

Investigation of the Frequency of Fever and Inflammation Responses in Patients Receiving Different Viscosities of Nutrients in a Recuperation Hospital [†]

Masanari TOGO^{*1}, Midori MURAKAMI^{*2}, Natsuki MINAGAWA^{*3}

Abstract:

Patients with suspected aspiration pneumonia, whose oral feeding is restricted, are managed by enteral nutrition. However, enteral nutrition often produces fever or increased inflammation responses. Semi-solid nutrient has been confirmed to prevent fever or inflammation responses. The purpose of the present study is to retrospectively examine the frequency of fever and inflammation responses in older patients in a recuperation hospital in order to determine whether varying the viscosity of nutrients is effective in reducing fever and inflammation responses.

The subjects of this research are twenty-one patients in their mid 70s -80s, receiving treatment in a recuperation hospital. They were divided into three groups. Seven subjects were assigned liquid nutrient (0 millipascal · second (mPa · s) group); seven were given 400 mPa · s of semi-solid nutrient (400 mPa · s group), and seven were administered 2000 mPa · s of semi-solid nutrient (2000 mPa · s group). The physiological (body temperature and number of fever episodes) and biochemical (White blood corpuscle (WBC) and C-reactive protein (CRP)) data were measured in each group.

The resulting data revealed that body temperature, number of fever episodes, WBC, and CRP variations were not significantly different for each group. Therefore, it was determined that administering a low-viscosity of semi-solid nutrient is not effective for improving fever and inflammation responses.

Keywords: *older patient, aspiration pneumonia, enteral nutrition, liquid nutrient, semi-solid nutrient*

[†] This study was conducted in full compliance with the ethical standards of the Helsinki Declaration.

^{*1} Assistant Professor, Food and Nutrition Major, Department of Life Science, Asahikawa University Junior College/ Senior Researcher, Research Organization of Science and Technology, Ritsumeikan University/ Registered Dietitian, Department of Nutrition, Muroran Taiheiyō Hospital

^{*2} Registered Dietitian, Department of Nutrition, Muroran Taiheiyō Hospital

^{*3} Medical Doctor, Minagawa House Call Clinic

E-mail:^{*1} togo@live.asahikawa-u.ac.jp, togo@fc.ritsumei.ac.jp, ma08t.nutrition@gmail.com

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1. Introduction

The rate of deaths from aspiration pneumonia among older patients has been increasing recently. In patients over the age of a 70, about 80% of pneumonia cases have been reported as aspiration type (Teramoto et al., 2008). Aspiration pneumonia is caused by the blockage of airways by food clots, saliva, bacteria, backwash of gastric fluid and gastric acid, and ingested foreign bodies, causing inflammation in the alveoli (Inada, 2001). It has been reported that the probable cause of developing aspiration pneumonia by dysphagia and respiratory disturbance among older patients is weakness of the muscles associated with swallowing and respiration (Maeda et al., 2015). In addition, gastroesophageal reflux of gastric contents has also been shown to lead to the development of aspiration pneumonia (Miyazawa, 2007). Therefore, it is thought that the prevention of symptoms of aspiration pneumonia in older patients can lead to a reduction in the death rate.

Older patients in recuperation hospitals often become unable to eat as a response to symptoms of aspiration pneumonia such as increased fever and inflammation. In recuperation hospitals, when orally fed patients are suspected of aspiration pneumonia due to increased fever and inflammation responses, their food intake is stopped as a specific primary disease treatment. If a patient who repeatedly suffers from increase of fever and inflammation responses is diagnosed as too weak for oral nutrition, their intake method is changed to enteral feeding either by a gastric fistula or an intestinal fistula. However, it is doubtful that selecting a nutritional supplementation method for parenteral intake leads to the prevention of aspiration pneumonia. As recuperation hospitals do not regularly sample patients' blood unless their condition worsens, no comparative study has been conducted on nutritional supplementation methods for elderly patients of recuperation hospitals whose condition is relatively stable.

