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ORIGINAL RESEARCH ARTICLE

Oral rehydration solution normalizes plasma renin and aldosterone levels in patients with ulcerative colitis after proctocolectomy

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Abstract:

Objectives: The possible effects and benefits of oral rehydration solution (ORS) on chronic dehydration after total proctocolectomy. Methods: To evaluate the effect of ORS on the renin-angiotensin system after remnant proctocolectomy in patients with ulcerative colitis (UC), we selected 20 patients after remnant proctocolectomy, ileal J pouch-anal anastomosis, and construction of a diverting ileostomy for UC. Patients were randomly divided into two groups, A (n=9) or B (n=11), 2 weeks after the surgery. In group A, ORS (1000 mL/day) was given for the first 7 days and mineral water (1000 mL/day) for the next 7 days. In group B, mineral water (1000 mL/day) was given for the first 7 days and ORS (1000 mL/day) for next 7 days. Plasma levels of renin, aldosterone and excretion of sodium in urine were evaluated at days 0, 7, and 14. We defined day 0 as the day of beginning this study. Results: Mean plasma renin levels on day 0 were six to eight times greater than the upper normal limit. In group A, ORS lowered plasma renin levels. In group B, plasma levels of renin and aldosterone after ORS were lower than those at days 0 and 7. Conclusions: ORS corrected increased plasma levels of renin and aldosterone to within the normal range in patients after proctocolectomy.

Keywords:

oral rehydration solution, ulcerative colitis, after proctocolectomy

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Introduction

Restorative proctocolectomy with ileal J pouch-anal anastomosis (IPAA) is the standard operative procedure for patients with UC. IPAA offers a good quality of life to the majority of patients[1-3)]. Nevertheless, IPAA complicates a number of postoperative problems, such as increased frequency of defecation, diarrhea, and dehydration, and these three complications are inter-related. Among these, dehydration is due to the loss of reabsorption in the colon, and thus, patients who undergo IPAA are considered in the state of "chronic dehydration." These patients' can become seriously dehydrated because of various systemic diseases, and these patients may require admission for intravenous rehydration. Therefore, dehydration impairs patients' quality of life.

The renin-angiotensin system plays an essential role in homeostasis of blood pressure, body fluid volume, and electrolyte metabolism. Dehydration and sodium deprivation induce hypersecretion of renin from the juxtaglomerular apparatus in the kidney[4-6)]. Renin finally increases the secretion of aldosterone and the antidiuretic hormone vasopressin via the angiotensin pathway. Hyperaldosteronism was observed after total colectomy in rats and after IPPA in humans[7,8)]. Measurement of renin and aldosterone levels should be used for evaluation of the severity of a sodium deficiency[9)].

The use of oral rehydration solution (ORS) revolutional-

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Table 1. Questionnaire for Symptoms and Its Classification.

Thirst	1 Not at all	2 Very little	3 Sometimes	4 Often	5 Always
General fatigue	1 Not at all	2 Very little	3 Sometimes	4 Often	5 Always
Appetite	1 Very good	2 Good	3 Fair	4 Poor	5 Bad
Sweat	1 Not at all	2 Very little	3 Sometimes	4 Often	5 Always
Dizziness	1 Not at all	2 Very little	3 Sometimes	4 Often	5 Always
Palpitations	1 Not at all	2 Very little	3 Sometimes	4 Often	5 Always
Abdominal plan	1 Not at all	2 Very little	3 Sometimes	4 Often	5 Always
Abdominal discomfort	1 Not at all	2 Very little	3 Sometimes	4 Often	5 Always

ized the management of acute diarrhea[10]. World Health Organization (WHO) and United Nations Children's Fund (UNICEF) recommend ORS as the treatment of clinical dehydration throughout the world. Since WHO adopted ORS in 1978 as its primary tool to treat diarrhea, the mortality rate in children suffering from acute diarrhea has decreased markedly from 5 million to 1.3 million deaths annually. The possible effects and benefits of ORS on chronic dehydration after restorative proctocolectomy, however, have not been investigated so far.

