



The impact of different 75 g oral glucose tolerance test target ranges within normal limits on neonatal outcomes: A validation study

Normal sınırlardaki farklı 75 gr oral glukoz tolerans test hedef aralıklarının neonatal sonuçlar üzerine etkisi: Bir geçerlilik çalışması

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Abstract

Objective: To investigate the impact of different 75 g glucose tolerance test (OGTT) target ranges within normal limits on neonatal outcomes, thus to investigate the validity of 75 g OGTT thresholds.

Materials and Methods: The normal 1-hour and 2-hour ranges of 75 g OGTT levels of 110 pregnant women with no gestational diabetes mellitus (GDM) were further divided into three different sub-groups; for the 1 hour as group 1 (<120 mg/dL), group 2 (120-140 mg/dL), group 3 (>140 mg/dL) and for the 2 hour as group 1 (<120 mg/dL), group 2 (120-135 mg/dL), and group 3 (>135 mg/dL).

Results: For the 1-hour results, there was no statistically significant difference between groups in terms of age, body mass index, multiparity, neonatal hypoglycemia, hyperbilirubinemia, neonatal intensive care unit admission, birth weight, and LGT rates; however, the rate of small-for-gestational-age (SGA) infants was significantly higher in group 2 compared with those in group 3. For the 2-hour results, statistically similar results were found between the groups.

Conclusion: A 2-hour 75 g OGTT has reliable threshold values for GDM screening. However, because there are still adverse neonatal outcomes in women with OGTT results below the current thresholds and the number of SGA fetuses is higher in the glucose range 120-140 mg/dL of the first hour, the validity of the 75 g OGTT thresholds still needs further investigation.

Keywords: Gestational diabetes mellitus, glucose tolerance test, neonatal outcome, screening, pregnancy

Öz

Amaç: Bu çalışma normal sınırlardaki farklı 75 gr oral glukoz tolerans test (OGTT) hedef aralıklarının yenidoğan sonuçlarına etkisini araştırarak 75 gr OGTT eşik değerlerinin geçerliliğini araştırmak için yapıldı.

Gereç ve Yöntemler: Gestasyonel diabetes mellitus (GDM) saptanmayan 110 gebe kadının normal sınırlardaki 1. saat ve 2. saat 75 gr OGTT değerleri 1. saat için grup 1 (<120 mg/dL), grup 2 (120-140 mg/dL), grup 3 (>140 mg/dL) olarak ve 2. saat için grup 1 (<120 mg), grup 2 (120-135 mg/dL), grup 3 (>135 mg/dL) olarak üç alt gruba ayrıldı.

Bulgular: Birinci saat sonuçlarda yaş, vücut kitle indeksi, multiparite, yenidoğan hipoglisemi, hiperbilirubinemi, yenidoğan yoğun bakım ünitesi ihtiyacı, doğum ağırlığı ve LGT oranları açısından gruplar arasında istatistiksel olarak anlamlı bir fark yoktu; bununla birlikte, grup 2'deki gebelik yaşı için küçük (SGA) bebeklerin oranı grup 3'e göre istatistiksel olarak anlamlı derecede yüksekti. İkinci saat sonuçlar gruplar arasında istatistiksel olarak benzer bulundu.

Sonuç: İki saatlik 75 gr OGTT, GDM taraması için güvenilir eşik değerlerine sahiptir. Bununla birlikte, mevcut eşik OGTT değerleri altında olan kadınlarda olumsuz yenidoğan sonuçlar olması ve birinci saat 120-140 mg/dL glukoz aralığında SGA fetüs sayısının yüksek olması nedeniyle 75 gr OGTT eşik değerlerinin geçerliliği hala araştırmayı gerektirmektedir.

Anahtar Kelimeler: Gestasyonel diabetes mellitus, glukoz tolerans testi, yenidoğan sonuç, tarama, gebelik

PRECIS: A 2-hour 75 g glucose tolerance test has reliable threshold values for gestational diabetes mellitus screening. However, the validity of the 75 g glucose tolerance test thresholds still needs further investigation.

