D-Xylose Absorption in Non-Chronic Diarrhea AIDS Patients with the Wasting Syndrome

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Abstract

Objective : To compare the intestinal absorptive capacity, permeability function and duodenal histopathology in human immunodeficiency virus (HIV) patients with or without wasting syndrome who had not suffered from chronic diarrhea.

Method : Adult HIV patients who attended Chulalongkorn Hospital were included. The subjects were classified into wasting and non-wasting groups (group I and group II). 25 g oral D-xylose test, oral phenolsulfonephthalein test and duodenal histopathology were performed.

Results : Of thirty-two HIV patients, aged between 25-50 years enrolled, there were 18 and 14 patients in group I and group II, respectively. In both groups, the baseline data, permeability function and histopathology were similar. Intestinal absorptive capacity was statistically different, i.e. 5-hour urine D-xylose was 3.96 $\pm$ 2.81 g and 5.95 $\pm$ 2.47 g in group I and group II respectively ($p < 0.05$).

Conclusion : This study demonstrated that D-xylose absorption was decreased in non-diarrheal, wasting HIV infected patients. Abnormal absorptive capacity is a common phenomenon found in HIV patients with wasting syndrome as determined by standard 25 g oral D-xylose test.

Key word : D-xylose Absorption, Permeability Function, HIV Wasting Syndrome

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Wasting syndrome in HIV-infected patients is considered to be an AIDS-defining condition. It was defined by the Center for Disease Control[1] as profound and involuntary loss of more than 10 per cent of baseline body weight in combination with chronic diarrhea or prolonged fever. It can be found in 5-20 per cent of HIV infected persons and 70 per cent with full blown AIDS and is independent of CD4 lymphocyte count[2-7]. It contributes to both morbidity and mortality[2-6]. Potential mechanisms of HIV wasting syndrome include increased energy expenditure, decreased energy intake, inefficient use of energy substrate, and hormonal factors[8-18]. Chronic diarrhea is the most common gastrointestinal symptom in HIV infection, mainly caused by opportunistic infections[1,10,11]. Small bowel malabsorption is postulated to be one of the important factors especially in AIDS with chronic diarrhea[19-27].

In HIV infected patients, the change in functional and histological of the small intestine can be found without correlation between the former and the latter[8,10,28-33]. Many studies conducted in chronic diarrheal HIV patients with wasting syndrome demonstrated markedly severe malabsorption[23,25,26,28]. So far, no study has assessed the absorptive function in non-diarrheal HIV wasting syndrome.

This study was designed to assess functional and histological abnormality in non-chronic diarrheal HIV patients with or without wasting. The research question was, "Is small bowel malabsorption one of the important factors in non-chronic diarrheal HIV wasting synndrome?".

MATERIAL AND METHOD

Thirty two HIV-infected patients who attended the Immunologic Clinic, King Chulalongkorn Memorial Hospital from January to December 1999, were included in this study. Patients with chronic diarrhea and prolonged fever were excluded. All patients gave written informed consent. The study subjects were classified into wasting and non-wasting groups (group I and group II). Wasting was defined as involuntary loss of more than 10 per cent of baseline body weight. Exclusion criteria were pulmonary tuberculosis; pneumocystis carinii pneumonia; severe oral candidiasis or candida esophagitis; previous protease inhibitor anti-retroviral treatment of more than 1 year duration; renal failure or serum creatinine more than 2 mg/dl.; detected ascites by physical examination; alcoholic drinking or NSAIDS use within 1 week before small intestinal function assessment. From the previous study by Ehrenpreis ED, et al[26]; the sample sizes calculated with assuming type I error of 0.05 and type II error of 0.1 were 11 per group.

All patients had complete medical history, physical examination, recorded height, body weight and blood test for complete blood count, creatinine, albumin and triglyceride. Absolute CD4 cell counts closest to the time of study were also recorded. The intestinal function test and endoscopy were done within 2 weeks. After overnight fast, all patients had a D-xylose test with ingestion of 25 g of D-xylose dissolved in 250 ml of water followed immediately by an additional 250 ml of water[34-39]. All urine specimens were collected within a 5 hour period and D-xylose was quantified with spectrophotometer. Normal values for 5-hour urine (> 4 g) D-xylose were established from previous studies[34]. On the successive day, after overnight fast, permeability function of all patients was assessed with ingestion of 30 mg of phenolsulfonephthalein (PSP) test in 250 ml of water[40,41]. All urine specimens were collected within a 24-hour period and PSP was quantified with spectrophotometer. Patients underwent upper GI endoscopy with biopsies from the second part of the duodenum. Duodenal histopathology under light microscopy was performed to verify villous height, crypt depth and cellular infiltration with H&E staining.