We hypothesized that early after IPAA (1) plasma levels of renin, aldosterone, and vasopressin are increased, and (2) administration of ORS decreases plasma levels of these hormones and thereby improves IPAA-associated dehydration. The aims of the present study were to investigate, (1) plasma levels of renin, aldosterone, and vasopressin after restorative proctocolectomy, and (2) whether ORS could improve the dehydration by reversing plasma levels of these hormones without adverse events.

Methods

Patients

Twenty patients were enrolled in this study, all of whom underwent three-staged operation for UC. In the first operation, we performed subtotal colectomy, construction of a rectal mucous fistula, and an end-ileostomy. After approximately 4-6 months, the second operation was carried out; after performing a transanal rectal mucosectomy for a 5-7 cm length, we performed a transabdominal resection of the remnant rectum and created the ileal J pouch using a linear stapler. A diverting loop ileostomy was made 40-50 cm proximal to the inlet of the ileal pouch after performing a transanal, hand-sewn IPAA. In the third operation performed 2-3 months later, the loop ileostomy was taken down, and closed with a side-to-side ileo-ileostomy. In this study, patients were evaluated 2-3 weeks after the second operation.

Study design

This study is prospective randomized cross-over design. The patients were assigned randomly into two groups using a table of random numbers. The patients in group A initially ingested ORS (Na^+ 50 mEq/L, K^+ 20 mEq/L, Cl^- 50 mEq/L, Mg^{2+} 2 mEq/L, P 2 mmol/L, Lactate 31 mEq/L, Glucose 1.8%) (1000 mL/day) for the first 7 days (days 1-7) and mineral water (Na^+ 0.49 mEq/L, K^+ 0.046 mEq/L, Mg2+ 0.44 mEq/L, Glucose 0%) (1000 mL/day) was given for the next 7 days (days 8-14). Conversely, patients in group B initially drank mineral water (1000 mL/day) for the first 7 days and ORS (1000 mL/day) was given for the next 7 days. We defined day 0 as the day of beginning this study each group. Food and the other liquid intake were not restricted and were allowed ad-libitum from day 1 to 14 in their daily life. All patients were given no intravenous fluid supplementation and any antidiarrheal during the study.

Analysis of laboratory data

We analyzed blood and urine samples and total 24 hour volume of urine at days 0, 7, and 14, after the start of the study. The blood and urine samples were taken regularly around 10 o'clock in the morning before the patients drank the ORS and mineral water of the day. Plasma levels of renin, aldosterone, and vasopressin, as well as routine laboratory data including osmotic pressure and creatinine, were evaluated. Osmotic pressure, glucose, protein, Na, K, Cl, creatinine were measured in urine samples at days 0, 7, and 14.

Clinical evaluation with questionnaire

The patients were inquired about thirst, general fatigue, appetite, sweat, dizziness, palpitations, abdominal pain, and abdominal discomfort at days 0, 7, and 14. Their symptoms were described on a five-score scale (Table 1).

Statistical analysis

The statistical comparison was executed with analysis of variance (ANOVA), and significant difference was defined by a p-value of less than 0.05.

Ethical compliance

This clinical was performed under institutional guidelines, and the protocol of this study was approved by the ethical committee of Tohoku university graduate school of medicine (2003-307). Written informed consent was obtained from each patient.

Results

There were no statistical differences in patients' back-

Table 2. Demographics of Patients in 2 Groups.

	Group A (N=9)	Group B (N=11)
Age (years)	31 ± 12	40 ± 12
Sex ratio (man:woman)	6:3	6:5
Days after the first operation	141 ± 29	216 ± 72
Days after the second operation	13 ± 4	17 ± 8
Blood loss during the second operation (mL)	608 ± 434	476 ± 238
Duration of the second operation (min)	352 ± 80	328 ± 86

