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Comparing the Effect of Erythromycin and Ginger Extract on the Gastric Residual Volume in Patients Receiving Enteral Nutrition Order in the Intensive Care Unit

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ABSTRACT

BACKGROUND AND OBJECTIVE: Gastric residual volume is considered as an important parameter for gastric emptying and feeding tolerance. This volume is measured before each time of feeding and it has direct effect on the volume and time of the next feeding. Ginger is one of the medicinal plants that have effect on gastric emptying rate. This study aims to compare the effect of erythromycin and ginger extract on gastric residual volume in patients receiving enteral nutrition order in the intensive care unit.

METHODS: This randomized clinical trial was conducted among 74 patients hospitalized in the intensive care unit. Patients were fed with similar nutrition formula every 3 hours for 24 hours. Before each gavage feeding, the gastric residual volume of patients was aspirated and recorded. The gastric residual volume of 28 patients (more than 200 cc) was allocated to one of the groups of erythromycin (n = 13) and ginger (n = 15). Patients were fed with 2.5 mg/kg erythromycin in 4 divided doses or 2 grams per day ginger extract in 4 divided doses. The gastric residual volume was recorded for 4 consecutive days and the data obtained from the two groups were compared (IRCT: 201505257494N13).

FINDINGS: The mean difference of gastric residual volume in erythromycin group was 111.71±7.04 cc before the intervention and 4 days after that, which was not statistically significant. This difference was 108.61±11.47 cc in ginger group. Results demonstrated that mean gastric residual volume in erythromycin and ginger groups were 98.52±27.88 cc and 95.71±18.91 cc, respectively during the first 4 days and there was not a statistically significant difference between these two groups.

CONCLUSION: Results of the study demonstrated that the effect of ginger is very similar to erythromycin. Therefore, ginger can be a proper substitute for erythromycin to prevent increased gastric residual volume in patients hospitalized in the intensive care unit.

KEY WORDS: *Enteral nutrition, Gastric Lavage, Erythromycin, Ginger, Residual volume, Intensive care unit*.

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Introduction

When oral nutrition is not possible or is inadequate for patients hospitalized in the intensive care unit, nutritional support as an integral part of patient care is crucial for them (1). Early enteral nutrition in patients with critical conditions hospitalized in the intensive care unit is associated with lower prevalence of infections and shorter length of stay at the hospital (2, 3). However, gastrointestinal motility is disrupted in these patients and subsequently, enteral nutrition cannot be tolerated (4).

Delayed gastric emptying puts patients at risk of complications such as vomiting, aspiration and ventilator-associated pneumonia (5-7). Delayed gastric emptying mostly causes enteral nutrition intolerance in 30 to 51% of patients hospitalized in the intensive care unit. Moreover, this delay may increase gastric residual volume in 39% of patients hospitalized in the intensive care unit (8). Increased gastric residual volume may increase the length of stay in the hospital (9,10). Gastric residual volume is considered as an important parameter for gastric emptying and feeding tolerance. The volume is measured before each feeding and it directly affects the volume and the time of next feeding (11). Volumes more than 200–250 cc are considered significant for patients hospitalized in the intensive care unit (12).

Various strategies have been proposed for reducing gastric residual volume in patients hospitalized in the intensive care unit. One of these strategies is post-pyloric nutrition and another one is the use of bowel function enhancement drugs such as metoclopramide, domperidone (13), erythromycin (14) and cisapride (16,15). Considering the technical problems associated with post-pyloric catheter placement and the mortality caused by infectious complications of intravenous feeding, treatment with prokinetic agents as first-line therapy is a priority (17). Prokinetic agents increase the contraction of the gastric antrum, correction of gastric dysrhythmias and improve the coordination between the antrum and duodenum and as a result improves gastric motility (14).

