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ORIGINAL ARTICLE

A home-based method for the detection of impaired glucose tolerance in hypertensive primary care patients

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Abstract

Objective. The aim of this project was to compare an oral glucose tolerance test (OGTT) partly performed in the patient's home (OGTTh) with a clinic-obtained OGTT with regard to the ability of the tests to identify patients with impaired glucose tolerance (IGT) and type 2 diabetes mellitus (DM-2). *Design*. A method comparison. *Setting*. The study was completed at two primary health care centres. *Subjects*. Fifty-one patients with hypertension aged 50–79 years completed both OGTT tests. *Main outcome measures*. Values for capillary P-glucose obtained two hours after a glucose load were compared between the two OGTT tests. Fasting plasma glucose (fP-glucose) and HbA1c were also measured. *Results*. Thirty-seven patients were classified in the same group (normal/IGT/DM-2) by the two tests. The index of validity based on the test's ability to identify normal or pathological values (≥ 8.9 mmol/l) was 0.75. The value for kappa was 0.66 with a sensitivity of 0.54 and a specificity of 0.82. *Conclusion*. OGTTh may be a useful screening method for IGT in risk groups such as hypertensive patients.

Key Words: *Diabetes, general practice, home test, hypertension, IGT, OGTT, Sweden, validity*

Introduction

Recent data indicate that approximately 150 million people have diabetes mellitus (DM) worldwide and that this number may double by the year 2025. Much of this increase will be due to population growth, ageing, unhealthy diets, obesity, and sedentary lifestyles [1–3].

More than 100 000 individuals in Sweden have a precursor of the disease in the form of impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) [3]. There is a significant relationship between IGT and the risk of cardiovascular and heart disease [4–6]. Subjects with IGT have an approximately 50% risk of developing type 2 diabetes (DM-2) over a 10-year period [7,8]. Several large studies have shown that the risk of developing DM-2 in persons with IGT can be reduced by lifestyle changes [5,6,9–11], with some studies showing a risk reduction of approximately 50–58% [5,6,12].

To identify individuals at high risk of developing DM-2, certain screening methods would appear to be appropriate, rather than a general screening of a healthy population [13]. Patients with hypertension have a 2.5 times greater likelihood of having DM-2 compared with normotensive patients, and screening for diabetes among hypertensive patients has been shown to be more cost-effective than universal screening, especially in the 55–75-year-old age group [14,15]. Screening has a relevant role to play in the prevalence of diagnosed diabetes that warrants the evaluation of screening activity on the part of general practitioners to optimize the identification of diabetic patients [16].

The World Health Organization (WHO) recommends retention of the oral glucose tolerance test (OGTT) as a diagnostic test because fP-glucose alone fails to diagnose approximately 30% of cases of previously undiagnosed DM-2 and because the OGTT is the only test that can identify people with IGT [7,14,15,17,18].

OGTT is used less and less in clinical practice most likely because the method is complicated. If the

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- A home-based oral glucose tolerance test (OGTTh) in which the glucose load was consumed at home was compared with a routine oral glucose tolerance test (OGTT) obtained in a clinic setting. The OGTTh classified 75% of the study participants in the same group as the clinic OGTT (normal/pathological).
- This study demonstrates that OGTTh is comparable to OGTT and that the home-based test may be a useful screening tool for the detection of impaired glucose tolerance (IGT) in hypertensive patients in the age range 50–79 years.

OGTT could be performed in a simpler and less time-consuming manner, it would most likely be used more often and thereby more at-risk individuals would be identified during the pre-diabetic stage when lifestyle interventions could prevent or delay the onset of DM- 2.

The aim of this project was to compare an OGTT partly performed in the patient's home with a clinic-obtained OGTT with regard to the tests' ability to identify patients with IGT and DM-2.

Material and methods

Settings and study population

A group of patients who had been diagnosed with hypertension at two primary healthcare centres (PHCs) during the year 2010 was selected [19]. At each clinic, 10 patients from each age group (50–59, 60–69, and 70–79), with five from each sex, were randomly selected and invited to participate in the study. Patients who were diagnosed with DM-2 were excluded.

Procedure

The individuals were invited by letter to take part in the study. Those who declined to participate were replaced with a new randomly selected individual of the same sex and age group. After written consent was obtained, the patients were sent 75 g of glucose in an envelope along with a description of the procedure and instructions regarding the performance of the procedure. Study participants were instructed to dissolve the glucose with 300 ml of water and to drink the mixture 1½ hours before an appointment time scheduled at the PHC and to record the exact time of the intake. For three days prior to the appointment, patients were to avoid nicotine and heavy physical activity. After eight o'clock on the evening prior to the test dose, patients were allowed only to drink water. Transportation to the PHC on the day of the test that did not involve physical effort was advised.