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Introduction

Gestational diabetes, which affects 3% to 6% of all pregnancies, is an important issue that should be handled with specific treatment in addition to routine antenatal care to reduce the risks of maternal and perinatal morbidity⁽¹⁾. It has been suggested that risks for adverse outcomes differ according to the single or combined thresholds selected⁽²⁾. The hyperglycemia and adverse pregnancy outcome (HAPO) study, pointed out the continuously increased risk between maternal glucose levels and adverse pregnancy outcomes even within ranges previously considered to be normal for pregnancy⁽³⁾. This study was the cornerstone for the diagnosis of gestational diabetes mellitus (GDM), identified using the 75 g oral glucose tolerance test (OGTT) when any of the following plasma glucose values are exceeded: fasting, ≥ 5.1 mmol/L (92 mg/dL); 1 h, ≥ 10 mmol/L (180 mg/dL); and 2 h, ≥ 8.5 mmol/L (153 mg/dL)⁽⁴⁾. These cut-offs recommended by the International Association of the Diabetes and Pregnancy Study Groups (IADPSG)⁽⁵⁾, have been adopted by the World Health Organization (WHO)⁽⁶⁾ and the American Diabetes Association (ADA)⁽⁴⁾. As a result of new diagnostic criteria, the increase in the incidence of GDM and use of treatment modalities will be inevitable; however, considering the increasing rates of obesity and diabetes globally, the changes are updated, and recommended to reduce adverse outcomes^(4,5,7). On the contrary, in 2015, the National Institute for Health and Care Excellence (NICE) opted for a higher fasting glucose threshold [fasting ≥ 5.6 mmol/L (≥ 101 mg/dL), and/or 2 h ≥ 7.8 mmol/L (≥ 140 mg/dL)]⁽⁸⁾.

The objective of this study was to investigate the validity of 75 g OGTT thresholds by evaluating the impact of different 75 g OGTT target ranges within normal limits on neonatal outcomes because the diagnostic dilemma on the most appropriate test for GDM and its thresholds is still ongoing.

Materials and Methods

This is a cross-sectional study of 110 consecutive pregnant women who attended our outpatient antenatal clinic and were diagnosed as having no GDM using the 75 g OGTT at 24-28 weeks of gestation. A 2 hour 75 g OGTT is performed for screening GDM at 24-28 weeks of gestation as a standard obstetric practice at our institution. The study protocol was approved by the Ethics Committee of Lütfi Kırdar Kartal Training and Research Hospital (89513307/1009/372). Written informed consent was obtained from all subjects before the study. The diagnosis of the GDM was made according to the ADA/IADPSG criteria, when any of the following plasma glucose values were exceeded: fasting, ≥ 92 mg/dL; 1 h, ≥ 180 mg/dL; 2 h, ≥ 153 mg/dL^(4,5). The exclusion criteria included women with GDM, pre-gestational diabetes mellitus (GDM), hypertension, multiple pregnancies, and fetal anomalies. The normal 1 h and 2 h ranges of 75 g OGTT levels of 110 pregnant women were further divided into three different sub-groups; for the 1 h as group 1 (<120 mg/dL), group 2 (120-140 mg/dL), group 3 (>140 mg/dL), and for the 2 h as group 1 (<120 mg/dL), group 2 (120-135 mg/dL), and group 3 (>135 mg/dL). Neonatal outcomes were compared between these new range groups. Neonatal hypoglycemia, hyperbilirubinemia, intensive care unit admission, large-for-gestational-age (LGA) and small-for-gestational-age (SGA) newborns were considered as adverse outcomes. The presence of one or more adverse outcome was determined as an abnormal result.

