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Preoperative fluid and electrolyte management with oral rehydration therapy

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Abstract
Purpose. We hypothesized that oral rehydration therapy using an oral rehydration solution may be effective for preoperative fluid and electrolyte management in surgical patients before the induction of general anesthesia, and we investigated the safety and effectiveness of oral rehydration therapy as compared with intravenous therapy.
Methods. Fifty female patients who underwent breast surgery were randomly allocated to two groups. Before entry to the operation room and the induction of general anesthesia, 25 patients drank 1000 ml of an oral rehydration solution ("oral group") and 25 patients were infused with 1000 ml of an intravenous electrolyte solution ("intravenous group"). Parameters such as electrolyte concentrations in serum and urine, urine volume, vital signs, vomiting and aspiration, volumes of esophageal-pharyngeal fluid and gastric fluid (EPGF), and patient satisfaction with the therapy (as surveyed by a questionnaire) were assessed.
Results. After treatment, the serum sodium concentration and the hematocrit value, which both declined within the normal limits, were significantly higher in the oral group than in the intravenous group (sodium, 140.8 ± 2.9 mEq·l^{-1} in the oral group and 138.7 ± 1.9 mEq·l^{-1} in the intravenous group; $P = 0.005$; hematocrit, 39.03 ± 4.16% in the oral group and 36.15 ± 3.41% in the intravenous group; $P = 0.01$). No significant difference was observed in serum glucose values. Urine volume was significantly larger in the oral group (864.9 ± 211.5 ml) than in the intravenous group (561.5 ± 216.0 ml; $P < 0.001$). The fractional excretion of sodium (FENa), as an index of renal blood flow, was increased in both groups following treatment (0.8 ± 0.5 in the oral group and 0.8 ± 0.3 in the intravenous group). Patient satisfaction with the therapy favored the oral rehydration therapy, as judged by factors such as "feeling of hunger", "occurrence of dry mouth", and "less restriction in physical activity". The volume of EPGF collected following the induction of anesthesia was significantly smaller in the oral group than in the intravenous group (6.03 ± 9.14 ml in the oral group and 21.76 ± 30.56 ml in the intravenous group; $P < 0.001$). No adverse events or adverse reactions were observed in either group.
Conclusion. The results suggest that the oral rehydration therapy with an oral rehydration solution before surgery is superior to the current preoperative intravenous therapy for the provision of water, electrolytes, and carbohydrates, and this therapy should be considered as an alternative to the intravenous therapy for preoperative fluid and electrolyte management in selected surgical patients in whom there is no reason to suspect delayed gastric emptying.

Key words Preoperative management · Fluids · Electrolytes · Oral rehydration therapy

Introduction

Since the 1970s, oral rehydration therapy has been recognized to be safe and clinically effective for the treatment of patients with cholera [1–4]; it is considered to be an effective therapy for the treatment of dehydration and has attracted a great deal of interest in the United States and European Union countries. Also, the use of oral rehydration solutions is recommended by the Centers for Disease Control and Prevention in the United States for the treatment of patients with mild to moderate dehydration [5].

With regard to the management of surgical patients, preoperative fasting from the day before surgery has been standard practice to prevent aspiration pneumonia in patients receiving general anesthesia [6]. However, due to a lack of sufficient scientific evidence, the period of preoperative fasting has recently been reevaluated, and societies of anesthesiology in the United States and most European countries have revised the practice guidelines for preoperative fasting, so that the oral intake of clear fluids may be permissible for up to 2 h before the induction of anesthesia for select groups of surgical patients in whom there is no reason to suspect

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delayed gastric emptying [7]. It has been shown that the oral intake of clear fluids up to 2 h before the induction of anesthesia usually does not increase the volume or the acidity of gastric fluid [7–10]. In addition, an approach for minimizing surgery-related stress by appropriate preoperative management and also reducing subsequent complications has been introduced by Fearon et al. [11], as the "enhanced recovery after surgery" (ERAS) protocol, addressing the disadvantage of preoperative fasting and the advantage of providing carbohydrates before surgery in reducing postoperative insulin resistance. As recommended by the World Health Organization (WHO), oral rehydration therapy [1] is considered to be effective for the treatment of dehydration, and this method is now preferred in the United States and European countries. With regard to the fluid and electrolyte management of surgical patients, intravenous fluid therapy before proceeding to surgery is still a standard practice in Japan [12].

