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Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation

Brief report

Reproducibility of multiple repeated oral glucose tolerance tests

B.A. Gordon [a,b,*], S.F. Fraser [c], S.R. Bird [a], A.C. Benson [a]

[a] Discipline of Exercise Sciences, School of Medical Sciences, RMIT University, Melbourne, Australia
[b] Physiotherapy Department, Austin Hospital, Austin Health, Melbourne, Australia
[c] School of Exercise and Nutrition Sciences, Deakin University, Melbourne, Australia

ARTICLE INFO

Article history:
Received 10 August 2011
Received in revised form
26 August 2011
Accepted 27 August 2011
Published on line 25 September 2011

Keywords:
Apparently healthy
Glucose tolerance
Insulin sensitivity
Hyperinsulinaemia
OGTT

ABSTRACT

We assessed the oral glucose tolerance test's (OGTT) ability to produce consistent results for estimating insulin sensitivity over four consecutive days. Individual coefficients of variation for OGIS and Stumvoll-ISI were 7.8% and 14.4% with no statistically significant difference between days. Thereby, indicating repeated OGTT's are reliable for estimating insulin sensitivity.

1. Introduction

Insulin sensitivity is regularly estimated through the use of an oral glucose tolerance test (OGTT) with a number of equations showing good correlation with the gold standard method, the euglycaemic hyperinsulinaemic clamp [1]. However, issues concerning glucose load (50–100 g), reproducibility and diurnal variation of the OGTT have been reported [2], with reliability questioned [3,4]. Reproducibility investigations have centred on variables around the testing conditions, including glucose load [5], time of day (6), and the fasting period prior to testing [6,7]. And while many studies have reported variations in glucose response from multiple or repeated OGTT's [3,4,6,8], none have looked at the reproducibility of OGTT's repeated on consecutive days. So in light of this, we believed it important to analyse the glucose and insulin responses in apparently healthy individuals to determine whether OGTT's are reliable to estimate insulin sensitivity on consecutive days. Therefore, the aim of this study was to investigate whether insulin sensitivity was affected by repeated daily OGTT's.

* *Corresponding author at*: School of Medical Sciences, RMIT University, PO Box 71, Bundoora, Victoria 3083, Australia. Tel.: +61 3 9925 7037; fax: +61 3 9467 8181.
E-mail address: brett.gordon@rmit.edu.au (B.A. Gordon).

Abbreviations: OGTT, oral glucose tolerance test; AUC, Area under the curve; OGIS, oral glucose insulin sensitivity index; ISI, insulin sensitivity index.

0168-8227/$ – see front matter
doi:10.1016/j.diabres.2011.08.025

2. Materials and methods

2.1. Participants and study design

Ten sedentary, apparently healthy individuals with no diagnosed metabolic conditions took part in this trial. Inclusion criteria were: aged 40–69 years, taking no medications influencing metabolism, and not having participated in resistance training in the last six months or undertaking regular aerobic exercise. Exclusion criteria included: recent coronary event or established heart disease, uncontrolled hypertension (>150/90 mm Hg), neuropathy and being unable to understand English or follow instructions. Participants completed the self-report International Physical Activity Questionnaire [9] and were instructed not to complete any structured or specific exercise during the study, record all food consumed in a food diary and replicate their diet before each OGTT. Participant characteristics are presented in Table 1.

Participants arrived at the research facility between 6 am and 9 am by private vehicle, following a 12-h overnight fast. Anthropometric measurements and a fasting blood sample were collected before participants undertook an OGTT to obtain baseline glucose and insulin responses [10]. Participants then returned to the research facility to undergo further OGTT's on the three subsequent mornings.

