Effects of β-Adrenoceptor Stimulation on Rectosigmoid Motility in Man

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Effects of selective β-adrenoceptor agonists on rectosigmoid motility during prolonged rectal distension were studied in 12 healthy volunteers in a double-blind, randomized fashion. Continuous distension was performed with a balloon in the proximal part of the rectum. Pressure was recorded by this balloon and by a catheter in the sigmoid. Contractile activity was quantified for three consecutive periods of 25 min. On separate days prenalterol (β-1 agonist), terbutaline (β-2 agonist), and placebo, respectively, were administered intravenously preceded by a control period. Terbutaline, 0.5 mg intravenously, was followed by a significant decrease of sigmoid motility from $4.3 \pm 1.5$ (SEM) kPa × min to $2.9 \pm 1.0$ kPa × min ($P < 0.01$) and of rectal motility from $4.3 \pm 1.3$ to $2.4 \pm 0.7$ kPa × min ($P < 0.05$). After placebo a slight, but not significant, increase of contractile activity was seen compared to the initial control period. The effects of prenalterol, 1.0 and 4.0 mg intravenously, on motility did not differ from that of placebo infusion. Both drugs caused a dose-dependent increase of systolic blood pressure and of heart rate. The study shows that β-2-adrenoceptor stimulation decreases rectosigmoid colonic pressure in man, while effects of β-1 stimulation on motility index do not differ from that of placebo.

The regulatory function of the sympathetic adrenergic nervous system in human gastrointestinal motility has been poorly known until recently. Gut motility is suppressed by sympathetic adrenergic activity under stressful conditions, such as postoperatively (1-4). There is also evidence for an adrenergic inhibitory influence on colonic motility under physiological conditions. In recent studies on patients with the irritable bowel syndrome (5) and in healthy volunteers (6), sigmoid motility increased significantly after administration of beta-blocking drugs.

Intestinal isolated smooth muscle contractions can be inhibited by the β-1 agonist prenalterol and by the β-2 selective agonist terbutaline (7). β-2-adrenoceptor agonists have been shown to relax the lower esophageal sphincter (8, 9) and slow down gastric emptying in man (10, 11), but effects of selective β-2 agonists on human colonic motility have not been studied. The present study was performed to determine the influence of a β-1 and a β-2 adrenoceptor agonist on rectal and sigmoid motility in healthy subjects.

MATERIALS AND METHODS

Subjects. Twelve healthy male subjects with a mean age of 27 years (22-40) participated in the study. They had no history of gastrointestinal disease or previous abdominal surgery and were taking no medications. They all belonged to the medical staff of the hospital. Before entering the study, each subject had a normal physical examination and showed normal findings on electrocardiogram. The study was approved by the Ethical Committee of the University of Göteborg.
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RECTOSIGMOID MOTILITY

![Fig. 1. Schematic diagram for experimental design. The shaded areas represent periods of 25 min for which rectal and sigmoid pressure were quantified after control infusion of saline and after infusion of the drugs tested (terbutaline, prenalterol, or placebo).](image)

**Drugs.** Prenalterol (Hyprenan, AB Hässle) was used as β-1 adrenergic agonist (12) and terbutaline (Bricanyl, AB Draco) as β-2 agonist (13).

**Experimental Design.** Motility was recorded after an overnight fast and after a spontaneous bowel movement at least 1 hr before the recording started. The pressure recording device was inserted through a sigmoidoscope without prior enemas and without air insufflation. Pressure was recorded from two separate locations. An open tip polyethylene catheter (ID 1.67 mm) perfused with water 3 ml/hr was placed in the sigmoid about 19 cm from the dentate line of the anus. A second recording catheter, to which a balloon of 5 cm length was connected, was placed in the rectum. The balloon lay between 9 and 14 cm from the dentate line and was continuously distended by 80 ml of air in order to give a steady local contact to the rectal wall. This volume of distension could be kept in all subjects without any discomfort or pain, as reported also by others using a similar balloon recording technique (14). To prevent the device from moving in the distal direction, a third catheter was fixed to it and placed just inside the anus. This catheter was connected to a balloon which lay between 3 and 8 cm from the dentate line and was continuously distended by 20 ml of air.

The two recording catheters were connected to pressure transducers (Statham P23Db) and recordings were made on a Grass 7 C polygraph. For assessing rectal and sigmoid motility, the area under the pressure curves was continuously determined by an integrator (Grass 7P10) as described previously (6). Total area minus the area under the estimated basal pressure line was used as an index of contractile activity and expressed as kilopascal x min (1 kPa x min = 7.5 mm Hg x min). The study was randomized and double blind. Calculations of motility index were done before the code for the drugs was randomized and double blind. Blood pressure and heart rate were measured by a sphygmomanometer (Figure 1).

Each subject was investigated on three different days with at least five days between each recording to exclude any possible interaction between the drugs. After 30 min of rest following sigmoidoscopy, motility was quantified for three periods of 25 min. The first period was preceded by an intravenous infusion of saline, 5 ml (1 ml/min), and assigned as the control period. The following two test periods were each preceded by an infusion of terbutaline 0.25 mg (0.05 mg/min for 5 min), and prenalterol 1 mg preceding the first test period and 4 mg preceding the second test period on the other day, and placebo 5 plus 5 ml (saline) on the third day according to the randomized schedule (Figure 1). For determination of drug plasma levels, blood samples were drawn from a venous cannula at 10 and 25 min after the end of each drug infusion. Blood was collected in heparinized test tubes and, after separation, the plasma samples were stored at -20°C until analysis. Plasma concentration of prenalterol was determined at the Department of Analytical Chemistry, AB Hässle (15), and plasma concentration of terbutaline determined at the Department of Analytical Chemistry, AB Draco (16).

**Methods of Evaluation.** Statistical analysis of occurrences of changes (increase or decrease) in motility index was made with the chi-square test. The occurrence of change in motility index from control to test period for each dose of active drug was compared to the corresponding placebo period. Index differences less than 0.10 kPa x min between control and a test period was assigned as no change.

**RESULTS**

**Basal Conditions and Effects of Placebo.** During the control period, following infusion of saline, sigmoid motility was characterized by periods of pressure waves with a frequency of 1-3/min with amplitudes < 4 kPa. The duration of pressure waves was generally between 10 and 25 sec. There were also frequent periods of only slight pressure waves. In four of the subjects there were periods of raised baseline pressure with superimposed waves corresponding to type III waves (17). The duration of these longer waves was generally between 30 and 90 sec with an amplitude of 1-3 kPa. The pressure wave recorded by the rectal balloon was mainly of the low frequency type without any periods of raised baseline pressure or superimposed waves. After placebo infusion, there was a tendency to an increased occurrence of pressure waves in the majority of the subjects with an increasing duration and amplitude of the waves during the recording.