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Prazosin inhibits small intestinal transit in the rat

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Gastric emptying, small intestinal transit, and colonic transit were measured in fasted rats preimplanted with either duodenal or colonic cannulae. At the doses stated, prazosin (given subcutaneously) had no effect on gastric emptying or colonic transit, whereas small intestinal transit was significantly delayed.

Introduction Earlier studies in our laboratory (Ruwart *et al.*, 1979a) have demonstrated that gastric emptying, small intestinal transit and colonic transit in the rat are affected differently by adrenergic and cholinergic stimulation or blockade. For example, atropine depresses gastric emptying and colonic transit, but not small intestinal transit (Ruwart *et al.*, 1979b); clonidine suppresses small intestinal transit without affecting gastric emptying (Ruwart *et al.*, 1980). In an attempt to define further the role of the adrenergic system in gastrointestinal transit in the rat, we examined the effects of the α_1-adrenoceptor antagonist prazosin.

Methods Male Upjohn Sprague Dawley rats (200–220 g) were fitted with duodenal or colonic cannulae as previously described (Ruwart *et al.*, 1979c). After a ten-day recovery period, they were fasted for 48 h but allowed water *ad libitum*. Prazosin hydrochloride was dissolved in saline and given subcutaneously to the rats 20 min prior to administration of transit markers.

For studies measuring gastric emptying and small intestinal transit, rats with duodenal cannulae were given simultaneously oral $Na_2^{51}CrO_4$ in saline (0.25 ml) and a bolus of black agar (0.25 ml) through the cannula (Ruwart *et al.*, 1979a). Forty-five minutes later, rats were killed by carbon dioxide asphyxiation, the pylorus and oesophagus were clamped and the stomach and small intestines removed. Small intestinal transit was expressed as the percentage of intestinal length travelled by the most distal edge of the agar bolus. The stomach and intestines were monitored separately for radioactivity and gastric emptying was expressed as the percentage of isotope which had entered the intestines.

For studies measuring colonic transit, rats with colonic cannulae were given a black agar bolus and killed 3 h later by carbon dioxide asphyxiation. The colon was removed and colonic transit expressed as the percentage of intestinal length travelled by the most distal edge of the agar marker.

Results Prazosin had no effect on gastric emptying; intestinal transit, however, was significantly depre-

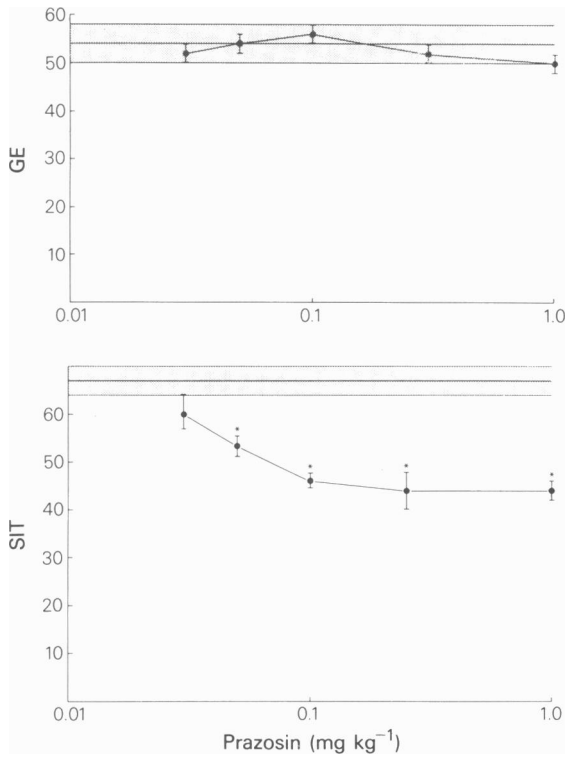

Figure 1 Gastric emptying (GE) and small intestinal transit (SIT) as a function of subcutaneous prazosin dose. The stippled area indicates the mean and s.e.mean for rats receiving vehicle only ($n = 10$). The points indicate mean for rats receiving various doses of prazosin ($n = 10$) with s.e.mean indicated by vertical lines. Values with asterisks indicate points significantly different ($P < 0.05$) from vehicle-only values.

ssed at 0.03 mg kg^{-1} and maximally decreased from 67% to 45% at 0.1 mg kg^{-1} (Figure 1). No significant change was observed in colonic transit between vehicle and prazosin (0.5 mg kg^{-1})-treated animals (53.2 ± 6.2 vs. 56.1 ± 6.6, respectively).

Discussion Prazosin might have been expected to have no influence on gastric emptying since phentolamine is also without effect (Ruwart *et al.*, 1979a). However, colonic transit was enhanced by phentolamine, suggesting that suppression of α-adrenoceptor-mediated activity would enhance transit in colon. The failure of prazosin to increase colonic transit might be due to its specificity of action on α_1-adrenoceptors, since phentolamine is generally thought to affect both α_1- and α_2-adrenoceptors.

Earlier studies have indicated that small intestinal transit in the rat, unlike man and dog, is minimally affected by atropine (Ruwart *et al.*, 1979b), suggesting that the primary stimulatory neurotransmitter may not be acetylcholine. The depression of small intestinal transit by prazosin may be another anomaly of rat small intestine, since antagonism of adrenergic transmission might have been expected to enhance, not delay, small intestinal transit (Dubois *et al.*, 1973; Ruwart *et al.*, 1979a,d). Furthermore, small intestinal transit is not completely suppressed, suggesting that stimulatory neurotransmission is not completely blocked by this agent.

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