The present study was conducted to investigate the safety and effectiveness of oral rehydration therapy as compared with intravenous therapy for the preoperative fluid and electrolyte management of patients receiving general anesthesia before breast surgery. Specifically, in the study, we hypothesized that preoperative replacement therapy with oral rehydration solution may not be inferior to the currently used intravenous solution, with equal volumes of the two solutions being used.

Subjects and methods

This study was approved by the institutional review board of the study institution (Kanagawa Cancer Center, Japan) and was conducted in accordance with the Declaration of Helsinki. Voluntary written informed consent was obtained from all subjects enrolled in the study.

The subjects were female patients with physical status classification I or II of the American Society of Anesthesiologists (ASA), who were scheduled to enter the operating room at 1300 hours to undergo breast surgery. Patients who had previously received gastroesophageal surgery; patients with a body weight of 40 kg or less or 70 kg or more; patients with abnormal glucose tolerance (fasting glucose level, more than 110 $mg \cdot dl^{-1}$); and patients taking medications affecting gastrointestinal function, such as laxatives, were excluded from the study.

Fifty patients were randomly allocated to two groups (25 patients in the intravenous group and 25 patients in the oral group), and all of these patients completed the treatment.

An intravenous maintenance electrolyte solution, containing water, fructose, and electrolytes, packaged in a 500-ml plastic bag (Fructlact Injection [classified as a drug in Japan]; Otsuka Pharmaceutical, Tokushima, Japan,) and an oral rehydration solution, containing water, glucose, and electrolytes, packaged in a 500-ml plastic bottle (OS-1; Otsuka Pharmaceutical), were used in the study. OS-1 is an oral rehydration solution based on the WHO oral rehydration therapy recommendations [13,14], and its composition is based on the guidelines of the American Academy of Pediatrics (AAP) [15]. In Japan, OS-1 has been approved as a food (classified as a food for special dietary use) and is useful for the provision and maintenance of water and electrolytes in patients with mild to moderate dehydration. In clinical studies, it has been shown to be effective for the provision of water and electrolytes in patients with dehydration, as well as postoperative patients [16,17]. The compositions of these study solutions are shown in Table 1.

The schedule of the study protocol is shown in Fig. 1. Patients consumed a standard diet at 1800 hours on the

Table 1. Compositions of oral rehydration solution and intravenous maintenance electrolyte solution

	Oral rehydration solution (OS-1)	Intravenous maintenance electrolyte solution (Fructlact Injection; Otsuka Pharmaceutical, Tokushima, Japan)
Volume (ml)	500	500
Energy (kcal)	50	54
Carbohydrate (%)	2.5 (glucose 1.8)	2.7 (fructose)
Electrolytes ($mEq \cdot l^{-1}$)		
Sodium (Na^+)	50	50
Potassium (K^+)	20	20
Magnesium (Mg^{2+})	2	—
Lactate	31	20
Chloride (Cl^-)	50	50
Phosphorus ($mmol \cdot l^{-1}$)	2	—
pH	3.9	4.8
Osmolarity	Approx. 270 $mOsm \cdot l^{-1}$	Approx. 290 $mOsm \cdot l^{-1}$