The results are presented as mean $\pm$ SD. Comparison was performed with paired student *t*-test. Differences were considered significant if $p < 0.05$.

RESULTS

Of thirty-two HIV patients, 11 females and 21 males aged between 25-50 years enrolled in the study, there were 18 and 14 patients in group I and group II, respectively. In both groups, the baseline data including age, body mass index (BMI), CD4 count, duration of HIV seropositivity, triglyceride level, serum creatinine, serum albumin, anti-retroviral treatment, co-trimoxazole prophylaxis were similar as shown in Table 1. More than ninety per cent of the patients in both groups received only 1 or 2 anti-retroviral drugs, which is not the standard regimen.

Results of oral D-xylose absorption test, oral PSP permeability test and duodenal histopathology are shown in Table 2. The 5-hour urine D-xylose was statistically different i.e. 3.96 $\pm$ 2.81 g in group I *versus* 5.95 $\pm$ 2.47 g in group II ($p < 0.05$). The 24-hour urine PSP was not different i.e. 9.7 $\pm$ 4.7 mg% in group I *versus* 8.2 $\pm$ 3.7 mg% in group II. In both groups, there was no difference in endoscopic find-

Table 1. The baseline data of 32 HIV-infected patients studied.

	Group I (n = 18)	Group II (n=14)	P-value
Sex Male : Female	12 : 6	9 : 5	
Age (yrs)	35.8 ± 5.9	34.4 ± 6.5	0.54
Duration of HIV seropositive (yrs)	4.2 ± 1.6	3.7 ± 1.8	0.41
Body mass index (kg/m^2)	21.4 ± 5.9	21.6 ± 2.7	0.92
CD_4 cell count (cells/μl)	144.6 ± 131.2	194 ± 148.4	0.33
Serum creatinine (mg/dl)	1.09 ± 0.14	1.0 ± 0.14	0.10
Serum albumin (g/dl)	3.9 ± 0.2	4.0 ± 0.3	0.59
Serum triglyceride (mg/dl)	211.4 ± 16.1	243.7 ± 12.5	0.29
Cotrimoxazole prophylaxis (n)	14/18	9/14	0.45
Antiretroviral treatment (n)	12/18	13/14	0.10

Table 2. D-xylose absorption test and PSP permeability test.

	Group I (n = 18)	Group II (n=14)	P-value
D-xylose test (g)	3.96 ± 2.8	5.95 ± 2.5	0.045 (0.005-3.93)
PSP test (mg%)	8.2 ± 3.7	9.7 ± 4.7	0.33

Table 3. UGI endoscopic findings and duodenal histopathology in the study patients.

	Group I (n = 18)	Group II (n = 14)	P-value
UGI endoscopic findings			0.22
Normal	17	14	
Gastritis	1	0	
Duodenal histopathology			
Villous height			
Normal	18	14	
Abnormal	0	0	
Crypt depth			
Normal	18	14	
Abnormal	0	0	
Cellular infiltration			
No	17	14	
Yes	1	0	

ings and duodenal histopathology under light microscopy, which included villous height, crypt depth and cellular infiltration by H&E staining, as shown in Table 3.

DISCUSSION

From the previous studies, the absorptive function test had been conducted in chronic diarrheal HIV patients with wasting syndrome and markedly severe malabsorption was found[23,25,26,28]. Therefore, small bowel malabsorption was postulated to be one of the important factors especially in AIDS with chronic diarrhea[19-27]. The main causes of chronic diarrhea in HIV patients are opportunistic infections which have an effect on the absorptive function[1, 10,11]. The present study was conducted in non-

Table 4. The baseline data and clinical characteristics of patients in subgroup analysis.

