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Randomized Controlled Trial

Effects of a novel method for enteral nutrition infusion involving a viscosity-regulating pectin solution: A multicenter randomized controlled trial

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SUMMARY

Background & Aims: The initial complications associated with infusion of enteral nutrition (EN) for clinical and nutritional care are vomiting, aspiration pneumonia, and diarrhea. There are many recommendations to prevent these complications. A novel method involving a viscosity-regulating pectin solution has been demonstrated. In Japan, this method along with the other so-called "semi-solid EN" approaches has been widely used in practice. However, there has been no randomized clinical trial to prove the efficiency and safety of a viscosity-regulating pectin solution in EN management. Therefore, we planned and initiated a multicenter randomized controlled trial to determine the efficiency and safety.
Methods: This study included 34 patients from 7 medical institutions who participated. Institutional review board (IRB) approval was obtained from all participating institutions. Patients who required EN management were enrolled and randomly assigned to the viscosity regulation of enteral feeding (VREF) group and control group. The VREF group (n = 15) was managed with the addition of a viscosity-regulating pectin solution. The control group (n = 12) was managed with conventional EN administration, usually in a gradual step-up method. Daily clinical symptoms of pneumonia, fever, vomiting, and diarrhea; defecation frequency; and stool form were observed in the 2 week trial period. The dose of EN and duration of infusion were also examined.
Results: A favorable trend for clinical symptoms was noticed in the VREF group. No significant differences were observed in episodes of pneumonia, fever, vomiting, and diarrhea between the 2 groups. An apparent reduction in infusion duration and hardening of stool form were noted in the VREF group.
Conclusions: The novel method involving a viscosity-regulating pectin solution with EN administration can be clinically performed safely and efficiently, similar to the conventional method. Moreover, there were benefits, such as improvement in stool form, a short time for EN infusion, and a reduction in vomiting episodes, with the use of the novel method. This indicates some potential advantages in the quality of life among patients receiving this novel method.

Abbreviations: AC, arm circumference; Alb, albumin; BMI, body mass index; CRP, C-reactive protein; EN, enteral nutrition; GER, gastroesophageal reflux; IRB, institutional review board; LM, low methoxide; QOL, quality of life; TSF, triceps skinfolds; TTR, transthyretin; VREF, viscosity regulation of enteral feeding.

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1. Introduction

The initial complications associated with infusion of enteral nutrition (EN) for clinical and nutritional care are aspiration pneumonia, vomiting that is often caused by gastroesophageal reflux (GER), and diarrhea associated with the osmolality of the EN solution and/or infusion speed (time). The EN solution delivered via bolus into the stomach through feeding tubes often causes vomiting and aspiration of gastric contents into the lungs, resulting in fatal pneumonia. Very high osmolality of the EN solution or very quick infusion of the solution into the intestine may cause diarrhea, resulting in malabsorption [1]. Studies in healthy volunteers and clinical case reports have mentioned that aspiration pneumonia can be prevented and that GER can be controlled by elevating the viscosity of the EN solution inside the stomach using a solution composed of pectin [2–4]. However, there have been no randomized clinical trials to prove the effects of using a viscosity-regulating pectin solution in EN management.

The idea of changing the viscosity of the EN formula inside the intestinal tract after infusion though a small bore feeding tube was introduced in the late 1990s in Japan [5]. There was a need for an EN formula and/or oral nutritional supplement that would not cause aspiration pneumonia in patients who were undergoing rehabilitation for dysphagia associated with their underlying disease. The problems with EN infusion were first thought to be associated with the morphology of the EN formula. The liquid EN formula would pose a risk for aspiration when passing though the throat of a patient with dysphagia. Therefore, the characterization of low methoxide (LM) pectin was used. LM pectin in the presence of ionized calcium elevates the viscosity of EN solution. Elevation of the viscosity of EN solution is anticipated to prevent aspiration and reflux of gastric content. Inada et al. reported experiencing an improvement in the incidence of aspiration pneumonia by using LM pectin solution (REF-P1) [3,4]. Additional benefits, such as prevention of GER along with stabilization of the blood sugar value, delay of the gastric emptying time, and prevention of aspiration pneumonia, with the use of LM pectin have been demonstrated [2,6–9]. Some clinical case reports support the use of so called “semi-solid EN” that is used in Japan [10–12]. The use of viscosity-regulating pectin solution, which is classified as a semi-solid EN method, allows infusion of EN through thin bore feeding tubes, allows administration of EN without the use of the EN pump system, and has gradually became popular as a practical management approach for the administration of EN in Japan.

