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ORAL GLUCOSE TOLERANCE TEST REVISITED

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ABSTRACT

Objective: The present review was undertaken to create the required utilization of oral glucose tolerance test in a developing country with a high prevalence of diabetes mellitus and its complications.

Sources of data: This review is primarily based on available literature on local and international studies on oral glucose tolerance test

Results: Pregnant and non-pregnant patient preparation; indications, contra indications and the diagnostic criteria for diabetes mellitus using oral glucose tolerance test was elucidated. Determinant for the usefulness or otherwise of oral glucose tolerance test for the diagnosis of diabetes mellitus was also discussed

Conclusion: Proper understanding of oral glucose tolerance test and teamwork of pathologist, physician, obstetrician, surgeon and pediatrician to face the challenges of diabetes mellitus and its unwanted complications is recommended.

INTRODUCTION

Oral glucose tolerance test [OGTT] is a specialised metabolic investigation that involves serial timed measurements of plasma [blood] glucose, preceding and post oral glucose load [1]. It is an investigation for the detection of early derangement of carbohydrate metabolism in which glucose is underutilised due either to absolute or relative deficiency of insulin resulting in hyperglycaemia. Such disorders produce medical, social, and economic problems particularly in developing countries[2-5] where the prevalence of diabetes mellitus and its complications are higher than in developed countries. An early diagnosis is essential to achieve an excellent glycaemic control that delays or even prevents diabetic complications, [6,7]. This is required in developing countries where there is low literacy level, scarce health education, inadequate health care facilities, insufficient qualified medical personnel, poverty and poor economic management, [8-9] that are known to increase the prevalence of diabetes mellitus and its complications. Notwithstanding, it is obviously not enough just to order specific investigations at specific times in a poor resource setting like Nigeria. Neither is it enough to justify investigations simply because they are routine. Considerations of cost in human, material and technological terms must impose a moratorium on test request [10]. However, in the Nigerian environment, even trained, qualified medical personnel including those in tertiary health institutions do not apply OGTT test appropriately. It was recently observed among others, that oral glucose tolerance test was requested for the management of already diagnosed diabetic patient with fasting hyperglycaemia of 17.1 mmol/l; a diabetic female with unequivocal fasting hyperglycaemia before and during the current pregnancy; and also in patients not known to be at risk of developing diabetes mellitus. Adequate awareness of the indications for OGTT and compliance with its principles are likely to prevent these abuses, and yield correct investigation appropriate for patient management. Therefore, there is a need for an urgent revisit of oral glucose tolerance test in our environment.

INDICATIONS FOR ORAL GLUCOSE TOLERANCE TEST

A standard method for discriminating healthy individuals from those with metabolic disorders of glucose utilisation by an investigation that is believed to be more sensitive than fasting plasma glucose determination [1,11,15,] requires the following indications:

- Abnormal previous glucose result of either impaired fasting plasma glucose ≥6.1mmol/l but < 7.0mmol/l[14;] or impaired glucose tolerance [two-hour post prandial of between 7.8 and 11.1[14] mmol/l. An OGTT sample result of ≥ 11.1 mmol/l] before the two hour post-prandial is also relevant. About 40% of subjects in these categories develop frank diabetes in 5-10 years[7] at an annual rate of 5% of patients [1,17].
- Potential diabetics – Subjects who are first-degree relatives of type II diabetic and are 25 years or older are candidates for this category. Type II diabetes mellitus is more common in individuals with a family history of the disease with the prevalence rate increasing with age.
- A second twin of a type II diabetic patient as the concordance rate for developing type II diabetes mellitus in an identical twin approaches 100% but less so in dizygotic twins[1,7].
- Diagnosis of gestational diabetes mellitus [GDM] and current diagnosis of patients previously diagnosed

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gestational diabetics. The prevalence may range from 1-14 % depending on the studied population [18-20]. Gestational diabetics are at an increased risk of developing diabetes in the next pregnancy with incidence rates ranging from 6-62% [13,14,15].The detection and appropriate treatment of GDM provides the opportunity to prevent adverse outcome for both mother and child

