Direct Mucosal Targeting of Colonic Receptors by Prokinetic Drugs in an Experimental Model

Y H Ho,*FAMS, FRCSEd, FRACS, D F Evans,**PhD, J D Hardcastle,***MD, FRCP, FRCS

Abstract

Isolated perfused segments of pig ileum and sigmoid colon were used as an extrinsically denervated model of intestinal fluid propulsion to compare the effects of intraluminal (IL) with intraarterial (IA) administration of cisapride and mebeverine. The ileal segments had a spontaneous mean activity of 0.008 (SEM 0.003) ml Krebs propelled aborally min^{-1}, with propulsive waves at a mean frequency of 8.3 (1.6) min^{-1}. The sigmoid colon segments ejected a mean of 0.013 (0.009) ml Krebs min^{-1}, with propulsive waves at 3.9 (0.8) min^{-1}. IL cisapride produced a dose-dependent response in the dose range 1 x $l0^{-9}$ M to 3 x 10^{-1} & 1-3 x 10^{-7} M in the ileum, and 3 x $l0^{-11}$ to 3 x 10^{-9} M in the colonic segments, IL cisapride was significantly more effective than IA delivery of equivalent doses. IL instilled mebeverine (1 x 10^{-6}M) inhibited the carbachol dose response of the ileal and colonic segments more than an equivalent dose of mebeverine infused IA. We conclude that the isolated perfused pig intestine is an effective model for studying the pharmacological effects of drugs and their routes of delivery. Cisapride and mebeverine were more effective per given concentration, when delivered IL than IA in both the ileum and sigmoid colon preparations. The qualitative effects of either IL or IA drug delivery were not affected by extrinsic denervation.

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