Differences in Postload Plasma Glucose Levels between 100-g and 75-g Oral Glucose Tolerance Tests in Normal Pregnant Women: A Potential Role of Early Insulin Secretion

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Objective: *To demonstrate a role of early insulin secretion on plasma glucose levels after different amounts of oral glucose loads in pregnant women.*
Material and Method: *Forty-one pregnant women with normal glucose tolerance according to the Carpenter and Coustan' s criteria and 25 non-pregnant women (control group) with normal glucose tolerance according to the World Health Organization criteria were enrolled. Each subject was randomly scheduled to perform both the 100-g and 75-g OGTT within a 1-week interval. Venous blood was drawn at fasting, 30-, 60-, 120-, and 180-minute intervals during both tests for determination of plasma glucose and serum insulin levels.*
Results: *The mean (± SE) ages of the pregnant and control groups were 33.3 ± 0.9 and 31.8 ± 1.4 years, respectively. The mean gestational age at the time of performing OGTT of the pregnant group was 28.7 ± 0.6 weeks. In the non-pregnant group, the plasma glucose concentrations were not different between 75-g and 100-g OGTT whereas the serum insulin levels at the 30 and 180 minutes of the 100-g OGTT were significantly higher than those of the 75-g OGTT. In the pregnant group, both plasma glucose and serum insulin concentrations at the 120 and 180 minutes of the 100-g OGTT were significantly higher than those of the 75-g OGTT.*
Conclusion: *The limited ability of early insulin secretion to increase when glucose load increased in the pregnant women could explain the high plasma glucose levels at 2 and 3 hours of 100-g OGTT compared to those of 75-g OGTT.*

Keywords: *Oral glucose tolerance test, Normal pregnant women, Plasma glucose, Insulin secretion*

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The oral glucose tolerance test (OGTT) is the gold standard for diagnosing gestational diabetes mellitus (GDM). However, there is still controversy regarding the amount of glucose load, duration of the test, and threshold values of plasma glucose. A commonly used OGTT for diagnosing GDM is 100-g 3-h OGTT using Carpenter and Coustan's criteria[1] as recommended by the American Diabetes Association (ADA)[2]. They define an individual as having GDM when two or more venous plasma glucose concentrations meet or exceed the following plasma glucose levels: fasting level of 5.3 mmol/l; 1-hour of 10 mmol/l; 2-hour of 8.6 mmol/l; and 3-hour of 7.8 mmol/l. In addition, the ADA has also recommended 75-g 2-h OGTT

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using the same criteria and reference values as the 100-g 3-h OGTT. However, previous studies found that plasma glucose concentrations after a 100-g glucose load were significantly higher than those after a 75-g glucose load in pregnant women, regardless of the glucose tolerance status[3,4].

It is well established that early insulin secretion plays a critical role in maintaining postmeal glucose homeostasis[5-8]. In contrast to the pregnant women, the subjects with normal glucose tolerance could maintain plasma glucose at the same levels despite different amounts of oral glucose load[9]. To demonstrate the ability of early insulin secretion to increase when glucose load increased in pregnant women, the authors compared plasma glucose and serum insulin levels between 75-g and 100-g OGTT in both pregnant and non-pregnant women who had normal glucose tolerance.

Material and Method

Forty-one pregnant women with normal glucose tolerance according to the Carpenter and Coustan' s criteria[1] and 25 non-pregnant women (control group) with normal glucose tolerance according to the World Health Organization criteria[10] were enrolled. Each subject was randomly scheduled to perform both 100-g and 75-g OGTT within a 1-week interval. The pregnant women were tested during 15-35 weeks' gestation. Each test was done in the morning after an overnight fast. As a more dilute oral glucose solution may affect the plasma glucose levels[11], 100-g glucose was dissolved in 300 ml of water and 75-g glucose was dissolved in 225 ml of water. The subjects remained seated during the test. Venous blood was drawn at fasting, 30-, 60-, 120-, and 180-minute intervals during both tests for determination of plasma glucose and serum insulin levels. Informed consent was obtained from all participants, and the present study was approved by the Ethics Committee of the Faculty of Medicine, Prince of Songkla University.