Exactly two hours after the home intake of glucose, the patients' capillary P-glucose was measured at the clinic. The capillary blood samples were obtained from the fingertips, collected in HemoCue Glucose cuvettes and immediately measured in a HemoCue Glucose Analyser 201 RT, which converts blood glucose (B-glucose) concentrations to equivalent P-glucose concentrations by multiplying by an adjustment factor of 1.11 [20]. This test is referred to as the home-based oral glucose tolerance test (OGTTh). At the clinic visit, patients' BMI, smoking habits, family history, physical activity level, and the method of transportation used to reach the PHC were also obtained. The patients were scheduled for an OGTT at the clinic one week later, which included both fP-glucose and HbA1c. When all the data were collected, the patients were informed of the results. Those who had a pathological value were followed up according to standard procedures for the new onset of IGT or DM-2. The WHO diagnostic criteria employed were capillary P-glucose ≥ 12.2 mmol/l for DM and, for IGT a capillary P-glucose ≥ 8.9 and < 12.2 mmol/l at two hours following the glucose load [1,21].

Statistics

The analysis primarily tested the degree of agreement between the OGTTh and OGTT with regard to the classification of study participants as "healthy", IGT, or DM-2. Analysis of coherence was performed with kappa statistics [22], where approximately 50–60 pairs of individual measurements provided the opportunity for inference. Descriptive statistics with an index of validity, sensitivity, and specificity were also used.

Ethics

The study was approved by the Regional Ethical Review Board in Lund. Dn 2011/806.

Results

Of the 113 individuals surveyed, 57 agreed to participate, of whom 51 completed all aspects of the study. Fifty-six individuals did not respond to the invitation or were not forthcoming for the study. Most patients declined to participate due to a lack of time or to the fact that they had already checked

their fP-glucose value recently. Six individuals discontinued the study after the OGTTh, mostly due to nausea from the sugar solution.

The study group is presented in Table I. The distribution between men and women was equal. There were more dropouts in the youngest age group. Among participants who had walked or biked to the PHC, six out of 10 had a lower value for OGTTh than OGTT, while 19 of 41 of participants who had taken a car or bus had a lower OGTTh value.

The median value for both OGTTh and OGTT was 7.9 (Table II). FP-glucose values showed a distribution range of 4.1 to 7.0 with a median value of 5.5. The participant with an fP-glucose of 7.0 had values ≥12.2 on both the OGTTh and OGTT. HbA1c values showed a range of 33 to 48 mmol/mol.

The two tests classified 37 persons in the same group: two with diabetes, four with IGT, and 31 as normal, which provides an index of validity of 0.73. Fourteen individuals were classified differently by the two tests: one had a diabetic value in one test and IGT in the other, and 13 had one pathological and one normal value (Table III). The minimum and maximum values for OGTTh were 4.6 and 15.2, and for OGTT were 3.2 and 14.1, respectively. The two tests' classifications of the two-hour values as normal or pathological (≥8.9) gives a kappa value of 0.66 with an index of validity 0.75, a sensitivity of 0.54, and a specificity of 0.82.

Discussion

An OGTT partly performed in the patient's home had an index of validity of 0.73 for classifying the participants' two-hour P-glucose values as normal, IGT, or DM and an index of validity of 0.75 for the classification of normal or pathological values with a kappa-value of 0.66. In a reproducibility study of OGTT performed with a six-week interval between the two tests, other investigators reported an index of validity of 0.66 [23]. The higher value in the index of validity in our study may be explained by the shorter period between the two tests. Nevertheless, the main finding in our study is that the agreement between the OGTTh and the OGTT appears to be as good as that between the two OGTTs.

False-positive two-hour P-glucose values are less likely because such values are likely to represent abnormal glucose tolerance, regardless of whether the glucose was consumed at home or in the clinic. False-negative values in OGTTh are more likely and may represent possible sources of error by the participants who may not have consumed the entire test solution or who were excessively physically active during the two-hour test interval.

Of the seven individuals who were classified into the lower glucose concentration category by the OGTTh but not by the OGTT, only one walked or biked to the PHC, which may indicate a lower likelihood of a falsely low value in this individual.

Two of the participants had a two-hour P-glucose value ≥12.2 on both tests, and they were thereby diagnosed with DM. One person was classified as having DM by one test and as having IGT by the other, and four were classified as having IGT by both tests. These five participants were diagnosed with IGT. The 13 participants who had one pathological and one normal value are likely to be at a higher risk of developing IGT/DM and should be monitored more closely. The remaining 31 participants were classified as normal by both tests.

