Improved gastric emptying in diabetic rats by irbesartan via decreased serum leptin and ameliorated gastric microcirculation

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Received May 23, 2013
Accepted January 23, 2014
Published September 5, 2014
DOI http://dx.doi.org/10.4238/2014.September.5.2

ABSTRACT. Diabetic gastroparesis (DG) is a common clinical complication of diabetes mellitus. Leptin may cause delayed gastric emptying in the central and peripheral pathways. Microcirculatory disturbances in the stomach make gastric smooth muscles and nerves hypoxic-ischemic, thereby impairing gastric motility. Irbesartan is an angiotensin II (ATII) receptor blocker that indirectly decreases serum leptin levels and improves blood vessel endothelia. This study examined the effect of irbesartan on DG and its relationship with serum leptin levels and microcirculatory disturbances of the stomach. Sprague-Dawley rats were injected with streptozotocin to induce diabetes and were then treated with or without 0.012 g·kg⁻¹·d⁻¹ irbesartan by gavage. After six weeks of treatment, the gastric evacuation rate (GER) was measured using phenol red. Serum leptin levels were detected using enzyme-linked immunosorbent assays. Endothelin (ET) in the stomach tissue was examined using a radioimmunoassay, whereas chemical colorimetry was used to measure the nitric oxide synthase (NOS) activity of stomach tissues. The mRNA expression of the ATII
receptor (AT1R) was assessed using reverse transcription-polymerase chain reaction. Treatment with irbesartan significantly increased the GER of diabetic rats and reduced the serum leptin levels, as well as decreased the ET content and AT1R mRNA expression in the stomach (P < 0.05). Changes in the cNOS activity after irbesartan intervention were not significant (P > 0.05), whereas iNOS activity was significantly decreased (P < 0.05). Irbesartan can alleviate hyperglycemia-induced delayed gastric emptying, which is associated with decreased serum leptin levels and improved microcirculation in the stomach.

**Key words:** Diabetes mellitus; Diabetic gastroparesis; Irbesartan; Gastric evacuation rate; Leptin; Endothelin