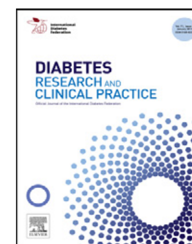
DIABETES RESEARCH AND CLINICAL PRACTICE 94 (2011) 404–409

Contents lists available at ScienceDirect

Diabetes Research and Clinical Practice

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



Protein oxidation markers in women with and without gestational diabetes mellitus: A possible relation with paraoxonase activity

Remise Gelisgen [a], Habibe Genc [a], Refik Kayali [b], Mahmut Oncul [c], Ali Benian [c,], Onur Guralp [c], Seyfettin Uludag [c], Ufuk Cakatay [d], Mustafa Albayrak [e], Hafize Uzun [a]*

[a] Istanbul University, Cerrahpasa Medical Faculty, Department of Biochemistry, Istanbul, Turkey
[b] Istanbul University, Cerrahpasa Medical Faculty, Department of Pediatrics, Laboratory of Biochemistry, Turkey
[c] Istanbul University, Cerrahpasa Medical Faculty, Department of Obstetrics and Gynecology, Turkey
[d] Istanbul University, Istanbul Medical Faculty, Central Laboratory of Clinical Biochemistry, Istanbul, Turkey
[e] Duzce University, Department of Obstetrics and Gynecology, Duzce, Turkey

ARTICLE INFO

Article history:
Received 1 July 2011
Received in revised form
28 July 2011
Accepted 2 August 2011
Published on line 31 August 2011

Keywords:
Gestational diabetes
Protein carbonyl
Paraoxonase
Protein hydroperoxides
Nitrotyrosine

ABSTRACT

Aims: To clarify the levels of protein oxidation markers such as protein carbonyl (PCO), protein hydroperoxides (P-OOH), advanced oxidation protein products (AOPP) and nitrotyrosine (NT), as well as antioxidative enzymes such as paraoxonase (PON-1) in women with and without gestational diabetes mellitus (GDM).

Methods: The study was conducted on 23 women with GDM and 22 women without GDM. The levels of the P-OOH, AOPP, and PON-1 were determined by colorimetric methods; whereas NT and PCO levels were measured by ELISA.

Results: The concentrations of protein oxidation markers were significantly increased and PON1 activity was significantly decreased in GDM group compared to those of normal pregnant women. The control group showed a significant negative correlation between PON-1 and PCO ($r = -0.451$, $p = 0.027$); whereas in GDM group, there was a significant positive correlation between P-OOH and HbA1c ($r = 0.89$, $p = 0.001$). There was no significant correlation between AOPP, PON-1, P-OOH, PCO, and HbA1c in either group.

Conclusions: There is evidence of a possible association between protein oxidation and decreased PON1 activity in GDM. The increase in protein oxidation parameters in the GDM group leading to decreased PON1 activity might, we think, create a predisposition for clinical complications in GDM group.

© 2011 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Free radicals are unstable and highly reactive. They become stable by acquiring electrons from nucleic acids, lipids, proteins, carbohydrates, or any nearby molecule causing a cascade of chain reactions resulting in cellular damage and disease. In normal cells, ROS (reactive oxygen species) and antioxidants are in homeostatic balance. When the redox balance is disrupted towards an overabundance of ROS, oxidative stress (OS) occurs. OS plays a role in conditions such as abortion, pre-eclampsia, hydatidiform mole, fetal embryopathy, preterm labor and pre-eclampsia, and gestational

* *Corresponding author at*: Istanbul Universitesi, Cerrahpasa Tip Fakultesi, Kadin Hastaliklari ve Dogum Anabilim Dali, Fatih, Istanbul 34980, Turkey. Tel.: +90 5424343032; fax: +90 2122730336.
E-mail address: abenian@hotmail.com (A. Benian).

0168-8227/$ – see front matter © 2011 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.diabres.2011.08.001

diabetes mellitus (GDM), which lead to an immense burden of maternal and fetal morbidity and mortality [1].

Paraoxonase1 (PON1) is a 355 aminoacid glycoprotein, which is synthesized in the liver and secreted into the blood, where it associates with HDL (high-density lipoprotein). PON1's free thiol at cysteine-284 is required to combat LDL oxidation and is thought to be the active site for its antioxidant activity [2]. On the other hand, PON1 was shown to possess peroxidase-like activity that can contribute to its protective effect against lipoprotein oxidation, as well as a homocysteine-thiolactonase activity that may be linked with its anti-atherogenic properties [3,4].

In former studies, lipid oxidation had been the center of scientific attraction instead of protein oxidation. However, due to their relatively high abundance, it has been recently recognized that proteins could be the main targets for oxidants. Moreover, the maintenance of protein redox status is considered to be of fundamental importance for cell function [5–7]; and metal-catalyzed protein oxidation characterized by carbonyl (PCO) formation [8–10], loss of protein thiol (–SH) groups [10–12], nitrotyrosine (NT) [8–10,13–16], and advanced oxidation protein products (AOPP) formation [17–19] may lead to structural changes.

