Hydroxystearic acid and diarrhoea following ileal resection

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SUMMARY The faecal outputs of 10 patients who complained of diarrhoea after ileal resection were measured whilst they consumed identical diets in which most of the fat was present as olive oil. No relationship was found between faecal weight and hydroxystearic acid production. In three patients the output of hydroxystearic acid was reduced by changing the dietary fat. There was no reduction in faecal weight. It is concluded that hydroxystearic acid does not contribute to diarrhoea in these cases.

In the first report (James, Webb, and Kellock, 1961) of the occurrence of 10-hydroxystearic acid in the faeces of patients with steatorrhoea the authors commented on the resemblance of its chemical structure to that of ricinoleic acid, 12-hydroxyoleic acid, which is the active constituent of castor oil. It was suggested therefore that 10-hydroxystearic acid might also have a cathartic effect and be responsible for the diarrhoea associated with steatorrhoea. A recent survey (Wiggins, Pearson, Walker, Russell, and Kellock, 1974) of a large group of patients showed that in most conditions 10-hydroxystearic acid increased as faecal fat increased, and faecal weight correlated as well with total fatty acids as with 10-hydroxystearic acid. One group of patients, those with ileal resections, differed in having relatively more 10-hydroxystearic acid than other patients with the same degree of steatorrhoea. Since diarrhoea is a prominent feature in patients with an ileal resection and it has been suggested (Hofman, Poley,

Mekhjjan, and Phillips, 1970) that 10-hydroxystearic acid may be responsible for this, these patients seemed an ideal group to examine for evidence of its cathartic action.

Patients

Nine patients who complained of diarrhoea following an ileal resection were studied, one being studied again after reconstructive surgery. In six patients the ileal resection was for Crohn's disease which was in remission at the time of study. The three other patients, including the one studied twice, had no residual bowel disease. Brief clinical details of these patients who have been described more fully (Cummings, James, and Wiggins, 1973) are given in table I.

Two types of study were done. In the first, faecal 10-hydroxystearic acid output and faecal weight were measured in each patient whilst they were eating identical diets. In the second investigation the effect on faecal weight and 10-hydroxystearic acid

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Patient	Sex	Age	Ileum Resected (cm)	Site of Anastomosis	Diagnosis
1	F	54	76	Ascending colon	Crohn's disease
2	M	58	122	Caecum	Vascular occlusion
3	F	39	61	Caecum	Volvulus
4 ¹	M	51	46	Ileum	Trauma
5	M	51	122	Mid transverse colon	Trauma
6	F	60	156	Hepatic flexure	Crohn's disease
7	M	40	46	Mid transverse colon	Crohn's disease
8	M	36	80	Descending colon	Crohn's disease
9	F	54	76	Rectum	Crohn's disease
10	F	45	259	Mid transverse colon	Crohn's disease

Table I Clinical details of patients studied

¹Patient 5 after reconstructive surgery.

output brought about by changing the composition of the dietary fat was measured. Both types of investigation were done under 'metabolic ward' conditions. A three-day rotating diet of 2200 calories containing 85 g fat was used. In the first type of study the major part of the fat, 70 g, was added as olive oil suitably mixed into the diet. In the second type of study the olive oil was replaced by equal weights of coconut oil in two patients and by corn oil in the third. Each bowel movement was collected separately and immediately frozen. The samples were pooled to make a three-day collection after an equilibration period of at least twice the mouth-to-anus transit time as determined with radioopaque shapes (Hinton, Lennard-Jones, and Young, 1969). Full details of the method of study have previously been reported (Cummings *et al*, 1973).

The pooled samples were unfrozen and homogenized while still cold. Aliquots of the homogenate were analysed for total fatty acids by the method of Kamer, Huinink, and Weyers (1949) except that toluene was used to extract the fatty acids as recommended by Jover and Gordon (1962). Aliquots of the toluene extract were dried down and the fatty acids esterified with freshly prepared diazomethane. The hydroxystearic acid content was determined by gas-liquid chromatography of the methyl esters using SE30 as stationary phase as previously described (Wiggins *et al*, 1973). The statistical procedures used were those described by Snedecor and Cochran (1967).

