OBSERVATIONS

Osteoprotegerin Levels in Women With Prior Gestational Diabetes Mellitus

Osteoprotegerin (OPG), an inhibitor of bone resorption, seems to be elevated in patients with diabetes as well as in nondiabetic subjects with cardiovascular disease (1).

Following a pregnancy complicated by gestational diabetes mellitus (GDM), women present with an increased prevalence of glucose intolerance and an unfavorable cardiovascular risk profile, although definite cardiovascular diseases or late diabetes complications have only rarely been confirmed (2).

Hence, our aim was to study OPG levels and their association with other cardiovascular risk factors in a sample of 30 former GDM (by World Health Organization criteria) and 14 age-matched women with normal glucose tolerance during pregnancy in an average 4 years after delivery. During the study investigation an assisted questionnaire was completed, followed by a detailed physical examination, and blood samples were drawn (after 12-h fasting). To compare groups, two-sample *t* tests and Fisher's exact tests were utilized as appropriate. To describe independent covariates of the fasting OPG values (dependent variable), multiple linear regression (stepwise forward method) was used entering the univariately significant parameters as possible covariates. $P < 0.05$ was considered significant.

Glucose intolerance (either diabetes or impaired glucose tolerance [IGT]) was more prevalent among prior GDM than among control subjects (18 of 30 vs. 2 of 14, $P = 0.008$). Prior GDM women were more commonly overweight (BMI: 27.4 ± 8.5 vs. 23.5 ± 3.0 kg/m^2) had higher homeostasis model assessment (3) insulin resistance (9.7 ± 3.7 vs. 4.4 ± 2.1), and had lower fasting C-peptide levels (1.31 ± 1.36 vs. 1.66 ± 0.74 ng/ml) compared with control subjects (all $P < 0.005$). There was no difference in OPG levels (ELISA, Biomedica; Halstenbek, Germany) between prior GDM and control subjects (3.35 ± 1.42 vs. 3.82 ± 1.38 pmol/l).

Henceforward, the data of prior GDM and control subjects were analyzed together. Higher serum OPG levels were associated with present glucose intolerance (4.04 ± 1.34 vs. 3.05 ± 1.32; $P = 0.018$); with older age ($r = 0.33$; $P = 0.031$); with higher triglycerides ($r = 0.38$; $P = 0.012$), C-peptide ($r = 0.50$; $P = 0.0001$), and γ-glutamyl transferase (GGT) ($r = 0.52$; $P = 0.0001$); and with lower HDL cholesterol ($r = -0.31$; $P = 0.004$) and serum calcium ($r = -0.503$; $P = 0.028$). No associations were found with BMI, waist-to-hip ratio, total cholesterol, fibrinogen, presence of hypertension, or a positive family history of either diabetes or cardiovascular disease.

OPG levels were independently associated ($r = 0.76$ for the whole model; $P < 0.0001$) with GGT ($\beta = 0.3$; $P < 0.0001$), fasting C-peptide ($\beta = 0.252$; $P = 0.014$), and current glucose intolerance ($\beta = 0.231$, $P = 0.037$). Age, fasting triglycerides, HDL cholesterol, and serum calcium were also available for selection to the model.

To our best knowledge, there is only one previous report on OPG levels in prior GDM women. Akinci et al. (4) reported that higher serum OPG levels were associated with older age, higher CRP and glucose levels, and higher carotid intima media thickness; however, they were also unable to prove a significant association with prior GDM status.

According to a recent study, elevated GGT should be included as a component of the metabolic syndrome to improve its cardiovascular predictive value (5). The interrelationships between glucose intolerance, liver function, and cardiovascular disease might partly explain our observation of an independent association between OPG and GGT. In summary, our data suggest that higher OPG levels are associated with present glucose intolerance, independently of the effect of prior GDM status.

ESZTER MADARASZ, MD[1,2,3]
GYULA TAMAS, MD, PHD[1,2]
ADAM G. TABAK, MD, PHD[1,2]
GABOR SPEER, MD, PHD[2]
PETER LAKATOS, MD, PHD, DSC[2]
ZSUZSA KERENYI, MD, PHD[1,3]

From the [1]National Center for Diabetes Care, Semmelweis University, Budapest, Hungary; the [2]1st Department of Medicine, Semmelweis University, Budapest, Hungary; and [3]Csepel Health Service, Department of Diabetology, Semmelweis University, Budapest, Hungary.

Corresponding author: Eszter Madarász, madeszt@yahoo.com.

DOI: 10.2337/dc08-1628

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