Hyperglycemia in diabetes is associated with increased glycation, oxidative stress, and nitrosative stress. GDM is defined as a glucose intolerance of varying severity with onset or first recognition during pregnancy [20].

Limited publications are available in the current literature regarding the presence of protein oxidation stress in women with GDM [21]. Serum PON1 is associated with high-density lipoprotein (HDL). Studies have shown that serum PON1 activity is reduced in diabetic subjects [21–23]. Furthermore, protein carbonylation rates in the plasma of pregnant rats with streptozotocin-induced diabetes were shown to be elevated [23,24].

The aim of this study was to investigate the plasma levels of the protein oxidation markers such as PCO, protein hydroperoxides (P-OOH), AOPP, and NT in GDM and normal pregnant women. This study also aims to evaluate whether or not PON1 inactivation results from an interaction of oxidized proteins with PON1's active thiol group. Additionally, we assessed the capability of PON1 to maintain redox status of proteins and to investigate the effect of protein oxidation on its antioxidant activity in GDM. If the complex oxidative interactions in plasma of GDM could be better understood, the complications of GDM would be prevented.

2. Materials and methods

2.1. *Subjects*

Overall, 45 women with a singleton pregnancy who were prospectively followed-up in our clinic were enrolled in the study. The first 23 consecutive women with GDM and the first 22 consecutive women without GDM were recruited.

Gestational age was confirmed in all pregnant women by a routine ultrasonographic examination performed during the first trimester of gestation. All women were nonsmokers and none used any antenatal medications except anti-anemic drugs. Inclusion criteria included a signed informed consent, absence of a clinically relevant illness, normal findings in the medical history and physical examination except for GDM, and normal laboratory values. Subjects were excluded if any clinically relevant abnormality was found during routine follow-up or in any of the laboratory tests including circulating anti-insulin antibodies and anti-islet cell antibodies. None of the subjects was on a special diet or reported intake of any medication, including "over-the-counter" drugs, at the time of blood sampling. Exclusion criteria for all subjects were taking medication, smoking, and high blood pressure for the control group. The study was approved by the Ethics Committee of Cerrahpasa Medical Faculty, and every patient gave informed consent.

All women were screened for GDM with 50 g glucose challenge test at 24th GW. The 50-g glucose screening test was carried out independent of the time of day or any previous meals at about 24 weeks gestation. An oral glucose tolerance test was recommended to all patients whose 1-h test result was equal to or exceeded 140 mg/dl (7.8 mmol/l).

A diagnosis of GDM was made by 100-g oral glucose tolerance test (OGTT) and results were evaluated according to the Carpenter-Coustan Criteria [25]. GDM was diagnosed if at least 2 abnormal values were met: fasting, $\geq$95 mg/dl (5.3 mmol/l); 1 h, $\geq$180 mg/dl (10.0 mmol/l); 2 h, $\geq$155 mg/dl (8.6 mmol/l); 3 h, $\geq$140 mg/dl (7.8 mmol/l). Women diagnosed with gestational diabetes were seen weekly and treatment consisted of dietary treatment (energy goals of 35 kcal/kg of ideal body weight), adapted to allow 0.2–0.5 kg weight gain per week. Antidiabetic diet was combined with insulin based on the patient's ability to achieve glycemic control within 0–2 weeks. Insulin therapy was initiated if blood glucose readings remained above target levels [5.8 mmol/l (105 mg/dl) before meals and 7.1 mmol/l (130 mg/dl) 2 h after meals] and was adjusted by the patient on a daily basis using a protocol of self-monitored blood glucose levels 3–4 times per day. Of the women with GDM, 19 were clinically managed by diet alone and 3 were prescribed insulin in addition to dietary management. The women were advised to keep daily records of food intake and document their blood glucose results, which were reviewed every 1–2 weeks. Treatment targets [5.8 mmol/l (105 mg/dl) before meals and 7.1 mmol/l (130 mg/dl) 2 h after meals] were achieved in all women. Timing of delivery was based primarily on obstetric indications.

2.2. *Study protocol*

2.2.1. *Blood samples*

After the completion of recruitment procedure, blood samples were taken between 24 and 28 gestational weeks in the morning, after a mild breakfast, to avoid the confounding effect of diurnal variation of oxidative stress parameters as reported previously [26]. Venous blood samples were drawn in the fasting state and processed within 1 h of collection. Blood samples were collected in tubes containing lithium heparin, EDTA, or no additive depending on the analysis. For protein oxidation parameters, all paraoxanase plasma samples containing lithium heparin were stored at −70 °C until analysis, and all other parameters were determined on the same day of collection.

Download English Version:

https://daneshyari.com/en/article/5900122

Download Persian Version:

https://daneshyari.com/article/5900122

Daneshyari.com