Treatment of acute diarrhoea in adults with dioctahedral smectite (Smecta): a prospective randomised study

使用雙八面體蒙脫石（思密達）治療成人急性腹瀉病者的一個前瞻性隨機化研究

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Background: Acute diarrhoea is a common presenting problem to the accident and emergency department. This study aimed to assess the efficacy of dioctahedral smectite (Smecta) in altering the duration and frequency of acute diarrhoea in the adult population in Hong Kong. ***Material and methods:*** This was a prospective, randomised controlled study carried out in the Accident and Emergency Department of Caritas Medical Centre from July 2005 to October 2005. One hundred and ninety eligible adult patients with acute diarrhoea lasting not more than 14 days were randomly assigned either (1) oral rehydration solution (ORS) one sachet three times daily and Smecta one sachet three times daily for two days; or (2) ORS one sachet three times daily for two days. The duration of diarrhoea, daily frequency of diarrhoea, presence of vomiting and fever following treatment were obtained by telephone interviews and mailed questionnaires. ***Results:*** For patients treated with or without Smecta, there was no statistically significant difference in the mean duration and daily frequency of diarrhoea in the first three days. ***Conclusion:*** The use of Smecta did not change the duration or frequency of acute diarrhoea in the adults in this study. (*Hong Kong j.emerg.med.* 2006;13:84-89)

背景：急性腹瀉是一個急症室常見的求診問題。是次研究旨在評估雙八面體蒙脫石（思密達）於改變香港成人病者腹瀉持續時間及頻率的功效。**資料及方法：**這是一個前瞻性、隨機化控制研究，於 2005 年 7 月至 10 月期間在明愛醫院急症室進行。合適的 190 名急性腹瀉持續不超過 14 天的成人病者被隨機分配兩天份量的（1）口服補充液及思密達，每日三次，每日一小包，或（2）口服補充液，每日三次，每次一小包。其後以電話訪問或郵寄問卷方式，取得他們腹瀉持續的時間，每天腹瀉的頻率，及治療後有否嘔吐或發燒。**結果：**病者接受思密達治療與否，他們腹瀉的平均持續時間及最初三天期間每天的腹瀉頻率沒有統計上顯著的差別。**結論：**在這研究中，使用思密達沒有改變成人病者急性腹瀉的持續期間或頻率。

Keywords: Acute disease, adult, anti-diarrhoeals, diarrhoea

關鍵詞：急性疾病、成年人、止瀉藥、腹瀉

Introduction

Acute diarrhoea is a common problem presenting to medical care. Globally, diarrhoea accounts for more than two million deaths annually.[1] In developed cities like Hong Kong, acute diarrhoea costs inconvenience and productivity loss. According to the data from the Department of Health of Hong Kong, the monthly consultation rates of acute diarrhoeal diseases at general outpatient and private clinics range from 4.1 to 35.3 per 1,000 consultations.[2]

Acute diarrhoea is defined as increase in fluidity or frequency of stool lasting not more than 14 days in duration.[3] The mainstay of treatment is fluid therapy

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and correcting electrolyte disturbance. Antimicrobial therapy is only indicated in selected cases.[4]

Anti-diarrhoeal agents are frequently prescribed by clinicians. According to current guidelines, they are not recommended for routine use in children with acute diarrhoea,[5,6] because of potential side effects and doubtful benefits. However, in adults, their use is more liberal. There are many over-the-counter anti-diarrhoeal agents and quite often patients request anti-diarrhoeal drugs during their consultations. The current anti-diarrhoeal agent of choice is loperamide (Imodium).[4,7] Other anti-diarrhoeal drugs available include diphenoxylate (Lomotil), bismuth subsalicylate, and adsorbents like kaolin-pectin and Smecta.