Our research examines whether enteral feeding for the prevention of aspiration decreases fever and inflammation responses, or not. Our study examines the frequency of fever and inflammation responses in patients receiving oral feeding, and compares them with patients receiving enteral feeding. As a result of enteral feeding, patients had higher body temperatures, more fever episodes, higher white blood cells counts (WBC), and C-reactive protein (CRP) than orally fed patients (Togo et al., 2018). This was because the lengthening of parenteral intake with the cessation of the diet for the purpose of treatment was unable to reduce the fever and inflammation responses, which are symptoms of aspiration pneumonia. Thus enteral feeding is not effective for the prevention and amelioration of aspiration pneumonia, but can be considered to be a factor that increases it. Therefore, long-term enteral feeding is not effective for improving fever and inflammation responses.

On the other hand, enteral feeding with semi-solid nutrients may be able to prevent aspiration and gastroesophageal reflex. Enteral feeding of patients with increased fever and inflammation responses is reported to engender aspiration of saliva secreted from the oropharynx (Marik, 2010) and gastroesophageal reflex (Adachi et al., 2010). Therefore, for enteral nutrition patients regular oral care and regulation by a nutrient injection method are necessary to prevent aspiration pneumonia. The effectiveness of semi-solid nutrients in the prevention of gastroesophageal reflux or diarrhea caused by nutrients was reported (Goda, 2016). Therefore, it is conceivable that semi-solid nutrients have a certain effect in the prevention of aspiration pneumonia. Our study (Togo et al., 2018) on enteral feeding patients included patients feeding on semi-solid nutrients, as it is thought necessary that different methods such as liquid nutrients and semi-solid nutrients could be used retrospectively to examine the frequency of fever and inflammation responses. In addition, it can be said that these

studies can clarify the characteristics of elderly patients in medical care hospitals where few research reports have been conducted, and provide useful data on the effects of long-term use of low-viscosity nutritional supplements. The purpose of the present study is to retrospectively examine the frequency of fever and inflammation responses in older patients receiving a variety of viscosity of nutrients in a recuperation hospital.

2. Method

1) Subjects

Twenty-one elderly patients admitted to recuperation Hospital 'A' participated. Their mean age was: 80.3 ± 6.3 yr; height: 155.5 ± 10.2 cm; weight: 42.9 ± 7.5 kg; BMI : 17.9 ± 3.3 kg/m². The ratio of males to females was 4 to 6. Subjects were randomly selected by a doctor from patients who: 1) Had previously been oral feeding, but who were suspected of having aspiration pneumonia due to an increase of fever and inflammation responses, and had been ingesting by enteral nutrition for more than one year, 2) Were stable in their symptoms, administration details and method of administering nutrients. All patients had been receiving a nutritional supplement of the target viscosity for at least six months, and the effects of long-term nutritional administration were examined. As is typical of elderly patients in recuperation hospitals, they were suffering from a number of diseases; the main ones being cerebrovascular disease, about 90%, and heart disease, about 10%. The disease status of each group was characteristic of elderly patients in medical treatment wards, and many secondary disease names were listed in addition to their main diseases. In addition, all patients were taking medications to treat their diseases according to their respective conditions.

Seven subjects were assigned liquid nutrient (0 millipascal · second (mPa · s) group: Asahikasei, Japan), seven were given 400 mPa · s of semi-solid nutrient (400 mPa · s group: Asahikasei, Japan), and seven were administered 2000 mPa · s of semi-solid nutrient (2000 mPa · s group: Terumo, Japan). Each nutrient was a semi-digestion nutrition agent. Nutrients of 400 and 2000 mPa · s were measured with a single cylindrical rotating viscosimeter (type B). The number of revolutions was determined at 12 revolutions per minute (rpm) for the 400 mPa · s group, and 6 rpm for the 2000 mPa · s group. All subjects were administered nutrients by gastric fistula and had good digestion and absorption through the intestine. In addition, patients of each group were in a stable condition and used a nutritional supplement similar in viscosity to the nutrients administered in an acute care hospital, and the dosing viscosity was reviewed.

