Original Article doi: 10.2176/nmc.oa.2020-0350

Neurol Med Chir (Tokyo) 61, 268–274, 2021 Online March 9, 2021

Effect of Enteral Nutrition on In-hospital Infection and Hospital Expense in Stroke Patients: A Retrospective Assessment

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Abstract

Infection is a common complication of stroke and is associated with unfavorable outcomes. Although nutritional intervention reduces the risk of postoperative infection, the impact of specific nutritional products remains unclear. From a hospital management perspective, we aimed to determine whether the provision of specific types of enteral nutrition in acute stroke patients affects infection control and hospital costs. In all, 45 acute hemorrhagic stroke patients receiving enteral nutrition in a single center (April 2017–March 2019) were retrospectively assessed. Patients were divided into two groups according to nutritional interventions: the 1.0-group with general nutrition (1.0 kcal/mL) (24 patients) and the 1.5+α-group with an initial high-protein, whey peptide-digested liquid diet (1.5 kcal/mL), followed by a highly fermentable fiber-containing liquid diet (1.5 kcal/mL initiated after 4 days) (21 patients). Changes in body mass index (BMI), duration of antibiotic use, incidence of postoperative infection, and medical cost were evaluated. Baseline patient characteristics were similar between groups. The mean BMI change was lower in the 1.5+α-group than in the 1.0-group, and the mean duration of antibiotic use throughout hospitalization was 12.8 and 18.3 days, respectively. Antibiotic use in the 1.5+α-group was lesser than that in Japanese patients from other hospitals. The incidence of postoperative infections was lower in the 1.5+α-group. Injection costs for the 1.5+α group (615 USD/patient) were lower than those for the 1.0-group. Enteral nutrition provided to acute stroke patients reduced the risk of hospital infection and medical costs.

Keywords: enteral nutrition, infection, stroke, medical expense

Introduction

Stroke is the second leading cause of mortality worldwide[1)] and caused 5.5 million deaths and 116.4 million disability-adjusted life years in 2016.[2)] A substantial proportion of stroke survivors suffer from post-stroke disability. Moreover, stroke is one of the most financially burdensome, commonly occurring medical conditions.[3)] Medical expenditures associated with stroke include (but are not limited to) surgeries, medications, medical supplies, hospitalization, and nutritional care; even greater costs are accrued when patients develop postoperative complications.

Of postoperative complications associated with stroke, infection is the most common, with a reported global incidence of 30%.[4)] Prevention of postoperative infection is extremely important because it affects patient prognosis and medical expenses.[4–6)] However, some reports suggest that the efficacy of prophylactic antibiotics provided to combat postoperative infection is limited.[7,8)] Furthermore, the immunosuppressed state of post-stroke patients contributes to increased infection rates. These issues lead physicians to investigate the efficacy of peripheral immune activation.[9)]

