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Enema volume and spreading

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Summary

The spreading of enema solutions has been monitored in four normal subjects using gamma scintigraphy. Two volumes, 50 ml and 200 ml, were administered on separate occasions. Enema dispersion was greater with the 200 ml dose but there was considerable variability. Enema administration and eating stimulated intraluminal colonic motility, but food taken 1 h after enema dosing did not affect spreading. Aboral movement of the colon contents appears to inhibit dispersion. It is concluded that 100 ml is the optimum enema solution volume for the delivery of topically active drugs to the descending colon.

Introduction

The administration of 100 ml doses of enema solution provides a reliable means of delivery of topically active drugs to the descending colon (Hardy et al., 1986a). Only occasionally, however, does the preparation spread into the ascending colon (Wood et al., 1985; Hardy et al., 1986a). Although the extent of dispersion of enema solutions is highly variable, the limited data available indicate that within the range 50 ml to 200 ml spreading is greater with larger administered volumes (Swarbrick et al., 1974; Hay, 1982).

Colonic motility is stimulated by enema administration and can be correlated with the degree of enema dispersion (Hardy et al., 1986a). On average the increase in colonic motility resulting from dosing with 100 ml enema was the same as that following a large meal. Food consumed immediately before enema dosing, however, did not enhance spreading.

The present study compares the dispersion of enemas having volumes of 50 ml and 200 ml. The effect of enema administration on colonic motility has been monitored. Additionally, food was consumed 1 h after dosing to investigate its influence on motility and enema spreading. The results of this study will aid in the optimization of dosage regimens for enema preparations.

Materials and Methods

Materials

The enema was 0.9% sodium chloride solution in 50 ml and 200 ml doses. Each dose was radiolabelled immediately prior to administration by the addition of 3 MBq ^{99m}Tc-labelled diethylenetriaminepentaacetic acid in 1 ml solution.

Colonic motility was monitored using pressure-sensitive radiotelemetry capsules, 28 mm long

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by 8 mm diameter (type 7014, Remote Control Systems, London). Each capsule contained a pressure-sensitive diaphragm and a radiotransmitter, and was calibrated at 50, 25 and 0 cm water at 37°C. The signals were detected by an aerial positioned against the abdomen, demodulated by a receiver (type 7040, Remote Control Systems) and recorded by a multichannel pen recorder (Grass Instruments, Quincy, MA, U.S.A.). The capsules were radiolabelled with 0.3 MBq indium-111 so that their positions could be identified within the gastrointestinal tract.

The radionuclide distributions were monitored using a gamma camera having a 40 cm diameter field of view and fitted with a medium energy (300 keV maximum) parallel hole collimator. The camera was tuned to detect, simultaneously but separately, the 140 keV radiation of technetium-99m and the 245 keV radiation of indium-111. The images were recorded by computer in a 128 × 128 matrix.

Subjects

Four healthy male volunteers, aged 21–23 years, participated. All were regular in their bowel habits and none was taking any medication. Each subject gave written informed consent prior to taking part and the study was approved by the local ethical committee.

Methods

At 23.30 h on the days before enema administration each subject swallowed a radiotelemetry capsule. Following an overnight fast, basal colonic pressure activity was recorded from 10.00 h to 11.00 h with each subject in the prone position. Capsule movements were monitored by reference to an anatomical reference marker radiolabelled with indium-111 taped to the subject's back, over the right lobe of the liver.

At 11.00 h two subjects were dosed with 50 ml enema and two with 200 ml. The solution was administered at room temperature with the subjects lying on their left sides. Following resumption of the prone position monitoring was continued for a further 3 h. Pressure measurements were recorded continuously, and at 15 min intervals posterior images of the abdomen were recorded using the gamma camera. One hour after enema administration, and whilst remaining prone, each subject consumed the 4200 kJ meal described by Snape et al. (1978). At the end of each study an anterior image was recorded with the subject supine.

One week later the study was repeated with each subject receiving the alternative volume of enema solution. On both occasions each subject consumed similar food on the day before the study.

The spreading of the enema was quantified from the technetium count rates from each section of the colon. The data were expressed as proportions of the administered dose as described by Wood and colleagues (1985). The location of the capsule was identified by reference to the enema distribution and the external references marker. Intraluminal colonic motility indices were calculated using the equation (Misiewicz et al., 1966):

$$\text{motility index} = \frac{\Sigma(\text{duration} \times \text{amplitude of pressure wave})}{\text{time}}$$

Results

There was considerable variation in the extent of enema spreading. In general, however, disper-

TABLE 1

ENEMA DISTRIBUTIONS AT 2 h AFTER DOSING

Subject	Enema volume (ml)	Proportion of dose (%)		
		Rectum/ sigmoid colon	Descending colon	Transverse colon
1	50	50	42	8
	200	42	52	6
2	50	100		
	200	29	57	14
3	50	98	2	
	200	82	18	
4	50	83	17	
	200	52	32	16

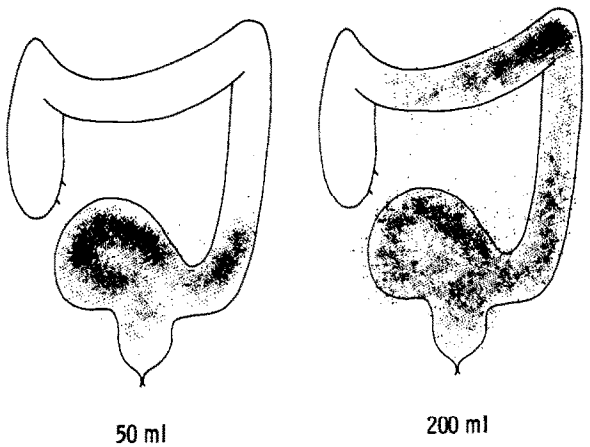

Fig. 1. Enema distributions in Subject 4, 3 h after dosing.

sion had ceased by 2 h. The distributions at this time are given in Table 1. In each subject there was a greater proportion of the 50 ml dose retained in the rectum and sigmoid colon than of the 200 ml dose (Fig. 1). In all four subjects the 200 ml dose spread into the descending colon and in three it entered the transverse colon. In contrast, the 50 ml dose was fully retained in the rectum and sigmoid colon in one subject and spread into the transverse colon in only one. The preparation was not detected in the ascending colon in any of the studies. The times between defaecation and enema dosing ranged from 1.8 to 38 h and there was no relationship between the defaecation times and the extent of spreading.

