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Absorption of L-Phenylalanine in Human Ileal Reservoirs Exposed to Urine

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Summary. The mucosa of ileal reservoirs exposed to urine undergoes successive structural changes, indicating a loss of absorptive capacity. In patients with urinary diversion via a continent ileal reservoir, the active absorption of L-phenylalanine from the reservoir was studied at different postoperative time intervals. A test solution containing L-phenylalanine was instilled into the resorvoir and samples were taken at intervals during a period of one hour for determination of phenylalanine. In one group of patients, urine from the kidneys by-passed the reservoir via a catheter inserted into the afferent segment. Within three months after construction of the ileal reservoir, the uptake was significantly slower than that in ileostomy reservoirs and the absorption decreased even more with longer observation times. Mixing of urine with the reservoir contents did not influence the uptake of L-phenylalanine to any significant degree. The reduced absorption of L-phenylalanine indicates that the uptake of other substances from this type of ileal reservoirs might be decreased also.

Key words: Continent ileal reservoir – Urinary diversion – L-phenylalanine absorption

Introduction

The increasing use of various parts of intestine to substitute for the urinary bladder makes it highly desirable to aquire information about the qualities of the intestine in its new position. It has previously been shown that exposure of the continent ileal reservoir to urine leads to remarkable structural changes in the mucosa [1, 4, 5]. In some areas, the villi and crypts disappear and the enterocytes are altered to cuboidal or flat epithelial cells without microvilli and without enzymatic activity. In other regions of the reservoir the mucosa has a "villous appearance", although also here the villi are smaller. These alterations of the ileal reservoir mucosa after exposure to urine indicate that the transport capacity of the mucosa is probably also changed.

The amino acid L-phenylalanine has previously been used in our laboratory to test the absorptive capactiy of intestinal reservoirs. This amino acid is actively absorbed, is stable and is not influenced by the presence of bacteria. When L-phenylalanine was instilled into the ileostomy reservoir it was found that the mucosa retained its absorptive capactiy during the study period comprising one year [3]. In a more recent study the uptake of L-phenylalanine in vitro was the same in biopsies from ileal urostomy and ileostomy reservoirs, while the in vivo uptake was significantly lower in the urinary reservoirs [4]. There was also a tendency to reduced phenylalanine absorption in the urinary reservoirs with the increasing postoperative interval. It was hypothesized that the addition of hypertonic urine may have caused a "paracellular bulkflow" of water into the reservoir, thereby hindering the paracellular uptake of phenylalanine and contributing to the low in-vivo uptake.

The present investigation was designed to study the absorption of L-phenylalanine in ileal urinary reservoirs with respect to the significance of the presence of urine in the reservoir and to the uptake as a function of postoperative time.

Material and Methods

Sixteen patients with urinary diversion via a continent ileal reservoir were included in the study. Seven of the patients were studied within 3 months after construction of the reservoir (Group A), while in the remaining 9 patients (Group B) the time interval from the operation to the investigation varied from 10 to 92 months.

The patients were supine on a couch during the investigation. A Nelaton catheter (Ch 12) was inserted into the reservoir which was emptied, thoroughly rinsed with saline, and refilled with the test solution. In patients from Group A, the reservoirs had not yet expanded to their ultimate size and, therefore, volumes of only 130–200 ml of the test solution were instilled. In the patients from Group B, the reservoirs were well established with good functional capacity and in these reservoirs volumes of 250 ml were instilled.

The test solution contained 20 mmol/l of L-phenylalanine dissolved in a Ringer-glucose solution (30 mmol/l glucose, pH 7.4) and a nonabsorbable volume marker, ^{51}Cr-EDTA (5 μCi/l).

Table 1. The amount of reflux to the afferent loop, amount of leakage through the outlet and difference between calculated and recovered volumes of reservoir contents recorded in patients from Group B

Pat.	Reflux, ml	Leakage through the outlet, ml	Difference between calculated and recovered volume, ml[a]
1	0	0	+7
2	0	7	−9
3	14	3	+22
4	4	0	−16
5	8	2	+32
6	0	0	+23
7	0	0	+14
8	2	10	−22
9	11	0	+27

[a] The difference is positive when the calculated volume is larger than the recovered volume

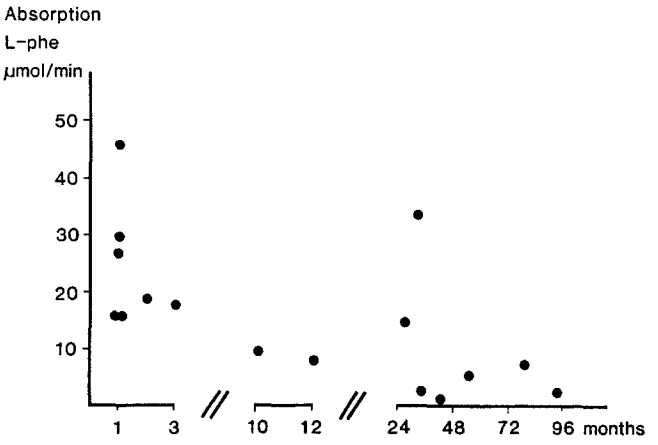

Fig. 2. Absorption of L-phenylalanine (μmol/min) in ileal urostomy reservoirs as a function of the postoperative time interval recorded in seven patients with reservoirs exposed to urine for less than 3 months (Group A) and in nine patients with reservoirs exposed to urine for more than 10 months (Group B)