Values are mean ± SD

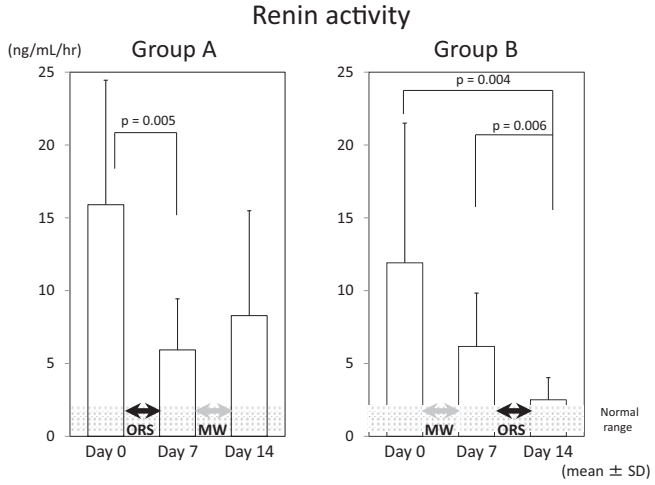

Figure 1. Renin levels in two groups. Plasma renin levels were about six to eight times higher than the upper limit of normal range in both groups at day 0. In group A, ORS lowered the plasma renin level on day 7 compared to day 0, but administration of mineral water thereafter increased renin levels on day 14. Plasma renin levels in group B on day 7 after administration of mineral water were decreased compared to day 0 with no statistical difference. ORS significantly decreased plasma renin levels on day 14 compared to days 0 and 7.

grounds between the two groups (mean age, sex ratio, days after the first and the second operations, blood loss and duration of the second operation, Table 2). These patients had no pre-operative complications such as renal failure, pulmonary diseases, cirrhosis, cardiac diseases, or malignant diseases. They did not have any postoperative complications including leakage or intestinal obstruction. Prednisolone (5-30 mg) by oral was administered in two patients in group A and three in group B during the study.

Laboratory data

Plasma renin activity was about six to eight times greater than the upper limit of normal range (0.1-2.0 ng/mL/h) in both groups at day 0 (Figure 1). In group A, ORS decreased the plasma renin level on day 7 (5.9 ± 3.5 ng/mL/h) compared to day 0 (15.9 ± 8.5 ng/mL/h, p=0.005). Administration of mineral water for the following week in group A slightly increased renin levels on day 14 with no statistical difference compared to days 0 and 7. Plasma renin levels in

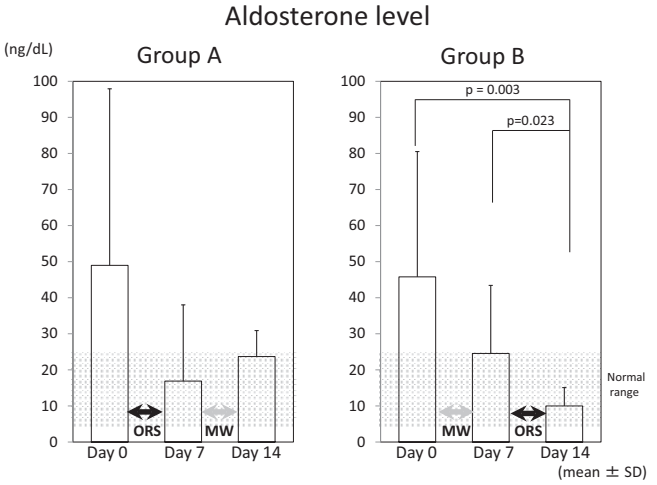

Figure 2. Aldosterone levels in two groups. Aldosterone levels at day 0 were about two times higher than the normal range in both groups. In group A, aldosterone levels on day 7 after ORS and day 14 after mineral water did not differ from those on day 0. In group B, aldosterone levels on day 7 after administration of mineral water were not different from those on day 0. Aldosterone levels on day 14 after ORS were lower than those on days 7 and 0.

group B on day 7 after administration of mineral water (6.17 ± 3.7 ng/mL/h) were decreased compared to day 0 (11.9 ± 9.6 ng/mL/h) with no statistical difference (p=0.079). ORS decreased plasma renin levels on day 14 (2.51 ± 1.5 ng/mL/h) compared to days 0 (p=0.004) and 7 (p=0.006).

Aldosterone levels at day 0 were about two times greater than the normal range (3.6-24.0 ng/dL) in both groups (Figure 2). In group A, aldosterone levels on days 7 after ORS and 14 after mineral water were not statistically different compared to day 0. In group B, the aldosterone levels on day 7 after administration of mineral water were not different from day 0 (p=0.09), but on day 14 after ORS, aldosterone levels were less than on days 7 (p=0.023) and 0 (p= 0.003). Although vasopressin levels varied between days 0, 7, and 14, these values were within or slightly above the normal range and did not differ from each other in both groups (Table 3).