- Poor obstetrics history – complications of pregnancy such as stillbirth, frequent spontaneous abortion, intrauterine foetal death, polyhydramnious, malformed baby, macrosomic baby and excessive weight gain in a diabetic during pregnancy are indications for gestational OGTT.
- Obesity usually defined as body mass index equal or greater than 30 kg/m^2, or a weight gain over 20% of the desired weight for the individual [21-22] is a common phenomenon in type II diabetics and may cause insulin resistance [1,23-25] in some of these diabetics.
- Diseases of endocrine origin like hypercortisolism, g lucagonoma, phaeochromocytoma, aldosteronism, acromegaly / gigantism produce hormones that oppose insulin action. Evaluation of therapy in diagnosed cases of these endocrine diseases is useful [1,14,19]. However, such conditions are rare in this environment.
- Evaluation of patients with unexplained diseases known to be complication of diabetes like; nephropathy, neuropathy, retinopathy, with a random plasma glucose level equal or greater than 7.8 mmol/l [1,12,26]. Abnormal results in these patients do not necessarily denote cause and affect relationship.Therefore, the need to meticulously consider and rule out causative diseases in these instances must be borne in mind.
- Subjects with genetic diseases like Down's syndrome, Klinefelter's syndrome, and Turner's syndrome [26,27] which are extremely rare[11]. Chronic pancreatitis, haemochromatosis,and fibrocalculous pancreatopathy[1,27] are diseases that require evaluation by OGTT.
- Population studies for epidemiological data are known indications for oral glucose tolerance test. However, it is not recommended for a poor resource setting like Nigeria.

Contra-indications of Oral Glucose Tolerance Test

Oral glucose tolerance test has numerous contraindications. These contraindications, when properly observed, will improve the quality of test and usefulness of OGTT, and curtail unnecessary OGTT requests as some of the indications are rare in this environment These contra-indications include:

- Already diagnosed diabetes mellitus,
- The unconscious patient,
- Patients who lack the ability to fast and
- Hospitalised ill patients[1,7,16].
- Patients with neurological diseases involving the brain,
- Patients on essential medications that influence OGTT results like corticosteroids replacement therapy and
- Less than 8 hours or longer than 14 hours' fast pre-glucose load[1,17].

Table 1: **Factors other than diabetes that may influence oral glucose tolerance test [1]**

Patient's preparation
- Duration of fast
- Prior carbohydrate intake
- Medications
- Trauma
- Intercurrent illness
- Age – glucose load depends on age
- Activity
- Weight

Administration of glucose
- Form of glucose (anhydrous or monohydrous)
- Quantity and concentration of glucose ingested
- Rate of ingestion

During the test
- Posture
- Anxiety
- Caffeine
- Smoking
- Activity
- Time of day

Table 2: **Criteria for the diagnoses of diabetes mellitus[14]**

a. Symptoms of diabetes plus casual plasma glucose concentration > 11.1mmol/L. Casual means any time of the day without regard to last meal.

b. Fasting plasma glucose ≥7.0mmol/L. Fasting is defined as no caloric intake for at least 8hr.

c. Two-hour plasma glucose ≥11.1mmol/L during an OGTT.

d. Fasting whole venous or capillary blood > 6.1 (mmol/L)

e. Random whole venous blood >10mmol/l or whole capillary blood > 11.1 mmol/l

Table 3: **Fasting Plasma Glucose cutpoints equivalent to the WHO 2-hr plasma glucose criteria of 11.1mmol/L**

Study	Method	Fasting plasma glucose
Pima Indians	ROC curves	6.9mmol/L[12]
Pima Indians	Equal prevalence	6.7mmol/L[12]
Several pacific populations	Equal prevalence	7.6mmol/L[30]
NHANES* 111	Equal prevalence	7.2mmol/L[14]
Egyptians	Bimodal frequency distribution	7.2mmol/L[13]

National Health and Nutrition Examination Survey

PATIENT PREPARATION

Scrupulous patient preparation is essential for a meaningful result of an OGTT investigation [see table 1]. Responsibilities of a laboratory physician in this regard include appropriate choice of the type of OGTT to recommend amongst gestational OGTT, adult non-pregnant OGTT, paediatric OGTT and intravenous glucose tolerance test. Requesting physician needs to properly inform the diagnostic laboratory of the request to allow proper patient preparation and prompt investigation. While this information allows the laboratory prepare adequately for the required dynamic investigation, the patient needs to be properly and prep aired, thus:

- Withdrawal of all medications that are known to influence OGTT result.
- Consumption of a balanced diet with at least 150 g of carbohydrate daily for at least three consecutive days before the day of the test.
- Performing test between 8 and 10 am to allow for comparability of result.
- No exercise during the fast and test periods. Patients must rest for 30 minutes on arrival to the laboratory before the commencement of OGTT investigation.
- No smoking, no ingestion of coffee [caffeine], alcohol intake during preparation and test periods. Patient education on the procedure and duration of the investigation usually allays anxiety knowledge of malabsorption; scars of gastrointestinal tract operation, hypothyroidism and chronic liver disease will guide the interpretation and avoid misinterpretation of investigation results. Strict adherence to instructions and appointments by patients are essential.

