Correspondence between first-trimester fasting glycaemia, and oral glucose tolerance test in gestational diabetes diagnosis

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Abstract

Aim. – To evaluate the correspondence between first-trimester fasting glycaemia and the results of the OGTT in diagnosing gestational diabetes (GDM).

Methods. – The medical records of all consecutive women who had undergone a diagnostic OGTT, performed according to the IADPSG, during the past year were retrospectively reviewed. All first-trimester fasting glucose values greater or equal to 5.1 mmol/L (92 mg/dL), recommended as a diagnostic value, were also verified for each patient in this cohort. Moreover, a ROC curve and a multiple logistic-regression model were constructed to calculate the predictive capability of this cut-off value in diagnosing GDM.

Results. – In our population of 738 eligible pregnant women, an 11.9% prevalence of GDM was revealed by OGTT. However, when the first-trimester fasting glucose value for each patient was retrospectively considered, there were a further 29 patients who should have been diagnosed as GDM cases (glycaemia ≥ 5.1 mmol/L), although their OGTT was normal. Yet, when the value of fasting glucose was considered not diagnostic, but only predictive, an AUC of 0.614 (95% CI: 0.544–0.684) and an aOR of 7.1 (95% CI: 3.8–13.1) was obtained in these patients compared with the reference group (fasting glucose < 5.1 mmol/L).

Conclusion. – There was no complete correspondence in diagnosing GDM between the first-trimester fasting glucose value and the results of a 2-h 75-g OGTT performed early in the third trimester. However, albeit not diagnostic, a fasting glucose value greater or equal to 5.1 mmol/L may be considered a highly predictive risk factor for GDM.

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Keywords: Gestational diabetes; First-trimester fasting glycaemia; Diagnostic criteria; OGTT; IADPSG Consensus Panel

Résumé

Relation entre la glycémie à jeun au premier trimestre et le résultat de l’hyperglycémie provoquée par voie orale réalisée au troisième trimestre dans le diagnostic du diabète gestationnel.

But. – L’objectif de notre étude était de déterminer la corrélation entre la glycémie à jeun au premier trimestre et le résultat du test d’hyperglycémie provoquée par voie orale (HGPO) dans le diagnostic du diabète gestationnel.

Méthodes. – Il s’agit d’une étude rétrospective. Nous avons dépouillé les dossiers médicaux de toutes les gestantes ayant effectué un test d’hyperglycémie provoquée par voie orale (HGPO). Notre période d’étude s’étendait du mois de mai 2010 à avril 2011. L’interprétation des résultats a été faite en se fondant sur les critères diagnostiques de l’IADPSG. Nous avons relevé la glycémie à jeun effectuée au premier trimestre de toutes les femmes enceintes. Pour calculer la valeur prédictive de la glycémie à considérer comme valeur-seuil (cut-off) (92 mg/dL), nous avons réalisé une courbe ROC et un modèle de régression logistique multiple.

Résultats. – De l’interprétation des résultats de l’HGPO il ressort que la prévalence du diabète gestationnel était de 11,9 % (88/738). En confrontant la valeur de la glycémie à jeun au premier trimestre et le résultat de l’HGPO, 29 gestantes dont la glycémie à jeun du premier trimestre était supérieure à 92 mg/dL avaient un test d’HGPO négatif. En écartant la valeur de la glycémie à jeun supérieure à 92 mg/dL comme critère diagnostique et en ne la considérant seulement pour sa valeur prédictive, nous avons obtenu un OR de 7.
1. Introduction

Gestational diabetes mellitus (GDM) has been defined as “any degree of glucose intolerance with onset or first recognition during pregnancy” [1]. Although there is a general consensus over this definition, there has never been universal consensus regarding screening for GDM and its diagnostic criteria. Last year (2010), on reviewing the published results of the Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) study [2], the International Association of Diabetes and Pregnancy Study Group (IADPSG) Consensus Panel suggested new criteria in an attempt to obtain worldwide consensus for GDM diagnosis [3]. They proposed a 2-h 75-g oral glucose tolerance test (OGTT) for all women not already known to be diabetic, and such a diagnosis was made if at least one value of fasting plasma glucose (FPG) concentration was greater or equal to the thresholds of 5.1, 10.0 and 8.5 mmol/L (for fasting, 1-h and 2-h post-glucose load, respectively). The IADPSG Consensus Panel chose these thresholds as the diagnostic criteria because they are the glucose concentrations at which the chances of the adverse perinatal outcome considered are 1.75 times the chances of the same outcome in the reference glucose group. Furthermore, the IADPSG Panel had previously recommended an FPG value greater or equal to 5.1 mmol/L as a diagnostic marker of GDM.

Thus, at least according to the IADPSG Panel’s suggestions, there are two ways to diagnose GDM, one during the first trimester, and the other early in the third trimester (by OGTT). For this reason, the aim of the present study was to verify the correspondence, for diagnostic purposes, between the first-trimester FPG value and the OGTT, evaluated according to IADPSG criteria at 24–28 weeks of gestation.