The administration speed of nutrients was varied according to each patient's condition and the type of nutrients. Oral care was implemented 3 to 4 times a day according to the level of contamination in the oral cavity. The concentration of nutrients was 1.0 or 1.5 kcal/ml for the 0 mPa · s group (non-water hydration type), 1.5 kcal/g for the 400 mPa · s group (non-water hydration type), and 0.55 or 0.75 kcal/g for the 2000 mPa · s group (water hydration type). For subjects in the 0 mPa · s and 400 mPa · s groups, water was administered before or after nutrient administration according to each patient. The 0 mPa · s and 400 mPa · s groups were calculated according to the concentration of intragastric nutrients added to water and dosed daily. To prevent backflow of the stomach contents, patients were kept on a bed inclined at 30 degrees for two hours after administration.

2) Examination of body temperature and number of fever episodes

Physiological data by body temperature and number of fever episodes was extracted from the medical records, and values for the past six months from the time of extraction were averaged. Body temperature was taken as the maximum daily temperature measured from the axilla. The number of fever episodes was recorded based on the clinical diagnosis criteria for aspiration pneumonia at 37.5 °C or higher (Deglutition Lung Disease Research Meeting, 2003).

3) Examination of inflammation response

Biochemical data about inflammation responses was extracted from the medical records, and values for the past six months from the time of extraction were averaged. In recuperation hospitals blood samples are checked on a temporary basis when the patient's condition deteriorates extremely. However, Hospital 'A' regularly collected blood samples every two weeks. In this study, WBC and CRP that were collected regularly were extracted as indicators of inflammatory reaction.

4) Ethical consideration

This study was conducted in compliance with the ethical norms of the Declaration of Helsinki. In consideration of protecting the personal information of patients, all data obtained in this study were managed in a format that could not identify individuals.

5) Statistical analysis

Values of concentration and dose of nutrients are expressed as a mean \pm SD. Values of Body temperature, number of fever episodes, and inflammation responses are expressed as a median (range). A one-way analysis of variance was used for comparison of each group examined regularly. The Kruskal-Wallis test was used when the normal distribution was not followed. The correlation between each index was examined using the Pearson correlation coefficient. Differences were considered significant when $p < 0.05$.

3. Results

1) Administration concentration and dose of nutrients

The concentration of nutrients administered was 0.59 ± 0.07 kcal/g in the 0 mPa \cdot s group, 0.69 ± 0.08 kcal/g in the 400 mPa \cdot s group, and 0.64 ± 0.10 kcal/g in the 2000 mPa \cdot s group, and the results were not found to be significantly different ($p=0.16$). The dose was 1686 ± 181 g/day in the 0 mPa \cdot s group, 1450 ± 239 g/day in the 400 mPa \cdot s group, and 1563 ± 149 g/day in the 2000 mPa \cdot s group, and the results were also not significantly different ($p=0.30$).