Smecta is the most commonly prescribed anti-diarrhoeal drug in some accident & emergency (A&E) departments (including the authors') and in general practice. Each sachet of Smecta contains three grams of dioctahedral smectite, which is an aluminium silicate. It is presented in powder form. During use, it is dissolved in 30-50 ml of boiled water or mixed with watery food. It is marketed as a gastrointestinal mucoprotective agent. It interacts with mucus molecules, strengthens mucosal barrier, and protects the apical poles of enterocytes and the tight junctions against bacteria and toxins within the gastrointestinal lumen.[8] As shown by in vitro studies, it is capable of adsorbing toxins, bacteria and rotavirus.[9] Some clinical studies showed that Smecta reduced the duration of diarrhoea in children.[10-14] However, comparative clinical studies involving the general adult population are lacking.[7]

The aim of our study was to assess the efficacy of Smecta in altering the duration and frequency of acute diarrhoea in the adult population in Hong Kong.

Study design and method

It was a single centre, prospective randomised clinical trial performed at the A&E Department of Caritas Medical Centre.

Adult patients with acute diarrhoea were recruited in the 3-month period from 23 July 2005 to 23 October 2005. The inclusion and exclusion criteria are shown in Table 1.

Eligible patients would be informed about the study and invited to participate in the study after detailed and clear explanation.

Patients were randomly allocated into one of the following two treatment regimes: (1) oral rehydration solution (ORS) one sachet three times daily plus Smecta one sachet three times daily for two days; or (2) ORS one sachet three times daily alone for two days. The former was the treatment group and the latter was the control group. Randomisation was done by the registration number: if the second last digit of the registration number was an odd number, the patient would be allocated into the treatment group; otherwise the patient would be in the control group.

Use of motility agents during the A&E consultation, namely metoclopramide, hyoscine, and Dologesic (dextropropoxyphene and paracetamol), were recorded. The onset of diarrhoea in terms of date and hour, vomiting and temperature were recorded. Each patient was given a questionnaire together with a self-addressed envelope, and was requested to fill in and mail back to

Table 1. Inclusion and exclusion criteria of the study

Inclusion criteria for patient enrolment, fulfilling both:
1. At least 18 years old
2. Acute diarrhoea (increase in frequency and fluidity of stool) at least three times a day, lasting not more than 14 days
Exclusion criteria for patient enrolment:
1. Exacerbation of chronic diarrhoea in inflammatory bowel disease or malabsorption
2. Presence of bloody diarrhoea
3. Intake of antibiotics in the previous three weeks
4. Chronic immunosuppressive conditions, including human immunodeficiency virus, chemotherapy and diabetes mellitus
5. Pregnant or lactating women
6. Admission required

the investigators. An English version of the questionnaire is shown in Figure 1. The patients were informed that a telephone interview would also take place three days after the consultation. In the telephone interview and questionnaire, the intake of medications, time of the last diarrhoea, and the daily frequency of diarrhoea after consultation were enquired. If the diarrhoea persisted, subsequent phone calls would be made to identify the time of the last diarrhoea. Special follow-up phone calls were made for patients having diarrhoea for more than five days.

The primary end-points of the study were to determine significant difference in duration of diarrhoea (measured in terms of hours) and the daily number of diarrhoea in the first three days following treatment in these two groups. The duration of diarrhoea after treatment means the time between the A&E consultation and the last diarrhoea. The first day of diarrhoea means the 24 hours following the A&E consultation, the second day means the 24 hours after the first day, and so on. Secondary end-points, including vomiting and presence of fever before and after treatment, were recorded.

Ref. no:

Caritas Medical Centre

Accident and Emergency Department

Questionnaire for research and follow up in acute diarrhoea

	Number of diarrhoea	Oral rehydration solution (√ if taken)	Smecta (√ if taken)	Vomiting (√ if present)	Fever (√ if present)
24 hours following A&E consultation (first day)					
Next 24 hours (second day)					
Next 24 hours (third day)					
Next 24 hours (fourth day)					
Next 24 hours (fifth day)					

Approximate time of the last diarrhoea: _____ (month) _____ (date) _____ (hour)

Name: _____

Please complete the questionnaire and return it to Caritas Medical Centre by the self-addressed envelope. Thank you.

