CHRONIC DIARRHOEA : A PROSPECTIVE STUDY IN THAI PATIENTS AT CHULALONGKORN UNIVERSITY HOSPITAL, BANGKOK

SATHAPORN MANATSATHIT, SACHAPAN ISRASENA, NUSONT KLADCHAROEN, PRASERT SITHICHAROENCHAI, SOMJAI ROENPRAYOON and PONGPEERA SUWANAKUL

Departments of Medicine, Parasitology, Microbiology, Faculty of Medicine, Chulalongkorn University, Bangkok, and Bamrasnaradura Infectious Diseases Hospital, Nonthaburi, Thailand.

INTRODUCTION

Acute diarrhoea is usually self-limiting and relatively easy to treat. Although the causes are most often infective, antibiotics are not always indicated. Rehydration is more important in the management of this condition. Chronic diarrhoea, on the other hand, is diagnosticly as well as therapeuticaly more difficult to manage. The prognosis can be assessed only when the specific aetiology is defined. In developing countries where diarrhoeal illnesses are highly prevalent, the proportion of chronic diarrhoea patients is obviously larger than in the developed countries (Barua, 1980). The aetiologic factors in chronic diarrhoea vary from one geographic region to another, depending on the local prevalence of parasitic and/or inflammatory bowel diseases.

Several studies on acute diarrhoea in Thai adults and children have been published (Workshop, 1984), but only a few reports on chronic diarrhoea. This study was aimed at thorough investigations of adult chronic diarrhoea, ultilising the existing facilities at Chulalongkorn University Hospital.

MATERIALS AND METHODS

Between April 1983 and March 1984, patients referred to the Gastrointestinal clinic, Chulalongkorn Hospital, with diarrhoea lasting longer than two weeks were screened for the study. Chronic diarrhoea was defined as passage of two or more loose stools daily for more than two weeks, with less-than-seven-day intervals of normal bowel movements. Foreign travellers and patients with other gastrointestinal disorders or a previous gastrointestinal operation were excluded.

The following tests were performed for all patients : complete blood count, fasting blood sugar, blood urea nitrogen and creatinine, serum electrolytes, two stool examinations and two stool cultures. Further investigations were selectively performed if all the above tests were normal, or if a relevant diagnosis could not be made, or if there were other indications. These included *Entamoeba histolytica* serology, rigid or flexible sigmoidoscopy, chest X-ray, barium enema, upper gastrointestinal radiology or endoscopy, jejunal and/or rectal biopsy, serum thyroxine, serum albumin and globulin, serum carotene, D-xylose test, and stool fat examination. All biochemical tests were carried out at Chulalongkorn Hospital Central Laboratory. A minimum of 2 fresh stool specimens collected on separate days were examined at the Department of Parasitology, using the ether sedimentation concentration method (Ritchie, 1948). Stool specimens transported in the Carry Blair and the Thio-Campy media were cultured at the Department of Microbiology. Routine identification was made for

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Vibrio cholerae, Non 0 - 1 vibrios, *Vibrio parahemolyticus*, *Shigella*, *Salmonella*, *Aeromonas*, *Plesiomonas*, *Yersinia*, and *Campylobacter jejuni*. Serology for *Entamoeba histolytica* was determined by haemagglutination-inhibition technique. Sigmoidoscopy was performed with either a 25-cm rigid sigmoidoscope (in the first few cases), or a 60-cm Olympus-SF flexible colonoscope (in all the subsequent cases).

Patients were given symptomatic medications (such as paracetamol, metoclopamide, diazepam) but antiperistaltics (such as codeine, diphenoxylate, loperamide and tincture belladonna) were not prescribed. Clinical progress and stool character were closely observed. Specific treatment was started whenever a definitive diagnosis was made. Cases with no specific diagnosis after thorough investigations were followed-up as outpatients as long as the symptoms persisted. Symptoms were labelled "subsided" if the bowel habit returned to normal, "improved" if stool frequency became less and the stool better-formed, and "persisting" if the improvement was only slight, transient, or negligible.

RESULTS

Of the 62 patients who fulfilled the study criteria, 55 completed the required investigations and formed the basis for the present study; the remaining 7 patients were lost to follow-up.

The patients characteristics and clinical profiles are shown in Table 1. Females outnumbered males by approximately three to one. The various investigations, and the frequencies with which they were performed for the entire group, are shown. in Table 2. Stool examinations were positive for fecal leucocytes with or without erythrocytes in only 5 patients. The parasites identified in 29 cases are shown in Table 3. Multiple parasitic infestations with doubtful relevance were noted in a few cases. Stool culture was positive for pathogenic organisms in 8 cases.

Table 1

Clinical profiles of 55 chronic diarrhoea patients at Chulalongkorn Hospital.

Sex	14 male, 41 female
Age	16-69 years (mean 33.5)
Duration	2 weeks - 4 weeks
Stool frequency	3-8 per day (mean 3.7)
Symptoms	
abdominal pain	94.2%
nausea	61.5%
vomiting	25.0%
weight loss	69.2%
nocturnal diarrhoea	48.1%

Table 2

Investigations in 55 chronic diarrhoea patients.