Total 24-hour volume of urine did not differ between days 0, 7, and 14 in both groups (Table 3). Urinary excretion of sodium after ORS on day 7 (59.4 ± 38.7 mEq/g CRE) increased compared to day 0 (15.2 ± 11.4 mEq/g CRE) in group A (p=0.005, Table 3), and administration of mineral water for 7 days thereafter decreased the urinary excretion of sodium on day 14; no statistical difference was observed between day 0 and 14 (Table 3). In group B, administration of mineral water increased the urinary excretion of sodium in urine on day 7 (42.8 ± 36.1 mEq/g CRE) compared to day 0 (17.4 ± 12.7 mEq/g CRE) (p=0.039). ORS further increased excretion of sodium in urine (103 ± 62.7 mEq/g CRE) compared to days 7 (p=0.012) and 0 (p<0.001, Table 3). Creatinine, Na, K and osmotic pressure in blood were not statistically different and were within the normal range for both groups (data not shown).

Table 3. Vasopressin Level, Volume of Urine and Urinary Excretion of Sodium in 2 Groups.

	*Vasopressin level (pg/mL)		Total 24 hour volume of urine (mL)		urinary excretion of sodium (mEq/g CRE)	
	Group A	Group B	Group A	Group B	Group A	Group B
Day 0	5.2 ± 3.7	2.7 ± 2.1	569 ± 258	911 ± 727	15.2 ± 11.4	17.4 ± 12.7
Day 7	3.5 ± 3.1	1.7 ± 0.8	616 ± 395	1449 ± 1109	59.4 ± 38.7	42.8 ± 36.1
Day 14	2.9 ± 2.2	1.6 ± 0.8	589 ± 382	1283 ± 1133	32.6 ± 28.8	103 ± 62.7

Values are mean ± SD *Normal level (0.3-4.2 pg/mL)

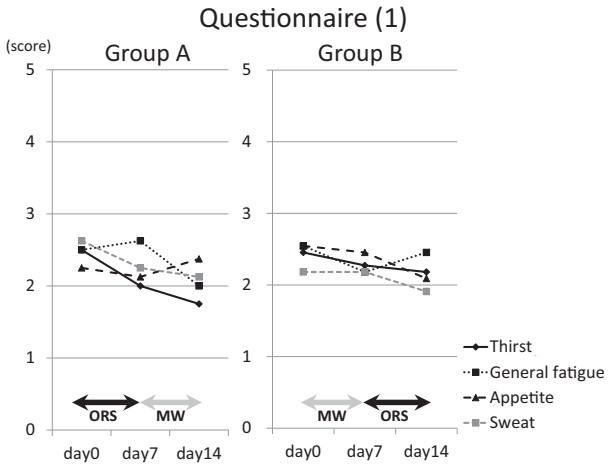

Figure 3. Results of questionnaire in two groups (1). In both groups, thirst, general fatigue, appetite and sweat on day 14 were better than day 0 with no statistical differences.

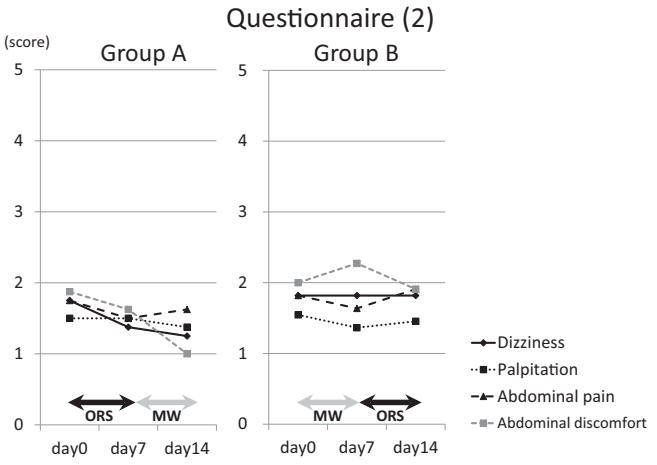

Figure 4. Results of questionnaire in two groups (2). There were no adverse events such as dizziness, palpitations, abdominal pain, and abdominal discomfort with neither ORS nor mineral water for both groups.