2) Body temperature and number of fever episodes

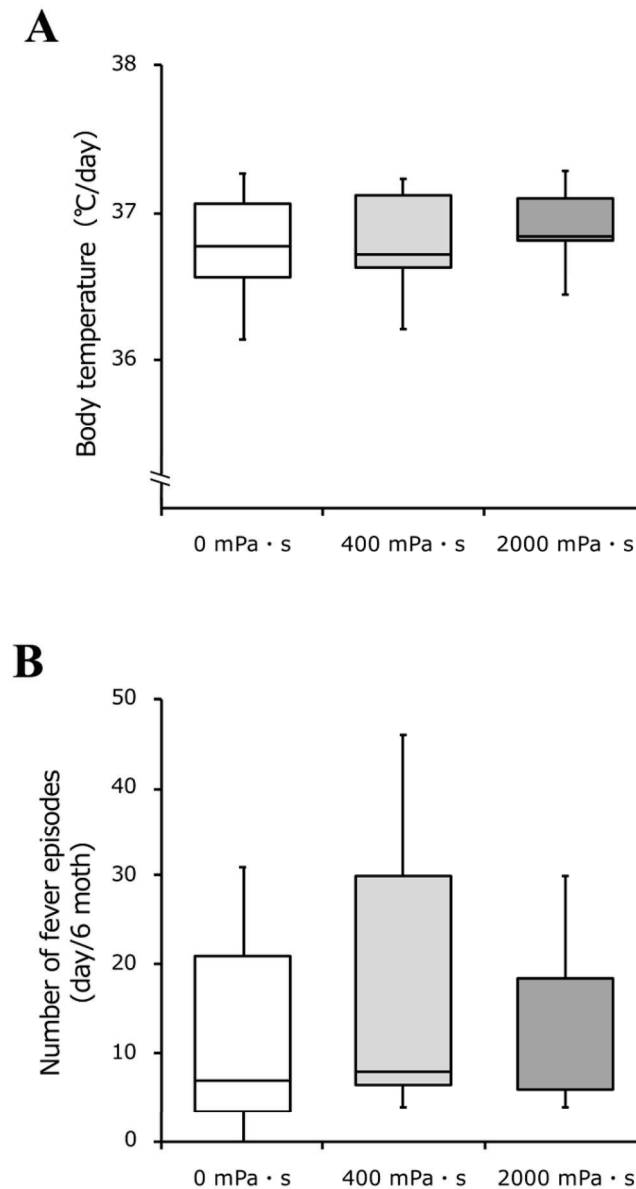


Figure 1. Comparison of body temperature (A) and number of fever episodes (B)

Body temperature and number of fever episodes are shown in Figure 1. Maximum daily temperature measured from the axilla was 36.8 (36.1-37.3) °C in the 0 mPa · s group, 36.7 (36.2-37.2) °C in the 400 mPa · s group, and 36.8 (36.4-37.3) °C in the 2000 mPa · s group, which were not significantly different (Fig.1A, $p=0.76$). The number of fever episodes above 37.5 °C was 7 (0-31) day in the 0 mPa · s group, 8 (4-46) day in the 400 mPa · s group, and 6 (4-30) day in the 2000 mPa · s group, and were also determined to be not significantly different (Fig.1B, $p=0.64$).

3) Inflammation response

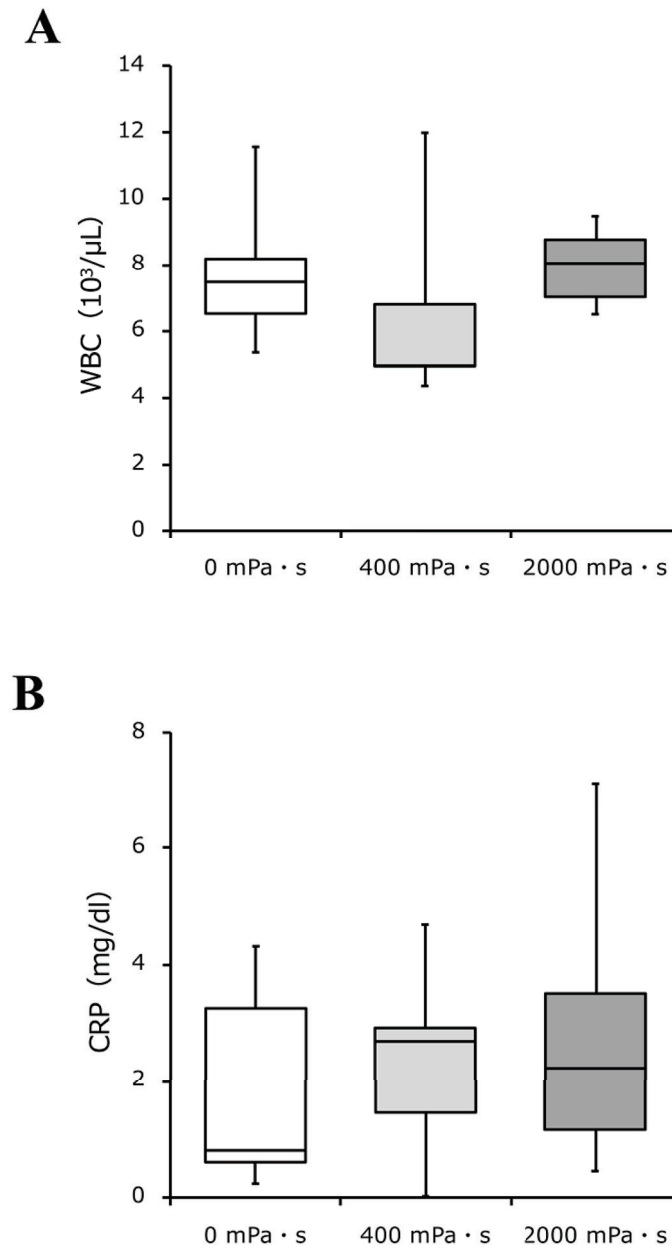


Figure 2. Comparison of WBC (A) and CRP (B)

