

Glucose tolerance test: A brief summary of basic principles and important considerations

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Fasting plasma glucose is the standard test for the diagnosis of diabetes mellitus (DM). However, there is another functional test which can give more details on the homeostasis of glucose in the patient, i.e., glucose tolerance test. There are two main types of glucose tolerance test: oral and intravenous methods. In this study the author reviews a summary on basic concepts and some important considerations on glucose tolerance test.

Keywords : *Glucose, Tolerance test.*

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การตรวจ *fasting plasma glucose* เป็นมาตรฐานสำหรับการวินิจฉัยโรคเบาหวาน อย่างไรก็ตามยังมีการทดสอบหน้าที่ชนิดอื่น ๆ ที่สามารถให้รายละเอียดของภาวะน้ำตาลของกลูโคสในร่างกายได้มากกว่า ซึ่งการทดสอบนั้นก็คือ การทดสอบความทนต่อกลูโคส โดยมีการทดสอบได้ 2 วิธี คือ การทดสอบทางการรับประทาน กับ การฉีดเข้าเส้นเลือดดำ ในบทความนี้ได้สรุปรวมเกี่ยวกับหลักการและข้อพิจารณาที่สำคัญบางประการของการทดสอบความทนต่อกลูโคส

คำสำคัญ : กลูโคส, ความทนต่อกลูโคส

Introduction to glucose and oral glucose tolerance test

Glucose is a monosaccharide, consisting of six carbon atoms. Glucose is the common sugar that is necessary for human metabolism. Basically, glucose is the sugar that the body uses for energy. In glucose homeostasis, both hormones and enzymes have their roles in regulating the metabolism of glucose. As for the hormones, insulin and glucagon from the pancreas play major roles in glucose homeostasis. An abnormality in glucose homeostasis results in several clinical disorders and the most well-known clinical disorder is diabetes mellitus (DM).

In the diagnosis of type 2 DM, fasting plasma glucose is the standard test. When available, the criteria required to justify population screening should be satisfied. However, there is another functional test which can give more details on glucose homeostasis in the patient, i.e., glucose tolerance test. The most common glucose tolerance test is oral glucose tolerance test (OGTT). In clinical practice, however, OGTT is mainly used in obstetrics. It is used to screen pregnant women for gestational diabetes between 24 and 28 weeks of pregnancy.⁽¹⁾ The glucose challenge and fasting glucose tests are leading contenders as appropriate screening tests to determine who should have the diagnostic glucose tolerance test.⁽¹⁾ It may also be used to diagnose diabetes in research studies and in cases where the disease is suspected despite a normal outcome of fasting blood glucose.

How to perform a glucose tolerance test?

1. OGTT⁽²⁻⁶⁾

A. Prenalytical phase

OGTT is a functional test. The basic principle of the test is to load the substance to test the down regulating property of the human body. As the influence of hematocrit is omitted by using plasma, it is suggested that the diagnostic glucose concentrations are measured in venous plasma. The required specimen is a venous blood sample. Hence, the principle of standard venepuncture is to be respected.⁽⁷⁾ The standard anticoagulant is fluoride (gray tube).⁽⁷⁾

After an overnight fast, the patient is required to drink a solution containing a known amount of glucose (usually 75 gram). A blood sample has to be obtained before the patient drinks the glucose solution; and blood is drawn again every 30 to 60 minutes after the glucose is consumed for up to 3 hours (depending on the amount of the loading dose).

B. Analytical phase

The analysis for OGTT is actually the analyses of the quantity of blood glucose. Fluoride blood samples can be processed by a standard enzymatic assay, which is usually a glucose oxidase method. In addition, the insulin level might be measured when it is needed.

When the blood glucose levels are above the normal limits at the times of measurement, it can be used to diagnose type 2 diabetes⁽⁸⁾ (Table 1) or gestational diabetes⁽⁹⁻¹⁰⁾ (Table 2). In addition, the insulin levels may also be measured. The interpretation of blood glucose level depends on the loading dose of glucose (Table 3).