Figure 1. Questionnaire of the study.

Sample size calculation

The sample size required was calculated by the sample size calculator – randomised controlled trial (quantitative outcome) of the Hospital Authority intranet. Using the data from a previous study (treatment effect of 10 hours, standard deviation of the effect at 24 hours),[10] 5% level of significance and 80% power, the sample size required in each group was 91.

Statistical methodology

The SPSS version 11.5 software programme was used for statistical analysis. The data was entered into the computer by the investigators. Continuous variables were compared by the independent t-test and discrete variables by the Chi-square test.

Ethical consideration, consent and confidentiality

The study was approved by the Clinical Research Ethics Committee of the Kowloon West Cluster. A written consent was obtained from each patient before the study began. Whether the patient participated or not would not affect the standard of care given. All information was kept confidential and assessed by the investigators only.

Results

We recruited 212 patients from 23 July 2005 to 23 October 2005; 22 of them were discarded (12 could not recall the details of the diarrhoea, 8 lost from follow up, 2 were subsequently admitted to hospital for the diarrhoea). As a result, 190 patients were eligible for our study.

There were 98 patients in the ORS plus Smecta treatment group and 92 patients in the ORS control group. The demographics and baseline symptom variables with regard to age, sex, duration of diarrhoea, presence of vomiting and fever before

treatment were comparable in both groups. The use of motility agents by the A&E department was the same in the two groups as well (Table 2).

Most of the results were obtained from telephone interviews alone (75.8%). Only a few results were obtained from mailed questionnaires alone (5.8%). Some were obtained from both telephone interviews and mailed questionnaires (18.4%). When there were discrepancies between the results from telephone interviews and mailed questionnaires, they were clarified by telephone interviews again.

All eligible patients took the prescribed drugs. The mean duration of diarrhoea after treatment was 26.3 hours in the ORS plus Smecta group, and 30.0 hours in the ORS group. There was no statistically significant difference between the two groups (p=0.405). There was also no statistically significant difference between the two study groups after treatment in the frequency of diarrhoea on the first day after treatment (p=0.191), second day after treatment (p=0.330), third day after treatment (p=0.991), presence of vomiting (p=0.280) and fever (p=0.496). The results are shown in Table 3.

Discussion

This study aimed to assess the clinical efficacy of

Table 2. Demographics and baseline symptom variables of the two study groups

	ORS + Smecta	ORS	P value
Male	46	49	0.384
Female	52	43	
Total	98	92	
	ORS + Smecta Mean (SD)	ORS Mean (SD)	P value (95% CI of difference)
Age (years)	39.02 (15.64)	37.38 (15.50)	0.645 (-3.42, 5.50)
Duration of diarrhoea before treatment (hours)	19.80 (27.27)	16.25 (20.90)	0.318 (-3.50, 10.53)
	ORS + Smecta No. of patients	ORS No. of patients	P value
Presence of vomiting before treatment	29 (29.59%)	28 (30.43%)	0.899
Presence of fever before treatment	12 (12.24%)	7 (7.61%)	0.287
Use of motility agent by A&E department	33 (33.67%)	31 (33.70%)	0.997

ORS = oral rehydration solution

Table 3. Duration of diarrhoea, frequency of diarrhoea, vomiting and fever after treatment in the two study groups

	ORS + Smecta Mean (SD)	ORS Mean (SD)	P value (95% CI of difference)
Duration of diarrhoea after treatment (hours)	26.27 (28.74)	29.96 (32.18)	0.405 (-12.41, 5.03)
Frequency of diarrhoea on the first day	3.20 (3.29)	3.90 (4.03)	0.191 (-1.75, 0.35)
Frequency of diarrhoea on the second day	0.76 (2.04)	1.08 (2.48)	0.330 (-0.97, 0.33)
Frequency of diarrhoea on the third day	0.31 (1.17)	0.30 (1.20)	0.991 (-0.32, 0.33)
	ORS + Smecta No. of patients	ORS No. of patients	P value
Presence of vomiting after treatment	8 (8.16%)	4 (4.35%)	0.280
Presence of fever after treatment	9 (9.18%)	6 (6.52%)	0.496

ORS = oral rehydration solution

Smecta in local adult patients with acute diarrhoea. It showed that Smecta had no statistically significant effect in altering the duration of diarrhoea or daily frequency of diarrhoea.