Clinical evaluation with questionnaire

In both groups, thirst, general fatigue, appetite, and sweat on day 14 were better than day 0 with no statistical differences (Figure 3). There were no adverse events such as dizziness, palpitations, abdominal pain, and abdominal discomfort with neither ORS nor mineral water for both groups (Figure 4).

Discussion

This study was performed as a cross-over design because of the limited number of patients. By using a cross-over design, we excluded the influence of different postoperative status by the time from the operation. We showed the possibility that ORS partially ameliorated dehydration by normalizing plasma renin activity and increasing the urinary excretion of sodium whether ORS was administered before or after mineral water. ORS also normalized the increased baseline aldosterone levels in the group in whom ORS was administered after mineral water but not in a group in whom ORS was administered before mineral water. These observations indicate that the effect of ORS to improve dehydration was more obvious when it was administered after mineral water. It is likely that administration of mineral water beforehand could be an enhancing factor for ORS to exert its effect on renin, aldosterone, and excretion of sodium in urine.

The present study showed that baseline plasma levels of renin and aldosterone, in these patients after the second operation for UC, were approximately six to eight and two times greater than the upper limit of normal range, respectively, before administration of ORS or mineral water on day 0 (2-3 weeks after IPAA and 20-30 weeks after subtotal colectomy). These results suggest that the patients after the second operation for UC were dehydrated even after 20-30 weeks had passed since the first operation in which the ileostomy was constructed. This result coincided with that in a previous study by Huber et al. that reported increased plasma levels of aldosterone in patients after total colectomy[8]. Delin et al. reported the shorter length of small bowel after proctocolectomy with various ileal resections, the more the increase in plasma levels of renin and aldosterone after the operation, and they concluded that measurement of renin and aldosterone levels should be used for evaluation of the severity of sodium deficiency[9]. We hypothesize that renin and aldosterone levels increase to compensate for loss of sodium associated with total proctocolectomy and the IPAA.

In the present study, although the effect was not so obvious as that of ORS, mineral water increased the urinary excretion of sodium when it was administered before ORS. These results suggest the possible improvement of post-colectomy dehydration with one liter of mineral water daily. In contrast, the clinical benefit of ORS was superior. The clinical benefit of ORS has been well documented in patients with severe diarrhea[11,12]. Dhaka et al. demonstrated that the mechanism of sodium and glucose co-transport remains intact in patients with cholera, and ORS can successfully rehydrate and maintain hydration in these patients[13]. Because ORS includes suitable sodium and glucose for absorption, we consider that ORS takes advantage of the active co-transport of sodium and glucose molecules at the intestinal brush border by the transported sodium glucose transporter to maintain hydration even after proctocolectomy. Therefore, we speculate that ORS would be more effective than mineral water for absorption of the remnant small intestine after total colectomy.

Our previous studies in rats demonstrated that the electrogenic Na+ channel (ENaC) and SGLT-1 were induced in the remnant ileum after total colectomy[14-16]. ENaC mediates Na+ entry through the apical membrane, whereas SGLT-1 facilitates co-transport across the luminal membrane. Glucose in the enterocyte is transported into the blood by glucose transporter type 2 (GLUT2) through the basolateral membrane[17-20]. These mechanisms are believed to contribute to the improvement of post-colectomy diarrhea. Changes in gene expression of these channels after administration of ORS should be investigated in the future.

We also showed that vasopressin levels were within or slightly above the normal range on day 0 before study and did not change after administration of ORS or mineral water; these results coincided with those in a previous study after proctocolectomy. Vasopressin is an antidiuretic hormone secreted from posterior pituitary gland, and an increase in plasma osmolarity or a decrease of blood pressure stimulates the release of vasopressin[21,22]. The unaltered plasma osmolarity throughout the present study may have explained the unchanged levels of plasma vasopressin.

In this study, we could not identify any changes in symptom scores associated with dehydration, such as thirst, sweat, and palpitationsm suggesting that changes in plasma renin and aldosterone levels shown in this study were not considered directly associated with symptom scores. Additionally, there were no abnormal symptoms, such as dizziness, palpitation, abdominal pain, and abdominal discomfort, with administration of ORS, suggesting that ORS can safely correct postoperative potential dehydration without any adverse reaction.

Acknowledgements

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Conflicts of Interest

There are no conflicts of interest.

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