Sibutramine accelerates gastric emptying, inhibits intestinal motility in conscious dogs

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**Background & Aims:** Sibutramine is a serotonin- norepinephrine uptake inhibitor, used in the treatment of obesity. It has never been reported whether sibutramine has any effects on GI motility and GI myoelectrical activity. The aim of this study was to evaluate the effects of sibutramine on gastric emptying, small bowel contractions, rectal tone and compliance and gastric/intestinal myoelectrical activity.

**Methods:** The study was performed in fourteen healthy female dogs (18-27 Kg); seven of fourteen dogs were surgically prepared for duodenal cannula and pacing wires implanted in gastric and small bowel serosa. It was composed of 3 separate experiments: gastric emptying of liquids and gastrointestinal slow waves; Small bowel contractions; and rectal tone and rectal compliance. Each experiment included two sessions: a control session and a treatment session with sibutramine (5mg/Kg p.o, Generic Meridia, United Pharmacies) administrated 2 hours before the recording. 7 cannula dogs underwent gastric emptying study with liquid meal and small bowel contractions study in the fed state. 7 dogs underwent a rectal barostat study.

**Results:**

1. Sibutramine significantly accelerated liquid gastric emptying at 75min and 90 min after the meal but did not alter gastric or intestinal slow waves. Gastric emptying was $61.42 \pm 19.34\%$ at 75 min and $66.32 \pm 19.38\%$ at 90 min in the control session, and increased to $71.27 \pm 13.5\%$ at 75min ($p = 0.046$, vs. control) and $75.93 \pm 15.05\%$ at 90min ($p = 0.036$, vs. control) in the session with sibutramine.

2. Sibutramine significantly inhibited postprandial small bowel contractions. The area under the curve (AUC) was $14.57 \pm 4.11$ in the control session and decreased to $10.64 \pm 4.18$ ($p = 0.014$, vs. control) in the session with sibutramine.

3. Sibutramine did not alter the rectal tone, but significantly increased rectal compliance. The rectal compliance expressed as the slope of the pressure-volume curve was significant increased from $7.59 \pm 2.05 \text{ml/mmHg}$ at baseline to $9.97 \pm 3.25 \text{ml/mmHg}$ after sibutramine administration ($p = 0.003$).

**Conclusions:** Sibutramine accelerates gastric emptying of liquids but inhibits small bowel contractions. These findings suggest the peripheral mechanisms of sibutramine in reducing food intake and causing weight loss in obesity patients.