Results

The results of the 10 studies using the identical olive oil diets are presented in table II where the patients are listed in order of increasing faecal output. The faecal weight ranges from 162 to 1528 g/day whereas output of 10-hydroxystearic acid varies from 0.09 to 9.7 g/day. These variables do not correlate with each other ($r = -0.07$) nor do the faecal weight and the concentration of 10-hydroxystearic acid expressed as mg/g of stool ($r = 0.05$). The results of the three experiments in which the amount of 10-hydroxystearic acid in the stools was changed by varying the type of fat in the diet are presented in table III. In two studies there was no significant change in the faecal weight or faecal fat output even when the output of 10-hydroxystearic acid increased several fold. In the third study the faecal weight decreased on the olive oil diet although the 10-hydroxystearic acid increased to 10 times its initial value.

The best correlation between any pair of the variables listed in table II is that between faecal fat and 10-hydroxystearic acid outputs ($r = 0.87$, $P < 0.01$). A considerable part of this correlation may derive from the method of calculating 10-hydroxystearic acid output, viz, % 10-hydroxystearic acid in faecal fat $\times$ total fat output. Fat output thus appears in both x and y . However, as the proportion of 10-hydroxystearic acid in the fatty acids and the faecal fat output are arithmetically independent the correlation ($r = 0.66$, $P < 0.05$) found between them

Patient	Faecal Weight (g/day)	10-Hydroxystearic Acid Output (g/day)	Faecal Fat (g/day)	Transit Time (hr)
1	162	4.0	13.3	22
2	238	3.5	14.5	48
3	250	0.14	2.4	24
4	281	0.49	3.6	29
5	664	3.4	19.8	20
6	810	9.7	26.0	23
7	987	1.5	7.3	18
8	1217	0.29	4.8	6
9	1277	0.09	8.8	5
10	1528	3.1	21.0	9

Table II Results of studies on olive oil diets

	Patient 2		Patient 5		Patient 6	
	Olive Oil Diet	Coconut Oil Diet	Olive Oil Diet	Corn Oil Diet	Olive Oil Diet	Coconut Oil Diet
10-Hydroxystearic acid (g/day)	3.5	0.7	3.4	1.9	9.7	0.3
Faecal weight (g/day)	238	224	664	689	810	1312
Faecal fat (g/day)	15	11 ¹	20	21	26	18 ¹

Table III Results of studies with variations in dietary fat

¹These values are corrected for equivalent weight differences by means of gas-liquid chromatography data.

Fig. The relationship between the proportion of 10-hydroxystearic acid and the faecal fat output. The numbers within the squares represent the transit time in hours of the particular patient.

is valid (see fig). The points that lie above the regression line in the figure are predominantly those from patients with the longest transit times suggesting that increased transit time may increase the level of 10-hydroxystearic acid. When the regression of the percentage of 10-hydroxystearic acid on both faecal fat output and transit time together was calculated the following equation was obtained:

$$y = 0.94 x_1 + 0.39 x_2 - 2.31$$

where y = % 10-hydroxystearic acid, x_1 = faecal fat g/day, x_2 = transit time.

The regression coefficient for faecal fat output, is significant ($P < 0.01$) as is that for transit time ($P < 0.05$). The proportion of the variation in the 10-hydroxystearic acid concentration that could be accounted for by changes in faecal fat output and transit time together was 0.60, an increase on that of faecal fat alone ($r^2 = 0.44$). The effect of faecal fat output was greater than that of transit time as shown

by standard partial regression coefficients of 0.69 and 0.44 respectively.