Investigation	No. of cases	No. positive
Stool microscopy	55	21
Stool culture	55	8
Routine blood chemistry	55	10
Sigmoidoscopy	45	10
E. histolytica serology	43	7
Barium enema	33	1
Chest X-ray	27	0
Rectal biopsy	19	5
Serum thyroxine	12	1
Serum carotene	10	1
D-xylose test	9	1
Jejunal fluid study	8	0
Upper GI and small bowel radiology	6	1
Upper GI endoscopy	5	0
Jejunal biopsy	1	1

Table 3

Intestinal parasites in 29 cases with a potitive stool examination-cultures.

Intestinal parasites	No. Cases (%)
Opistorchis	8 (24.2)
Hookworm	8 (24.2)
E. histolytica	5 (15.2)
Giardia lamblia	4 (12.1)
Entamoeba coli	2 (6.1)
Strongyloides	2 (6.1)
Trichomonas hominis	1 (3.0)
Capillaria philippinensis	1 (3.0)
Hymenolepis diminuta	1 (3.0)
Endolimax nana	1 (3.0)
Pleisiomonas shigelloides	3 (9.1)
Salmonella group E	2 (6.1)
Salmonella group C_1	1 (3.0)
Campylobacter jejuni	1 (3.0)
Shigella flexneri	1 (3.0)

The peripheral blood was normal in nearly all cases, except for anemia (hemoglobin below 12 gm%) in three, leucocytosis above 10,000/c. mm in five, and leucopenia below 5,000 cell/c. mm in two patients. Eosinophilia over 7% was noted in six patients, including one case of Strongyloidiasis with 43% eosinophils. Fasting blood sugar, blood urea nitrogen, creatinine, and electrolytes were normal in all. *Entamoeba histolytica* serology was positive in 7 cases (1 : 320 in one, 1 : 160 in three, and 1 : 80 in another three cases).

Sigmoidoscopic findings were unremarkable in 35 of the 45 patients examined. A benign rectal ulcer was found in two patients, a cauliflower rectal mass (adenocarcinoma) in one patient, and a retained surgical pack discovered and removed at sigmoidoscopy in another female patient whose chronic diarrhea followed its inadvertent insertion during a Caesarean operation 6 weeks previously. Four patients had inactive haemorrhoids. Two patients had non-specific proctitis which was absent on a subsequent examination. Except for one case of amyloidosis and one case of rectal adenocarcinoma, rectal biopsy in the rest revealed only minor and non-specific mucosal changes. Biopsy in the two rectal ulcer cases showed active and chronic proctitis with ulceration, while that in the case with retained rectal foreign body revealed granulation tissue with mucosal inflammation.

Thyrotoxicosis was diagnosed from a high serum thyroxine in one patient. Mucosal abnormalities on gastrointestinal X-ray led to the discovery of amyloidosis in one case. In another patient with persistent leucopenia, bone marrow aspirate showed considerable plasmacytosis consistent with multiple myeloma. The D-xylose test in this latter case was also compatible with an extensive mucosal disease. With the exception of excess faecal fat (by the stool Sudan test) in the case with amyloidosis, gross malabsorption was not documented in any patient. Serum albumin was below 3 g/100 ml in 5 patients, including those with amyloidosis, multiple myeloma, and capillariasis. All the other selectively performed investigations, namely chest radiograph, upper GI and small bowel study, flexible sigmoidoscopy, oral cholycystography, and ultrasonography of the pancreas, were non-informative.

A definitive aetiologic diagnosis was reached in 21 cases. In another 16 patients the final diagnosis remained uncertain although certain pathogenetic factors or agents were noted. In the remaining 18 patients with entirely negative investigations, the diagnosis of "irritable bowel syndrome" was given.

The clinical outcomes in the three groups of patients are shown in Table 4. Five patients were lost to follow-up so that their progress was not known. Most patients were followed up between four to six weeks, the longest follow-up being 9 months on the one case of strongyloidiasis.

Table 4

Clinical outcome in the different groups based on diagnosis.

Group diagnosis	No. of cases	Outcome			
		Subsided	Improved	Persist.	Lost to follow-up
Definitive	21	10	6	4	1
Uncertain	16	2	6	7	1
Unknown	18	1	5	10	3
Total	55	13	17	21	5

Table 5

Clinical profiles in the infective and the non-infective group.

	Infective diarrhoea (n=14)	Non-infective diarrhoea (n=7)
Mean age (years) ± S.D.	28.5 ± 8.4	38.5 ± 14.3
Mean duration (weeks) ± S.D.	23.4 ± 51.6	54.5 ± 85.0
Mean frequency/day ± S.D.	3.8 ± 1.3	3.8 ± 0.8
Abdominal pain (%)	92.3	87.5
Nausea (%)	38.5	73.4
Vomiting (%)	8.0	50.0
Weight loss (%)	76.9	62.5
Nocturnal diarrhoea (%)	46.2	62.5

The clinical profiles of the infective and the non-infective cases are compared in Table 5. In the former group, the mean age (28.5 years) was lower, the average duration of diarrhoea shorter, and nausea and vomiting less frequent than in the latter group, but the differences were not statistically significant.