Received October 9, 2020; Accepted November 24, 2020

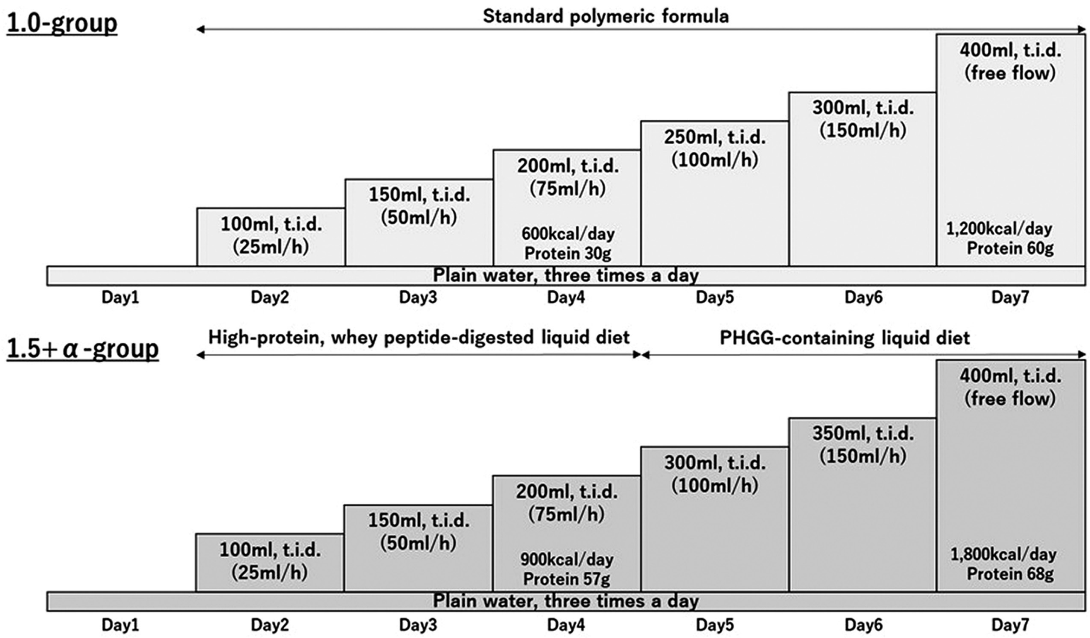

Fig. 1 Nutritional care protocol for stroke patient, namely Driving Surf protocol. In the both protocols, all the following conditions should be met to move on to the next step: (1) GRVs ≤100 mL, (2) no constipation, (3) no vomiting, and (4) no diarrhea. GRV: gastric residual volume, PHGG: partially hydrolyzed guar gum.

Many stroke patients experience postoperative malnutrition,[10] which has been associated with infection in non-stroke patients.[11] Based on these reports, we hypothesized that appropriate postoperative nutritional intervention to prevent malnutrition in stroke patients may decrease the postoperative risk of infection. Previous research has shown that malnutrition can be prevented by providing the patients with a high-protein, whey peptide-digested liquid diet using an early enteral nutritional intervention protocol.[12] In this study, we retrospectively analyzed clinical data to assess whether the implementation of the protocol reduced the postoperative infection risk and expense of stroke treatment.

Materials and Methods

Study design and setting

This retrospective cohort study used data derived from medical records and inpatient claims from an acute hospital (St. Marianna University School of Medicine, Yokohama City Seibu Hospital, Kanagawa, Japan), and it was conducted with the approval of the St. Marianna University School of Medicine Institutional Review Board (approval number 4190) and was performed in accordance with the Declaration of Helsinki. Because this was a retrospective study, the Institutional Review Board waived the need for patient consent. Hemorrhagic stroke patients who were admitted and received early enteral nutrition within 3 days of hospitalization between April 2017 and March 2019 were included in the study. Patients who could not start early enteral nutrition, such as those with serious comorbidities, were not included. The patients were classified into two groups based on the early enteral nutritional protocol (Driving Surf protocol, DS-prt), which comprises seven steps (Fig. 1).[12] The protocol involves the administration of 100 mL water and medications (0.5 g *Clostridium butyricum* preparations, 2.5 g daikenchuto, and 5 g mosapride citrate hydrate) via a nasogastric tube within 48 hours. The quantity of enteral nutrition provided is gradually increased when none of the following symptoms are observed: diarrhea, constipation for three consecutive days, vomiting, and the presence of 100 mL or greater gastric remnants. In the present study, we analyzed the following enteral nutrition protocols: A 1.0-group, which was provided 1.0 kcal/mL standard polymeric formula, and a 1.5+α-group, which was given an initial 1.5 kcal/mL high-protein, whey peptide-digested liquid diet, followed by a 1.5 kcal/mL highly fermentable dietary fiber-containing liquid diet (containing partially hydrolyzed guar gum [PHGG]) (Supplementary table, available online). Patients received antibiotics as directed by clinicians.