Statistical Analysis

All data were analyzed using SPSS Statistics for Windows, Version 22 (IBM Corp, Armonk, NY) and p values <0.05 were considered to be statistically significant. Continuous variables

Table 1. Maternal characteristics and neonatal outcomes of groups according to different 75 g oral glucose tolerance test target 1 h ranges within normal limits

	Group 1 (n=50)	Group 2 (n=32)	Group 3 (n=28)	P
OGTT 1 h cut-off (mg/dL)	<120	(120-140)	(>140)	
Age (years)	28.26±5.00	29.31±6.96	31.53±5.24	0.056
BMI (kg/m ²)	28.33±3.98	27.57±3.95	28.46±3.89	0.617
Multiparous	32 (64)	19 (59.4)	16 (57.1)	0.819
Neonatal hypoglycemia	5 (10)	1 (3.1)	0 (0)	0.138
Neonatal hyperbilirubinemia	13 (26)	13 (40.6)	9 (32.1)	0.382
NICU admission	7 (14)	5 (15.6)	6 (21.4)	0.690
SGA	8 (16)	11 (34.3)	1 (3.6)	0.007 ^a
LGA	5 (10)	5 (15.6)	3 (10.7)	0.727
Birth weight (g)	3296.9±527.5	3305.1±592.5	3437.1±583.8	0.538
Abnormal result	23 (46)	23 (71.9)	13 (46.4)	0.05

Values are expressed as mean ± standard deviation or n (%). OGTT: Oral glucose tolerance test, NICU: Neonatal intensive care unit, SGA: Small for gestational age, LGA: Large for gestational age, BMI: Body mass index, ^a: Group 2 vs group 3 p<0.05

are presented as mean \pm standard deviation and categorical variables as numbers and percentages. For the analysis of qualitative data, the chi-square test was used. For the analysis of quantitative data, One-Way ANOVA and Kruskal-Wallis tests were used.

Results

One hundred ten pregnant women without GDM were enrolled in the study. The women were further divided into subgroups according to different ranges of normal 75 g OGTT results to compare neonatal outcomes.

The number and percentage of the subjects were 50 (45.5%), 32 (29%) and 28 (25.5%) for the first hour (Table 1), and 82 (74.5%), 14 (12.7%), and 14 (12.7%) (Table 2) for the second hour, for groups 1-3, respectively. For the 1 h results, there was no statistically significant difference between the groups in terms of age, body mass index (BMI), multiparity, neonatal hypoglycemia, hyperbilirubinemia, intensive care unit admission, birth weight, abnormal results, and LGA rates; however, the rate of SGA infants was statistically significantly higher in group 2 compared with group 3 (Table 1). For the 2 h results, statistically similar results were found between the groups ($p>0.05$) (Table 2).

Table 2. Maternal characteristics and neonatal outcomes of groups according to different 75 g oral glucose tolerance test target 2 h ranges within normal limits

	Group 1 (n=82)	Group 2 (n=14)	Group 3 (n=14)	P
OGTT 2 h cut-off (mg/dL)	<120	(120-135)	(>135)	
Age (years)	29.17 \pm 5.78	28.57 \pm 5.85	31.57 \pm 5.77	0.308
BMI (kg/m ²)	28.32 \pm 4.26	26.70 \pm 2.42	28.57 \pm 2.90	0.335
Multiparous	50 (61)	8 (57.1)	9 (64.3)	0.927
Neonatal hypoglycemia	3 (3.7)	2 (14.3)	1 (7.1)	0.258
Neonatal hyperbilirubinemia	26 (31.7)	6 (42.9)	3 (21.4)	0.476
NICU admission	13 (15.9)	3 (21.4)	2 (14.3)	0.763
SGA	14 (17.1)	5 (35.7)	1 (7.1)	0.128
LGA	10 (12.2)	1 (7.1)	2 (14.3)	0.824
Birth weight (g)	3328.1 \pm 555.8	3141.7 \pm 642	3568.2 \pm 433	0.128
Abnormal result	43 (52.4)	11 (78.6)	5 (35.7)	0.132

Values are expressed as mean \pm standard deviation or n (%). OGTT: Oral glucose tolerance test, NICU: Neonatal intensive care unit, SGA: Small for gestational age, LGA: Large for gestational age, BMI: Body mass index

