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AEP397

Exposure to phenolic compounds (Bisphenol A and Methyl Paraben) in pregnancy and its relationship with gestational diabetes mellitus, insulin homeostasis and pancreatic beta cell function

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Objectives
The effect of exposure to endocrine disruptors (exogenous chemical compounds that interfere with hormonal homeostasis), such as Bisphenol A (BPA) and Methyl Paraben (MPB), on gestational diabetes mellitus (GDM) has only been investigated in a small number of studies, with inconclusive results. Our objective was to investigate the association between concentrations of BPA and MPB in urine and the presence of DMG, insulin sensitivity and function of beta cells in a cohort of pregnant women in the Mediterranean area.
Material and methods
Multicenter case-control study, nested in a gestational cohort. Sequential sampling of women with pathological O'Sullivan (week 24–27 gestation), and indication of GDM confirmation test (OGTT 100 g, 3 h) was performed. We analyzed the presence of GDM (Carpenter and Coustan), insulin sensitivity through Matsuda-SOG Index (WBSII), and beta cell function by a trapezoidal model with calculation of the incremental area of insulin and glucose under the curve (AUCins and AUGglu, respectively), and by disposition index (DI) [(AUCins / AUGglu) * WBSII]. Concomitantly, urine concentrations of BPA and MPB were quantified by liquid chromatography coupled to mass spectrometry (HPLC-MS). The relationship between the urinary levels of BPA and MPB with the dependent variables was studied using Spearman correlation tests and multivariate logistic and linear regression models.
Results
Of the 110 women included 34.5 [29–38] years old, 26 [24.7–28] weeks of gestation, BMI 27.9 [24–32] kg/m^2, 40.4% of them met the GDM criteria. The study population had a urinary concentrations of BPA 2.95 [1.17–4] µg/l, and MPB 12.1 [4.4–35.4] µg/l. BPA levels of the 3rd vs 1st tertile were not associated with an increased risk of GDM [OR 0.84 (0.3–2.3)], neither with differences in WBSII or DI. These variables were also not correlated by Spearman. 3rd vs MPB levels 1st tertile were not associated with an increased risk of GDM [0.76 (0.3–1.9)], but with a higher WBSII ($P<0.01$). A negative correlation was also found between MPB and HbA1c, HOMA-IR, AUCins / AUGglu and positive with WBSII ($P<0.05$). This relationship disappears when a multivariate linear regression analysis is performed, in which it is found that BMI (B = –0.1, $P=0.002$) would be the only independent factor associated with WBSII.
Conclusions
In pregnant women with pathological O'Sullivan, higher concentrations of BPA or MPB in urine were not associated with an increased risk of GDM, lower insulin sensitivity, or lower beta cell function.

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The prophylactic effects of metoprolol, diltiazem and pilocarpine on hypoglycemia-induced prolongation of QT interval

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Background
Insulin-induced hypoglycemia has been demonstrated to prolong the corrected QT (QTc) interval. Prolongation of QTc interval, especially in diabetic patients using insulin, can cause fatal ventricular arrhythmias. The aim of this study was to evaluate the effects of metoprolol, diltiazem and pilocarpine on hypoglycemia-induced QTc prolongation.
Methods
Thirty rats were randomly distributed into the following five groups: Group 1 (1 ml/kg saline, $n=6$), Group 2 (40 U/kg crystalline insulin + saline, $n=6$), Group 3 (40 U/kg crystalline insulin + 1 mg/kg metoprolol, $n=6$), Group 4 (40 U/kg crystalline insulin + 0.8 mg/kg pilocarpine, $n=6$), Group 5 (40 U/kg crystalline insulin + 2 mg/kg diltiazem, $n=6$). Three hours after insulin injection, blood glucose level was measured in all groups. Blood glucose <40 mg/dl was defined as hypoglycemia. Electrocardiograms (ECG) were taken in lead I (DI) and QTc was calculated by using Bazett' s formula.
Results
Group 2 (insulin + saline) showed that they had significantly prolonged QTc interval compared to control group ($P<0.0001$). However, treatments of the rats with metoprolol, pilocarpine and diltiazem significantly prevented the prolongation of QTc interval compared to insulin + saline group ($P<0.005$, $P<0.005$ and $P<0.01$, respectively).
Conclusion
The findings of the present study demonstrated the efficacy of metoprolol, pilocarpine and diltiazem in the prevention of hypoglycemia-induced QTc prolongation. These agents may be considered in the prophylactic therapy of high-risk patients who are using insulin.

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Serum vaspin level in patients with diabetes mellitus type 2 as a predictive index of atherosclerosis

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Background
It has been proved that the adipose tissue is an active endocrine organ. It secretes a large number of adipokineswhich are involved in and affect regulation of metabolic process and can influence pathogenesis of atherosclerosis. Vaspin-new representative of adipokineswhich is secreted by adipose tissue and have an insulin-sensitizing properties. Vaspin engagement into atherosclerotic process poorly investigated.
Aim
To establish the value of plasma vaspin level in patients with diabetes mellitus type 2 (DM2) for prediction cardiovascular disease.
Methods
Thirty-one patient (55.1 ± 1.9 years) with DM2 (9.1 ± 2.8 years of duration) who do not have major adverse cardiovascular events were included to the study. The BMI (28.18 ± 0.8 kg/m^2), fasting plasma glucose level (FPG), HbA_1c, total cholesterol (TC), low-density lipoproteins (LDL), triglycerides (TG), C reactive protein (CRP) serum vaspin level and intima media thickness of carotid arteries (IMT CA) by ultrasound were measured. Control group healthy volunteers (54.8 ± 1.1 years) matched for age, gender and BMI.
Results
The study results showed that all patients had an adequate control of DM2 by oral hypoglycemic agents FPG 8.18 ± 0.92 mmol/l; HbA_1c 7.49 ± 0.21%. Dyslipidemia was present TC 6.40 ± 0.63 mmol/l; LDL 3.39 ± 0.52 mmol/l, TG 2.35 ± 0.15 mmol/l and there is no active process of inflammation CRP 1.33 ± 0.12. Serum vaspin level was significantly higher in patients with DM2 than in control group 3.47 ± 0.42 pg/ml vs 2.42 ± 0.19 pg/ml, $P<0.05$). In multivariate analysis after adjusting for atherosclerotic risk factors vaspin had positive correlation with IMT CA 1.02 ± 0.23 mm vs 0.71 ± 0.11 mm ($r=0,37$, $P<0,02$); immunoreactive insulin (0.6 $P<0,001$) FPG (0.62 $P<0,001$), HbA_1c (0.56, $P<0,001$), TG ($r=0,31$, $P<0,04$). No significant correlation was found between vaspin and BMI, TC, LDL, and plaque existence in carotid arteries.
Conclusions
Serum vaspin level was found significantly higher in patients with DM2 and thicker intima media than age-matched healthy subjects with normal IMT. The vaspin level had significant correlation with all known parameters which are involved in and promoted atherogenesis. Therefore, vaspin may have a pleiotropic effects and can be engaged in atherosclerosis development.

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