Measurement of variables

For both groups assessed, the following features were evaluated: prospective payment for the DPC

Table 1 Patients' characteristics and outcomes

Characteristics	1.0-group (n = 24)	1.5+α-group (n = 21)	p value
Age, mean (SD)	70.5 (11.6)	68.4 (14.3)	0.724
Female, n (%)	14 (58.3)	11 (52.3)	0.769
BMI at admission (kg/m^2), mean (SD)	23.2 (6.1)	24.6 (4.6)	0.258
BMI at 4 weeks (kg/m^2), mean (SD)	21.4 (5.4)	23.5 (3.7) n = 16[a]	0.060
BMI change (kg/m^2), mean (SD)	1.8 (2.3)	0.7 (1.7) n = 16[a]	0.007
GNRI, n (%)			0.660
High risk (<82)	0	0	
Moderate risk (82–<92)	2 (8.3)	2 (9.5)	
Low risk (92–98)	3 (12.5)	1 (4.8)	
No risk (>98)	19 (79.2)	18 (85.7)	
SGA, n(%)			1.000
Well nourished	24	21	
Moderately malnourished	0	0	
Severely malnourished	0	0	
Stroke subtype, n (%)			0.377
SAH	15 (62.5)	10 (47.6)	
ICH	9 (37.5)	11 (52.3)	
Operation			1.000
Craniotomy, n (%)	20 (83.3)	18 (85.7)	
Endovascular surgery, n (%)	4 (16.7)	3 (14.3)	
GCS on admission, n (%)			0.759
Score 13–14	3 (12.5)	3 (14.3)	
Score 9–12	9 (37.5)	8 (38.1)	
Score 3–8	12 (50.0)	10 (47.6)	
Comorbidity, n (%)			
Hypertension	16 (66.7)	13 (61.9)	0.765
Diabetes	6 (25.0)	6 (28.6)	1.000
Hyperlipidemia	5 (20.8)	5 (23.8)	1.000
Urinary catheterization, n (%)	24 (100)	21 (100)	1.000
Length of hospital stay, mean (SD)	49.0 (13.5)	49.3 (19.6)	0.991
Days of antibiotics use, mean (SD)	18.3 (12.4)	12.8 (5.5)	0.110
Days of therapy (per 100 bed-days)	37.4	26.0	–

[a]Only patients for whom data were not missing are included in the tabulation. BMI: body mass index, GCS: Glasgow Coma Scale, GNRI: Geriatric Nutritional Risk Index, ICH: intracranial hemorrhage, SAH: subarachnoid hemorrhage, SD: standard deviation, SGA: Subjective Global Assessment.

system[13] and actual cost (the cost of admission, examination, medication, and pharmacological treatment; 1 USD = 110 JPY), the length of hospital stay, body mass index (BMI) at admission and at 4 weeks after surgery, days of antibiotic use (excepting intraoperative use), days of therapy (days of antibiotic use/100 bed-days), and the incidence of three types of nosocomial infections (ventilator-associated pneumonia, catheter-related bloodstream infection, and urinary tract infection). The number of postoperative infections was compared with the number of incidences in other departments of our hospital and in other institutions belonging to the Japan Nosocomial Infections Surveillance (JANIS),[14] which

Table 2 Comparison of incidence of nosocomial infections

Incidence of infection	VAP	CBI[a]	UTI[a]
JANIS member hospitals (2017–2018)	1.3	0.6–0.7	0.7–0.8
Our hospital (2017–2018)	2.5–4.4	0.0–0.5	0.0–2.5
1.0-group	1.7	0	0.9
1.5+α-group	1.0	0	0

[a]Results are expressed as number of cases per 1000 patients per day. CBI: catheter-related bloodstream infections, JANIS: Japan Nosocomial Infections Surveillance[14], UTI: urinary tract infections occurring in intensive care unit, VAP: ventilator-associated pneumonia.

