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Brief report

Effect of glucose ingestion in plasma markers of inflammation and oxidative stress: Analysis of 16 plasma markers from oral glucose tolerance test samples of normal and diabetic patients

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ABSTRACT

Sixteen plasma markers of inflammation and oxidative stress were measured during OGTT in 54 subjects. Leptin, RBP4, CRP, OPN, ANG, MDC, and MCSF concentrations significantly decreased during OGTT ($P < 0.05$). IL6, IL8, and MCP3 concentrations significantly increased during OGTT ($P < 0.05$). These results provide evidence that glucose ingestion affects systemic inflammation and oxidative stress.

1. Introduction

In recent years, numerous studies have suggested that inflammation and oxidative stress play a major role in the pathologic process of diabetes [1,2]. Many studies have shown that acute hyperglycemia or food intake increases markers of inflammation and oxidative stress [3–6] and decreases adiponectin and leptin [7]. However, the effect of glucose ingestion on numerous other plasma markers, including some major cytokines involved in inflammation, has not yet been investigated. In addition, the effect of glucose ingestion on these plasma markers has not been fully investigated in

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Abbreviations: OGTT, oral glucose tolerance test; TRX, thioredoxin; RBP4, retinol-binding protein-4; CRP, C-reactive protein; IL6, interleukin-6; IL8, interleukin-8; TNFSF14, tumor necrosis factor superfamily member 14; OPN, osteopontin; ANG, angiogenin; VEGF, vascular endothelial growth factor; MCP1, monocyte chemoattractant protein-1; MCP3, monocyte chemoattractant protine-3; MDC, macrophage derived chemokine; MCSF, macrophage colony stimulating factor.

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diabetic patients. Thus, the aim of the present study was to investigate the effect of glucose ingestion in various plasma markers of inflammation and oxidative stress in both normal subjects and diabetic patients.

2. Subjects and methods

Subjects were recruited from the Korean Genome Epidemiology Study (KoGES) [8]. Subjects with a previous history of diabetes or any malignant disease were excluded. A total of 54 subjects were included in the present study and underwent an OGTT. Subjects were classified into normal, newly diagnosed prediabetes or newly diagnosed diabetes groups according to the American Diabetes Association Criteria (2009).

After an overnight fast, subjects ingested 75 g glucose, and blood samples were taken at 0, 60, and 120 min. Plasma glucose, insulin, thioredoxin (TRX), retinol-binding protein-4 (RBP4) were measured using ADVIA1660 Auto Analyzer (Siemens Medical Sol, USA), Gamma counter (D5010, Packard Bioscience Co., USA), thioredoxin ELISA kit (Redox Bio Science Inc., Japan) and RBP4 ELISA kit (Immundiagnostik Inc., Germany) were used, respectively. For all other measurements, including adiponectin, leptin, resistin, CRP, IL6, interleukin-8 (IL8), tumor necrosis factor superfamily member 14 (TNFSF14), osteopontin (OPN), angiogenin (ANG), vascular endothelial growth factor (VEGF), monocyte chemoattractant protein-1 (MCP1), monocyte chemoattractant protine-3 (MCP3), macrophage derived chemokine (MDC), and macrophage colony stimulating factor (MCSF), ELISA kits from R&D systems Inc. (USA) were used.

Values are given as mean ± SD. *t*-Tests were used to evaluate differences in baseline characteristics between groups. Concentrations of plasma markers were log-transformed for analyses. To examine the effect of time and whether plasma concentration variation patterns during OGTT were different between diagnosis groups, we used two-way repeated measures ANOVA with time and group as independent variables and interaction term between time and group (time × group). Additionally, paired *t*-tests were used separately for each time point and each diagnosis group. A *P* value less than 0.05 was considered to be statistically significant. All evaluations were performed with statistical software package SPSS version (version 17.0, SPSS Inc., USA).

3. Results

According to OGTT, the subjects were classified as normal ($n = 30$), prediabetes ($n = 14$) or diabetes ($n = 10$). Table 1 gives an overview of the characteristics of study subjects.