When some motilin receptor agonists such as erythromycin are fed orally, gastric emptying increases and the symptoms are improved (4). Erythromycin is a motilin receptor agonist that pushes the stomach contents through the aforementioned mechanisms. As an antibiotic, erythromycin is also accompanied by several complications (15). Since patient's safety is the highest priority of nursing care, substituting these medicines with a safe medicine with similar functionality seems necessary. One of the herbal factors that affects gastric emptying rate is ginger. Ginger, scientifically known as Zingiber officinale Roscoe, is recognized in the pharmacopoeia of many countries including Iran (5). There are active compounds in ginger that affect digestive system. These compounds include Shogaols volatile oil, which has anti-nausea properties and Gingerols volatile oil, which increases bowel movements (16). These two compounds can accelerate gastric emptying (18). Unlike most anti-nausea drugs that work by affecting the central nervous system, the anti-nausea effect of ginger is the result of local function on the digestive system (19).

Considering that a limited number of studies have been dedicated to the effects of ginger on gastric emptying rate and decreased gastric residual volume (8,20) and since no comparison has been made between ginger and erythromycin, which is used as a routine medication in some health centers to decrease the gastric residual volume in patients hospitalized in the intensive care unit (21), the present study was conducted to compare the effect of erythromycin and ginger extract on gastric residual volume in patients receiving enteral nutrition order in the intensive care unit. In this way, we can find an appropriate and safe substitute to decrease gastric residual volume.

Methods

This single-blinded, randomized, controlled clinical trial was carried out after receiving permission from the ethics committee of Mazandaran University of Medical Sciences (IR.MAZUMS.REC.95.1503) and the clinical trial registration number IRCT: 201505257494N13. Convenience sampling was performed among 74 patients under mechanical ventilation, hospitalized in the intensive care unit of an Educational Hospital in Babol based on inclusion and exclusion criteria. Patients aged 18 to 75 years old (22), feeding through a nasogastric tube, hospitalized because of internal and neurological diseases (since the study was conducted in the internal intensive care unit), lack of pregnancy and breastfeeding, being under mechanical ventilation, no history of gallstones (because of the stone making properties of ginger) and over 24 hours of admission to the intensive care unit (based on clinical guidelines of nutrition in patients) (23) were included in the study. Patients with any type

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of food allergy noted in their medical record and allergy to medication during the study, use of drugs that enhance bowel movements, receiving corticosteroids and immunosuppressive medications, malignancies, diseases and gastrointestinal ulcers (20,24), active bleeding and patients at risk of bleeding due to the effects of ginger in inhibiting the synthesis of thromboxane (25), occurrence of intestinal paralysis and use of laxatives were excluded from the study. After selecting samples, written informed consents were obtained from patients or their families.

Then, the social, demographic and medical information of patients was recorded and the necessary descriptions for the procedure were presented to the patients or their families. The patients had nasogastric or orogastric tube before admission to the intensive care unit. In cases where the patients did not have nasogastric or orogastric tube, the tube was placed in the absence of contraindications. After 24 hours of NPO (5), enteral nutrition started for 74 patients. Since 25 Kcal/kg is accepted as an average standard, the nutritional support was done based on 20 – 30 Kcal/kg energy (21). Since hospital nutritional formulas have 1 Kcal/cc energy, nutrition started with 30 cc volume every three hours and gradually increased to 250 – 300 cc every three hours depending on patient's tolerance. The amount of energy received was calculated to be 25 kcal per kilogram of body weight (20). The patients in both groups were gavage fed with similar nutritional formula in 7 divided doses in 24 hours every 3 hours. The patient's bed had a 30 – 45 degrees angle to reduce the risk of aspiration (5,26).

