

Postprandial hyperglucagonemia accompanies morbid obesity even in non-diabetic patients

E.A. Shestakova, I.A. Sklyanik, A.S. Panevina, L.V. Nikankina, M.V. Shestakova, I.I. Dedov

Endocrinology Research Centre, Moscow, Russian Federation

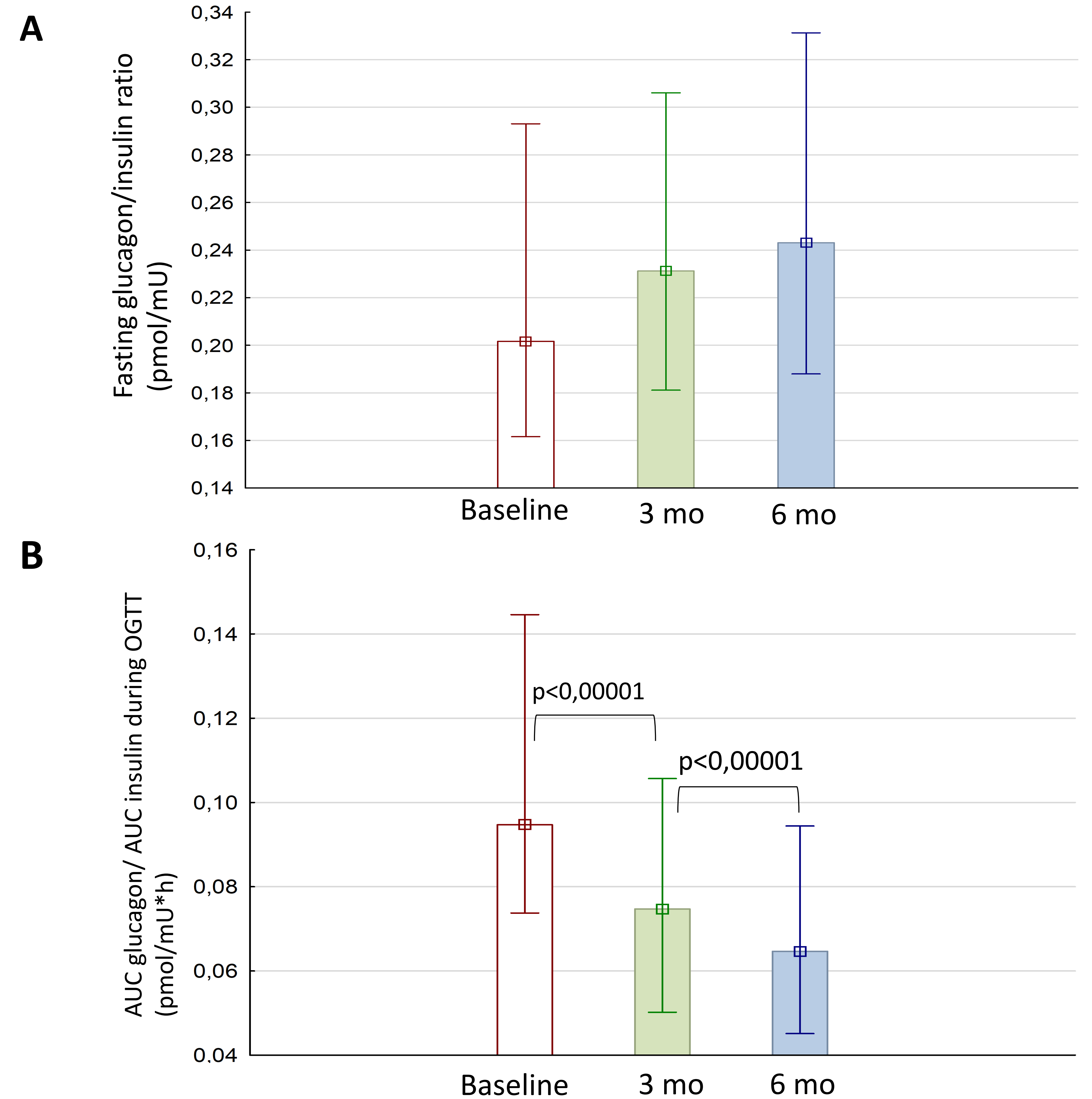
Background and aims: Hyperglucagonemia is one of the pathophysiological mechanisms for type 2 diabetes development. Whether glucagon is increased in obese patients without glucose disturbances is less known.

Materials and methods: Study population included 44 patients with morbid obesity and normal glucose metabolism. All patients went through gastric bypass or biliopancreatic diversion and were followed-up at 3 and 6 months after surgery. At baseline, 3 and 6 months patients passed euglycemic hyperinsulinemic clamp-test and oral glucose tolerance test (OGTT) with plasma glucose, insulin, glucagon, GLP-1 measured at 0', 30' and 120' minutes after glucose load. We calculated fasting and postprandial glucagon/insulin ratio as well as GLP-1 AUC during OGTT. Values are presented as median [Q1; Q3]. Statistical analysis was performed in Statistica 13.3.

Results: BMI (kg/m^2) dramatically decreased in all patients during the study: 43,2 [40,3; 46,5] at baseline vs 37,0 [34,3; 40,2] at 3 months and 33,6 [31,0; 37,3] at 6 months, $p < 0,00001$. Though HbA1c (%) was normal at beginning (5,5 [5,3; 5,8]) it still improved alongside with weight reduction: 5,35 [5,2; 5,5] at 3 months and 5,2 [5,1; 5,4] at 6 months, $p < 0,00001$. According to M-index ($\text{mg}/\text{kg} \cdot \text{min}$) measured in clamp-test patients had mild-to-moderate insulin resistance at baseline (4,06 [3,14; 4,96]) that decreased during follow-up (4,91 [3,83; 5,59] at 3 months and 5,11 [4,23; 6,18] at 6 months, $p < 0,00001$). Fasting glucagon/insulin ratio didn't change significantly during the study, while postprandial glucagon/insulin ratio (AUC glucagonOGTT/AUC insulinOGTT) declined (Fig. 1) due to insulin increase and glucagon reduction. These changes were followed by GLP-1 secretion improvement (AUC GLP-1OGTT 68,8 [51,4; 84,8] $\text{pmol}/\text{l} \cdot \text{h}$ at baseline vs 78,5 [54,1; 92,3] $\text{pmol}/\text{l} \cdot \text{h}$ at 3 months vs 81,9 [60,3; 99,2] $\text{pmol}/\text{l} \cdot \text{h}$, $p < 0,00001$). GLP-1 secretion at baseline negatively correlated with glucagon level ($r = -0,62$, $p < 0,00001$).

Conclusion: Morbid obesity without glucose intolerance is accompanied by relatively high postprandial glucagon level. Weight reduction causes decrease in hyperglucagonemia and restoration of normal postprandial insulin/glucagon regulation which may be due to GLP-1 secretion improvement.

Fig. 1. Fasting (A) and postprandial (B) glucagon/insulin ratio at baseline and in 3 and 6 months after bariatric surgery



Support: Grant 17-15-01435 Russian Science Foundation