Our study result might be due to the fact that most diarrhoeal illnesses are due to viral causes and are self-limiting. Acute diarrhoea in the general population lasts less than one day in nearly half of the cases.[15] Supportive fluid therapy is usually sufficient.[7] Anti-diarrhoeal agents may not produce clinically significant effect.

The findings in our study have both clinical and financial implications. From the patients' perspective, their main concerns are the duration and frequency of diarrhoea. The prescription of Smecta has not been shown to be effective in reducing the severity of acute diarrhoea in adults in our study. More importantly, the treatment of diarrhoeal diseases should be focused on rehydration and maintaining electrolyte balance. For financial consideration, among the various anti-diarrhoeal agents, Smecta is a rather costly drug (HK$1.5 per pack). [Drug Formulary 2002, Caritas Medical Centre, Hong Kong] It is about seven times the cost of kaopectate or Imodium, and ten times the cost of Lomotil. Therefore, clinicians should exercise judgement regarding its use.

As regard to the side effects of Smecta, there were no adverse effects demonstrated in our study. The results were consistent with previous studies.[10,11] The safety profile of Smecta may be better than loperamide and diphenoxylate, which can cause toxic megacolon in patients with *Clostridium difficile* infection, and haemolytic-uraemic syndrome in children infected with enterohaemorrhagic *Escherichia coli*.[16]

In our study, microbiological investigation was not required for inclusion. It was because most diarrhoeal diseases were treated on clinical grounds without the results of stool culture. According to the data from the Department of Health of Hong Kong, among stool samples collected from stable patients with acute diarrhoea, the positive isolation rates for viruses and bacteria were 12% and 16% respectively. Although viruses are more common than bacteria in acute diarrhoea, the former are more difficult to culture. The commonest viral isolates were Norwalk-like virus (80% of the total viral isolates) and rotavirus (18%). The commonest bacterial isolates were *Salmonella* species (25% of the total bacterial isolates), *Vibrio parahemolyticus* (22%) and *Campylobacter* species (20%).[2] The treatment in most cases would not be changed by stool culture results.

Strengths and weaknesses

The measured baseline characteristics of both the treatment and control groups were comparable. This minimises confounding factors in affecting the clinical outcomes.

One of the limitations of this study was that both the patients and the doctors were not blinded to the treatment, and there was no placebo used in the control arm. It was thought that the frequency of diarrhoea was an objective clinical feature, and placebo might have little effect. Another limitation is recall bias. Patients might not recall accurately the time of onset and the time of the last diarrhoea. In order to reduce this possibility, diaries for patients to record the bowel motion were given, and telephone interviews were conducted timely. Apart from the above limitations, it would theoretically be more appropriate in reflecting the effectiveness of Smecta if the duration and frequency of diarrhoea were counted after the intake of medication, instead of after the time of A&E consultation. However, problems of patient compliance to the study and recall bias would be magnified if the patients were required to count their bowel motions from the time of medication intake. Finally, the effect of antipyretic use was not taken into account in assessing fever in the two study groups.

Conclusion

The use of Smecta did not result in a change in duration or frequency of acute diarrhoea in adults in our study. The most important aspect of treatment in acute

diarrhoea is fluid and electrolyte balance. However, up to now, Smecta has not been found to be associated with harmful effects. Its use should be left to clinical judgement.

Declaration of interest

The authors declared no conflicts of interest or sources of funding.

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