The WBC and CRP on inflammation responses are shown in Figure 2. WBC was 7.5 (5.4-11.6) 10³/μl in the 0 mPa · s group, 5.0 (4.3-12.0) 10³/μl in the 400 mPa · s group, and 8.0 (6.5-9.5) 10³/μl in the 2000 mPa · s group, which were not significantly different (Fig.2A, $p=0.16$). CRP was 0.8 (0.2-4.3) mg/dl in the 0 mPa · s group, 2.7 (0.0-4.7) mg/dl in the 400 mPa · s group, and 2.2 (0.5-7.1) mg/dl in the 2000 mPa · s group, which were also not significantly different (Fig.2B, $p=0.76$).

4) Relationship of body temperature and WBC, CRP

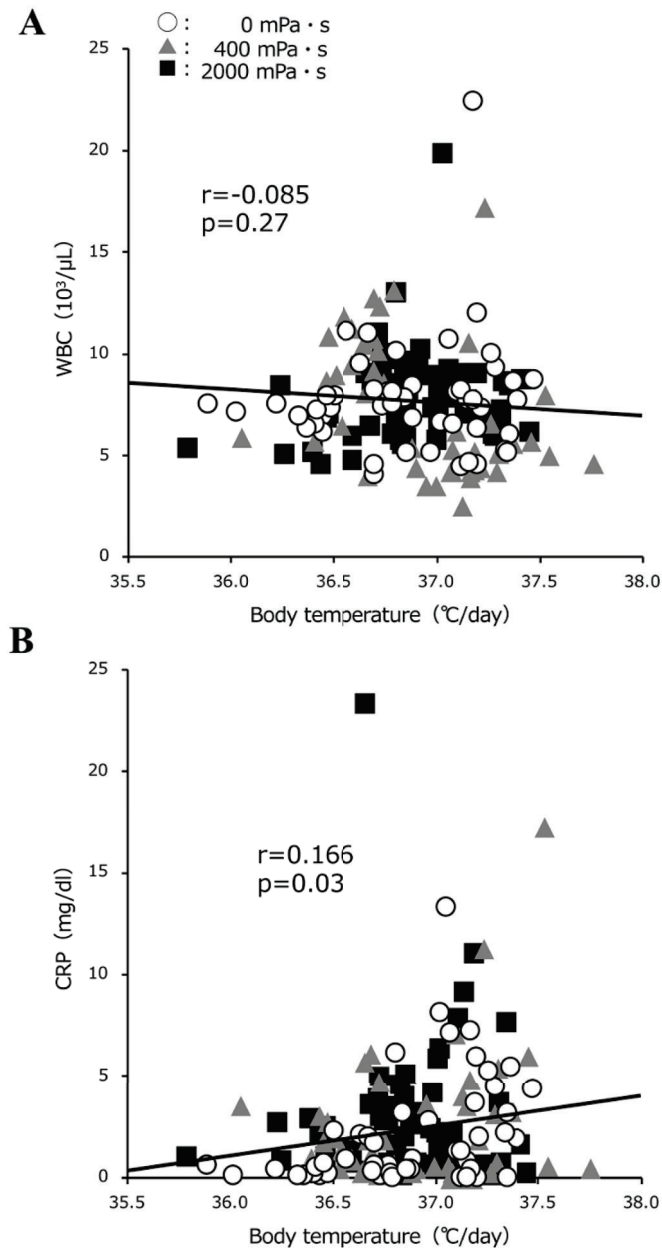


Figure 3. Comparison of Relationship of body temperature and WBC (A) or CRP (B)

In the results, body temperature and WBC did not show any significant relationship (Fig.3A, $r = -0.085$, $p = 0.27$). Body temperature and CRP also did not show any significant relationship (Fig.3B, $r = 0.166$, $p = 0.03$). In addition, the relationship between body temperature and CRP for each group did not show any distribution bias by group.