All patients had nasogastric or orogastric tube, 16 FR and gavage feeding was done using the gravity and without any pump. Before each session of gavage feeding, the gastric residual volume was aspirated and recorded with graduated cylinder. If the gastric residual volume was less than or equal to 200 cc, the aspirated volume was returned and nutrition continued. If the gastric residual volume was more than 200 cc, 200 cc of the aspirated volume was returned and the rest was thrown away (21). The feeding tube was washed with 30 cc water and one hour after the process was stopped, the residual volume was examined again (5). If the patient's lavage was more than 200 cc again, the patient was placed in one of the groups of erythromycin and ginger through random allocation method. Patients received 2.5 mg/kg erythromycin syrup (Tehran Chemical Co., Iran) in four divided doses (27) or 2 g ginger extract (28) (Aromin – Yas Daroo Co., Iran) (every 120 drops of ginger extract equals 1 g)(29). Overall, patients received 8 g (24 cc) ginger in 24 hours. Medications were administered in four divided doses. Erythromycin syrup or ginger extract were administered every 6 hours (at 5, 11, 17, and 23) up to 4 days. To synchronize the volume of the received drug, the first group received 2.5 mg/kg erythromycin syrup (equivalent to 5 cc drug) plus 25 cc water; a total volume of 30 cc. The second group received 17 cc ginger extract plus 13 cc water; a total volume of 30 cc.

According to the instructions, the water used for washing the nutritional tube can be 20 to 100 cc (5, 26,30); 30 cc water was used in the present study. When the gastric residual volume decreased up to less than 200 cc in both groups, gavage feeding was increased to reach the target level (250 – 300 cc every 3 hours) and after this step, erythromycin and ginger extract were stopped. It is worth noting that whenever the gastric residual volume exceeded 500 cc, the patient experienced NPO (31), was excluded from the study and was seen by a gastroenterologist. For the study to be single-blind, the patients were not informed of the type of medication they received (erythromycin or ginger).

The collected data were analyzed and compared using SPSS Ver. 21 and Kolmogorov, x2 and independent t-test. The gastric residual volume was analyzed using descriptive statistics (mean ± SD) and the two groups were compared using one-way repeated measures ANOVA within 4 days. To compare the duration of gastric residual volume reduction to normal level, the log-rank test was used and $p<0.05$ was considered significant.

Results

Of 74 studied patients, 40 patients were male (54.8%) and 34 patients were female (45.2%). Of 28 patients undergoing intervention, 15 patients were in erythromycin group (53.3%), out of which, 8 patients were male (53.3%) and 7 patients were female (46.7%). Of 13 patients in ginger group, 9 patients were male (62.9%) and 4 patients were female (30.8%). The mean age of patients was 56.24±14.12 years (ranging from 23 to 75 years old). Of the 74 patients participating in the study, the gastric residual volume did not increase in 46 patients, while 28 patients experienced increased gastric residual volume and were randomly divided into two groups of

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erythromycin (15 patients) and ginger (13 patients). The mean age of these 28 patients was 59.24±13.05 years and there was not a statistically significant difference between the two groups in terms of age. Moreover, the test results of these two groups were similar in terms of sex. Of 74 studied patients, 61 patients (71.8%) had an underlying disease and 13 patients (28.2%) lacked an underlying disease. In erythromycin group, 3 patients (20%) lacked an underlying disease and 12 patients (80%) had an underlying disease. In ginger group, 3 patients (23.1%) lacked an underlying disease and 10 patients (76.9%) had an underlying disease. The most prevalent underlying disease in erythromycin group was cardiovascular disease, while diabetes was the most prevalent underlying disease in ginger group and control group. There was no significant difference between the groups in term of underlying disease. Patients' gastric residual volume was measured and recorded. At the beginning of intervention, the mean gastric residual volume was 210.23±11.87 cc in erythromycin group and 204.31±16.41 cc in ginger group and there was no significant difference between the two groups in term of mean gastric residual volume. The gastric residual volume was also measured and recorded every 3 hours during intervention. After 4 days of receiving erythromycin or ginger extract, the mean gastric residual volume was 98.52±18.91 cc in erythromycin group and 95.71±27.88 cc in ginger group. There was no significant difference between the two groups in term of mean gastric residual volume after 4 days (Fig 1). The difference between mean gastric residual volume before the intervention and four days after intervention was 111.71 ± 7.04 cc in erythromycin group and 108.61 ± 11.47 cc in ginger group, which was not significant in any of the groups. Results of the present study demonstrated that the average time for gastric residual volume to reach an acceptable level (less than 200 cc) was 6.8 days in erythromycin group and 7.46 days in ginger group and the difference was not statistically significant.