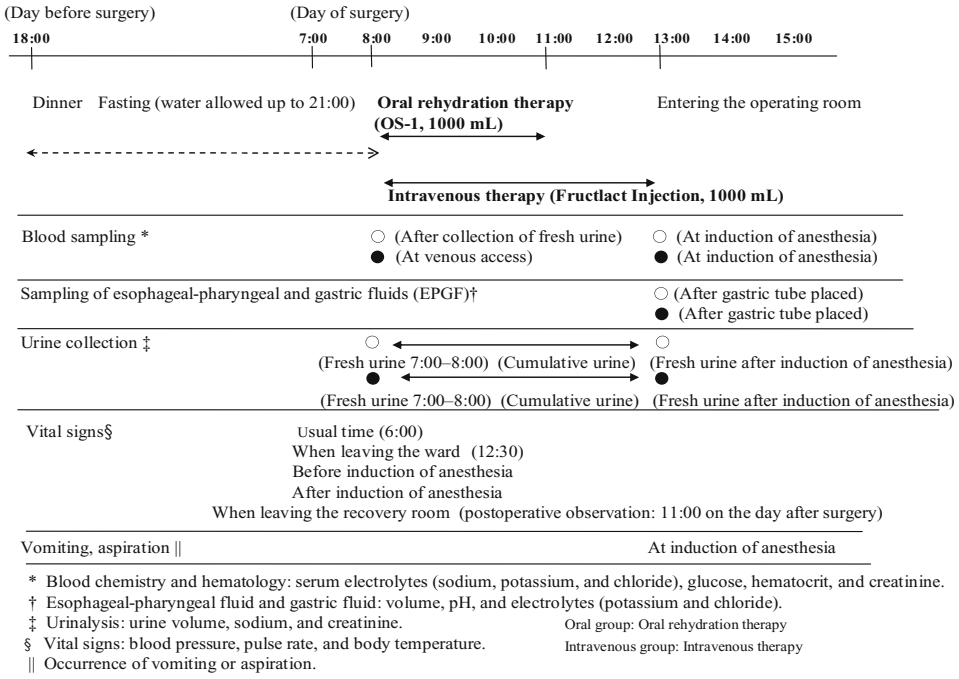


Fig. 1. Schedule of the study and laboratory examinations in the oral (*open circles*) and intravenous (*closed circles*) groups. *Fructlact Injection* (Otsuka Pharmaceutical, Tokushima, Japan). *OS-1*, oral rehydration solution (Otsuka Pharmaceutical)

day before surgery and subsequently fasted (with water permitted until 2100 hours). At 0800 hours on the day of surgery, blood and urine were sampled as before-administration data (Fig. 1). Then the patients in the intravenous group received 1000 ml of the intravenous maintenance electrolyte solution at a rate of 200 ml·h^{-1} given over a 5-h period until entry to the operating room. The patients in the oral group consumed 1000 ml of the oral rehydration solution at a rate of 333 ml·h^{-1} from 0800 hours to 1100 hours. With regard to the administration dose, 1000 ml was selected for both groups, based on the volume of rehydration required for a period of about 12 h in healthy subjects weighing 50 kg, as calculated by the 4:2:1 rule [18]. In both groups, there was no restriction of activity in the ward. With regard to environmental conditions, room temperature was maintained at around 24°C.

The patients were not premedicated and they walked into the operating room. Anesthesia was induced with propofol (1.5 mg·kg^{-1}), fentanyl citrate (2.0 µg·kg^{-1}), and vecuronium bromide (0.1 mg·kg^{-1}). A laryngeal mask (Proseal #3; Laryngeal Mask Company, Henley-on-Thames, UK) was used to secure the airway. Blood and urine were sampled as after-administration data (Fig. 1) within 3 min after the induction of anesthesia, and the volume of intravenous solution administered during that period was less than 10 ml.

A gastric tube (14-Fr, Terumo, Tokyo, Japan) was inserted 75 cm from the tip of the drain tube of the laryngeal mask to sample gastric fluid. The tube was then pulled back to 45 cm from the tip of the drain tube to sample esophageal fluid. This procedure was repeated three times, and the gastric tube was then pulled back into the pharynx to sample pharyngeal fluid. Sampling of esophageal-pharyngeal fluid and gastric fluid (EPGF) was conducted by the same person.