4. Discussion

The purpose of the present study was to retrospectively examine the frequency of fever and inflammation responses in older patients to determine whether varying the viscosity of nutrients is effective in reducing fever and inflammation responses. In the results, fever and inflammation

responses were not significantly different (Fig.1, 2). In addition, body temperature and CRP also did not show any significant relationship. However, the relationship of body temperature to WBC or CRP for each group did not show any distribution bias by group (Fig.3AB). The mean body temperature of each group was normal, but the WBC and CRP of all groups were shown to be higher, and a fever of over 37.5 °C was a frequent occurrence. In this present study, as subjects did not receive an inspection by chest X-ray or CT, it cannot be ascertained whether or not they had developed aspiration pneumonia. However, the administration of nutrients up to 2000 mPa · s was confirmed as not being able to improve the fever and inflammation responses that are indicative of aspiration pneumonia.

The concentration or volume of nutrients administered was similar for each group. Disease complications resulting from the enteral nutrition method (i.e., gastric or intestinal fistula) were reported as aspiration pneumonia or gastroesophagitis reflux attended by gastroesophageal reflux (Miyazawa, 2007). In this study, the frequency of oral care was according to subjects oral condition. Regarding the intraoral being kept relatively clean, there was no difference between the groups. The main factors causing an increase in aspiration pneumonia or gastroesophagitis reflux attended by gastroesophageal reflux were reported to be the administration speed, concentration, volume and viscosity of the nutrients (Miyazawa, 2007). In this study, the administration speed of nutrients was varied among patients with consideration for gastroesophageal reflux and diarrhea. In addition, there were no significant differences in the concentration and volume of administered nutrients between the groups. Therefore, differences in administration speed, concentration and volume of nutrients are thought to have no effect.

Regarding the fever and inflammation responses, there was no significant difference between the groups. These factors are thought to be due to administering a lower viscosity of nutrients. Semi-solid nutrient has been reportedly confirmed to prevent aspiration pneumonia attend by gastroesophageal reflux (Goda, 2016). In this study, nutrients of 400 mPa · s group were designed for the purpose of spontaneous dripping and improvement of feculent. Administration nutrients of 400 mPa · s have been revealed to be effective in gastrointestinal symptoms such as vomiting or gastroesophageal reflux (Tatsumi et al., 2015). The nutrients of the 2000 mPa · s group were designed for the purpose of preventing gastroesophageal reflux in addition to natural dripping¹ and improvement of feculent. Semi-solid nutrients of 2000 mPa · s have been reported to reduce the pathogenesis rate of complication in patients with gastric fistula (Mizuno et al., 2015). Based on these factors, a viscosity of between 400 and 2000 mPa · s was considered to be effective for preventing fever and inflammation responses, but the results for each group were not significantly different (Fig. 1). Ohura et al. (2001) examined the effectiveness of nutrients with a viscosity of 2200 - 2500 mPa · s in elderly patients with gastroesophageal reflux and diarrhea. In the result, nutrients of a viscosity of 2200 - 2500 mPa · s have been reported to be effective for suppressing gastroesophageal reflux, diarrhea and decubitus. On the other hand, in a study targeting elderly patients, semi-solid nutrients of a viscosity of about 2000 mPa · s failed to sufficiently suppress gastroesophageal reflux (Adachi et al., 2009). Shimizu (2018) investigated the effective viscosity for gastroesophageal reflux with different viscosities of 2000 mPa · s, 6000 mPa · s and 10000 mPa · s. In the result, a viscosity of 6000 mPa · s was observed to suppress gastroesophageal backflow, and the incidence was further increased at 10000 mPa · s. However, nutrients of 2000 mPa · s were effective in reducing diarrhea, but have not been shown to be

1 Nutrients with low viscosity up to 2000 mPa · s are dripped naturally using gravity. However, 20000 mPa · s high-viscosity nutrients are dropped using a pressure bag.