	D-xylose test (mean ± SD)	
	Abnormal	Normal
Wasting group (group I)		
Patients (n)	12	4
Age (yrs)	35.8 ± 5.99	36.8 ± 9.43
Duration of HIV seropositive (yrs)	4.7 ± 1.67	5.0 ± 1.41
Body mass index (kg/m^2)	19.8 ± 3.84	18.7 ± 0.83
CD_4 cell count (cells/μl)	151 ± 127	153.8 ± 207.6
Serum creatinine (mg/dl)	1.1 ± 0.13	1.0 ± 0.16
Serum albumin (g/dl)	3.9 ± 0.21	4.0 ± 0.17
Serum triglyceride (mg/dl)	213.3 ± 18.4	214.3 ± 25.97
Non-wasting group (group II)		
Patients (n)	6	10
Age (yrs)	35.8 ± 6.21	33.5 ± 5.23
Duration of HIV seropositive (yrs)	3.3 ± 1.03	3.2 ± 1.73
Body mass index ** (kg/m^2)	24.5 ± 8.35	22.7 ± 2.33
CD_4 count (cells/μl)	130 ± 150	210.1 ± 128.16
Serum creatinine (mg/dl)	1.1 ± 0.16	1.0 ± 0.14
Serum albumin (g/dl)	4.0 ± 0.28	4.0 ± 0.37
Serum triglyceride (mg/dl)	207.8 ± 10.5	255.5 ± 147.68

** Statistical significant p-valve = 0.007 (95% confidence interval = 1.33-6.64)

Table 5. Correlation between 5- hours urine D-xylose with body mass index and CD_4 count.

	Correlation coefficient	P-value
Wasting group (group I)		
Body mass index	0.19	0.49
CD_4 cell count	0.12	0.63
Non-wasting group (group II)		
Body mass index	0.66	0.01**
CD_4 cell count	0.45	0.11

** Statistical significant

chronic diarrheal HIV patients with or without wasting. The authors aimed to postulate that small bowel malabsorption is one of the important factors in non-chronic diarrheal HIV wasting syndrome.

The 5-hour urine D-xylose was statistically different i.e. 3.96 ± 2.81 g in group I *versus* 5.95 ± 2.47 g in group II (p = 0.045). The present data suggested that small bowel malabsorption plays an important role in non-chronic diarrheal HIV wasting syndrome without association with CD4 cell count, anti-retroviral treatment and co-trimoxazole prophylaxis. The abnormal absorptive capacity was a common phenomenon found in HIV patients with wasting syndrome as determined by standard 25 g oral D-xylose test.

In general, 5 hour urine D-xylose was considered normal when it was ≥ 4 g. For subgroup analysis in group I, there was no difference in most parameters such as age, CD4 count, duration of HIV serpositivity, triglyceride level, serum creatinine, serum albumin, anti-retroviral treatment, co-trimoxazole prophylaxis and BMI. However, subgroup analysis in group II revealed that most parameters were also similar, except BMI. In the abnormal D-xylose subgroup, BMI was 18.7 ± 0.83 g, compared with 22.7 ± 2.33 g in the normal D-xylose subgroup. It

was statistically significant with p = 0.007 as shown in Table 4. A significant association between low BMI and poor absorptive capacity was observed with a correlation coefficient of 0.66 (p = 0.01) as shown in Table 5. In conclusion, D-xylose absorption was reduced in non-diarrheal, non-wasting HIV-infected patients with early weight reduction as well as in non-diarrheal, wasting HIV patients. This may be a useful test to predict the potential weight loss in HIV infected patients.

HIV enteropathy was associated with many structural changes such as villous atrophy and hyperplasia of crypts. There was no correlation between structural change and other parameters, such as small bowel function (absorption and permeability), staging of HIV- infection and CD4 cell count[8,10,28-33]. The present study suggested that there was no correlation among absorptive function, permeability function, and structural change in non-chronic diarrheal HIV-wasting syndrome.

SUMMARY

This study demonstrated that D-xylose absorption was decreased in non-diarrheal, wasting HIV-infected patients. The reduction of D-xylose absorption was also seen in non-diarrheal, non-wasting HIV infected patients with early weight reduction. The abnormal absorptive capacity was a common phenomenon found in HIV-patients with wasting syndrome as determined by standard 25 g oral D-xylose test. This might be a useful test to predict the potential weight loss in HIV-infected patients.

