Investigation of Regional Differences in Water and Electrolyte Absorption Across the Human Colon by in vivo Perfusion Method

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Colonic perfusion studies were performed to evaluate regional differences in water and electrolyte absorption across the human colon. In 19 healthy male volunteers, a 5-lumen tube with two balloons was inserted into the colon by the endoscopic retrograde bowel insertion (ERBI) method and a 25 cm segment of either the right or the left colon was perfused with an isotonic electrolyte solution simulating the fasting ileal content at a rate of 5 ml/min. Additionally into 5 subjects of the right colon and 5 subjects of the left colon, PSP solution was injected and mean transit time was calculated by the dilution method. Higher absorption rates of water, Na and Cl were observed in the right than in the left colon. Mean transit time was longer in the left than in the right colon. It was considered that the right colon had greater absorptive capacity than the left. The colonic perfusion study by the use of ERBI method made it possible to determine the absorption of water and electrolytes in the right and left colon directly in man, and would be useful to elucidate the pathophysiology of colonic diarrhea.

Key Words: Segmental colonic perfusion, Endoscopic retrograde, Bowel insertion method

It is well known that water and electrolytes are absorbed and secreted in the small intestine and colon. In adults, about 10 liters of fluid, which consists of dietary fluid and salivary, gastric, biliary, pancreatic and intestinal secretions, enter the human intestine every 24 hours. Most of the fluid is absorbed in the small intestine, and normal ileal flow into the cecum is estimated to be 1.5–2.0 liters per day,^{1, 2)} indicating a colonic absorption rate of 1.4–1.9 liters per day.

It is generally considered that more water is absorbed in the right than in the left colon in man, but a few reports have been made for regional differences in absorptive function of the human colon in vivo.^{3, 4)} Peroral or pernasal intubation to the cecum made it possible to investigate colonic absorption and regional differences in vivo, but many hours were required to intubate

the cecum from above. In addition, it is impossible to make a colonic segment and to elucidate segmental transit times in this way. For these reasons, we developed a new colonic perfusion method to study regional differences in water and electrolyte absorption across the human colon by the use of the endoscopic retrograde bowel insertion (ERBI) method.⁵⁾

MATERIALS AND METHODS

ERBI method was attempted on 29 volunteers, all of whom were healthy males ranging in age from 18 to 29 years. 14 subjects were intubated into the right colon (ascending-transverse colon) and 15 into the left colon (descending-sigmoid colon). Written informed consent was obtained from each subject before participation in the study and all experiments were conducted in accordance

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with the Declaration of Helsinki.

Technique of colonic intubation: A 5-lumen tube reformed from a Cliny balloon sonde 42C (F 18, 4 lumens, 2 balloons) was used. The tube had a test segment 25 cm long. Subjects were prepared the day before the colonoscopy by ingestion of a low residual diet and an oral dose of dioctyl sodium sulfosuccinate (DSS) 90 mg and dantron 75 mg. They fasted the morning of the study and were prepared with a 4 mg intramuscular injection of butropium bromide. A 5-lumen tube was inserted into the right or the left colon from below by the ERBI method.

ERBI method consisted of 5 steps: 1) A colonofiberscope (Olympus Company, CF-LB₃R), partially covered with a stiffening cuff, was introduced into the right or the left colon under fluoroscopic control. 2) A guide wire of 300 cm (maximum diameter of 1.2 mm) was passed through the channel of the colonofiberscope which was thereafter withdrawn while the guide wire was retained in position. 3) A 5-lumen tube was inserted as far as the guide wire. 4) The guide wire and stiffening cuff were removed, leaving the tube and balloons in position. 5) The proximal balloon was inflated with 30 ml of water and the distal balloon

with 50–100 ml of air; in this way the tube was fixed in position.

Test solution and experimental technique (Fig. 1): After intubation the test segment was rinsed rapidly with 500 ml of warm saline, until the recovery from the distal point was free of feces and mucus. 1–2 hours were allowed to expel or absorb the saline remaining in the colon.⁶⁾ Test solution was an isotonic electrolyte solution simulating the ileal content,²⁾ containing Na⁺ 145, K⁺ 10, Cl⁻ 110, HCO₃⁻ 45 mEq/L and polyethylene glycol (PEG) 4000 5 g/L as a non-absorbable marker. A 25 cm segment of either the right or the left colon was perfused with the test solution at a rate of 5 ml/min. The recovery from the distal point was collected at 10 minute intervals. Additionally in 5 subjects of the right colon and 5 subjects of the left colon, the perfusion was interrupted for 1 minute to inject 10 mg of phenol-sulfonphthalein (PSP) from the proximal point. Concentration of PSP in samples collected from the distal point at 5–10 minute intervals after injection was used to determine the colonic transit time for PSP.

Analyses and calculations: Na⁺ and K⁺ were measured by flame photometry (Model 205,

Fig. 1. Schema of colonic perfusion technique. A 25 cm segment of either the right or the left colon was perfused with the test solution at a rate of 5 ml/min.

