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Original paper

A comparative study of insulin resistance for Saudi and Caucasian subjects across a range of glycaemic categories

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ABSTRACT

Aim: Saudi and Caucasian subjects, matched for adiposity, and of differing glycaemic status were compared using several insulin sensitivity indices and to also to assess insulin, glucose and insulin-like growth factor binding protein-1 (IGFBP-1) responses to intravenous glucose.
Methods: Subjects with normal glucose tolerance (NGT; $n = 24$), impaired fasting glucose (IFG; $n = 12$), impaired glucose tolerance (IGT; $n = 12$), and type 2 diabetes (DM; $n = 13$) were recruited from Saudi ($n = 33$) and Caucasian ($n = 28$) populations. All had specimens taken in the context of a standard oral glucose tolerance test at their first visit and had the insulin sensitivity parameter (Si) determined by frequently-sampled intravenous glucose tolerance test (FSIVGTT) at a second visit.
Results: Saudis in the NGT and pooled glucose intolerance categories had significantly higher diastolic blood pressure ($p < 0.001$, $p < 0.05$ respectively) and HbA1c ($p < 0.01$, $p < 0.05$ respectively) compared to Caucasians. Caucasians in the NGT category had significantly higher Si, fasting and 2 h IGFBP-1 ($p < 0.01$, $p < 0.05$ and $p < 0.01$ respectively) compared to Saudis. Two hours following oral or intravenous glucose serum IGFBP-1 decreased to 44% ($p < 0.001$) and 50% ($p < 0.05$) of baseline levels respectively.
Conclusions: Our data suggest that adult Saudis with normal glucose tolerance appear to be more insulin resistant than Caucasians matched for adiposity. In normal individuals at 2 h the IGFBP-1 level will be about half the baseline level regardless of the route of glucose administration.

1. Introduction

Metabolic syndrome is an important and increasingly common public health problem both in the western world and Middle East. While the prevalence of metabolic syndrome among Caucasians has been reported to be approximately 16% [1], its prevalence in the Saudi population has been reported at almost one third [2]. The presence of metabolic syndrome is associated with an increased future risk of developing cardiovascular disease and type 2 diabetes, and there is a very high prevalence of both latter conditions in the Saudi population [3,4]. The reasons for this are believed to be both environmental and dietary [5,6] and may also be partly genetically determined. In particular, recent changes in nutrient intake and physical inactivity are thought to be contributory factors [4,6].

Insulin resistance is an essential component of the metabolic syndrome, and appears to develop early. Prospective studies have shown that metabolic syndrome is a powerful predictor of the likelihood of an individual developing diabetes or cardiovascular disease in Caucasian populations [7] and therefore it may be useful to be able to assess insulin sensitivity in individuals. We have previously reviewed the assessment of insulin resistance by various different techniques [8]. The frequently sampled intravenous glucose tolerance test (FSIVGTT) is considered a useful alternative to the hyperinsulinaemic euglycaemic clamp which is the gold standard method. However, owing to the difficulties and technical requirements of both these techniques, simpler methods for assessing insulin sensitivity have been proposed such as homeostasis model assessment (HOMA-IR) and quantitative insulin sensitivity check index (QUICKI) which are based on modelling of fasting glucose–insulin kinetics. Even simpler techniques for estimating insulin sensitivity involve measurement

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Table 1
Comparison of clinical, baseline and 2 h biochemical data in Saudi and Caucasian subjects. Subjects were classified as NGT and glucose intolerance (combined IFG and IGT) categories in each of the two populations.

	NGT		Glucose intolerance	
	Saudi ($n = 13$)	Caucasian ($n = 11$)	Saudi ($n = 12$)	Caucasian ($n = 12$)
Male (%)	77%	64%	58%	83%
Age (years)	39.4 ± 13	42.7 ± 17.8	47.6 ± 7.2	54.1 ± 7.4*
BMI (kg/m^2)	26.1 ± 4.6	26.4 ± 5.2	31.8 ± 2.2	29.8 ± 3.0
%TBF	25.4 ± 10.2	25.5 ± 11.6	36.5 ± 8.3	32.3 ± 7.0
WHR	0.90 ± 0.10	0.90 ± 0.10	0.93 ± 0.10	0.96 ± 0.10
SBP (mmHg)	118 ± 7	115 ± 20	127 ± 9	126 ± 16
DBP (mmHg)	73 ± 9	64 ± 4***	84 ± 10	74 ± 11*
TC (mmol/l)	4.5 ± 1.2	4.6 ± 1.2	4.7 ± 0.9	4.6 ± 0.8
HDLC (mmol/l)	1.2 ± 0.2	1.4 ± 0.4	1.1 ± 0.3	1.2 ± 0.2
LDLC (mmol/l)	2.7 ± 0.8	2.7 ± 1.3	2.9 ± 0.6	1.2 ± 0.2*
TG (mmol/l)	1.7 ± 1.0	1.1 ± 0.6	1.4 ± 0.7	1.9 ± 0.9
Uric acid (μmol/l)	322 ± 48	323 ± 47	331 ± 48	362 ± 68
%HbA1c	5.6 ± 0.5	5.2 ± 0.4**	6.1 ± 0.5	5.8 ± 0.4*
Glucose (mmol/l)	5.4 ± 0.4	5.2 ± 0.5	6.5 ± 0.4	6.0 ± 0.7*
Glucose (2 h) (mmol/l)	5.4 ± 1.4	5.5 ± 1.0	7.8 ± 1.6	8.5 ± 1.2
Insulin (pmol/l)	70 ± 26	87 ± 49	123 ± 34	138 ± 57
Insulin 2 h (pmol/l)	296 (190–403)	272 (126–418)	734 (640–828)	668 (557–778)
IGFBP-1 (μg/l)	3.7 (1.8–5.6)	9.8 (5.6–14.0)**	3.3 (1.7–4.8)	4.3 (2.1–6.5)
IGFBP-1 (2 h) (μg/l)	1.2 (0.5–1.9)	4.5 (2.1–7.0)*	0.7 (0.3–1.0)	1.7 (0.5–2.9)
IGF-I (nmol/l)	21.9 ± 8.7	20.6 ± 8.7	13.1 ± 3.3	17.3 ± 6.1