  The protocol below is followed for OGTT:

Non-pregnant adult subjects:

- Confirm compliance to the requirements for OGTT.
- Patient should be in sitting position, which facilitates gastric emptying [14].
- Dissolve 75 g of anhydrous or 82 g of monohydrate glucose [1,16,29] in 250-300 ml of water. Lemon additive to the solution for patient that may not tolerate glucose solution or a calculated volume of appropriate preparations for example 371 ml of lucozade[26] or orange squash may be used
- Take fasting venous specimen and allow the patient to ingest the solution within 5 minutes.
- Canulate the patient and take venous specimen every 30 minutes after ingestion of the glucose solution for two hours. This may be extended to 5 hours in extended OGTT.

Paediatric subjects:

Dissolve 1.75 g/kg or 1.92 g/kg body weight of anhydrous or monohydrate glucose to a maximum of 75 g and 82 g respectively [1,16,29] for paediatric subjects

Gestational diabetes mellitus:

A glucose load is required both for screening and for diagnostic tests; fasting is not necessary for the screening phase that requires a glucose load of 50 g irrespective of the time of the day[14]. The screening allows the choice for subjects that will require gestational OGTT. An extended OGTT of 3 hours after a loading dose of 100 g is required for pregnant women. Gestational diabetes is indicated when two or more of the following values are exceeded [33]:

One hour value >10.5mmol/l
Two-hour value >9.2mmol/l
Three-hour value >7.8mmol/l

Collection of urine sample for analysis during OGTT is essential for determining renal glycosuria but not essential for routine OGTT as it is an unnecessary additional cost that deserves consideration in a resource poor environment like Nigeria. Unless a result obtained from OGTT investigation is initially grossly abnormal, two separate OGTT tests on separate occasions are required to confirm diabetes mellitus. Diabetic glucose tolerance curve peaks at about one hour while that of healthy subjects peaks at about half an hour[33]. The diagnostic cutpoint of 11.1mmol/L for the 2-hr PG was originally adopted as the prevalence of microvascular disease sharply increased above a 2-hr PG level of 11.1mmol/L; a fact supported by an epidemiological data [14]. However, when the need for OGTT arise, the conclusion reached from the laboratory results is likely to be correct when carried out appropriately [10]. Though early detection, treatment, and planned preventive measures to curtail complications of diabetes mellitus are important, considerations of cost in human, material and technological terms must necessarily advise strict compliance with established guidelines if results are to be of any clinical usefulness.

REFERENCES

1. **Sacks DB.** Carbohydrates . In Burtis CA and Ashwood ER: Tietz text book of Clinical Chemistry' 3rd Edition. WB Saunders Co Philadelphia , 1999; 750–808.

2. **Singh DL, Bharttai MD, Maskey A.** Demographic profile of diabetic patients admitted to the medical wards of Bir Hospital,Nepal,1990 to 1994. Int. Diab. Digest 6;4: 87–88.

3. **Okesina AB, Bojuwoye BJ, Gadzama AA, Ogunriola EO.** Prevalence and sex distrubution of complications in diabetic patients from Ilorin, Nigeria. . Int. Diab. Digest 1999;3: 63–64.

4. **Mayes W.** Fighting a global epidemic with simple weapons. IDF Bulletin 1993; 38: 4.

5. **Park JE, Park K.** Park's textbook of Social and Preventive Medicine. Jabalpur: Banasidas. Bhanot. 1991: 257–260.

6. **Hardy KJ Scarpello JHB.** Diabetic Retinopathy. Int. Diab Dig. 1994; 5: 38–46.

7. **Wang PH, Lau J, Chalmers TC.** Meta analysis of intensive blood glucose control on late complications of type 1 Diabetes. Lancet. 1993; 341: 1306-1309.