Fig. 1 shows the effect of glucose ingestion in plasma marker concentrations during OGTT according to each diagnosis group. Leptin, RBP4, CRP, OPN, ANG, MDC, and MCSF concentrations decreased during OGTT while IL6, IL8, and MCP3 increased during OGTT (effect of time *P* value < 0.05 and paired *t*-test *P* value < 0.05).

Interestingly, TRX concentration significantly increased at 1 h and 2 h in the normal group (paired *t*-test $P < 0.05$); however, in the diabetes group, TRX concentration decreased at 2 h, although not significantly (paired *t*-test $P > 0.05$) (Supplemental Fig. 1). There was a significant interaction between the effects of time and group for TRX from two-way repeated measures ANOVA analysis (time × group interaction *P* value < 0.05), which indicates that the effect of time on the TRX concentration is different between normal, prediabetes and diabetes groups.

Table 1 – Baseline characteristics of study subjects.

Variables	Normal	Pre-diabetes	Diabetes	Total
Number (male/female)	30 (14/16)	14 (4/10)	10 (7/3)	54 (25/29)
Age (yr)	56.5 ± 6.8	59.4 ± 8.3	60.0 ± 9.5	57.9 ± 7.7
BMI (kg/m^2)	24.5 ± 2.3	25.0 ± 3.0	25.6 ± 3.5	24.8 ± 2.7
Waist circumference (cm)	82.0 ± 6.0	81.8 ± 6.3	85.9 ± 7.2	82.7 ± 6.4
Hip circumference (cm)	92.0 ± 3.7	93.2 ± 5.1	95.0 ± 4.3	92.9 ± 4.3
Waist-to-hip ratio	0.89 ± 04.04	0.88 ± 0.05	0.90 ± 0.05	0.89 ± 0.04
Triglyceride (mmol/L)	1.54 ± 0.85	1.28 ± 0.55	1.63 ± 0.69	1.48 ± 0.76
Total cholesterol (mmol/L)	5.33 ± 1.02	5.34 ± 1.00	5.32 ± 0.84	5.33 ± 0.97
HDL cholesterol (mmol/L)	1.16 ± 0.25	[a]1.33 ± 0.23	1.08 ± 0.25	1.19 ± 0.26
HbA_1c (%)	5.4 ± 0.3	5.6 ± 0.4	[a]6.4 ± 0.9	5.6 ± 0.6
HbA_1c (mmol/mol)	36 ± 3	38 ± 4	46 ± 10	38 ± 7
Fasting glucose (mmol/L)	4.67 ± 0.40	4.97 ± 0.57	[a]6.34 ± 1.49	5.06 ± 0.97
1 h glucose (mmol/L)	6.82 ± 2.08	[a]9.72 ± 2.55	[a]13.67 ± 2.97	8.84 ± 3.52
2 h glucose (mmol/L)	6.02 ± 1.12	[a]8.93 ± 0.79	[a]13.72 ± 1.90	8.20 ± 3.16
Fasting insulin (pmol/L)	56.9 ± 17.4	70.1 ± 25.7	63.9 ± 22.2	61.8 ± 20.8
1 h insulin (pmol/L)	234.0 ± 267.4	[a]433.4 ± 385.4	145.8 ± 79.2	269.5 ± 295.2
2 h insulin (pmol/L)	192.4 ± 187.5	[a]370.9 ± 290.3	291.0 ± 168.1	257.0 ± 225.0
HOMA-IR	1.71 ± 0.57	[a]2.27 ± 0.95	[a]2.62 ± 1.11	2.02 ± 0.87
HOMA-B	3.81 ± 1.15	4.33 ± 1.46	3.18 ± 1.40	3.83 ± 1.31
QUICKI	0.355 ± 0.016	0.344 ± 0.024	[a]0.336 ± 0.022	0.349 ± 0.021
Matsuda index	9.15 ± 3.87	[a]5.18 ± 2.74	[a]4.89 ± 1.44	7.33 ± 3.82

Data are given as absolute numbers (*n*), means ± SD.
[a] $P < 0.05$ compared with normal group.