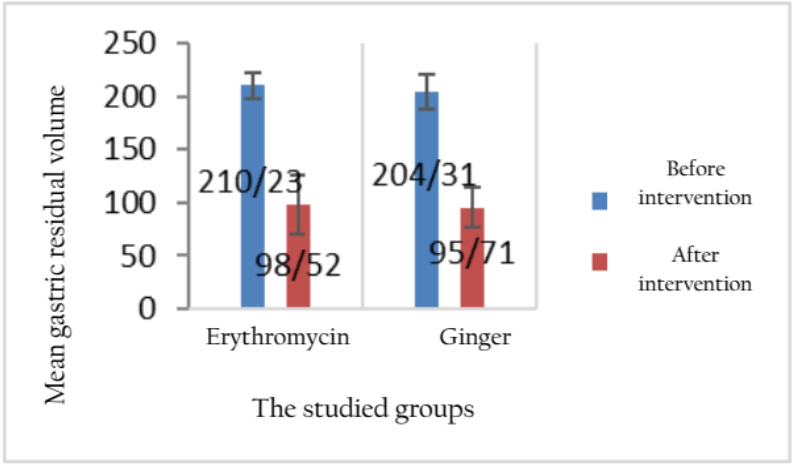

Figure 1. Comparison of mean gastric residual volume (cc) before the intervention and four days after intervention in the groups receiving erythromycin and ginger

Discussion

Results of this study demonstrated that similar to erythromycin, ginger extract decreases gastric residual volume and the difference between these two is not statistically significant. Similar to the results of the present study, a study demonstrated that erythromycin decreases gastric residual volume and increases nutritional tolerance (31). In another study, the preventive effect of oral erythromycin on milk tolerance in preterm infants indicated that low-dose erythromycin (2.5 mg/kg every 6 hours) increases gastric peristalsis and thus decreases gastric residual volume (27). Result of another study demonstrated that low-dose erythromycin may increase the chance of successful enteral nutrition in patients hospitalized in the intensive care unit (32). Results of a study in Iran demonstrated that ginger extract decreases gastric residual volume in patients hospitalized in the intensive care unit compared with the placebo-receiving group (8). Another study demonstrated that ginger decreases gastric residual volume in healthy people (33). Results of a study indicated that enteral

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feeding with ginger extract decreases gastric emptying duration and decreases the incidence of ventilator-associated pneumonia (20). Moreover, results of a study by Montazeri et al. proved that the use of ginger is effective in preventing nausea after surgery and can be used as a safe anti-nausea medication after surgery (34). Another study demonstrated an increase in gastric emptying after using ginger (35). Results of investigating the prokinetic effect of hydroalcoholic ginger extract on rat stomach indicated that ginger extract causes prokinetic activity in rat stomach (36). Since increased prokinetic activity is associated with faster gastric emptying, the results of this study are consistent with the present study.

One of the limitations of the present study was the short period of the study. In addition, due to the special color of erythromycin syrup, having a double-blind study was not possible. Moreover, since the environment of the study was limited to the internal intensive care unit, we could not generalize the results to trauma patients. The present study demonstrated that similar to erythromycin, ginger extract can decrease the gastric residual volume in patients under mechanical ventilation, hospitalized in the intensive care unit. Since there is no significant difference between erythromycin and ginger extract in decreasing the gastric residual volume and since feeding intolerance and malnutrition caused by this problem are quite common in patients hospitalized in the intensive care unit, the usual dose of ginger extract (which was reported to be without side effects in this study and other studies) is suggested to be used to improve gastrointestinal motility and nutritional tolerance in these patients. By improving the nutrition process in these patients, we can prevent the complications of malnutrition caused by increased gastric residual volume and nutritional intolerance. In addition, decreasing the gastric residual volume decreases the risk of aspiration of gastric contents and as a result, the length of stay in the intensive care unit decreases. It is suggested that the effect of ginger on nutritional adequacy in patients hospitalized in the intensive care unit be investigated in future studies. Moreover, future studies can analyze the comparative effect of ginger extract and ampoule of metoclopramide on the gastric residual volume in patients hospitalized in the intensive care unit.

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