Plasma glucose levels were determined by the glucose hexokinase method using an automated Hitachi model 917 machine. Intra-assay coefficient of variations (CVs) were 0.90 and 0.77% at mean concentrations of 5.2 and 13.3 mmol/l, respectively. Interassay CVs were 1.62 and 1.70% at mean concentrations of 5.5 and 14.1 mmol/l, respectively. Serum insulin concentrations were determined by radioimmunoassay (Diagnostic Products Corporation, CA, USA). Intra-assay CVs were 5.8 and 4.2% at mean concentrations of 252 and 804 pmol/l. Interassay CVs were 8.0 and 7.0% at mean concentrations of 234 and 984 pmol/l, respectively.

Statistical analysis

All results were expressed as mean $\pm$ SE (standard error of mean). The serum insulin and insulin/glucose ratio results were log transformed before analysis because of the positively skewed distribution. Differences in mean values within groups were tested by ANOVA with repeated measurement and Student paired *t*-test. A probability (p) value of less than 0.05 was considered statistically significant. The authors used SPSS 12.0 for Windows for computations.

Results

The mean ages of the pregnant and control groups were 33.3 ± 0.9 and 31.8 ± 1.4 years, respectively. The mean gestational age at the time of performing OGTT of the pregnant group was 28.7 ± 0.6 weeks. The time interval between performing the 75-g and 100-g OGTT was 3.3 ± 0.2 days. In the non-pregnant group, plasma glucose concentrations were not different between 75-gand 100-g OGTT, whereas the serum insulin at the 30 and 180 minutes of the 100-g OGTT were significantly higher than those of the 75-g OGTT (Fig. 1). In the pregnant group, both plasma glucose and serum insulin concentrations at the 120 and 180 minutes of the 100-g OGTT were significantly higher than those of the 75-g OGTT (Fig. 2). Since the insulin levels were accompanied by the glucose levels, the authors also compared insulin/glucose ratios between the 100-g and 75-g OGTT. The results remained unchanged when the data were analyzed by using the insulin/glucose ratio (Fig. 3).

Discussion

Suppression of endogenous glucose production by early prandial insulin secretion is an important mechanism for maintaining normal plasma glucose levels after glucose load[5-8]. Mitrakou et al found that 2-hour plasma glucose levels negatively correlated with 30-minute plasma insulin concentrations but positively correlated with 2-hour plasma insulin concentrations[12]. These findings suggest that blunting of early-phase prandial insulin secretion results in postprandial hyperglycemia and late hyperinsulinemia. Consistent with the findings by Metrakou et al, non-significant rising of the 30-minute insulin levels after increased glucose load in the pregnant group demonstrated by the present study could explain why the 2- and 3-hour plasma glucose concentrations of 100-g OGTT were

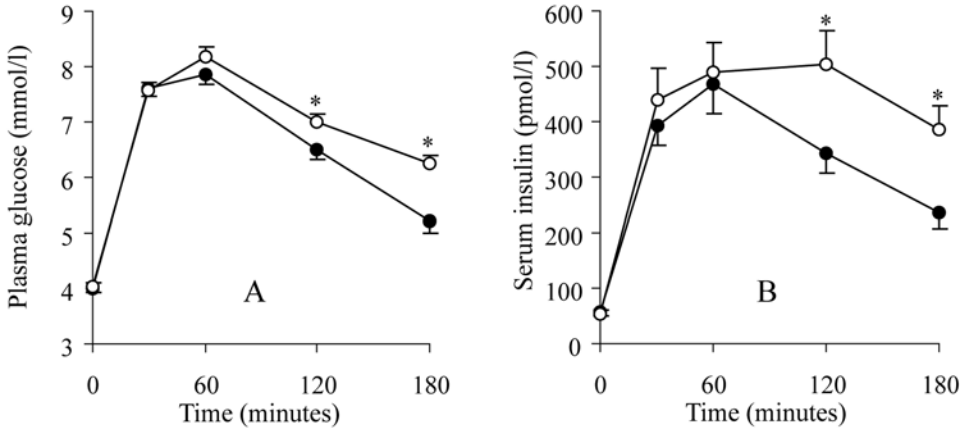

Fig. 1 Plasma glucose (A) and serum insulin concentrations (B) after 75-g (•) and 100-g (o) oral glucose load in pregnant women (* $p < 0.05$)