The examination and observation parameters and schedules are shown in Fig. 1. After the surgery, patients were surveyed by a questionnaire about their satisfaction with the fluid therapy. We compared the incidence of vomiting and aspiration at the time of induction of anesthesia between the two groups, and EPGF was compared with regard to volume and composition. Pulmonary aspiration was examined by monitoring oxygenation (using a pulse oximeter) and chest X-rays the day after surgery. Silent regurgitation was not examined. For the analysis of the composition of EPGF, the concentrations of chloride and potassium were assessed as indices of the presence of residual oral rehydration solution. The sodium concentration was not assessed because its composition is similar in gastric fluid and the oral rehydration solution. The effects of the provision of water, electrolytes, and carbohydrates were mainly assessed by evaluating changes in clinical laboratory data. The changes in serum electrolyte (sodium, potassium, and chloride), glucose, creatinine, and hematocrit values, as well as urinary values (preoperative urine volumes, sodium, and creatinine), were compared between the two groups. In order to estimate renal blood flow, the fractional excretion of sodium (FENa) and the change in FENa (ΔFENa) following rehydration were compared between the groups. Blood pressure, pulse rate, and body temperature at 0600 hours and 1230 hours (when moving from the ward to the

operating room) on the day of surgery, before and after induction of anesthesia, and at 1100 hours on the day after surgery were compared between the groups. Blood pressure and pulse rate were measured at the upper arm bound with a cuff, using a bedside monitor (BSM-2301; Nihon Koden, Tokyo, Japan). Body temperature was measured at the right axilla, using an electronic thermometer (ET-C202P01; Terumo).

In addition to the above efficacy assessment based on the results of clinical laboratory data, the incidence rates of a feeling of hunger, dry mouth, and a feeling of restriction in physical activity, surveyed using the questionnaire given to the patients after the surgery, were compared between the two groups to assess the patients' satisfaction with the fluid therapy.

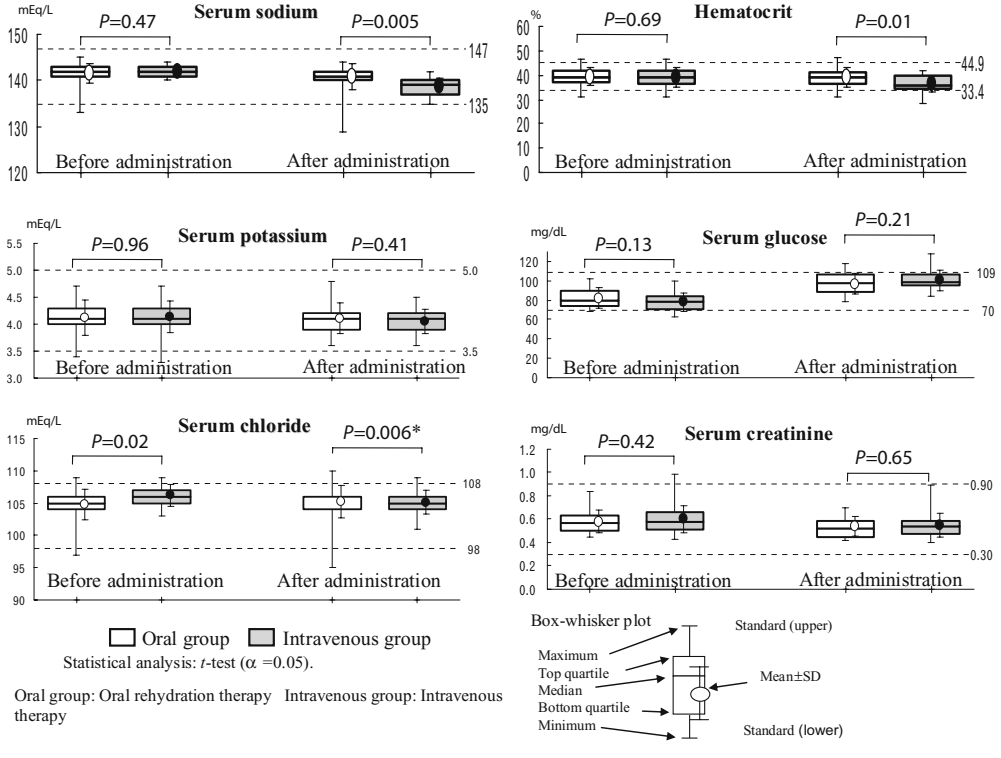
The serum electrolyte and glucose concentrations, urine, and EPGF were measured with an automatic analyzer (Hitachi 7170S; Hitachi High-Technologies, Tokyo, Japan), blood cell counts were measured with an automatic blood cell analyzer (Sysmex XE-2100; Sysmex TMC, Kobe, Japan), and pH was measured with a pH meter (B-211; Horiba, Kyoto, Japan).