2. Patients and methods

The present retrospective study was carried out in our department and involved the use of a 2-h 75-g OGTT according to the IADPSG Consensus Panel criteria (May 2010), and was concluded a year later. The study protocol received the approval of the Institutional Review Board, and all participating patients gave their consent regarding the collection of anamnestic data.

All consecutive Caucasian women scheduled for an OGTT early in the third trimester of pregnancy were enrolled, and prepregnancy body mass index (BMI), age, parity and gestational age were registered for each patient. All of the women were also asked to provide their laboratory results for their first-trimester fasting glucose values, if available, to the outpatients service, and these were also duly registered on their charts. Almost all patients had a first-trimester FPG value, as this test is free of charge to everyone in our country. If this value was not greater or equal to 7.0 mmol/L, the patient then underwent a 2-h 75-g OGTT and the resulting values were evaluated according to IADPSG criteria (5.1, 10.0 and 8.5 mmol/L for fasting, 1-h and 2-h glucose concentrations, respectively). In addition, the laboratory was blinded to any pre-existing values of fasting glucose.

At the end of the observational period, the women’s charts were reviewed and the correspondence between the two different diagnostic strategies compared.

2.1. Statistics

SPSS Statistics 17.0 computer software (SPSS, Inc, Chicago, IL, USA) was used for the statistical analysis. The variables were expressed as means ± SD or n (%). Differences among the groups were analyzed by analysis of variance (ANOVA) or Chi-square tests. A receiver operating characteristic (ROC) curve was constructed to test the ability of the first-trimester FPG values to discriminate patients with a diagnosis of GDM. The area under the curve (AUC) was calculated using the trapezoidal rule.

Multiple logistic-regression analysis was used to assess the Odds ratios (ORs) of the independent variables, and 95% confidence intervals (CI) were calculated as well. In addition, as maternal age and prepregnancy BMI were considered confounding factors, adjusted ORs (aORs) were also calculated. Finally, P<0.05 was considered significant for all of the data analyzed.

3. Results

During the present study period, a total of 775 consecutive Caucasian pregnant women were referred to our department for a 2-h 75-g OGTT. However, 12 women were excluded because they were twin pregnancies, 18 because they had no first-trimester fasting glucose assay, six because of an FPG value determined after the first trimester of pregnancy, and one because of a first-trimester FPG that was already diagnostic of pregestational diabetes (≥ 7.1 mmol/L).

Among the 738 eligible patients, the OGTT identified 88 cases of GDM (11.9%), according to the criteria of the American Diabetes Association (ADA) [4]. Of these 88 GDM cases, only 24 had a first-trimester fasting glucose greater or equal to 5.1 mmol/L. Of the 650 patients with values below the thresholds of diagnosis by OGTT, 29 women had a first-trimester FPG greater or equal to 5.1 mmol/L. At this point, the patients who were positive according to the OGTT showed an 11.9%
Table 1
Characteristics of all consecutive women undergoing the oral glucose tolerance test, comparing those with a first-trimester fasting plasma glucose (FPG) greater or equal to 5.1 mmol/L and those with an FPG less than 5.1 mmol/L.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>FPG &lt; 5.1 mmol/L (n = 685)</th>
<th>FPG ≥ 5.1 mmol/L (n = 53)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>30.63 ± 5.24</td>
<td>33.42 ± 4.36</td>
<td><em>P</em> = 0.0001</td>
</tr>
<tr>
<td>Prepregnancy BMI (kg/m²)</td>
<td>23.80 ± 7.32</td>
<td>27.9 ± 5.81</td>
<td><em>P</em> = 0.0001</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>26.0 ± 2.7</td>
<td>25.3 ± 2.3</td>
<td><em>P</em> = 0.064</td>
</tr>
<tr>
<td>Parity &gt; 1 [n (%)]</td>
<td>318 (46.4%)</td>
<td>31 (58.4%)</td>
<td><em>P</em> = 0.1</td>
</tr>
<tr>
<td>First-trimester FPG (mmol/L)</td>
<td>4.3 ± 0.4</td>
<td>5.3 ± 0.16</td>
<td><em>P</em> = 0.0001</td>
</tr>
<tr>
<td>Prevalence of GDM [n (%)]</td>
<td>64 (9.3%)</td>
<td>24 (45.3%)</td>
<td><em>P</em> = 0.0001</td>
</tr>
</tbody>
</table>

Data are expressed as means ± SD unless otherwise specified; BMI: body mass index; GDM: gestational diabetes mellitus.

prevalence of GDM in our population whereas, on also considering the women with a positive first-trimester fasting glucose (n = 29, 3.9%), the prevalence was 15.8%.