2.2. Blood sampling and analysis

A cannula was inserted into an antecubital vein with blood samples obtained before consuming 75 g of glucose in 300 mL of water (Gluco Scan, BIOCORP Aust Pty. Ltd.). Further blood samples were collected at 30, 60, 90 and 120 min after consuming the glucose, with patency maintained by flushing with saline, and the first 2 mL of blood collected being discarded. The study protocol is presented schematically in Fig. 1 and was approved by the RMIT University Human Research Ethics Committee with written informed consent obtained prior to participation. Lipid profiles and glycaemic control (HbA1c) were measured in a commercial laboratory. Glucose and insulin were measured using the YSI 2300 Stat Plus analyser (Yellow Springs, USA) and Millipore human insulin ELISA kits respectively. Area under the curve (AUC) was calculated by a computer-based trapezoidal model and insulin sensitivity estimated by the oral glucose insulin sensitivity (OGIS) index [11] and the Stumvoll insulin sensitivity index (ISI) equation [12].

Table 1 – Participant demographics.

Outcome measure (units)	Mean (SD)
Male/female	3/7
Age (years)	54.6 (6.5)
Weight (kg)	93.4 (16.4)
Height (cm)	167.7 (6.8)
BMI (kg m^{-2})	33.3 (6.3)
Waist circumference (cm)	98.8 (12.6)
Waist:hip	0.88 (0.08)
SBP (mm Hg)	126 (14)
DBP (mm Hg)	83 (10)
Cholesterol (mmol L^{-1})	4.9 (1.2)
LDL-C (mmol L^{-1})	2.8 (1.0)
HDL-C (mmol L^{-1})	1.42 (0.24)
Triglycerides (mmol L^{-1})	1.6 (0.5)
HbA1c (%)	5.5 (0.3)
Glucose (mmol L^{-1})	5.3 (0.3)
Insulin (pmol L^{-1})	130.1 (82.1)
Activity (MET-min wk^{-1})	1428 (1365)
Sedentary time (min)	435 (207)

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol; HbA1c, glycated haemoglobin; MET, metabolic equivalents.

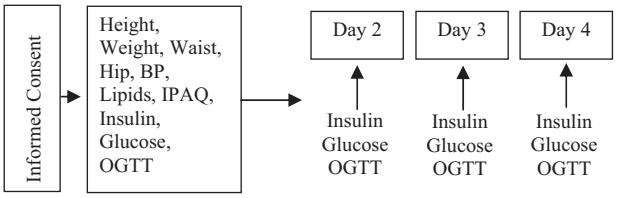

Fig. 1 – Study protocol.

2.3. Statistical methods

All data were analysed using SPSS version 18 for Windows (SPSS, Chicago, IL) with significance set at an alpha level of $p = 0.05$ and a Bonferroni correction made for multiple analyses. A repeated measures analysis of variance (ANOVA) was completed to determine change over time of the overall outcomes and to determine the reliability of the change scores from each independent time-point for each repeated measure. Change was calculated by subtracting the follow-up score from the initial score and to provide an indication of repeatability, coefficient of variation (CV) was calculated for each individual by dividing the standard deviation of their results from their four tests by their mean result. Data are presented as means (95% confidence intervals (CI)) unless otherwise indicated. Approximately 4% of glucose and insulin data points were missing (due to occlusions within the cannula) and were substituted by bringing the last known value for that time point forward to ensure AUC was calculated from five time-points [13].

3. Results

We failed to detect any statistically significant change in glucose or insulin response or insulin sensitivity over the 4-days of repeated, daily OGTT's (Table 2; $p = 0.20$). There were also no significant differences in the change scores for glucose AUC ($p = 0.37$), insulin AUC ($p = 0.22$), OGIS ($p = 0.41$) or Stumvoll ISI ($p = 0.12$; Table 3).

At baseline, two participants were considered to have extreme hyperinsulinaemia (insulin ≥200 pmol L^{-1}). One individual with extreme hyperinsulinaemia was classified as having impaired glucose tolerance (2-h glucose ≥7.8 mmol L^{-1}) 1) using the World Health Organisation criteria [10] at baseline, 24-h and 48-h testing, before reverting to a classification of normal glucose tolerance at the final test. At baseline, all other