8. **Jean- Claude Mbanya.** Diabetic care in Cameroun. Int. Diab Digest. 1993; 4: 146–150.

9. **Bakari AG, Oyemeluke GC, Sani BG, Hassan SS and Aliyu TM.** Prevalence of Diabetes in suburban Northern Nigeria: Results of public screening survey. Int. Diab. Digest 1999 ;9:(3) 59–60.

10. **Akanji AO.** Laboratory investigations in patient care. Afr. J. Med. Med. Sci. 1994;23: 3–7.

11. **McCance DR, Hanson RL, Pettit DG.,Bennett,PH, Hadden, DR, Knowler, WC.** Diagnosing Diabetes mellitus. Do we need new criteria? Diabetologia. 1997; 40: 247–255.

12. **McCance DR, Hanson RL, Chades MA, Jacobsson LTH, Pettit DJ, .,Bennett,PH, Knowler, WC** Comparison of tests for glycated Haemoglobin and fasting and two hours' plasma glucose concentration as diagnostic methods for Diabetes .British Medical Journal. 1994; 308: 1323–1328.

13. **Engelgau MM, Thompson TJ Herma WH Boyle JP, Albert, RE.,Kenny ST.,Badran,A, Sous, ES Ali, MA.** Comparative and fasting and two hours glucose and HbA1c. Levels for diagnosing Diabetes. Diagnostic criteria and performance revisited. Diabetic care. 1997;20: 785–791.

14. American Diabetes Association. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes care. 1997; 20:1183–1201.

15. **Sacks DB.** Implications of the revised criteria for the diagnosis and classification of diabetes mellitus. Clin Chem. 1997; 43: 2230–32.

16. **Daniel ES, Christopher MC, Jeffery HS et al.** Test of glycaemia in Diabetes mellitus. Their use in establishing a diagnosis and in treatment. Ann Intern. Med.1989; 110: 125–137.

17. **Yudkin JS, Alberti KJ, Mclarty DG et al.** Impaired glucose tolerance test. BMJ. 1990;301: 397–402.

18. **Engelgau MM, Herman WH, Smith PJ et al.** The epidemiology of diabetes and pregnancy in the US.,1998. Diabetes care. 1995;18: 1029–1033.

19. **Smith AF, Beckett GJ, Walker SW et al.** Disorders of Carbohydrate Metabolism. Lecture notes on Clinical Biochemistry., 6th Ed. Blackwell Science Ltd. United Kingdom.1998; 149–164.

20. **O'Sulivan JB.** Diabetes mellitus after gestational Diabetes mellitus. Diabetes. 1991; 40: 131–135.

21. **Gary T.** As Obesity rises. Expert's struggle to explain why. Science.1998;280: 1367–8.

22. **Michael R Rodolph ll, Jules H.** Obesity. Medical progress. NEJM .1997;337: 396–407.

23. American Diabetes Association. Report of the expert committee on the screening of type 2 diabetes.. Diabetes care. 1998; 21:220–222.

24. **Alberty JS.** Current views on Obesity.Am. J. Med.1996; 100: 230–236.

25. Reaven GM.Pathophysiology of insulin resistance in Humans. Physiol. Rev. 1995; 75: 473–486.

26. National Diabetes Data Group. Classification and diagnosis of Diabetes and other categories of glucose intolerance. Diabetes. 1979; 28:1039–1057.

27. **James JC, Ramzi SC.** The Pancrease. In Cotran RS, Kumar V, and Collins T.Robins. Pathological basis of diseases. 6th ed., W.B. Saunders Co. Philadelphia. 1999; 902–929.

28. **Geof G.** Editorial. Diabetes International. 2001; 11: 66.

29. **Weiner K.** What is 75 g of glucose? Ann. Clin. Biochem. 1990; 27:283–284.

30. **Finch, CF., Zimmet,PA, Albert, KGMM.** Determining diabetes prevalence; a rational basis for the use of fasting plasma glucose concentration? Diabet. Med. 1990: 7; 603–610.

31. National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. Diabetes 1979:28;1039–1057.

32. World Health Organization; Diabetes mellitus report of WHO Study group. Geneva, World Health Organization. 1985 Tech. Rep. Ser. No. 727.

33. **Dods RF.** Diabetes Mellitus In. Kaplan LA, Pesce AJ. Clinical Chemistry, Theory analysis, correlation. 3rd edition. Mosby Co. Philadelphia. 1996: 628–630