Discussion

The failure to find a correlation between faecal 10-hydroxystearic acid content and faecal weight does not necessarily indicate the absence of a relationship, but shows that in this group of patients with ileal resection and diarrhoea any cathartic effect that 10-hydroxystearic acid may be exerting is masked by other factors such as differences in the extent of the resections (Cummings *et al*, 1973). Our second investigation, however, in which each patient acted as his or her own control, being studied under conditions which differed only in the nature of the dietary fat and hence the amount of hydroxystearic acid in the stools, shows that 10-hydroxystearic acid is no more cathartic than other faecal fatty acids. Indeed the results of one study (patient 6, table III) suggests that 10-hydroxystearic acid is less cathartic than the medium chain fatty acids found in coconut oil. The two types of investigation, taken together, demonstrate clearly that the severity of the diarrhoea following ileal resection is not related to the amount of 10-hydroxystearic acid present in the stools. Other workers, however, have claimed that 10-hydroxystearic acid does have a cathartic effect in such patients (Hofman *et al*, 1970; Soong, Thompson, Poley, and Hess, 1972). The most detailed exposition of this view (Soong *et al*, 1972) is based on a temporal correlation between 10-hydroxystearic acid output and faecal weight. One of their studies of a patient similar to patient 6 (table III) showed a marked decrease in faecal weight and 10-hydroxystearic acid when dietary fat was replaced by medium chain triglycerides. As the drop in the total fatty acid output (85%) was as large as the drop in 10-hydroxystearic acid (89%), this experiment is not comparable with the three reported here.

The reason for suspecting that 10-hydroxystearic acid may be cathartic is because its chemical formula is similar to that of ricinoleic acid. However, the saturation of the double bond is very important because it changes both the shape of the molecule and its physical properties. Moreover for the idea to be tenable, hydrogenated ricinoleic acid (12-hydroxystearic acid) should also be cathartic but Masri, Goldblatt, De Eds, and Kohler (1962) have shown that at comparable doses hydrogenated castor oil has no cathartic effect. Watson, Karmen, and Jover (1963) found that normal volunteers receiving a 4 g dose of castor oil had no alteration in bowel function, so that levels of 10-hydroxystearic acid in excess of 4 g would be the minimum requirement for it to have a cathartic effect. Only one of the patients

in our study exceeded this level. The remainder excreted less 10-hydroxystearic acid than the minimum effective dose of castor oil when taken all at once on an empty stomach (Fingl, 1970).

The output of 10-hydroxystearic acid varied widely from patient to patient although all of them had had ileal resections and were on identical diets. A possible explanation might be a difference in bacterial flora. However, this seems unlikely since Pearson (1973) has shown that the ability to hydrate oleic acid is widespread amongst the groups of organisms that inhabit the intestine and found no clear difference between the quantitative bacteriology of stools containing high or low levels of 10-hydroxystearic acid. The results from patient 2 in the second study, when a change from olive oil (75% oleic acid) to corn oil (30% oleic acid) in the diet produced a marked drop in faecal 10-hydroxystearic acid confirm the observation *in vitro* (Pearson, 1973) that oleic acid is a more effective precursor of 10-hydroxystearic acid than linoleic acid, the major component of corn oil. If it is accepted that the bacteria that synthesize 10-hydroxystearic acid from oleic acid are abundant in the colon and are therefore not a limiting factor in the production of 10-hydroxystearic acid then the amount of this fatty acid in the stools will be determined mainly by the amount of oleic acid entering the colon, ie, the degree of fat malabsorption, and the time it remains there. That these factors are important in determining the 10-hydroxystearic acid content of stools is shown by the multiple regression analysis which indicates that they account for 60% of the variation in faecal output.

In this study, the amounts of 10-hydroxystearic acid in the stools were greatly increased over those usually found in patients with ileal resection by using olive oil as the principle dietary fat. The failure to find any evidence of a cathartic effect even under these conditions demonstrates that 10-hydroxy-

stearic acid plays no significant part in postileal resection diarrhoea.

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