Statistical analysis

The incidence rates of vomiting and aspiration were analyzed using the χ^2 test (two-sided at $\alpha = 0.05$). Descriptive statistics were obtained for the volume and composition of EPGF in each group and analyzed using the Wilcoxon test (two-sided at $\alpha = 0.05$). Descriptive statistics for serum electrolytes (sodium, potassium, and chloride), serum glucose, serum creatinine, hematocrit, urine volume, urinary sodium, and urinary creatinine were analyzed using the unpaired *t*-test (two-sided at $\alpha = 0.05$). When differences in pretreatment values were observed between the groups (two-sided at $\alpha = 0.05$), the post-treatment values were adjusted (tested for least square means of post-treatment values using pretreatment values as covariates), including the pretreatment values in the analysis model (two-sided at $\alpha = 0.05$). With regard to vital signs, descriptive statistics were obtained for each group at each measurement time point and analyzed for differences in mean values over time using marginal models [19]. FENa values were analyzed using the Wilcoxon test (two-sided at $\alpha = 0.05$). Parameters for the assessment of patient satisfaction were analyzed using the χ^2 test (two-sided at $\alpha = 0.05$). For statistical analysis, a software package (Release 8.2 TS Level 02M0; SAS Institute Japan, Tokyo, Japan) was used.

Results

No significant differences were observed for age, body weight, height, primary disease, ASA physical status, or surgical procedure between the two groups (Table 2). There were no differences between the two groups in the pretreatment laboratory data, except for serum chloride (Fig. 2). The concomitant medications of the



Oral group: Oral rehydration therapy Intravenous group: Intravenous therapy

Fig. 2. Serum electrolyte (sodium, potassium, and chloride), hematocrit, serum glucose, and serum creatinine values. *$P = 0.006$ was obtained from analysis adjusted by including pretreatment values in the analysis model

Table 2. Baseline characteristics of patients

	Oral group	Intravenous group	Statistical analysis[a] *P* value
Number of patients, female	25	25	
Age (years)			
≥20, <40	3	0	*P* = 0.29
≥40, <60	12	15	
≥60, <80	10	10	
≥80	0	0	
Mean ± SD	55.8 ± 11.4	57.3 ± 10.0	
Body weight (kg)			
<50	4	5	*P* = 1.00
≥50, <60	14	14	
≥60, <70	7	6	
Mean ± SD	56.3 ± 6.6	54.8 ± 7.1	
Height (cm)			
<150	3	3	*P* = 0.44
≥150, <160	18	14	
≥160, <170	4	8	
Mean ±SD	155.0 ± 4.5	156.3 ± 6.7	
Diagnosis			
Breast cancer	25	25	
Other	0	0	
ASA physical status classification			
ASA I	18	23	*P* = 0.14
ASA II	7	2	
Surgical procedure			
Mastectomy	2	4	*P* = 0.67
Conservative	23	21	

The oral group received oral rehydration therapy and the intravenous group received an intravenous maintenance electrolyte solution
ASA, American Society of Anesthesiologists
[a] Fisher's exact test (α = 0.15)