However, when the first-trimester fasting glucose value was not considered a diagnostic test for GDM, as suggested by the IADPSG Consensus Panel [3], but only as a screening test, there were 685 negative patients and 53 patients with an FPG greater or equal to 5.1 mmol/L. The characteristics of our two groups of patients are shown in Table 1. Of the 53 patients with a fasting glycaemia greater or equal to 5.1 mmol/L, 24 were later confirmed by OGTT as having GDM with, in particular, six patients who had values greater or equal to 5.6 mmol/L, whereas 29 failed to meet the diagnostic criteria. Given the cut-off value (≥ 5.1 mmol/L) used in the present study, there was a false-negative rate (FNR) of 9.8% and a false-positive rate (FPR) of 4.4%. In women who had a first-trimester FPG greater or equal to 5.1 mmol/L, the calculated crude OR for GDM was 8.0 (95% CI: 4.4–14.6), with an aOR of 7.1 (95% CI: 3.8–13.1) adjusted for prepregnancy BMI and maternal age, compared with the other group (FPG < 5.1 mmol/L). In the constructed ROC curve that included all eligible patients, distinguishing between those with a first-trimester value greater or equal to 5.1 mmol/L, and the negative patients, and considering only those patients with a positive OGTT as GDM cases, the AUC was 0.614 (95% CI: 0.544–0.684; Fig. 1).

4. Discussion

There was no complete correspondence between the first-trimester fasting glucose value and the 2-h 75-g OGTT in the diagnosis of GDM. Thus, if the OGTT is considered the gold standard for diagnosing GDM [4], then an FPG greater or equal to 5.1 mmol/L, but less than 7.0 mmol/L, during the first trimester of pregnancy should not be considered a diagnostic criterion of GDM.

Nevertheless, it is not clear why the IADPSG Panel [3] first stated that “there have not been sufficient studies performed to know whether there is the benefit of generalized testing to diagnose and treat GDM before 24–28 weeks’ gestation”, and then surprisingly concluded that “it is recommended that a FPG value in early pregnancy greater or equal to 5.1 mmol/L might also be classified as GDM”.

In fact, fasting glycaemia is the most studied biomarker of early pregnancy as a predictor of gestational diabetes later in pregnancy, but it was never proposed as a diagnostic test. The Riskin-Mashiah et al. [5] study (cited by the IADPSG Consensus Panel) reported the high predictive value of the first-trimester FPG level with an aOR of 8.63 (95% CI: 4.13–18.04) for the categorization of fasting glycaemia between 5.3 and 5.5 mmol/L. However, in addition to these interesting results, the authors also considered the FPG as a screening test, not a diagnostic test, with a suggested cut-off value. Indeed, they even specified that “there is no clear threshold for a fasting glucose level that puts pregnant women at a significantly increased risk”. The same recommendation was reported in the prospective study by Lopez Caudana et al. [6], who found a relative risk (RR) of 5.8 (95% CI: 1.9–17.5) in the group with first-trimester glycaemia between 5.1 and 6.8 mmol/L compared with the group with values less than 4.5 mmol/L that served as a reference.

Fig. 1. Receiver operating characteristic (ROC) curve using first-trimester fasting glucose values greater or equal to 5.1 mmol/L to screen for gestational diabetes mellitus (GDM).
In the present study, a strong, graded association between fasting glucose levels and ORs for GDM was also registered. The aOR of 7.1 for women with a first-trimester FPG greater or equal to 5.1 mmol/L suggested the highly predictive significance of this threshold. However, it also means that, if this cut-off value is considered diagnostic, it will increase the prevalence of GDM even further at a time when the prevalence has already been nearly doubled by the new ADA criteria [4]. Indeed, our present study found an additional 3.9% of patients who should have been monitored and treated for perhaps no obvious reason early in pregnancy. These extra 29 patients, diagnosed because of a first-trimester FPG greater or equal to 5.1 mmol/L, but less than 7.0 mmol/L, represent the FPR of a test that exposes women diagnosed as GDM to the likely medicalization of otherwise healthy pregnancies. Moreover, as paradoxically suggested by Ryan [7], an FPG of 5.1 mmol/L to diagnose GDM should be considered, as this value is considered normal in the non-pregnant state.

The limitations of our present study are, of course, its retrospective design and the small sample size, which might have lowered, but not completely cancelled, the FPR. In addition, the lack of a standardized protocol for reporting first-trimester fasting glucose values could be considered a limitation, even though it probably reflects routine clinical practice.

In conclusion, it is likely that the first-trimester fasting glucose value is important especially in the diagnosis of pregestational diabetes. Indeed, when this possibility was not considered, those patients were then classified as having GDM whereas all they actually needed was closer monitoring and appropriate treatment as early as possible. Nevertheless, a first-trimester fasting glucose value of 5.1–6.9 mmol/L should be considered as only a predictive value like other markers (such as previous GDM, macrosomia, obesity or a family history of diabetes), but not a diagnostic test for GDM, as proposed by the IADPSG Consensus Panel.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References