

Role of incretins in metabolic surgery-induced remission of type 2 diabetes.

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Two hypotheses are proposed as a mechanism for remission of type 2 diabetes (T2DM) in metabolic surgery; one is foregut hypothesis associated with the exclusion of the duodenojejunum from the nutrient exposure, while another one is hindgut hypothesis associated with the rapid exposure of the ileum to the bile and nutrients. These hypotheses are tested using rat models of T2DM, including Goto-Kakizaki rats and obese Zucker rats. Two most representative procedures of metabolic surgery in rats are ileal interposition (II) and duodenojejunal bypass (DJB). II is considered as a model for hindgut hypothesis, whereas DJB as a model for foregut and partly hindgut hypothesis. These 2 procedures improve glucose metabolism, and there are no differences in T2DM remission effects between 2 procedures. Incretins including GIP and GLP-1 are assumed to play an important role in remission of T2DM in these procedures. Most studies reported that II does not affect fasted plasma GLP-1 levels but increases those after glucose or meal administration. Effects of II on the fasted and postprandial plasma GIP levels are still controversial. The effects of DJB on plasma GLP-1 and GIP levels are also controversial, and mechanisms independent of incretin are assumed in DJB-induced remission of T2DM. Clinically, ileal interposition with sleeve gastrectomy (II-SG) and ileal interposition with diverted sleeve gastrectomy (II-DSG) are being attempted. More than 90% of patients achieved adequate glycemic control (HbA1C<7%). Plasma levels of GLP-1, GIP, and PYY significantly increased, while plasma levels of ghrelin significantly decreased, after II-SG and II-DSG in the fasted and postprandial states. These results indicate the important role of incretins in metabolic surgery-induced remission of T2DM, but mechanisms other than incretins are also likely.