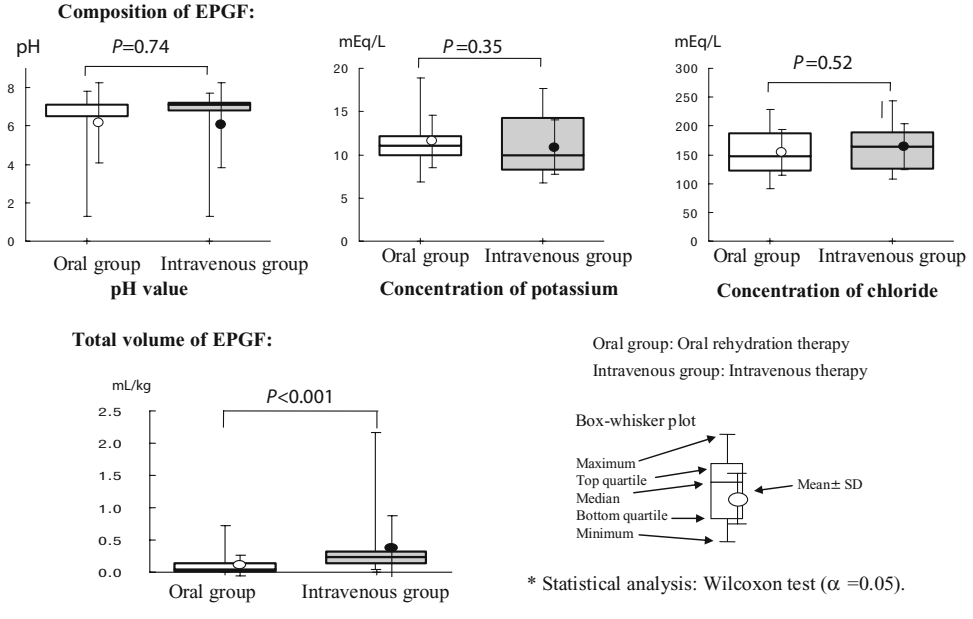


Fig. 3. Composition and total volume of esophageal-pharyngeal fluid and gastric fluid (*EPGF*)

patients were similar, and no diuretics were used. Creatinine clearance values for 24 h were within normal limits. Overall, the baseline characteristics of the two groups showed no differences that would affect the interpretation of the study results.

Events such as vomiting and aspiration associated with the induction of general anesthesia were not observed. Figure 3 shows the results for EPGF data. The volume of EPGF was significantly smaller in the oral group (6 ± 9 ml in the oral group and 22 ± 31 ml in

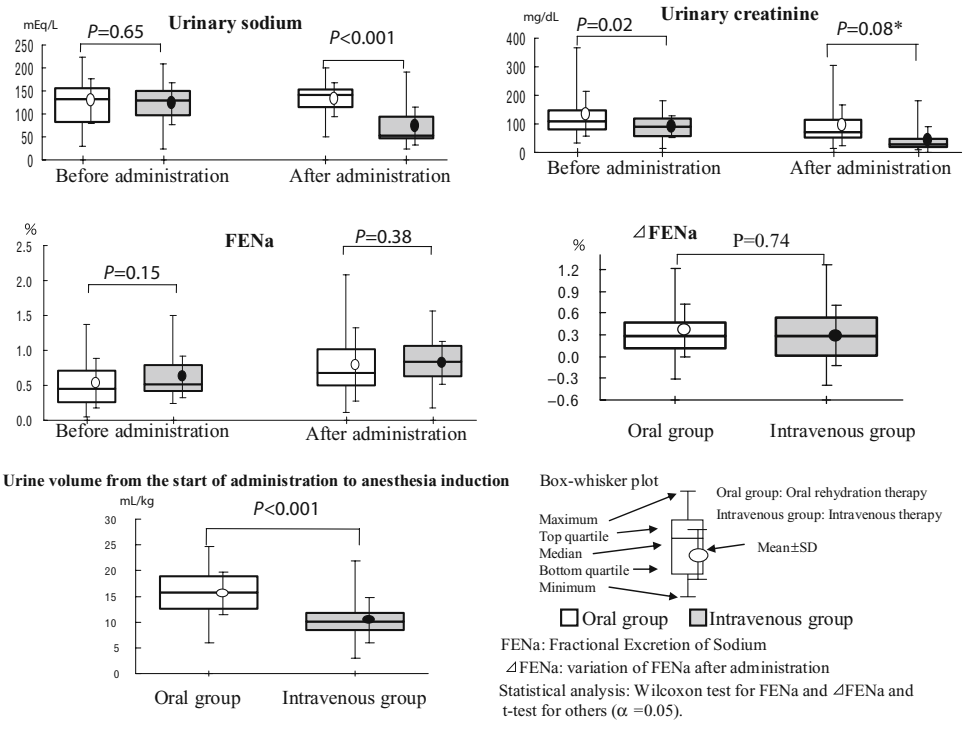


Fig. 4. Urinary sodium, creatinine, FENa, ΔFENa, and urine volume (from the start of rehydration to induction of anesthesia). Urinary sodium excretion was 117.9 ± 51.2 mEq in the oral group and 36.8 ± 18.0 mEq in the intravenous group. *$P = 0.08$ was obtained from analysis adjusted by including pretreatment values in the analysis model