If OGTTh had been used as a screening method in this study population, and if all subjects whose two-hour value was ≥8.9 had been retested with an OGTT, the following results would have been obtained: OGTTh classified 37 participants as normal with no further testing and classified 14 participants as abnormal. Of these 14 participants with

Table I. Description of the study group (n = 51).[1]

		q_3–q_1
Sex: men/women (n)	26/25	
Age (median):	64.0	72.0–59.0
50–59 years (n)	14	
60–69 years (n)	19	
70–79 years (n)	18	
Method of transportation to the PHC:		
Walking or bicycle (n)	10	
Car or bus (n)	41	

Note: [1]Values refer to median values and interquartile ranges.

Table II. Study groups' values for the different blood samples: Median and interquartile ranges (n = 51).

	median	q_3–q_1
OGTTh (mmol/l)	7.9	9.3–6.6
OGTT (mmol/l)	7.9	9.2–6.8
fP-glucose (mmol/l)	5.5	5.9–5.1
HbA1c (mmol/mol)	39	42–36

Table III. The two tests' classification of the participants (n = 51) as DM (≥12.2), IGT (8.9–12.1), or normal (<8.9).

		OGTT (mmol/l)			
		≥12.2	8.9–12.1	<8.9	Total
OGTTh (mmol/l)	≥12.2	2	0	1	3
	8.9–12.1	1	4	6	11
	<8.9	1	5	31	37
	Total	4	9	38	51

abnormal OGTTh values, two would have been classified as having DM and five as having IGT after a traditional OGTT retest. The remaining seven participants would undergo closer follow-up. This mock two-step screening procedure would have detected the two persons with DM, all five with IGT, and seven of the 13 participants who should receive closer follow-up.

HbA1c may also be used to detect DM-2 and pre-diabetes using a value $\geq$ 48 mmol/mol (according to the IFCC) and values from 39 to 46 mmol/mol for IGT [24,25]. At the ADA (American Diabetes Association) detection threshold, one of the two participants with DM-2 on both tests would have been classified as having DM-2 using HbA1c. However, it is intriguing that only 60% (3/5) of the participants classified as having IGT were also detected by HbA1c. This finding indicates that HbA1c is not a sensitive test for the detection of IGT.

The highest fP-glucose value obtained was 7.0. The participant also had values $\geq$ 12.2 by both OGTTh and OGTT and thus was diagnosed with diabetes. A review article concluded that both HbA1c and fP-glucose are effective tools for detecting DM-2 compared with OGTT (sensitivity 78–81% and specificity 79–84%, respectively), but they are poor tests to detect individuals with IGT [24].

Confirmed diabetes can be diagnosed by either capillary B-glucose or venous P-glucose. Capillary B-glucose may be more convenient than venous P-glucose in general practice [26]. The IFCC document recommends using a constant factor of 1.11 for converting the concentration of glucose in whole blood to concentrations in plasma, based on water concentrations in the two sample types [20].

OGTTh has proven feasibility. None of the participants consumed the test solution at the incorrect time. All of the participants recorded the ingestion time of the glucose load and arrived at the PHC at the desired time. However, there were difficulties in enrolling 60 participants, primarily due to the time limit. For each invited participant who did not respond to the enrolment request, a reminder was issued followed by a waiting period to allow for a definite "no" or "no response" before we could enrol additional participants.

The median age among those who chose not to participate in the study was 58 years versus 64 years in the study population. This may indicate that the method's usefulness as a screening examination is of limited value to younger age groups.

Because of an imbalance between the values in Table III, the kappa value was calculated due to the index of validity and the index by chance [22]. In light of the cited weaknesses, the results from this small study necessitate validation in larger study populations.

The OGTT remains the recommended test to find individuals with IGT compared with many other methods tested. A simplified test that is as sensitive as OGTT would offer a form of screening that is probably more time efficient and less expensive. Whether the OGTTh is simple and time-saving remains to be investigated. However, this study shows that OGTTh may be a useful screening method for IGT in risk groups such as hypertensive patients.

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Declaration of interest

The authors report no conflict of interest. The authors alone are responsible for the content and writing of the paper.

References

[1] World Health Organization. Definition, diagnosis of diabetes mellitus and intermediate hyperglycemia. Technical report and recommendations. Geneva: World Health Organization; 2006.

[2] Franciosi M, De Berardis G, Rossi MC, Sacco M, Belfiglio M, Pellegrini F, et al. Use of the diabetes risk score for opportunistic screening of undiagnosed diabetes and impaired glucose tolerance. Diabetes Care 2005;28:1187–94.

[3] Tamayo-Marco B, Faure-Nogueras E, Roche-Asensio MJ, Rubio-Calvo E, Sánchez-Oriz E, Salvador-Oliván JA. Prevalence of diabetes and impaired glucose tolerance in Aragon, Spain. Diabetes Care 1997; 20:534–6.

