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Effect of oral antidiabetic agents on the concentration of FGF-21s: The newly identified molecular effects of antidiabetic agents

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Background: Fibroblast growth factor 21 (FGF21) is an endocrine hormone that exhibits anti-obesity and anti-diabetes effects. Recently was presented that metformin in patients with type 2 diabetes modulates FGF21 expression and glood concentration. Results indicate that metformin and other oral antidiabetic drugs induced expression of FGF21 through an ATF4-dependent mechanism by inhibiting mitochondrial respiration independently of AMPK and it´s concentration in blood.

Aim: Studying the effect of metformin, derivates of sulphonylurea, glinidines, gliptines, glitazones on the concentration of FGF21 in serum in type 2 diabetes patients.

Methods: The study was approved by the Ethics Commission of the Hospital Šternberk, Czech Republic. Study was monocentric, prospective and randomized. A total of 196 individuals were recruited for our study (18 healthy controls (HC), 18 T2D individuals without diabetes therapy (W), 18 T2D individuals, diabetes monotherapy with derivates of sullfonylurea (SU),18 T2D individuals diabetes monotherapy with 500 mg metformin per day (M5), 18 T2D individuals diabetes therapy with 1000 mg metformin per day (M10), 18 T2D individuals, diabetes monotherapy therapy 1500 mg metformin per day (M15), 18 T2D individuals, diabetes monotherapy with 2000 mg metformin per day (M2), 18 T2D individuals diabetes monotherapy with SU derivates (SU), 18 T2D individuals diabetes monotherapy with gliptines (GP), 18 T2D individuals diabetes monotherapy with glitazones (GL), 18 T2D individuals diabetes monotherapy with glinidines (GN). Anthropometric (height, weight, BMI, waist circumference (WC)), clinical (systolic and diastolic pressures) and laboratory fasting analyses were performed. Blood samples were drawn under aseptic precautions from vena cubiti, after a several-minute rest in the half-sitting position. Serum samples were separated in a cooled centrifuge at 3000 g for 20 minutes and immediatelly analyzed for total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, glucose, high sensitivity CRP, creatinine, uric acid, AST, ALT (all Siemens, Advia 1800). FGF21 serum level was determined by a commercially available ELISA kit (Biovendor, Czech Republic) in serum samples stored at -80°C.

Results: The study analyzed 196 subjects, of which 18 were in good health while 180 probands suffered from type 2 diabetes. In-defined subgroups, no significant differences were found by gender in FGF21 concentration. Healthy individuals had the lowest values of FGF21, other subjects increased by the value of the diagnosis, the type of metformin therapy and dose (HC 84.2 ng/l vs. W 111.6; P<0.01) (M5 269.7 vs. M10 404.1 vs. M15 558.7, M2 711.4 ng/l; P<0.01). High values of FGF21 were found in patients with the highest dose of metformin 2000/mg per day. Changes remained significant after adjustment for age, sex and BMI. The values of FGF21 in patients treated with SU, GL, GP and GN did not differ significantly from diabetic patients without therapy (SU 115 ng/l, GL 121 ng/l, GN 105 ng/l, GP 127 ng/l).

Conclusion: In randomized prospective study we or the first time confirmed the recently presented hypothesis that metformin leads to the rise of FGF21 (unlike other antifdiabetic drugs). GF21 induction by metformin might explain a portion of the beneficial metabolic effects of metformin.

Biography

David Stejskal, MD has completed his Ph.D at the age of 38 years from Palacký University Olomouc, Czech Republic and postdoctoral studies from Palacký University Olomouc, CZ, too. He is the medical director of Agel Laboratories and head of Department of Laboratory Medicine Central Moravian Hospital Group. He has published more than 175 papers in reputed journals and serving as an editorial board member of two repute journals. He is specialisated in laboratory problems in cardiology, neurology and oncology.

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