DISCUSSION

Adult diarrhoeal illnesses usually affect both sexes equally. The apparent female preponderance in this study was probably due to the small number of cases. Abdominal pain, nausea, vomiting, weight loss and nocturnal diarrhoea were present in about half of the patients. Neither significant malabsorption nor steatorrhea was documented, although milder degrees of malabsorption could have been present in some patients with anaemia and hypoalbuminemia.

In Western countries, the irritable bowel syndrome and the inflammatory bowel diseases are the leading causes of adult chronic diarrhoea. Our results suggest that this may not be so in the tropics, where, as in the case of acute diarrhoea, infective and parasitic diseases are more likely to head the list. Fourteen of the 21 cases with an identifiable aetiology were found to harbour either

parasitic or bacterial infections. Amoebiasis and giardiasis were more common than expected (9 out of 13 cases). A similar finding has been reported by Butler *et al.*, (1973). Giardiasis is worldwide and was the commonest parasitic cause of chronic diarrhoea in American servicemen in Vietnam, (Butler *et al.*, 1973) and in the natives of Australia (Doe and Barr, 1981). The demonstration of amoebic trophozoites requires a fresh warm stool, while it is possible to identify *Giardia* in 85% of the cases by using the stool formal ether concentration method, and in the remaining 15% by examining a fresh smear of aspirated duodenal or jejunal fluid, or otherwise biopsy specimens of the duodenal mucosa (Manson Bahr and Apted, 1982). Other parasitic causes in our patients included strongyloidiasis, hymenolepiasis and capillariasis. Hymenolepiasis is a rather uncommon infestation capable of causing chronic diarrhoea (Cooper *et al.*, 1981). Capillariasis is found not only in the Philippines but also in certain northeastern areas in Thailand (Pathnacharoen *et al.*, 1983).

It was not able that amoebiasis and giardiasis were quite prominent among those cases with a known infective cause. In addition, the diarrhoea in 3 of the 16 cases with uncertain diagnosis in whom *E. histolytica* serology was qualitatively positive appeared to improve with anti-amoebic treatment. In such an endemic area, it is tempting, therefore, to recommend an anti-protozoal therapeutic trial in cases of chronic diarrhoea with persistently negative initial investigations before proceeding to the more elaborate tests. A similar approach has been suggested by Doe *et al.*, (1981) working on the problem of persistent diarrhoea in Australia.

The non-infective causes of chronic diarrhoea vary from one geographic area to another. Variations are also seen within similar geographic zones, most likely due to different selection criteria in the reported studies. For instance, unusual causes such as small - intestinal lymphoma, intestinal tuberculosis, bacterial overgrowth syndrome, tropical sprue, hyperthyroidism, diabetes mellitus, chronic renal failure, "A.P.U.D." tumour, systemic lupus erythematosus, etc., were quite prominent in the study in Thai patients by Vanasin *et al.*, (1984) in which most of the cases studied sufferred from quite prolonged and severe diarrhoea. In the present study, on the other hand, non-infective causes appeared only occasionally, with amyloidosis, multiple myeloma, benign rectal ulcer and rectal foreign body being quite unexpected.

In 16 patients, there was some evidence pointing to a specific pathogen but a direct pathogenetic role was difficult to ascertain. For instance, only one of the four patients with hookworm improved after mebendazole treatment, while the two cases with positive stool culture for *Pleisiomonas shigelloides* did not improve much even after appropriate antibiotic treatment. Similarly the discovery of certain enteric bacteria (e.g. *Shigella flexneri*, *Salmonella*, *Campylobacter jejuni* and *Plesiomonas shigelloides*) in the stools of 7 patients was probably coincidental, as their subsequent disappearance did not herald clinical improvement. The aetiologic diagnosis in this group of patients was therefore considered "uncertain".

It is apparent from Table 2 that stool microscopy is the most rewarding single investigation in chronic diarrhoea. Multiple stool microscopy alone, using the concentration technique, led to the discovery of significant organisms in 21 of the 55 cases. In 12 of these, the identified agent was thought directly pathogenetic for the patients diarrhoea (Table 5). Microscopic examination of multiple stool specimens using the ether-sedimentation technique is highly recommended, therefore, as an essential investigation that should precede other more complicated procedures in the routine workup of chronic

diarrhoea. The physician should specificaly request for the concentration technique for stool microscopy, not merely a simple microscopic examination of fresh stool.

SUMMARY

Fifty-five Thai patients with chronic diarrhoea were prospectively studied to find out the underlying causes. The aetiology was identified in 38.2%, uncertain in 29.1%, and unknown in 32.7% of the patients. In the group with a definitive aetiologic diagnosis, parasitic and infective causes were commoner than non-infective causes. Amoebiasis and giardiasis were more frequent than expected, such that empirical therapeutic trial with an antiprotozoal may be justified if initial routine investigations fail to uncover the cause of the diarrhoea. No significant clinical features were noted between the infective and the non-infective groups. Overall, repeated stool microscopy using the concentration technique was the most useful single investigation in approaching the chronic diarrhoea problem.

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