[4] Unwin N, Shaw J, Zimmet P, Alberti KG. Alberti KGMM. Impaired glucose tolerance and impaired fasting glycaemia: The current status on definition and intervention. Diabet Med 2002; 19:708–23.

[5] Isomaa B, Almgren P, Tuomi T, Forsén B, Lahti K, Nissén M, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. Diabetes Care 2001; 24:683–9.

[6] Tenerz Å, Norhammar A, Silveira A, Hamsten A, Nilsson G, Rydén L, et al. Diabetes, insulin resistance, and the metabolic syndrome in patients with acute myocardial infarction without previously known diabetes. Diabetes Care 2003;26: 2770–6.

[7] Tuomilehto J, Lindström J, Hellmich M, Lehmacher W, Westermeier T, Evers T, et al. Development and validation of a risk-score model for subjects with impaired glucose tolerance for the assessment of the risk of type 2 diabetes mellitus: The STOP-NIDDM risk-score. Diabetes Res Clin Pract 2010; 87:267–74.

[8] Horton ES. Effects of lifestyle changes to reduce risks of diabetes and associated cardiovascular risks: Results from large scale efficacy trials. Obesity 2009;17:43–8.

[9] Lindström J, Eriksson JG, Valle TT, Aunola S, Cepaitis Z, Hakumäki M, et al. Prevention of diabetes mellitus in subjects with impaired glucose tolerance in the Finnish diabetes prevention study: Results from a randomized clinical trial. J Am Soc Nephrol 2003;14:108–13.

[10] Meier JJ, Baller B, Menge BA, Gallwitz B, Schmidt WE, Nauck MA. Excess glycemic excursions after an oral glucose tolerance test compared with a mixed meal challenge and self-measured home glucose profiles: Is the OGTT a valid predictor of postprandial hyperglycemia and vice versa? Diabetes Obesity Metab 2009;11:213–22.

[11] Gillies et al. Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: Systematic review and meta-analysis. BMJ 2007:1–9.

[12] Diabetes Prevention Program Research Group. 10-year follow up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet 2009;374:1677–86.

[13] Echouffo-Tcheugui JB, Ali MK, Griffin SJ, Venkat Narayan KM. Screening for Type 2 diabetes and dysglycemia. Epidemiol Rev 2011;33:63–87.

[14] Karam JG, McFarlane SI. Update on the prevention of Type 2 diabetes. Curr Diab Rep 2011;11:56–63.

[15] Hoerger TJ, Harris R, Hicks KA, Donahue K, Sorensen S, Engelgau M. Screening for Type 2 diabetes mellitus: A cost-effectiveness analysis. Ann Intern Med 2004;140:689–709.

[16] Spigt M, Rikkers A, Doornbos M, Wouters E, Spitz I, Amelsvoort LV, et al. The effect of screening on the prevalence of diagnosed type 2 diabetes in primary care. Scand J Prim Health Care 2009;27:232–7.

[17] Rolka DB, Venkat Narayan KM, Thompson TJ, Goldman D, Lindenmayer J, Alich K, et al. Performance of recommended screening tests for undiagnosed diabetes and dysglycemia. Diabetes Care 2001; 24:1899–903.

[18] Bennet CM, Guo M, Dharmage SC. HbA1c as a screening tool for detection of Type 2 diabetes: A systematic review. Diabet Med 2007;24:333–43.

[19] World Health Organization. International statistical classification of diseases and related health problems, tenth revision (ICD-10). Geneva: WHO; 1997.

[20] Burnett RW, D'Orazio P, Fogh-Andersen N, Kuwa K, Külpmann WR, Larsson L, et al. IFCC recommendation on reporting results for blood glucose. Clinica Chemica Acta 2001;307:205–9.

[21] World Health Organization. Definition, diagnosis of diabetes mellitus and intermediate hyperglycemia. Report of a WHO consultation. Geneva: WHO;1999.

[22] Feinstein AR, Cicchetti DV. High agreement but low kappa II: Resolving the paradoxes. J Clin Epidemiol 1990; 43:551–8.

[23] Ko GT, Chan JC, Woo J, Lau E, Yeung VT, Chow CC, et al. The reproducibility and usefulness of the oral glucose tolerance test in screening for diabetes and other cardiovascular risk factors. Ann Clin Biochem 1998;35:62–7.

[24] American Diabetes Association. Diagnoses and classification of diabetes mellitus. Diabetes Care 2011;34:62–9.

[25] American Diabetes Association. Standards of medical care in diabetes – 2013. Diabetes Care 2013;36:11–66.

[26] Sandbæk A, Lauritzen T, Borch-Johnsen K, Mai K, Christiansen JS. The comparison of venous plasma glucose and whole blood capillary glucose in diagnoses of Type 2 diabetes: A population-based screening study. Diabetes Med 2005;22:1173–7.