the intravenous group; $P < 0.001$, expressed as 0.1 ± 0.2 ml·kg^{-1} in the oral group and 0.4 ± 0.5 ml·kg^{-1} in the intravenous group; $P < 0.001$). The maximum volume of EPGF was 42 ml in the oral group and 130 ml in the intravenous group, and no difference in the composition of the fluids was observed between the two groups. Based on the electrolyte concentrations and pH values, the sampled EPGF in the oral group appeared to be a mixture of gastric fluid and pharyngeal fluid.

The laboratory data are shown in Figs. 2 and 4. After treatment (rehydration), the serum concentration of sodium and the hematocrit value, which were similar in the two groups before treatment, were reduced in the intravenous group (sodium, 140.8 ± 2.9 mEq·l^{-1} in the oral group and 138.7 ± 1.9 mEq·l^{-1} in the intravenous group; $P = 0.005$; hematocrit, 39.03 ± 4.16 % in the oral group and 36.15 ± 3.41% in the intravenous group; $P = 0.01$). The serum concentration of chloride after treatment was similar in the two groups (105.2 ± 2.6 mEq·l^{-1} in the oral group and 105.2 ± 1.8 mEq·l^{-1} in the intravenous group), but a significant difference was observed ($P = 0.006$) when adjusted with pretreatment values (tested for least square means of post-treatment values using pretreatment values as covariates). No significant differences were observed in serum creatinine and glucose values following treatment. The urinary concentration of sodium following treatment was significantly higher in the oral group (132 ± 36 mEq·l^{-1} in the oral group and 74 ± 42 mEq·l^{-1} in the intravenous group; $P < 0.001$), and urine volume was also significantly larger in the oral group (864.9 ± 211.5 ml in the oral group and 561.5 ± 216.0 ml in the intravenous group; $P < 0.001$, expressed as 15.6 ± 4.2 ml·kg^{-1} in the oral group and 10.4 ± 4.4 ml·kg^{-1} in the intravenous group; $P < 0.001$: urinary sodium excretion was 117.9 ± 51.2 mEq in the oral group and 36.8 ± 18.0 mEq in the intravenous group). FENa was increased in both groups following treatment (0.8 ± 0.5 in the oral group and 0.8 ± 0.3 in the intravenous group) and ΔFENa showed no significant difference between the groups. With regard to vital signs, blood pressure (systolic/diastolic) and pulse rate were not significantly different between the groups. There was a significant difference in body temperature between the groups ($P = 0.01$).

The questions and answers in the questionnaire survey are shown in Table 3. Answers were obtained from all 50 patients (100% response rate). Fewer patients in the oral group reported a feeling of hunger, dry mouth, and restriction in physical activity while waiting for surgery ($P = 0.04$, $P = 0.001$, and $P < 0.001$, respectively). Favorable results (i.e., favorable responses) were obtained in the oral group.

No adverse events or adverse reactions such as vomiting and pulmonary aspiration were observed in either of the groups.

Discussion

We considered that an oral rehydration solution might be effective for the preoperative fluid and electrolyte management of surgical patients who may develop

Table 3. Patient satisfaction (Q & A) with the therapy (oral rehydration therapy or intravenous therapy)

Questions	Groups	Answers: Number and % of patients	Statistical analysis[a] *P* value
Q 1 Did you feel hungry before surgery? (feeling of hunger)	Oral group	Yes 5 (20%) No 20 (80%)	$P = 0.04$
	Intravenous group	Yes 12 (48%) No 12 (48%) Difficult to answer 1 (4%)	
Q 2 Did you have a dry mouth before surgery? (dry mouth)	Oral group	Yes 4 (16%) No 21 (84%)	$P = 0.001$
	Intravenous group	Yes 16 (64%) No 9 (36%)	
Q 3 Did you feel restriction in physical activity during the therapy? (feeling of restriction in physical activity)	Oral group	Yes 1 (4%) No 24 (96%)	$P < 0.001$
	Intravenous group	Yes 16 (64%) No 9 (36%)	

Oral group, 25 patients; intravenous group, 25 patients
Q & A, question and answer
[a] χ^2 test, $\alpha = 0.05$

dehydration, and we investigated the safety and effectiveness of oral rehydration therapy as compared with intravenous therapy.

