values $\geq$ 90 mg/dl and 2-h post-prandial $\geq$ 120 mg/dl were considered abnormal. Patients who had an altered glucose profile underwent insulin therapy according to a mixed-multiple regimen. The degree of insulin need was determined on the basis of a blood glucose profile. We then divided the patients into two groups based on a cutoff value of a 15% reduction from normal values of the glucose load (i.e, 90-165-145-125). Patients who had at least one value above this cutoff point were includede in the first group (63 patients); patients who had no value above this sutoff were included in the second group (15 patients).

RESULTS

Fourteen patients out of 63 in group 1 (20%) and three patients of group 2 required insulin therapy. Based on an evaluation of insulin requirements, it was determined that 11 of the 14 patients needing insulin from group 1 required a dose greater than 10 IU/day.

The results of using a cutoff point of "–15%" as a predictor of insulin requirement during pregnancy are presented in Table 1. Statistical analysis demonstrated that the positive predictive value in Group 1 was 79% and the negative predictive value in Group 2 was 80%. The occurence of at least another value above the "–15%" cutoff in the glucose tolerance test was associated with a good probability of the need for insulin therapy. On the other hand, normality of the remaining values (i.e., only one value above the cutoff) indicated only a minimal probability of the need for insulin therapy during the course of the pregnancy.

Table 1. – *Predictivity of the insulin need of IGGT patients, according to residual values (–15% cutoff) of the Glucose Tolerance Test.*

	One value above cutoff (n=63)	All values under cutoff (n=15)
Sensitivity	79	82
Specificity	25	20
Positive PV	79	22
Negative PV	25	80
Accuracy	65	33

DISCUSSION

Early diagnosis and treatment of gestational diabetes are associated with a reduction in perinatal mortality and morbidity. The clinical significance of one abnormal value in the glucose tolerance test in not as clear, however, as seen in the contrasting data published recently. Several studies have indicated that impaired gestational glucose tolerance is definitely not a normal metabolic condition. Langer *et al.* ([2]), using normally glucose tolerance test values from the National Diabetes Group, have reported that IGGT patients are at risk for an unfavourable pregnancy outcome; if not treated, such patients have a greater incidence of fetal macrosomia and neonatal metabolic disorders with respect to pregnant women having a normal glucose tolerance test. In another study ([3]), the incidence of gestational hypertensive disorders was found to be significantly increased in women with IGGT. Neiger and Coustan ([12]), have identified in IGGT patients a significant increase (+34%) in the risk of developing gestational diabetes in the course of their pregnancies. Another study by Langer ([13]), showed that treating IGGT patients with insulin reduced the incidence of fetal macrosomia and neonatal metabolic problems to values similar to normal subjects.

In contrast to the above, however, other recent works have indicated that IGGT cannot be equated to gestational diabetes. Roberts *et al.* ([11]), evaluating perinatal outcome in women with IGGT (defined according to WHO criteria), did not find any significant increase in the incidence of perinatal complications. Li *et al.* ([5]), found that perinatal outcome in insulin treated IGGT subjects was almost equivalent to that found in non-treated IGGT patients under the same circumstances.

Based on reviews of the most recent medical literature and the results of our study, we can affirm that patients with a clinical diagnosis of impaired gestational glucose tolerance are not a homogeneous group. Within the classification of IGGT there are patients whose metabolic alterations are severe enough to require insulin therapy (20% of the patients in our study) and there are patients with a minimal and stable reduction in their gestational glucose tolerance who do not require any pharmacological therapy (80% of our study). The need to select the patients at increased risk, not to mention the time and cost of "universal" IGGT monitoring, have pushed us to seek out more selective criteria. The introduction of a cutoff point of 15% less than normal values as a second criterion for an evaluation glucose tolerance (based on US National Diabetes Group Criteria), has resulted in an accurate technique to differentiate those patients who are in need of more strict control of their gluco-metabolic conditions. To date, our monitoring has resulted in the establishment of an individual glucose profile, but we are looking forward to other deeper biophysical assessments, including the measurement of fetal interventricular septum thickness, which is a marker of maternal hyperglycemia ([14]). However wider studies may be required, to better establish a reliable procedure to detect patients at risk and to reduce possible adverse perinatal outcomes in a condition, that seems much more like frank gestational diabetes than normal pregnancy.

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