

## Immunohistochemistry evidence for gastric ghrelin cells hypertrophy in obese patients

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Ghrelin cells are endocrine cells of the gastrointestinal tract mainly present in the glands of the stomach. They produce the "hunger hormone" that promotes appetite and adiposity in animal and human models. In response to these anabolic effects, several elements have suggested the influence of ghrelin on the regulation of metabolic functions and the development of obesity-related disorders. However, its physiologic significance is quite complex and some of the effects of ghrelin are still debated in the literature. Recent evidence suggests that ghrelin influences glucose homeostasis through the modulation of insulin secretion and insulin receptor signalling. T2 diabetes is the most frequent metabolic disorder associated with obesity. To date, the most effective treatment of obesity is bariatric surgery and one of the most used techniques is sleeve gastrectomy. It consists in the resection of 25% of the stomach producing a neo anatomy in which this organ becomes a tube-like structure, lacking the ghrelin-rich part. Forty-seven percent of T2 diabetic obese patients treated by sleeve gastrectomy rescue their diabetic condition just after surgery and before any weight reduction. This clinical evidence clearly connects this new morphology of the stomach with the positive metabolic improvement and suggests that ghrelin could play a key role in this striking effect. We studied the gastric mucosa of the fundus of sleeve gastrectomized T2 diabetic-obese patients (n.5) by immunohistochemistry with Anti- Ghrelin antibody to verify the ghrelin cell morphology, immunoreactivity and density. Anti- Chromogranin A antibody was used to detect the whole endocrine population of gastric glands. We used the normal part of the gastric fundus removed from patients (n.3) suffering for gastric cancer, as control. Ghrelin receptor has been shown on peripheral nerve fibers of the autonomous nervous system, and because a direct innervation of Langerhans islets by intestinal neurons have been shown in the past, we extended our immunohistochemistry analyses to neuronal antigens in order to study the nervous network of gastric mucosae in these surgical samples. Results show that ghrelin cells in T2 diabetic obese patients represented a consistent percentage (48.4% vs 38% in controls) of chromogranin A immunoreactive cell population. Furthermore, ghrelin cells were hypertrophic and intensely immunostained when compared with those found in gastric mucosae of controls. Neuronal specific enolase immunoreactivity was clearly enhanced in the gastric mucosae of obese patients. These data suggest that the stomach of T2 diabetic obese patients increase ghrelin content and that sleeve gastrectomy could have an important metabolic role by anatomical reduction of this hormone. Furthermore, our result suggest a possible paracrine effect on the peripheral neuronal population that could also be implicated in this complex and striking clinical effect of bariatric surgery.

### References

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### Keywords

Ghrelin , humans, stomach, T2 diabetes, obesity, sleeve gastrectomy, immunohistochemistry.