effective in the prevention of aspiration pneumonia, and the viscosity for gastroesophageal backflow suppression was concluded to be a nutrient of 6000 mPa · s or higher (Shimizu, 2018). It has been reported that the backflow of nutrient and also diarrhea can be prevented by the regulation of semi-solid nutrient at about 20000 mPa · s and administering it for a short time of 15 minutes (Goda, 2008). A study on the effect of low-viscosity semi-solid nutrients (0 - 2000 mPa · s) on gastroesophageal reflux that can spontaneously occur during natural-dripping is a study of the reduced pathogenesis rate of complication (Mizuno et al., 2015), or a study considers it is effective if there are no symptoms of aspiration pneumonia (Tatsumi, 2015; Ohura et al., 2007), study of the effectiveness cannot be clearly shown because there were no symptoms (Adachi, 2009; Shimizu, 2018). Among these studies, a unified opinion has not been obtained at present. Therefore in this present study, which used nutrients of lower viscosity, it can be said that this factor is ineffective.

Nutrients of low-viscosity may have possible backflow due to less irritation of the gastric contents. In general, the ingestion of food promotes the excretion of gastric contents by causing receptivity relaxation in the proximal part of the stomach. However, the administration of liquid nutrient from nasal or gastric fistula was reported not to give irritation causing receptivity relaxation in the proximal part of the stomach as compared to the swallowing of food (Ichimasa et al., 2010; Goda, 2008). In addition, the suppression of gastric emptying may cause gastroesophageal backflow (Ichimasa et al., 2010; Goda, 2008). The nutrient of low-viscosity can be administered by a natural dripping method, but it was reported to have an increased risk of gastroesophageal backflow and diarrhea in many patients (Goda, 2016). One reason for the lack of a unified view on nutrients of low-viscosity is thought to be that nutrients of low-viscosity may have individual differences in stimulation causing receptivity relaxation in the proximal part of the stomach during administration. Thus, the three nutrient groups used in this study are low viscosity, do not give irritation causing receptivity relaxation in the proximal part of the stomach, and so an increased risk of backflow into the esophagus is inferred. Therefore, to prevent aspiration due to gastroesophageal backflow, administering semi-solid nutrients with a viscosity of at least 2000 mPa · s or over and using a pressurized bag are considered to be effective. In addition, if saliva and gastroesophageal backflow may be considered, it has also been reported as effective to make the route of administration an intestinal fistula (Iijima, 2013). Recently, the usefulness of a liquid nutrient type solidified by gastric acid has also been reported (Yamada, 2017). Therefore, it can be said that it is necessary to consider this altogether. In addition, it can be said that it is necessary to clarify the cause of whether or not aspiration can be improved and to determine a treatment policy such as an administration method.

This present study has shown that different administrations of low-viscosity nutrient did not affect body temperature, frequency of fever, and inflammation responses. In our research, we examined a 6-month retrospective study of older patients in the same recuperation hospital. It was reported that their mean body temperature was 36.5 ± 0.3 °C, the frequency of fever was 9.2 ± 17.4 days, the mean WBC was 5.1 ± 2.1 $10^3/\mu\text{l}$, and the CRP was 1.1 ± 1.3 mg/dl (Togo et al., 2018). Considering the results obtained in the present study, administering nutrients of different viscosity by gastric fistula to the three groups is thought to cause higher fever and inflammation responses than in oral intake patients of the same recuperation hospital. The present study's limitation is that it was a retrospective study, therefore it is necessary to conduct an intervention study to select a nutrient choice for the prevention and improvement of aspiration pneumonia. Each group was small with seven subjects; therefore, in the next study it is also necessary to increase the number of subjects. This study was conducted using a low-viscosity nutritional supplement, but it also is necessary to consider a

nutritional supplement of over 6000 mPa · s. Moreover, research on patients in recuperation Hospital 'A' was limited in implementation under the same environmental conditions such as the review period, blood sampling etc.

5. Conclusion

The purpose of this study was to retrospectively examine the frequency of fever and inflammation responses in older patients in a recuperation hospital receiving a variety of viscosity of nutrients via a gastric fistula. After carefully examining all the data, it was determined that administering a low-viscosity of semi-solid nutrient was not effective for improving fever and inflammation responses to aspiration pneumonia.

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