Considering that the efficiency and safety of a viscosity-regulating pectin solution are unclear, we planned and initiated a multicenter randomized controlled trial to clarify the clinical efficiency and safety of a viscosity-regulating pectin solution in EN management.

2. Materials and methods

2.1. Ethical approval

This study was registered in the Center for Clinical Trials, Japan Medical Association (ID: JMA-IIA00085), and the study protocol was approved by the institutional review board (IRB) of The Jikei University School of Medicine and 6 other participating institutions (Tsuchida Hospital, Saiseikai Fukuoka General Hospital, Ushiku Aiwa General Hospital, Ota Hospital, Chiba Kashiwa Tanaka Hospital, and Shin-Yurigaoka General Hospital). All study procedures were performed in accordance with the Declaration of Helsinki. All patients provided written informed consent.

2.2. Study design

This VREF (Viscosity Regulation of Enteral Feeding) study was an open, multicenter, block randomized (four patients per block, and a block was allocated to a center one by one) study with a parallel group design in a clinical trial center.

2.3. Patients

Eligible patients (aged ≥20 years) were those who needed nutritional therapy intervention because oral intake was not possible for any reason. Ongoing or planned EN management by percutaneous endoscopic gastrostomy, percutaneous transesophageal gastro-tubing, or a nasogastric tube, was considered, although the site of administration was limited to the stomach. Only planned nutrition management for more than 14 days was considered.

The exclusion criteria were inability to receive EN management because of conditions that cause low digestion and absorption function, such as inflammatory bowel disease, fever (temperature ≥37.5 °C), obvious infection, severe complications (heart disease, pulmonary fibrosis/interstitial pneumonia, bleeding tendency, uncontrolled hypertension, diabetes, etc.), administration of drugs with side effects of diarrhea and vomiting, presence of diarrhea and vomiting owing to an underlying disease, diagnosis of GER before the start of the study, pneumonia, and diarrhea at the start of the study. Additionally, patients who were determined to be unsuitable for the study by the attending physician were excluded.

2.4. Materials

A viscosity-regulating pectin solution (REF-P1®; Kewpie Corporation, Tokyo, Japan), which contained 1.4 g fiber, 120 mg sodium, and 87.8 g water per bag (90 g, 5 kcal), was used.

Pectin is a high molecular polysaccharide extracted from an edible plant (dietary fiber), usually citrus fruits and apples. The type of pectin contained in REF-P1 is LM pectin, which has less than 50% of the carboxyl groups showing methyl esterification, with the characteristics of forming a gel. It thickens the viscosity of a solution and acts as a viscosity-regulating solution. When it is mixed with EN containing liberated calcium ions, the viscosity rises to 1000–2000 mPa s to form a thick gel solution equivalent to the viscosity of tomato ketchup. REF-P1 itself has a viscosity of only 10 mPa s, enabling easy administration through a small-bore 8-Fr. enteral feeding tube using a syringe.

The liquid EN diet (K-LEC®; Kewpie Corporation) used in this study is a conventional and commonly used commercial product in Japan, containing 3.5 g protein, 3.3 g fat, 14.1 g carbohydrate, and other essential macro- and micronutrients per 100 mL (100 kcal). The viscosity of this EN solution is 5 mPa s at room temperature. One serving of this EN solution is 400 ml and is known to contain liberated calcium ions that can bind to LM pectin. When this solution is mixed with one packet of REF-P1 (90 g), the viscosity increases to a semi-solid form of EN (mean viscosity, 1000 mPa s). All viscosity values were measured using a Brookfield Viscometer (type B; Toki Sangyo Co., Ltd, Tokyo, Japan) device at a rotation of 20 rpm at 23 °C ± 2 °C.

2.5. Study protocol

Patients were randomly assigned to the following 2 groups: the viscosity-regulating pectin solution group (VREF group) and the conventional enteral nutrition group (control group).

Total required calories (maintenance calories) for each patient were administered via the liquid diet from the starting date of EN in

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