Spread of steroid-containing foam after intrarectal administration

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Summary and conclusions

The spread of a steroid-containing foam from the rectum was studied in eight normal controls and eight patients with ulcerative colitis proved by biopsy. A standard dose of foam was labelled with technetium-99m adsorbed on to microspheres of Amberlite resin. Immediately after the foam was administered the extent of spread varied considerably, though in no instance did it extend beyond the rectosigmoid. Further scans at 120 and 240 minutes showed no further spread.

It is concluded that a steroid-containing foam has a topical effect only on the rectal mucosa.

Introduction

The local application of corticosteroids has long been recognised to be of considerable value in treating patients with ulcerative colitis. In 1956 Truelove¹ described the intrarectal infusion of an alcoholic solution of hydrocortisone by means of a drip set and rubber catheter. This gave satisfactory results, which were improved further by using an aqueous solution of hydrocortisone hemisuccinate. In 1960 a prednisolone sodium phosphate enema was shown by Matts² to be an effective treatment for colitis and simple to administer. In the same trial a preliminary study was performed whereby 100 ml of dilute barium solution was substituted for the enema fluid. This showed that such an enema can spread a considerable way into the colon and often well beyond the splenic flexure, provided that the patient lies on his face for a few minutes after administration. Although effective, the prednisolone sodium phosphate enema has notable disadvantages. It is often uncomfortable, and many patients find it difficult to retain even when the foot of the bed is raised.

Recently a steroid-containing foam (Colifoam) has been used to treat patients with ulcerative colitis. It is undoubtedly more comfortable for most patients and obviates the necessity to lie down after administration. Several trials have been performed,^{3,4} which report excellent patient tolerance. The foam has been suggested to be as effective in treating ulcerative colitis as the retention enema.⁵ Our clinical impression, however, has been that while the foam is effective in proctitis and the most distal ulcerative colitis it is of less value in more proximal disease. How far the foam spreads is uncertain but has a bearing on patient management. In this study, therefore, we have aimed to assess the spread of a steroid-containing foam enema within the bowel.

Subjects and methods

We labelled the foam (Colifoam) with technetium-99m, an isotope emitting γ -rays; as the pertechnetate ion, this was adsorbed on to microspheres of Amberlite CG400(CL) exchange resin. A measured quantity of the resulting dried powder, such that the activity was no more than 100 μ Ci, was placed in the nozzle of a foam applicator (fig 1), which was then filled from the pressurised dispenser in the usual way causing the powder to be dispersed throughout the foam.

FIG 1—Equipment for applying the foam. The Amberlite resin microspheres are dispersed by filling the applicator in the usual way.

The loaded applicator was then agitated with a mechanical stirrer. Preliminary studies were carried out to assess the spread of activity in the foam. The labelled foam was spread from the applicator on to a black background and a Polaroid photograph taken. A gamma-camera was then used to scan the same lines of foam and the scan photographed. The distribution of activity within the foam was sufficiently even (fig 2) to form a valid basis for studying the spread of the preparation in the rectum. The radiation doses to the subjects were calculated, and after being passed by the Isotope Advisory Panel the project was accepted by the area ethical committee on 3 February 1978.

FIG 2—Polaroid photographs: (a) of lines of foam on black background and (b) of gamma-camera scan of same lines of foam.

We studied 16 subjects. Eight were medical staff or students (controls) who had no symptoms of bowel disease. Eight were patients who had ulcerative colitis proved by sigmoidoscopy and biopsy. All subjects gave informed consent in writing. At the time of the study all the patients with colitis were being managed as outpatients and their bowel habit varied from two to six loose stools per day.

The standard dose of foam was labelled as described above and placed in the rectum of each subject. Scans were performed at 15, 120, and 240 minutes in an anteroposterior plane in all subjects while they were prone on a couch. In addition, scans were performed in a lateral plane in three of the controls and four of the patients with ulcerative colitis. All subjects were ambulant while not being scanned, and no restrictions were placed on food intake or bowel actions, although no subject found it necessary to defecate during the study. The extent of spread of the foam was assessed by laying on the subject a Perspex rod

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containing technetium in small cavities at 2.5 cm intervals, the lower end of the rod being positioned at the level of the anus. This produced a series of graduations along the side of the scan, against which the length of the column of intrarectal activity was compared.