Data are mean ± SD or with 95% confidence intervals. Key: BMI, body mass index; HDLC, high density lipoprotein cholesterol; LDLC, low density lipoprotein cholesterol; TBF, total body fat; TC, total cholesterol; WHR, waste hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglycerides; HbA1c, glycated haemoglobin.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

of a single protein in serum such as the fasting insulin level or insulin-like growth hormone binding protein-1 (IGFBP-1) [9,10] and may be of particular value in epidemiological studies.

IGFBP-1 is of particular interest in the context of assessing insulin resistance as its plasma concentrations are reciprocally regulated by insulin. Furthermore, IGFBP-1 is capable of modulating the actions of insulin-like growth factors which could be due to the different circulating forms of IGFBP-1 [11,12]. Up to five different forms of plasma IGFBP-1 have been identified; part of this heterogeneity being different degrees of serine phosphorylation [13]. In plasma IGFBP-1 is mostly phosphorylated whereas in amniotic fluid and fetal serum non-phosphorylated (np), and less-phosphorylated (lp) variants predominate [14,15].

To date there have been no studies that have directly compared insulin resistance in matched Saudi and Caucasian subjects. This current study was therefore set up to assess and compare insulin sensitivity in subjects from the two populations using Si and various surrogate techniques and including subjects from across the glycaemic spectrum. Investigators have previously studied the dynamic effect of intravenous glucose boluses upon serum glucose, insulin and total IGFBP-1 levels [16,17]. Here we have extended this study to the two different ethnic groups and refined it by investigating the response of the lp IGFBP-1 rather than total IGFBP-1.

2. Subjects and methods

2.1. Subjects

Saudi ($n = 33$) and white Caucasian ($n = 28$) subjects participated in this study which was approved by the ethical committee of King Khalid National Guard Hospital (Jeddah, Saudi Arabia) and South West Surrey Local Research Ethics Committee (Guildford, UK). All subjects attended on two occasions. A standard 75 g oral glucose tolerance test (GTT) was carried out during the first visit and glycaemic status subsequently classified according to WHO criteria [18]. The subjects were classified into four categories as follows: normal glucose tolerance (NGT, $n = 24$), impaired fasting glucose (IFG, $n = 12$), impaired glucose tolerance (IGT, $n = 12$) and type 2 diabetes (DM, $n = 13$). DM subjects were either newly diagnosed or achieving good glycaemic control by dietary means alone. None of the diabetic subjects were treated with oral hypoglycaemic agents, insulin or agents such as steroids that might modify insulin sensitivity. For the purposes of this paper the IFG and IGT categories are collectively referred to as 'glucose intolerance' categories. Clinical characteristics of the subjects are shown in Table 1. Subjects were aged between 20 and 65 years with BMI > 20 and <35 kg/m^2 and were matched as closely as possible in each ethnic group. Subjects of the NGT category of each ethnic group were similar in BMI, age and physical activity. Percentage total body fat (%TBF) was estimated using a Tanita BF-680 tetra-polar bioelectric impedance device. Other clinical measurements taken were blood pressure (BP) and waist–hip ratio (WHR).

2.1.1. Assays

Insulin was measured by solid phase two-site ELISA (Mercodia, Uppsala, Sweden) which had a sensitivity of <7.0 pmol/l and maximum analytical CV of 4.9%. At both study sites glucose, uric acid and lipids were assayed in accredited laboratories on Bayer Advia 1650 auto-analysers using the same quality control specimens. Glycated haemoglobin (HbA1c) analysis was by a high pressure liquid chromatography technique on a Biorad Variant II instrument at both sites. All other assays were carried out in Guildford, UK. Samples were transported on dry ice by air from Saudi Arabia to UK. Serum IGF-I was determined by immunoassay using Immulite kits (kindly donated by Siemens Diagnostics UK, Al-Redwan KSA). IGFBP-1 was assayed by in-house ELISA using R&D analytical components. The capture antibody (R&D cat. no. MAB675) has been validated for binding with different forms of IGFBP-1 using western blotting technique and dephosphorylation by alkaline phosphatase. This capture antibody has the potential to bind preferentially to non-phosphorylated and less-phosphorylated forms of IGFBP-1 rather than to the highly phosphorylated form (data not shown). Assay had a sensitivity of 0.01 μg/l and maximum analytical CVs of 7.0% and 9.1% for intra- and inter-assay