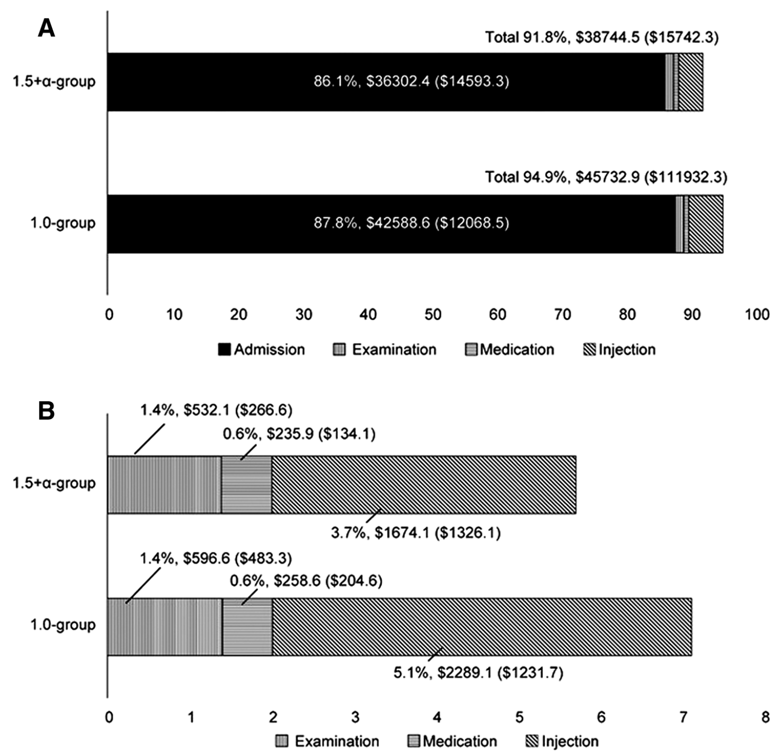

Fig. 2 Costs associated with acute stroke treatment. (A) Proportion of actual cost associated with admission, examination, medication, and injection relative to prospective cost percentage and mean actual cost (standard deviation). (B) Examination, medication, and injection costs extracted from (A).

is a national surveillance program organized by the Ministry of Health, Labour and Welfare of Japan. It is designed to provide basic information on the incidence and prevalence of nosocomial infections and antimicrobial-resistant bacteria in Japanese medical settings. Data on the incidence of ventilator-associated pneumonia, catheter-related bloodstream infection, and urinary tract infection in the intensive care unit (ICU) were continuously collected and analyzed.

Statistical analysis

The sample size of this observational study was determined based on the number of hemorrhagic stroke patients admitted during the study period. The Kolmogorov–Smirnov test was used to assess the data normality, and continuous variables were analyzed using the Mann–Whitney U test. Categorical variables were analyzed using Fisher's exact test. P values <0.05 were considered statistically significant (two-sided). Statistical analyses were

Table 3 Cost of care for acute stroke patients

	1.0-group (n = 24)		1.5+α-group (n = 21)	
	Actual cost ($), mean (SD)	Actual cost/prospective payment (%)	Actual cost ($), mean (SD)	Actual cost/prospective payment (%)
Total	45,732.9 (11,932.3)	94.9	38,744.5 (15,742.3)	91.8
Admission	42,588.6 (12,068.5)	87.8	36,302.4 (14,593.3)	86.1
Examination	596.6 (483.3)	1.4	532.1 (266.6)	1.4
Medication	258.6 (204.0)	0.6	235.9 (134.1)	0.6
Injection	2289.1 (1231.7)	5.1	1674.1 (1326.1)	3.7

SD: standard deviation.

performed using SPSS 22.0 software (IBM Japan, Tokyo, Japan).

Results

The baseline characteristics determined for both groups were similar (Table 1). The reduction in BMI after surgery was lesser in the 1.5+α-group than in the 1.0-group. Additionally, the mean number of days patients were prescribed antibiotics throughout hospitalization was 18.3 and 12.8 in the 1.0- and 1.5+α-groups, respectively. However, differences between the groups were not statistically different ($p = 0.110$). The mean number of days of therapy (i.e., antibiotic use days/100 bed-days) was 37.4 and 26.0 in the 1.0- and 1.5+α-groups, respectively. Furthermore, the incidence of the three types of nosocomial infections (ventilator-associated pneumonia, catheter-related bloodstream infections, and urinary tract infections) was lower in the 1.5+α-group than in other institutions in Japan (Table 2).

The mean length of hospital stay was 48.1 days in the 1.0-group and 49.3 days in the 1.5+α-group (Table 1). Injection costs associated with the treatment of patients in the 1.5+α- and 1.0-groups showed larger differences than did the other assessed costs. To cover the costs of examination, medication, and injections, the 1.0-group required approximately 700 USD/patient more than did the 1.5+α-group (i.e., 22% decrease in the 1.5+α-group relative to the 1.0-group) (Fig. 2, Table 3). Furthermore, the proportion of injection costs relative to the prospective total costs was 3.7% for the 1.5+α-group.