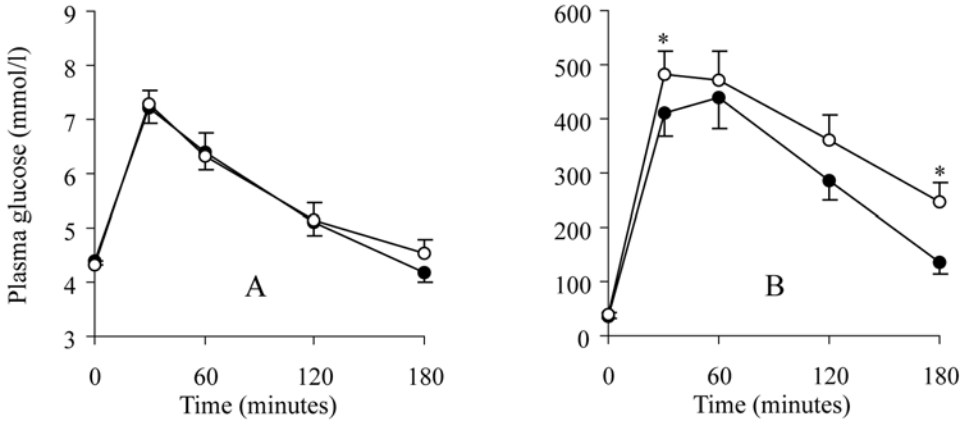

Fig. 2 Plasma glucose (A) and serum insulin concentrations (B) after 75-g (•) and 100-g (o) oral glucose load in non-pregnant women (B) (* $p < 0.05$)

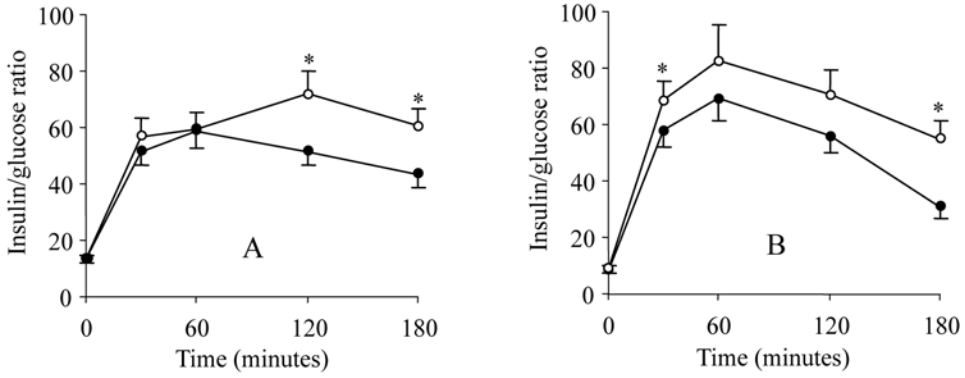

Fig. 3 Insulin/glucose ratio after 75-g (•) and 100-g (o) oral glucose loads in pregnant (A) and non-pregnant women (B) (* $p < 0.05$)

significantly higher than those of the 75-g OGTT. In contrast, an adequate increase in the 30-minute insulin levels after the 100-g oral glucose load in the non-pregnant group resulted in similar plasma glucose concentrations between the 100-g and 75-g OGTT. These phenomena are also demonstrated in subjects with different glucose tolerances. de Novel et al[9] found that plasma glucose levels after oral glucose loads of 100-g were higher than those of 50-g in subjects with slightly impaired glucose tolerance, while they were not different in subjects with normal glucose tolerance. They also found that plasma insulin levels at 30 minutes of 100-g glucose load were higher than those of 50-g glucose load in subjects with normal glucose tolerance, while they were not different in subjects with impaired glucose tolerance. The increase in plasma glucose concentrations after 100-g oral glucose loads in both pregnant women and subjects with impaired glucose tolerance could be explained by the limited increase in the early prandial insulin secretion. Previous studies demonstrated that women with GDM had impaired early phase insulin secretion when compared with pregnant women with normal glucose tolerance[13,14]. By demonstrating the role of insulin secretion in coping with different amounts of oral glucose loads, the authors found that pregnant women with normal glucose tolerance also had impairment of early insulin secretion when compared with non-pregnant women.