TABLE 2

POSITIONS OF THE RADIOTELEMETRY CAPSULES FOLLOWING ENEMA ADMINISTRATION

Subject	Enema volume (ml)	Location of capsule			
		0.1 h	1 h	2 h	3 h
1	50	SC	SC	SC	SC
	200	AC	AC *	HF	HF
2	50	TC	TC	SF	SF
	200	TC	HF	HF	HF
3	50	Cae	AC	SF	SF
	200	SF	SF	DC	DC
4	50	SI	AC	SF	SF
	200	SI	Cae	Cae	Cae

Key: SI = small intestine; Cae-caecum; AC = ascending colon; HF = hepatic flexure; TC = transverse colon; SF = splenic flexure; DC = descending colon; SC = sigmoid colon.
* Capsule in different location.

At the time of enema dosing the radiotelemetry capsule was in the colon in 6 of the 8 studies. Within the colon aboral movement of the capsule was detected during five studies and retrograde movement on just one occasion (Table 2). In only one study (200 ml dose to Subject 1) did enema spread into the transverse colon when aboral

TABLE 3

COLONIC MOTILITY INDICES BEFORE AND AFTER ENEMA DOSING AND FOOD

Subject	Enema volume (ml)	Motility index			
		Pre-enema	Post-enema (1st hour)	Postprandial	
				(1st hour)	(2nd hour)
1	50	0.4	1.8	20	18
	200	0	1.0	14	15
2	50	22	47	44	46
	200				
3	50	SI	2.9	38	33
	200	22	20	18	13
4	50	SI	19	29	46
	200	SI	22	42	40

SI = capsule in small intestine.

movement of the capsule occurred. In this subject a maximum of 10% of the 200 ml dose entered the transverse colon, compared with 23% of the 50 ml dose in the absence of aboral movement. The most rapid and extensive spreading of solution from the rectum and sigmoid colon occurred after dosing Subject 2 with 200 ml. This was accompanied by retrograde movement of the capsule.

Capsule movement occurred during the hour before enema dosing in two subjects. On both occasions the capsule was in the small intestine. Movement of the capsule within the colon was observed during the first hour after enema dosing in five studies and during the second hour also in five studies. The frequency of capsule movement was the same following the 50 ml dose as after the 200 ml dose. In none of the studies was there capsule movement during the third hour after enema administration.

Pressure measurements were obtained during seven of the eight studies; the exception being from Subject 2 during the 200 ml enema study. The colonic motility indices are listed in Table 3. In general the values were higher after the enema and food, although the responses showed considerable variability.

Discussion

In previous studies in normal subjects, carried out under similar conditions, the preparation spread into the transverse colon on about 40% of the occasions following dosing with 100 ml enema solution (Wood et al., 1985; Hardy et al., 1986a). During the current investigations three of the four 200 ml doses and one of the 50 ml doses dispersed into the transverse colon. Hay (1982) also found that 100 ml doses spread further than 50 ml doses and Swarbrick and co-workers (1974) reported a tendency for greater dispersion with increasing volume over the range 50 ml to 200 ml. In the present studies none of the preparations spread into the ascending colon, although this had been observed occasionally with 100 ml doses (Wood et al., 1985; Hardy et al., 1986a). While two of the 50 ml doses were almost completely retained in the rectum and sigmoid colon, this only occurred with the 100 ml enemas when the subjects were dosed soon after defaecation (Wood et al., 1985).

Hardy and colleagues (1986a) found that enema spreading could be correlated with colonic motility. Administration of enema solution stimulated colonic motility to the same extent as a substantial meal. Enema dispersion was, however, the same whether the subjects were dosed fasted or after a meal. In the present study colonic motility was, in general, greater after enema administration and food. The meal, however, did not stimulate enema dispersion nor movement of the capsule.

Changes in capsule location provided an indication of the movement of the bulk of the colon contents. Aboral progression through the colon is characterized by periods of propulsion separated by intervals of stasis which may last for several hours (Hardy et al., 1985). In agreement with earlier findings (Hardy et al., 1986a), aboral movement of the colon contents was associated with diminished enema spreading. Although retrograde movement of colonic contents is a relatively uncommon occurrence (Hardy et al., 1986b) it can lead to enhancement of enema dispersion. Thus it seems that movement of the bulk of the colon contents is a major factor influencing enema spread.

In conclusion, 100 ml enema solution volumes seem optimum for the delivery of topically active drugs to the descending colon, particularly since it has been suggested that enema spreading is greater in patients with active colitis (Swarbrick et al., 1974; Farthing et al., 1979). Increasing the volume to 200 ml did not enhance dispersion into the ascending colon and 50 ml doses showed less spreading. For the treatment of disease confined to the rectum and sigmoid colon, foam preparations may be more appropriate than solutions since they tend to be more convenient and comfortable to use (Clark, 1977; Hay, 1982). Oral dosing is a more appropriate route for drug delivery to the proximal colon (Hardy et al., 1985).

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