Discussion

Preventing postoperative infection among stroke patients is crucial to improve the treatment and management of stroke. Postoperative infection control is important in all fields of surgery. In the neurosurgical field, infection has been reported to worsen the patient prognosis.[4–6] In this study, we observed a diminished reduction in postoperative BMI in the patients provided with an enhanced enteral nutrition diet (1.5+α-group). Furthermore, the number of cases with postoperative ventilator-associated pneumonia, catheter-related bloodstream infection, and urinary tract infection in the ICU was lower in the 1.5+α-group (1.0, 0, and 0 cases per 1000 patients per day, respectively) than in the 1.0-group (1.7, 0, and 0.9 cases per 1000 patients per day, respectively). These numbers were lower than the values determined for JANIS members, which included more than 150 hospitals (with more than 200 beds) that voluntarily participated.

Multiple studies have indicated the clinical importance of postoperative nutritional management with enteral nutrition for stroke patients.[15,16] We have also previously reported that the 1.5+α-group protocol prevented patients from developing intolerance resulting from vomiting and diarrhea.[12] Regarding the 1.5+α-group feeding protocol, the following three mechanisms of infection prevention should be considered. First is the maintenance of a well-nourished state. Bodyweight is one of the most important indicators of a patient's nutritional state. Infection may have been prevented here because patients remained well-nourished with an early enteral nutritional intake of highly absorbent whey peptides. Second is the prevention of intolerance. Enteral nutrition-related intolerance, such as vomiting, puts patients at a risk of infection due to aspiration. The fact that the development of intolerance was suppressed with enhanced enteral nutrition diet suggested its role in preventing infection. Third is the improvement of peripheral immune function. PHGG, a highly fermentable dietary fiber, is known to enhance the production of butyric acid by enteric bacteria.[17] It has been reported that short-chain fatty acids derived from dietary fiber, particularly butyric acid, prevent infection by affecting the immune system.[18] Improved peripheral immune functioning may have prevented the infection.

Additionally, for the 1.5+α-group, injection costs were lower than those for the 1.0-group, signifying reduced overall medical costs for patients provided with enteric nutrition. This is in accordance with a report involving stroke patients by Vera Spatenkova.[6] The price of enteral nutrition varies depending on the ingredients, nutritional content, and calories provided to patients. Enteral nutrition is cheaper than medications such as antibiotics and surgery. The fact that a US$700 reduction in the cost of care is possible by appropriately providing enteral nutrition and nutritional intervention highlights the extreme efficiency of appropriately managing enteral nutrition in patients from a medical economic standpoint.

Because this is a retrospective study, it has all the limitations and risks associated with other retrospective investigations. Importantly, the experimental design did not allow researchers to infer causality. Moreover, the potential for selection bias was evident, considering all patients were recruited from one university hospital. Further multicenter prospective studies are required to validate the findings.

In conclusion, patients with acute stroke can experience a reduced risk of postoperative infections if provided with appropriate nutrition, which can also contribute significantly to reducing medical costs. We believe that these observations are worthy of further analysis and warrant a future prospective study.

Acknowledgments

The authors would like to thank all the members of the Nutrition Support Team and Infection Control Team of St. Marianna University School of Medicine, Yokohama City Seibu Hospital, for participating in this study despite their busy schedules. We would also like to thank Editage (www.editage.com) for English language editing.

Statement of Authorship

Hidetaka Onodera: conceptualization, methodology, and writing—original draft preparation. Takuma Mogamiya: validation, formal analysis, and writing—review & editing. Shinya Matsushima: writing—review & editing. Taigen Sase: writing—review & editing. Homare Nakamura: writing—review & editing. Yohtaro Sakakibara: supervision. All authors have read and approved the final version of this manuscript.

Funding

This work was supported by a Grant-in-Aid for Scientific Research (KAKENHI) from the Japan Society for the Promotion of Science (JSPS) [grant number 18K17868]. The funding agency had no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

Conflicts of Interest Disclosure

Hidetaka Onodera received lecture fees from Nestle Japan Ltd. The other authors have no conflicts of interest to disclose.

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