Results

Figures 3 and 4 represent two series of scans in two patients. Fig 3 shows that the extent of spread in case 11 at 15 minutes was 12.5 cm, which had increased by 240 minutes to 17.5 cm. This was the greatest extent of spread observed in any subject. Fig 4 shows a much more typical series of pictures. Here the spread was 5.1 cm at 15 minutes, which had not changed by 240 minutes. Tables I and II

FIG 3—Anteroposterior scan showing spread of foam in case 11. The foam extended to 12.5 cm at 15 minutes and 17.5 cm at 120 and 240 minutes. The line of dots is the Perspex scale containing technetium.

FIG 4—Lateral scan showing spread of foam in case 15. Foam extended to 5.1 cm at 15 minutes and had not changed by 120 or 240 minutes.

TABLE I—Extent of spread of foam from anus (cm) in control subjects as seen on anteroposterior scans. (Results obtained from lateral scans shown in parentheses)

Case No	Time of scan after administration of foam (min)		
	15	120	240
1	10.1	10.1	10.1
2	10.1	10.1	10.1
3	11.4	12.7	12.7
4	7.6	7.6	8.9
5	10.1	11.4	11.4
6	16.5 (12.7)	16.5 (15.2)	15.2 (14.0)
7	11.4 (8.9)	8.9 (8.9)	11.4 (12.7)
8	11.4 (10.2)	11.4 (10.2)	11.4 (11.4)
Mean	11.1 (10.6)	11.1 (11.4)	11.4 (12.7)

TABLE II—Extent of spread of foam from anus (cm) in patients as seen on anteroposterior scans. (Results obtained from lateral scans shown in parentheses)

Case No	Time of scan after administration of foam (min)		
	15	120	240
9	14.0	15.2	14.0
10	8.9	8.9	10.1
11	12.5	17.5	17.5
12	11.4	11.4	11.4
13	15.2 (17.8)	15.2 (15.2)	15.2 (14.0)
14	8.9 (8.9)	8.9 (8.9)	11.4 (10.2)
15	8.9 (5.1)	8.9 (5.1)	8.9 (5.1)
16	10.2 (10.2)	8.9 (10.2)	8.9 (8.9)
Mean	11.3 (10.5)	11.9 (9.8)	12.2 (9.5)

summarise the results for all subjects. The mean values for the extent of spread of foam are given at the bottom of each column, from which we constructed the graphs in figs 5 and 6.

FIG 5—Mean extent of spread of foam (and 95% confidence limits) as seen on anteroposterior scans in patients and controls.

FIG 6—Mean extent of spread of foam (and 95% confidence limits) as seen on lateral scans in patients and controls.

For the purposes of statistical analysis the results were considered in four groups—namely, anteroposterior scans (controls and patients) and lateral scans (controls and patients). A two-way analysis of variance with repeated measures⁶ was performed on both sets of scan results (table III). The results showed a wide variation between subjects in the extent of initial distribution of the foam, with no significant further spread occurring. There was no significant difference in the behaviour of the foam between controls and patients with colitis. The results obtained with the lateral scans confirmed those obtained with the anteroposterior scans.

TABLE III—Results of two-way analysis of variance with repeated measures using anteroposterior and lateral scans

Effect	Sum of squares	DF	Mean squares	F	DF	Significance of F
<i>Anteroposterior scans</i>						
Residual	28.468	28	1.017			
Time	3.125	2	1.563	1.54	2/28	P>0.1
Group by time	0.960	2	0.480	0.47	2/28	P>0.1
Subject within group	292.549	14	20.896	20.55	14/28	P<0.001*
Group	3.968	1	3.968	0.19	1/14	P>0.1
<i>Lateral scans</i>						
Residual	14.918	10	1.492			
Time	1.309	2	0.654	0.439	2/10	P>0.1
Group by time	7.976	2	3.988	2.673	2/10	P>0.1
Subject within group	195.809	5	39.162	39.162	2/10	P<0.05*
Group	13.349	1	13.349	0.341	1/5	P>0.1

DF = Degrees of freedom.

