OBSERVATIONS

Low Plasma Apelin in Newly Diagnosed Type 2 Diabetes in Chinese People

It has been unclear whether there is a pathway that regulates plasma glucose through the action of peripheral tissue of apelin with the secretory function of insulin, which exerts a control in adipocytes in addition to the direct regulation of plasma glucose. Our study was designed to identify the changes in plasma apelin levels in newly diagnosed type 2 diabetes in Chinese people. We also tried to investigate the possible association of apelin, the status of hyperglycemia, and insulin secretion.

The study population consisted of 75 patients with newly diagnosed and untreated type 2 diabetes and 36 healthy control subjects matched for age, sex, and BMI. Fasting plasma glucose (FPG), fasting serum insulin, A1C, and C-reactive protein (CRP) were measured. A steady-state model (homeostasis model assessment [HOMA]) (1) was used to assess insulin resistance (HOMA-IR) and β-cell function. Plasma apelin-17 levels were determined by radioimmunoassay (RIA) (human apelin-17 ^{125}I-tracer RIA kit; Bachem Americas) (sensitivity: [minimum detectable concentration] = 0.1 ng/ml, IntraCV:5% and InterCV:10%). An unpaired Student *t* test and Mann-Whitney *U* test were used to compare mean values among the type 2 diabetic control subjects and the healthy control group. Spearman rank correlation test and multiple stepwise regression analysis were used to show the relationship among HOMA-insulin sensitivity (IS), apelin, FPG, and A1C.

Plasma apelin levels were significantly lower in the diabetic group compared with the control subjects (0.11 vs. 0.25 ng/ml, $P < 0.0001$). Apelin levels were negatively correlated with CRP ($r = -0.357$, $P = 0.001$), HOMA-IR ($r = -0.509$, $P < 0.0001$), FPG ($r = -0.607$, $P < 0.0001$), and A1C ($r = -0.467$, $P < 0.0001$) and positively correlated with HOMA-IS ($r = 0.566$, $P < 0.0001$). Multiple stepwise regression analysis showed that apelin increased 565 fg/ml along with 1 SD, which increased in HOMA-IS in our subjects ($R^2 = 0.107$, $P = 0.002$). Compared with the lowest quartile, the highest quartile of HOMA-IS had significantly higher plasma apelin level (0.27 vs. 0.07 ng/ml, $P < 0.0001$). Such results were also obtained in FPG and A1C ($P < 0.0001$ for both).

The data showed the consistent results with those of Erdem et al. (2) that plasma apelin levels were lower in newly diagnosed and untreated type 2 diabetic subjects than in healthy control subjects, whereas Li et al. (3) reported the opposite results with type 2 diabetic subjects who were already under treatment. Boucher et al. (4) reported upregulation of apelin synthesis and secretion from the adipose tissue by insulin, whereas Dray et al. (5) revealed apelin as a new endocrine regulator of AMP kinase and strengthened the cross talk between adipose tissue and skeletal muscle. So our results were a possible clue that apelin, which is upregulated at the adipocyte tissue by insulin, may independently impact glucose metabolism indirectly besides the direct action on the glucose uptake of insulin.

The study was an observational study but not a perspective one. However, the hypothesis that apelin could impact the uptake of glucose at the skeletal muscle and adipose tissue levels, thus inducing the status of hyperglycemia or diabetes, needs to be further studied. It is expected that apelin might be a potential target for the treatment of diabetes.

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