β-Cell dysfunction and insulin resistance in gestational glucose intolerance

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Gestational diabetes mellitus (GDM) is defined as glucose intolerance of variable severity with onset or first recognition during pregnancy. Therefore, one cannot exclude the possibility that undiagnosed glucose intolerance antedated or began concomitantly with the pregnancy. Recently, the International Association of Diabetes and Pregnancy Study Groups recommended that high-risk women found to have diabetes based on standard criteria at their initial prenatal visit should be considered to have overt, not gestational, diabetes mellitus [1]. Moreover, they recommended new criteria for diagnosing GDM using a 75-g oral glucose tolerance test (OGTT). The new criteria require only one abnormal value to make the diagnosis of GDM compared with the two abnormal values required in the criteria using a 100-g OGTT. In 2011, the American College of Obstetricians and Gynecologists announced that they continue to recommend use of the old diagnostic criteria for GDM. Although several countries and international organizations have adopted the new criteria, the World Health Organization has not released its report on this topic. The United States National Institutes of Health plan to hold a conference in 2013 to develop consensus on this topic. The Korean Diabetes Association suggested both old and new criteria for the diagnosis of GDM, depending on the decision of clinicians.

GDM is associated with increased risks of maternal, fetal, and neonatal adverse outcomes, depending on the degree of hyperglycemia. Furthermore, GDM has long-term sequelae for both the mother and offspring after delivery. Several studies have reported postpartum type 2 diabetes mellitus (T2DM) rates ranging from 3% to 38% within 1 year after delivery, depending on ethnicity and the proportion of participants with severe hyperglycemia during pregnancy. Cho et al. [2] found that the incidence of T2DM was approximately 41% in Korean women with previous GDM.

Like prediabetes, gestational impaired glucose tolerance (GIGT) can be diagnosed when only one abnormal glucose value is seen on the 100-g OGTT. GIGT was thought to be an intermediate phenotype between normal glucose tolerance (NGT) and GDM. However, recent studies showed that the maternal and fetal outcomes are poorer if GIGT is not treated [3,4]. In this issue of The Korean Journal of Internal Medicine, Yang et al. [5] analyzed various indices of insulin resistance and insulin secretion in 1,163 pregnant Korean women undergoing 100-g OGTT. Based on the OGTT...
results, the study subjects were subdivided into three groups: NGT, GIGT (only one abnormal value based on the criteria of Carpenter and Coustan), and GDM. The subjects with GDM were older than the subjects with NGT and had a higher prepregnancy body mass index (BMI). In addition, the GDM group had higher insulin resistance indexes and lower insulin secretion indexes, as compared to the NGT group. These findings are similar to those of previous reports. It was thought that GDM develops when β-cells fail to adapt to the increasing demand for insulin release during the second half of pregnancy, when insulin resistance is greatest. Buchanan et al. [6] showed that insulin secretion during pregnancy increases in parallel in women with and without GDM, but from a lower starting point in women with GDM. This means that the β-cell defect in GDM is somewhat chronic, rather than acquired during pregnancy. Consequently, the β-cell dysfunction in GDM may worsen over time, which results in overt diabetes mellitus postpartum.

Yang et al. [5] found that the insulin resistance indexes were significantly worse in the GDM group than in the GIGT group, as expected. However, the insulin levels at each time point in the 100-g OGTT and the area under the curve for insulin were significantly higher in the GIGT group than in the GDM group. This suggests that compensation for insulin secretion occurs in the GIGT group. Insulin secretion indexes were significantly lower in subjects with GDM compared with the other two groups. Among the subjects with GIGT, the 1-hour abnormal group had a significantly greater weight gain during pregnancy, and the values from the 50-g OGTT were higher than in the other two groups. Although the insulin resistance indexes among the three groups were not different, HOMA-β as an index of insulin secretion capacity was lowest in the 1-hour abnormal group, which means that an insulin secretion defect is prominent in that group. This finding is similar to that of Retnakaran et al. [7]. However, recent studies suggest that women with a single abnormal glucose value at 1 hour on the OGTT had a metabolic phenotype similar to GDM, whereas GIGT at 2 or 3 hours on the OGTT is similar to NGT. Retnakaran et al. [7] reported that the caesarian section rate was higher in women with an abnormal glucose value at 1 hour on the OGTT, and this was associated with postpartum glycemia, insulin resistance, and β-cell dysfunction.

Compared with Caucasians, Asians have a smaller β-cell mass with a lower insulin secretion capacity, whereas visceral adiposity with greater insulin resistance is common in Asians, even with a lower BMI. These pathophysiological differences between Caucasians and Asians could explain the recent abrupt increase in the prevalence of type 2 diabetes in Asian countries. In a study that assessed the changes in insulin resistance and β-cell function in a multiethnic population-based cohort of pregnant women [8], the increase in insulin resistance was similar across the ethnic groups. However, the increase in β-cell function was significantly lower for East and South Asians compared with Western Europeans. This suggests that there are similar pathophysiological differences between Asians and Caucasians in pregnancy.

Gestational diabetes is a very interesting disease entity because it has a natural course similar to that of type 2 diabetes, which is characterized by two main pathogenic factors: insulin resistance and an insulin secretion defect. Furthermore, most GDM disappears after delivery, which provides a clue to the mechanisms for reversing type 2 diabetes to NGT. Recently, Kwak et al. [9] reported that obesity was a risk factor for both early (2 months postpartum) and late (more than 1 year after delivery) type 2 diabetes converters in women with a history of GDM. In addition, early converters had more pronounced defects in β-cell function. If there is a genetic component of the insulin secretory defect in Asian women, a reduction in insulin resistance after delivery might be the only way to prevent future type 2 diabetes in women with previous GDM.

Conflict of interest
No potential conflict of interest relevant to this article is reported.

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