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ความสามารถในการดูดซึมของลำไส้เล็กในผู้ป่วยภูมิคุ้มกันเสื่อมจากเชื้อเอ็ชไอวีที่มีปัญหาน้ำหนักลด ในผู้ป่วยกลุ่มที่ไม่มีอุจจาระร่วงเรื้อรัง

สมชาย เหลืองจารุ, พบ, เกียรติ รักษ์รุ่งธรรม, พบ**, นฤมล วิเศษโอภาส, พ.บ***, วโรชา มหาชัย, พบ***

วัตถุประสงค์ : เพื่อเปรียบเทียบความสามารถในการดูดซึม, การยอมให้สารต่าง ๆ ซึบซาบผ่านและลักษณะทางพยาธิวิทยาของลำไส้เล็กในผู้ป่วยภูมิคุ้มกันเสื่อมจากเชื้อเอ็ชไอวีที่มีและไม่มีปัญหาน้ำหนักลด ในผู้ป่วยกลุ่มที่ไม่มีอุจจาระร่วงเรื้อรัง

ผู้ป่วยและวิธีการ : ผู้ป่วยติดเชื้อไวรัสเอ็ชไอวี (อายุ 15–70 ปี) ที่มารับการรักษาที่โรงพยาบาลจุฬาลงกรณ์ แบ่งผู้ป่วยเป็น 2 กลุ่ม กลุ่มที่มีปัญหาน้ำหนักลดมากกว่าร้อยละ 10 ของน้ำหนักเดิมและน้ำหนักลดน้อยกว่าร้อยละ 10 การทดสอบความสามารถในการดูดซึมตรวจด้วยวิธี 25 g D-xylose test การยอมให้สารต่าง ๆ ซึบซาบผ่านตรวจด้วยวิธี Phenolsulfonephthalein test และลักษณะทางพยาธิวิทยาของลำไส้

ผลการศึกษา : ผู้ป่วยทั้งหมด 32 ราย เพศหญิง 11 ราย เพศชาย 21 ราย อายุระหว่าง 25–50 ปี โดยแบ่งเป็นกลุ่มน้ำหนักตัวลด 18 รายและน้ำหนักตัวไม่ลด 14 ราย ในทั้ง 2 กลุ่มไม่พบมีความแตกต่างอย่างมีนัยสำคัญในเรื่องอายุ, ค่าดัชนีมวลรวมของร่างกาย, ปริมาณเม็ดเลือดขาว CD4 T-lymphocytes, ระยะเวลาของการติดเชื้อเอ็ชไอวี, ค่าไตรกลีเซอไรด์, ค่าอัลบูมิน, การยอมให้สารต่าง ๆ ซึบซาบผ่านและลักษณะทางพยาธิวิทยาของลำไส้เล็ก ยกเว้น ความสามารถในการดูดซึมของลำไส้เล็ก โดยที่ค่าน้ำตาล D-xylose ในปัสสาวะ 5 ชั่วโมงเป็น 3.96 $\pm$ 2.81 กรัมและ 5.95 $\pm$ 2.47 กรัมในกลุ่มน้ำหนักตัวลดและกลุ่มน้ำหนักตัวไม่ลดตามลำดับ ซึ่งมีความแตกต่างอย่างมีนัยสำคัญทางสถิติ (ความน่าจะเป็นน้อยกว่า 0.05)

สรุป : พบมีการลดลงของการดูดซึม D-xylose ในผู้ป่วยติดเชื้อเอ็ชไอวีที่มีปัญหาน้ำหนักลดและไม่มีปัญหาอุจจาระร่วงเรื้อรัง ซึ่งทดสอบได้ด้วยวิธี 25 g D-xylose test

คำสำคัญ : ความสามารถในการดูดซึมของลำไส้เล็ก, การยอมให้สารต่าง ๆ ซึบซาบผ่านและลักษณะทางพยาธิวิทยาของลำไส้เล็ก, ผู้ป่วยภูมิคุ้มกันเสื่อมจากเชื้อเอ็ชไอวีที่มีปัญหาน้ำหนักลด

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