HITACHI), Cl^- by coulometry (CL-3, HIRANUMA), and HCO_3^- by auto burette (EST 882, COPENHAGEN). PEG 4000 was determined by turbidimetry⁸⁾ and PSP by spectrophotometry. It was considered that the steady state was attained when PEG concentration of successive samples varied by less than 10% of the average value. The equations used in the calculations of net water and electrolyte absorption (+) or secretion (-) were:³⁾

Net volume change (ml/min) =

$$[\text{V}_{\text{in}}] - [\text{V}_{\text{in}}] \left(\frac{\text{PEG}_{\text{in}}}{\text{PEG}_{\text{re}}} \right)$$

Net electrolyte change (mEq/min) =

$$[(\text{E}_{\text{in}}) (\text{V}_{\text{in}})] - [(\text{E}_{\text{re}}) (\text{V}_{\text{in}}) \left(\frac{\text{PEG}_{\text{in}}}{\text{PEG}_{\text{re}}} \right)]$$

V_{in} = volume infused, ml/min

PEG_{in} = PEG concentration in infused fluid

PEG_{re} = PEG concentration in recovered sample

E_{in} = concentration of electrolyte in infused fluid, mEq/ml

E_{re} = concentration of electrolyte in recovered sample, mEq/ml

In additional study, dye dilution curves were constructed from the concentration of PSP at the distal point.⁷⁾ The mean transit time in minutes was calculated according to Zierler.⁹⁾

Fig. 2. Absorption of water in different sides of the colon. Larger absorption rate of water was observed in the right than in the left colon.

Data were expressed as Mean $\pm$ SD without description and analyzed by Student's t-test.

RESULTS

Technique of ERBI method and perfusion study: Intubation was successful in all subjects, 14 into the right colon and 15 into the left colon. Perfusion studies failed in 4 of 14 subjects (right) and 6 of 15 subjects (left). In 5 subjects, the sampling tube was obstructed by stool, in 2 subjects the tube displaced during perfusion, and in 3 subjects a large volume of perfusion solution refluxed into the oral side of the balloon continuously. Eventually 10 subjects (right colon) and 9 subjects (left colon) were investigated.

Absorption of water and electrolytes in different sides of the colon: The results obtained in each subject are shown in Figs. 2, 3. Larger absorption rates of water, Na^+ and Cl^- were observed in the right than in the left colon. However, there was no significant difference in K^+ and HCO_3^- . There was a significant correlation between Na^+ absorption and water, Cl^- absorption in both sides.

Dye dilution curve and mean transit time of PSP: Dye dilution curves were constructed from the concentration of PSP at the distal point. In the right colon, the concentration of PSP increased rapidly and disappeared after 65 minutes in all cases. In the left colon, PSP increased gradually and disappeared slowly (Fig. 4). Mean transit

Fig. 3. Absorption of Na^+ and Cl^- in different sides of the colon. Larger absorption rates of Na^+ and Cl^- were observed in the right than in the left colon.

Fig. 4. Dye dilution curves for PSP in different sides of the colon. In the right colon, the concentration of PSP increased and disappeared rapidly. In the left colon, PSP increased gradually and disappeared slowly.

Fig. 5. Mean transit time for PSP in different sides of the colon. It was longer in the left than in the right colon.

time calculated from dye dilution curves was about twice as long in the left as in the right colon (Fig. 5).

DISCUSSION

The colon is thought to play an important role in water and electrolyte absorption. Moreover, it is important to know the colonic absorptive function for understanding the pathophysiology of

colectomy and diarrhea.

With a standard diet, 1500 ml of water, 200 mEq of Na^+ , 100 mEq of Cl^- , and 10 mEq of K^+ entered the colon daily in healthy individuals.¹⁾ It is considered that most of these are absorbed in the proximal segment of the colon. Levitan et al³⁾ showed that more Na^+ , Cl^- and water were absorbed in the cecum and the transverse colon than in the distal colon. Devroede et al⁴⁾ made a more direct observation by instilling radioactive Na and heavy water into different segments of the human colon. They all intubated the long tube into the cecum from above for these investigations, but many hours were required for intubation and the volunteer had to be restrained for some days. For these reasons we have developed a new colonic perfusion technique by the use of ERBI method. This technique made it possible to investigate regional differences in the absorption rate and to measure transit times in different segments of the human colon.

Regional differences in water and electrolyte absorption have been shown for rat¹⁰⁻¹³⁾, rabbit¹⁴⁾, guinea pig¹⁵⁾, pony¹⁶⁾ and man.^{3, 4, 17)} Results of many experiments indicated that the cecum and the proximal colon were capable of absorbing the excess of fluid, and the distal colon contributed little to water and Na^+ absorption. However, some authors reported that there was no difference be-

tween the proximal and the distal parts of the colon in water and electrolyte absorption.^{13, 15)} In man,^{3, 4)} two studies indicated that the absorptive capacity of the proximal colon was much higher than that of the distal colon, and these results were similar to our findings.

Two hypotheses have been presented to explain this difference. One is that the right colon has a larger absorptive area than the left, and the other is that transit is more rapid in the left colon than in the right. The report concerning the mucosal area indicated that the right colon had about two times larger mucosal area than the left.¹⁸⁾ If the right colon has approximately twice as large an absorptive area as the left, our results indicate that the absorptive rate per cm² of the right colon is roughly equal to that of the left. However, as transit time in the right colon is shorter than in the left, it is considered that the right colon has a greater absorptive capacity than the left. For regional difference of fluid transit, there has been no investigation by the use of the same solution. There were a few reports in rat¹⁶⁾ and man¹⁹⁾ for the transit of colonic fluid. These suggested that during perfusion, liquids were trapped in the right colon and passed through the left colon rapidly. In contrast to this data, our results by the use of the same solution and PSP indicated that liquids passed through the right colon more rapidly than the left.

We have described a simple and safe method for intubation of the colon in man. The technique is applicable to adults of all ages. The major advantage of our technique is that it reduces the time and discomfort associated with introducing a tube into the cecum from above. Moreover, this method makes it possible to perfuse optional sites of the colon. It must be considered, however, that a tube and balloons in the colon and the preparation for colonoscopy might have unknown effects on colonic functions.

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