Discussion

The accurate diagnosis of GDM and prompt and proper precautions to prevent adverse outcomes are crucial for both the mother and the fetus. There are many studies in the literature about the adverse effects of gestational diabetes on pregnancy outcomes^(3,9-13). The initial criteria for the diagnosis was determined more than 40 years ago⁽¹⁴⁾; however, the ongoing debate about the thresholds of the OGTT is yet to be concluded. The HAPO study, with a large, multinational cohort of 25505 pregnant women, showed a continuous relationship between maternal glycemia and adverse outcomes, with no obvious thresholds at which risks increased⁽³⁾. With the results showing a strong and continuous association between adverse outcomes and higher levels of maternal glucose, which are lower than those diagnostic of diabetes, and with the inclusion of a large number of subjects from a broad geographic area of the participating centers; this study changed the concept, and was the basis for the IADPSG new criteria, which was also adopted by WHO and ADA^(4,7). Considering the continuous relationship between glycemia and adverse outcomes, in our study, we investigated different 75 g OGTT target ranges within normal limits on neonatal outcomes and found adverse outcomes even in pregnant women with no GDM. The 2 h results were similar among groups in terms of age, BMI, multiparity, neonatal hypoglycemia, hyperbilirubinemia, intensive care unit admission, birth weight, abnormal result, SGA and LGA rates; however, for the 1 h results, the rate of SGA infants was statistically significantly higher in group 2 (120-140 mg/dL), compared with group 3 (>140 mg/dL). The American College of Obstetricians and Gynecologists reported that the one-step approach would increase the prevalence of GDM and health care costs without evidence for clinical improvements in maternal and neonatal outcomes, and favored the two-step approach⁽¹⁵⁾. In a recent study, it has been suggested that the one-step method identifies high-risk women at least as well as the two-step method⁽¹⁶⁾. Identifying subjects at risk and prompt, specific interventions to reduce maternal hyperglycemia can reduce maternal and perinatal morbidity^(1,17,18). In this present study, the 75 g OGTT one-step approach was used, and to minimize the risk the neonatal outcomes, the results were compared between different ranges, within the normal limits of the IADPSG/ADA criteria. In 2015, NICE recommended new diagnostic thresholds for the diagnosis of GDM, with a higher fasting but lower 2 h post-load glucose thresholds of those proposed by the IADPSG⁽⁸⁾. In a study to identify ethnic-specific criteria for the diagnosis of GDM, it was suggested that the United Kingdom NICE might have underestimated the prevalence of gestational diabetes, especially in south Asian women⁽¹⁹⁾. In another recent study that evaluated neonatal and obstetric outcomes among women who were test positive for the IADPSG criteria but negative for the NICE 2015 criteria, a higher risk for LGA, cesarean delivery, and polyhydramnios was suggested compared with women with negative screening

results and no OGTT. The IADPSG criteria was determined to identify women at substantial risk of complications who would not be identified by the NICE 2015 criteria. As a result, it was reported that according to the NICE criteria, a high-risk group could be unidentified and left untreated depending on the higher fasting threshold, and a low-risk group could be treated instead depending on the lower 2 h threshold.⁽²⁰⁾

Study Limitations

The limitation of the study is its small sample size. The validity of the 75 g OGTT thresholds still needs to be investigated and verified by large studies.

Conclusion

This study demonstrates that the 75 g OGTT (IADPSG/ADA) has reliable threshold values for GDM screening as the neonatal outcomes do not differ between the low normal and high normal levels of the first and second-hour test results, and provides evidence that there are still adverse neonatal outcomes in women with OGTT results below the current thresholds. The study also reports a higher number of SGA in the glucose range 120-140 mg/dL of the first hour, which needs further evaluation. As a result, the validity of the 75 g OGTT thresholds still needs to be investigated and verified by large studies.

Ethics

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of Lütfi Kırdar Kartal Training and Research Hospital (approval number: 89513307/1009/372)

Informed Consent: Consent form was filled out by all participants.

Peer-review: External and internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.S., Concept: Z.M.P., Design: Z.M.P., Data Collection or Processing: S.S., Analysis or Interpretation: G.A.İ., Literature Search: S.S., G.A.İ., Writing: G.A.İ.

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