Although no case of aspiration or vomiting at induction of general anesthesia was observed in the present study, there were not enough cases from which to draw valid conclusions about the risk of gastric regurgitation or pulmonary aspiration with preoperative oral rehydration. It has been reported that there is a risk of aspiration if the volume of the gastric contents exceeds 200 ml at the time of induction of anesthesia [7], but in the present study, no patient in either group was found to have a volume of gastric contents greater than 200 ml as the total volume of EPGF. It was observed that the total EPGF volume was smaller in the oral group than in the intravenous group, and the reason for this finding may be due to the osmolarity, caloric density, and pH of the administered oral rehydration solution, stimulating gastric motility. The pH value of EPGF was high, which may have been due to contamination by saliva, because the samples also included secretions obtained near the pharynx. With regard to the effectiveness of the oral therapy and intravenous therapy, FENa was assessed as an index reflecting the effect on water supplementation. FENa is a value that indicates the percentage of sodium filtered by the renal glomerular capillaries and may be a sensitive index of the renal blood flow in subjects with normal renal function, such as those enrolled in the present study [20]. In the present study, due to the effect of preoperative fasting from the evening before the day of surgery, many patients showed low FENa, which was increased by rehydration with the study solutions. Following rehydration, the serum sodium and hematocrit were lower in the intravenous group than in the oral group. Considering that the urinary excretion and concentration of sodium were high in the oral group, the difference observed in the serum sodium values between the groups (as well as the difference in hematocrit values) was thought to be related to differences between the groups in the rehydration rates and the times of rehydration. Generally, when the circulating blood volume increases with rehydration, the increase in renal blood flow would be detected by the renal juxtaglomerular cells, and as a result, renin secretion would be suppressed and angiotensin-aldosterone secretion would also be reduced. In the present study, we found that the urine volume and the urinary excretion of sodium were greater in the oral group, and this finding could be interpreted to mean that fluids and electrolytes are more rapidly absorbed from the gastrointestinal tract following bolus feeding than with continuous intravenous administration (as performed in the intravenous group), and consequently renin and aldosterone would have been suppressed in the oral group. However, based on the findings that, after rehydration, the serum concentration of sodium and the hematocrit value were reduced and no significant differences between the two groups were observed in FENa and ΔFENa, blood pressure, and pulse rate, it can be concluded that oral rehydration is effective for water and electrolyte supplementation and maintenance in preoperative patients.

Because the study solution (OS-1) used in the present study contains 2.5% carbohydrate, serum glucose concentrations following treatment were within normal limits. It has been reported that carbohydrate loading before surgery minimizes postoperative insulin resistance and postoperative immune suppression, thus helping to reduce postoperative complications [21,22]; the oral intake of fluids containing an appropriate car-

bohydrate content is therefore considered to be a suitable means of providing a source of carbohydrates.

Finally, with regard to patient satisfaction with the therapy, the patients in the oral group expressed higher satisfaction. As reported by Nygren et al. [23], the preoperative oral provision of carbohydrates helps to alleviate anxiety and also reduces dry mouth and the feeling of hunger. Providing carbohydrates and water orally may have contributed to the higher satisfaction observed in the oral group in the present study.

Conclusions

In the present study, oral rehydration therapy with 1000 ml of solution before surgery was effective for providing fluid and electrolytes, and showed no untoward effects on clinical parameters; the therapy was also favorably accepted by the patients, as judged by factors such as a feeling of hunger, occurrence of dry mouth, and a feeling of restriction of physical activity, as compared to intravenous therapy. These results suggest that oral rehydration therapy is superior to current preoperative intravenous therapy for the provision of water, electrolytes, and carbohydrates, and this oral therapy should be considered as an alternative to the intravenous therapy for the preoperative fluid and electrolyte management of selected surgical patients in whom there is no reason to suspect delayed gastric emptying.

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