*Can be tested if a negligible interaction between subjects within group and time is assumed.

Discussion

Our results indicate that using the foam results in a good topical application of steroid to the lower rectum but that more proximal spread is limited and infrequent. One criticism that could be put forward is that we made no attempt to ensure that the rectum was clear of any hard faecal matter that might prevent the spread of the foam. All the patients, however, had loose stools, and the foam spread no further in them than in the controls.

The aim of the study was simply to assess the extent of spread of the foam after rectal administration and not to attempt to compare the product with any other in terms of extent of spread or efficacy. Certain clinical implications, however, could not be avoided. On the basis of topical application alone the product is a rational treatment for only proctitis and mild distal ulcerative colitis. It would, however, seem illogical to use it for more proximal disease, and our clinical impression has been that under these circumstances it is less effective. If it is of benefit in more proximal disease this can be assumed to be only the result of absorption of the steroid from the foam by the rectal mucosa, any effect being that of systemic steroid. Of the clinical trials

quoted by the manufacturer, only that of Scherl and Scherl⁴ attempted to differentiate between patients with proximal or distal disease. Unquestionably, however, the foam is more comfortable and easier to retain than a retention enema, and since the patient need not be immobilised, the foam obviously has a place in outpatient practice for patients with proctitis and distal ulcerative colitis.

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Improved glucose control in maturity-onset diabetes treated with high-carbohydrate-modified fat diet

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Summary and conclusions

Fourteen patients with established maturity-onset diabetes were treated as outpatients with a high-carbohydrate-(about 60% of total daily energy requirements)-modified fat diet (ratio of polyunsaturated fatty acids to other fatty acids 1:1) for six weeks. Commercially available and acceptable cereal foods and tuberous vegetables high in both digestible and non-digestible carbohydrates were used. Simple sugars were restricted. Compared with their usual, low-carbohydrate diabetic diet this diet resulted in a fall in basal plasma glucose concentration (average of values measured at 0300, 0500, and 0700), mean preprandial plasma glucose concentration (average of values measured at 0800, 1230, and 1730), and percentage of glycosylated haemoglobin. Modifying dietary fat also decreased the fasting plasma cholesterol concentration.

The findings suggest that it is no longer justifiable to prescribe a low-carbohydrate diet for maturity-onset diabetes.

Introduction

Since insulin became routinely available over 50 years ago there has been some relaxation in restricting dietary carbohydrate in diabetic clinics. Despite this, in 1971 most clinics in Great Britain were still recommending a low-carbohydrate diet (carbohydrate constituting about 40% of total daily energy) for both maturity-onset and insulin-requiring disease.¹ Increasing evidence suggests, however, that dietary carbohydrate is not detrimental to blood sugar control.² An average carbohydrate-containing diet (carbohydrate providing 50-55% of total energy) gives a similar improvement in fasting blood sugar values to that obtained with the lower carbohydrate diet when recommended in newly diagnosed maturity-onset diabetes.³ Several workers⁴⁻⁵ have suggested that much higher carbohydrate-containing diets reduce the fasting blood sugar concentration. More recently it has been shown that increasing the dietary fibre,⁶ particularly guar or pectin,⁷ reduces the postprandial blood sugar concentration. These studies, however, used formula diets,⁴⁻⁶ unacceptably high amounts of carbohydrate,⁴⁻⁵ and carbohydrate foods likely to be unpalatable to some patients.⁷ Furthermore, measures of diabetic control used were principally confined to fasting blood glucose and 24-hour urinary glucose values.

We therefore decided to examine in greater detail the effect in maturity-onset diabetes of an acceptable, high-carbohydrate diet composed of commercially available high-carbohydrate foods such as wholemeal bread and tuberous vegetables.

Patients and methods

Eighteen patients with established maturity-onset diabetes (15 men and three women) were recruited into the study. Their mean age ($\pm$ SE of mean) was 54 ± 2.0 years and mean percentage of ideal body weight ($\pm$ SE of mean; Metropolitan Life Assurance Co) 106.3 ± 3.3 . All were considered to be clinically and chemically stable (14 taking sulphonylureas and the remainder dietary treatment alone), their mean

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