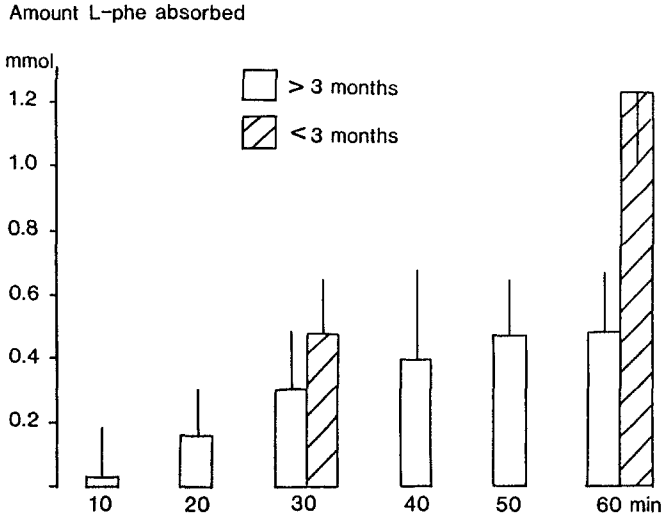

Fig. 1. Absorption of L-phenylalanine measured during 6 x 10 min periods in ileal reservoirs exposed to urine for one to three months (Group A) and for 10 to 92 months (Group B)

In Group A, samples from the reservoirs were taken 10, 30 and 60 minutes and in Group B 2, 10, 20, 30, 40, 50 and 60 minutes after instillation of the test solution. The samples were taken after thorough mixing of the content by repeated aspirations and injections through the reservoir catheter. Phenylalanine was determined by ion exchange chromotography (Contron Liquamate 3) and ^{51}Cr-EDTA activity in a gamma-counter (Selelectronic).

By measuring the ^{51}Cr-EDTA activity and the concentration of phenylalanine the absorbed amount of phenylalanine could be determined for each interval. Using linear regression analysis the absorption rate (μmol/min) for each patient was also calculated.

In the patients from Group B, an additional measure was taken in order to by-pass the urine from the afferent segment to the exterior. Under cystoscopic control a wire-guided Foley-catheter (Ch 14) was inserted through the antireflux valve into the afferent segment. The balloon was inflated with 5 ml of fluid and the catheter was gently pulled so that the balloon blocked the connection between the afferent segment and the reservoir. The Foley-catheter was kept open and samples were taken for determination of ^{51}Cr-EDTA activity. In this way any possible reflux of test solution from the reservoir to the afferent segment could be detected and the amount calculated.

In order to detect and calculate possible leaks through the continence-providing valve in those patients with two catheters through the valve (Group B), a compress wrapped around the catheters was analysed with regard to ^{51}Cr-EDTA activity.

Student's *t*-test was used for statistical analyses.

Results

The amounts of reflux to the afferent loop and the leakage through the outlet recorded in the patients from Group B were minute (Table 1). The differences between calculated and recovered volumes were insignificant. In the patients in Group A, who had only one catheter in the reservoir during the examination, no leakage through the stoma occurred.

The amount of L-phenylalanine absorbed from the reservoirs was proportional to the time after instillation of the test solution (Fig. 1). A significantly greater amount had been absorbed in Group A than in Group B after 60 minutes ($p < 0.05$). The absorption of L-phenylalanine as a function of postoperative time interval is given in Fig. 2. The uptake of L-phenylalanine in Group A was 24.2 ± 4.19 μmol/min (mean ± SEM) and in Group B 9.1 ± 3.32 μmol/min ($p < 0.02$).

Discussion

Shortly after construction of the ileostomy reservoir, the mucosa undergoes moderate alterations consisting mainly of a shortening of the villi and an increase in mitotic activity. Both the microvilli and the enzymatic activity remain

intact. Furthermore, these mucosal changes tend to return to normal with longer observation times [2].

In contrast to these moderate and regressive changes in the mucosa of the ileostomy reservoir, the mucous membrane of the ileal reservoir exposed to urine exhibited prominent structural alterations including loss of microvilli in large areas and reduction in enzymatic activity [1, 5]. Consequently, it is reasonable to expect that these structural variations should be reflected also in the transport capacity of the mucous membrane.

The amounts of reflux to the afferent loop and the leakage through the outlet were small in the patients from Group B and could easily be corrected for when calculating the volumes of the reservoir contents. The differences between calculated and recovered volumes of reservoir contents were only in two cases more than 10% of the instilled volume and considerably less in the majority.

The present investigation together with previous studies clearly demonstrates that exposing ileal mucosa to urine reduces its absorptive capacity. The absorption of L-phenylalanine was significantly higher ($p < 0.02$) in the ileostomy reservoirs (49.9 ± 7.85 μmol/min) than in the urostomy reservoirs both when exposed to urine for less than 3 months (24.2 ± 4.19 μmol/min) and when exposed for more than 10 months (9.1 ± 3.32 μmol/min). The figure for the absorption in ileostomy reservoirs is cited from a previous investigation in our laboratory [4]. It was also demonstrated that the minimal uptake of the substance in urostomy reservoirs was not due to the presence of urine. The decrease in active absorption appears very soon after construction of the reservoir, as shown by the declining uptake in the patients studied within 3 months after construction compared to the "normal" uptake in ileostomy reservoirs. In the latter type of reservoir, there was no change in uptake along the time axis [3].

The decrease in uptake of L-phenylalanine in ileal reservoirs exposed to urine indicates that the uptake of urinary components might be decreased in this type of urinary receptacle.

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