In conclusion, the 2- and 3-hour plasma glucose levels of 100-g OGTT were higher than those of 75-g OGTT in pregnant women with normal glucose tolerance. This could be explained by the limited ability of early insulin secretion to increase when glucose load increased. It is therefore not justifiable to use 75-g 2-h OGTT for diagnosing GDM using the same criteria and reference values as 100-g 3-h OGTT as suggested by the ADA.

Acknowledgement

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ความแตกต่างของระดับกลูโคสในเลือดขณะทำ 100 กรัม และ 75 กรัม oral glucose tolerance test ในสตรีตั้งครรภ์ปกติ: บทบาทของการหลั่งอินซูลินระยะแรก

กรณ์รัตน์ สุนทรพันธ์, สุภมัย สุนทรพันธ์, อัจฉรา ธรรมประสิทธิ์, จิราภรณ์ อักษรถึง

วัตถุประสงค์: *ศึกษาบทบาทของการหลั่งอินซูลินระยะแรกต่อระดับกลูโคสในเลือดหลังดื่มกลูโคสในจำนวนที่แตกต่างกันในสตรีตั้งครรภ์*

วัสดุและวิธีการ: *สตรีตั้งครรภ์จำนวน 41 คนที่มี glucose tolerance ปกติตามเกณฑ์ของ Carpenter และ Coustan และสตรีไม่ตั้งครรภ์จำนวน 25 คนที่มี glucose tolerance ปกติตามเกณฑ์ขององค์การอนามัยโลกเข้าร่วมการศึกษา ทุกคนได้รับการทำ 75 กรัม และ 100 กรัม OGTT โดยสุ่มภายใน 1 สัปดาห์ เจาะเลือดที่ 0, 30, 60, 120, และ 180 นาที ขณะทำ OGTT เพื่อตรวจระดับกลูโคสและอินซูลิน*

ผลการศึกษา: *อายุเฉลี่ย (± ความคลาดเคลื่อนมาตรฐาน) ของสตรีตั้งครรภ์และสตรีไม่ตั้งครรภ์เท่ากับ 33.3 ± 0.9 และ 31.8 ± 1.4 ปี ตามลำดับ ค่าเฉลี่ยของอายุครรภ์ขณะทำ OGTT ในกลุ่มสตรีตั้งครรภ์เท่ากับ 28.7 ± 0.6 สัปดาห์ ในกลุ่มสตรีไม่ตั้งครรภ์ ระดับกลูโคสในเลือดไม่แตกต่างกันระหว่าง 75 กรัม และ 100 กรัม OGTT ขณะที่ระดับอินซูลินในเลือดที่ 30 และ 180 นาที ของ 100 กรัม OGTT สูงกว่าของ 75 กรัม OGTT อย่างมีนัยสำคัญทางสถิติ ในกลุ่มสตรีตั้งครรภ์ ทั้งระดับกลูโคสและอินซูลินในเลือดที่ 120 และ 180 นาที ของ 100 กรัม OGTT สูงกว่าของ 75 กรัม OGTT อย่างมีนัยสำคัญทางสถิติ*

สรุป: *จากการหลั่งอินซูลินที่จำกัดเมื่อดื่มกลูโคสจำนวนมากขึ้นในสตรีตั้งครรภ์ สามารถอธิบายระดับกลูโคสในเลือดที่ 2 และ 3 ชั่วโมง ของ 100 กรัม OGTT ที่สูงกว่าของ 75 กรัม OGTT*