Table 1. Diagnosis criteria for type 2 DM. ⁽⁸⁾

Type of investigation	Criteria
Random glucose	Symptoms of DM plus a casual plasma glucose concentration of 200 mg/dL or greater
Fasting glucose	Fasting plasma glucose of 126 mg/dL or greater
75-gram OGTT	Two-hour plasma glucose of 200 mg/dL or greater

Table 2. Diagnosis of gestational DM with a 100-gram or 75-gram OGTT. ⁽¹⁰⁾

Type of OGTT	Level (mg/dL)			
	Fasting	1 hour	2 hour	3 hour
100-gram OGTT	95	180	155	140
75-gram OGTT	95	180	155	N/A*

*N/A means not applicable

Table 3. Interpretation for OGTT.

Loading dose	Normal value
75-gram	<ul style="list-style-type: none"> ● fasting: 60 to 110 mg/dL ● 1 hour: less than 200 mg/dL ● 2 hours: less than 140 mg/dL. Between 140-200 mg/dL is considered impaired glucose tolerance or pre-diabetes. This group is at increased risk of developing diabetes. Greater than 200 mg/dL is diagnostic of DM.
100-gram	<ul style="list-style-type: none"> ● fasting: less than 95 mg/dL ● 1 hour: less than 180 mg/dL ● 2 hour: less than 155 mg/dL ● 3 hour: less than 140 mg/dL

* There is another variety of OGTT called 50-gram OGTT. This test is actually a loading test with one measurement at 1 hour (no fasting measurement) and normal values of blood glucose at 1 hour are less than 140 mg/dL.

2. Intravenous glucose tolerance test (IGTT)⁽²⁻⁶⁾

IGTT is, however, not often used. The main indication for the test is to investigate a suspected glucose intolerance in patients who are unable to take an oral glucose load, such as in prolonged *hyperemesis gravidarum*, but only when random or fasting glucose concentrations are not diagnostic for DM. Similar to OGTT, fasting is required. In this test, patients are intravenously injected with a known amount of glucose (usually 50mL of 50 % glucose in adult or 1mL of 50 % glucose per kg body weight in childhood) by vein for 3–4 minutes, and blood insulin levels (if measured) are measured before glucose and at 1 and 3 minutes.

The analytic principle of IGTT is similar to that of OGTT. Regarding the interpretation of the result, measured glucose concentrations are plotted on 2-cycle semi-LOG paper, using the linear X scale for time and the log Y scale for glucose concentration. The glucose concentrations measured between 20 and 60 minutes should fall on a straight line indicating exponential decay. If exponential decay is demonstrated, the half life (in minutes) of glucose is to be calculated. Using the half life to calculate the decay constant K_g using the formula: " $K_g = 69.3 T_{1/2}$ ". In non-diabetic subjects, the average K_g is approximately 1.7 (normal range 1-3). In the elderly, however, the K_g may decline to 1.3. In diabetic subjects, the K_g value is usually less than 0.9. Values between 0.9 and 1.1 are considered borderline. Regarding insulin, the insulin levels below a standard threshold may predict a development of type 1 diabetes in some patients.

Some consideration on glucose tolerance test:

A. Quality control

Indeed, quality control is necessary for all laboratory tests. The control of pre-analytical,

analytical and post-analytical periods in glucose tolerance test is recommended. Most of the problematic cases for glucose tolerance test are in the pre-analytical phase. *Hyperemesis gravidarum* is the main interference of OGTT which can result in the abnormally low glucose level and can be an unacceptable aberrant laboratory result.⁽¹¹⁾

In addition to *hyperemesis gravidarum*, the inference from drug is another important factor contributing to aberrant OGTT results. The drugs include thiazide diuretics, beta-blockers, oral contraceptives and prednisone.

B. Complications of glucose tolerance test

Similar to other tests, complications due to blood collection can be expected in glucose tolerance test. However, other complications are also reported. Hypoglycemia following fasting in OGTT is serious complication. According to a recent report by Weissman et al, the incidence of reactive hypoglycemia during 100-g oral glucose tolerance test was 6.3 %.⁽¹²⁾ Therefore, observation of profound hypoglycemia that can lead to death is necessary. For the perinatal significance of hypoglycemia in OGTT in pregnant subjects, women who experience hypoglycemia during the test had low neonatal birth weights.⁽¹²⁾

Another uncommon complication of glucose tolerance test, in IGTT, is thrombophlebitis. Vallerand and Kavanagh reported that the adverse reaction is the result of an interaction between whole body cooling or vasoconstriction and the hypertonicity of the dextrose solution.⁽¹³⁾

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