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Early Versus Late Enteral Nutrition in Patients with Acute Severe Cerebral Stroke and Dysphagian

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Abstract

Background: Malnutrition is well recognized as an important cause of increased mortality in patients with stroke. In this study, we compared the effects of early and late enteral nutrition on dysphagic patients with acute severe cerebral stroke.

Methods: Eligible patients were randomized to early enteral nutrition (EN) group (initiated within 24 hours after onset of stroke) and late EN group (initiated more than 7 days after stroke onset). The levels of albumin and hemoglobin, nosocomial infection, National Institutes of Health Stroke Scale (NIHSS) scores, length of intensive care unit (ICU) stay, and mortality rate were recorded at 1, 7, 30, or 90 days after onset of symptoms.

Results: We found that the early EN group showed a better nutritional status and reduced nosocomial infection and shorter ICU stay compared with the late EN group at 7 and 30 days follow-up. The early EN group had a lower NIHSS score than the late EN group at 7 and 30 days follow-up. However, there was not significant difference in NIHSS scores in both groups on 90 days follow-up. In addition, lower mortality rate was not shown in the early EN group.

Conclusion: These data show that early EN may be beneficial in acute stroke patients with dysphagia.

Keywords: Enteral nutrition, Dysphagia, National Institutes of Health Stroke Scale scores Nosocomial infection, Stroke

Abbreviations: CRP: C-reactive Protein; EN: Enteral Nutrition; GPx: Glutathione Peroxidase; ICU: Intensive Care Unit; IL-6: Interleukin 6; mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; PICC: Peripherally Inserted Central Catheter; RCTs: Randomised Controlled Trials

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Introduction

Stroke is one of the most common causes of acquired adult disability and death [1]. In the acute stage of stroke, about 30 to 50% of patients suffer from dysphagia, while the incidence drops to around 10% after six months [2]. Dysphagia has been associated with decreased nutritional intake, dehydration, and aspiration pneumonia. Several studies have shown that the risk of these complications was significantly increased in dysphagic stroke patients [3-7]. Because of these potentially life-threatening complications, mortality rate is significantly increased in dysphagic stroke patients compared to non-dysphagic stroke victims [8,9].

In a meta-analysis of 6 randomised controlled, Doig et al. [10] reported that early enteral nutrition (EN), initiated within 24 hours of injury or intensive care unit admission, significantly reduces mortality rate and incidence of pneumonia in critically ill patients. In a recent study, Zheng et al. found that patients receiving early enteral nutritional support had a better nutritional status, lower score on the National Institutes of Health Stroke Scale (NIHSS), and reduced nosocomial infection and mortality rate than the family managed nutrition group [11]. However, the timing of the early enteral nutritional support and the effects of the late EN on nosocomial infection were not investigated. In the FOOD trial, the authors found that early tube feeding was associated with

an absolute reduction in risk of death of 5.8% and a reduction in death or poor outcome of 1.2% [12]. However, the Food trial did not evaluate the effects of early EN (initiated within 24 hours of stroke) on nutritional status, nosocomial infection, length of intensive care unit (ICU) stay in patients with acute cerebral stroke. We set up this study was to investigate the effects of early and late EN on dysphagic stroke patients.

Materials and methods

Subjects

A total of 42 patients admitted to the neurological intensive care units (NICU) of the First Affiliated Hospital of Chongqing Medical University due to acute ischemic stroke or intracerebral hemorrhage were enrolled into the study. Patients were randomized to receive early EN (initiated within 24 hours of stroke) by using a nasogastric tube or late EN (initiated more than 7 days after stroke) until the patient tolerated oral feeding. A randomization list was used. Patients with singular number entered the early EN group, and those with even number were allocated into the late EN group. Twenty-two patients (14 men, 8 women) were admitted to the early EN group. The average age was 66.4 years in the early EN group. Twenty patients (12 men, 8 women) were admitted to the late EN group. The average age was 69.1 years in the late EN group. 3 patients were discharged in each group because family members of those patients gave up further treatment for the very serious condition of patients. The criteria for enrollment were as follows: (1) Ischemic stroke and intracerebral hemorrhage were all confirmed by brain CT scan or MRI; (2) the NIHSS scores were between 10 and 25; (3) all patients had dysphagia; (4) the symptoms and signs of all patients persisted for more than 24 hours. Exclusion criteria: unable to tolerate EN, subarachnoid hemorrhage, liver or kidney failure, Acquired Immune Deficiency Syndrome, leukemia, aplastic anemia, thrombocytopenia, chronic obstructive pulmonary emphysema, pulmonary heart disease, and peptic ulcer disease. The two groups received the same neurological treatments, including rehabilitation management.

Nutritional management

Early EN was initiated within 24 hours after stroke. Late EN started after 7 days of stroke, but parenteral nutrition was needed to give full nutritional support in the first 7 days. The parenteral nutritional support, which consists of Intralipid 20% (20% I.V. Fat Emulsion), 8.5% amino acid and glucose, is given through a peripherally inserted central catheter (PICC). The head was elevated to an angle of 30–45°. Intermittent feeding or small residual amount feeding were used to deliver the nasogastric tube feeding. The calorie need was calculated from the estimated weight (subjective clinical evaluation) at the rate of 35 kcal/kg/d. The ratio of calorie and nitrogen was 100:1, and the ratio of carbohydrate and fat was 6: 4.

Measurements

We measured dysphagia and its severity through Water swallow test. Dysphagia refers that Water swallow test is level 3-5. On 1, 7, 30, or 90 days of admission, levels of albumin and hemoglobin, nosocomial infection, NIHSS scores, length of ICU stay, and mortality rate were measured.

Ethics

The study was approved by the Research Ethics Committee of the First Affiliated Hospital of Chongqing Medical University.

Statistical analysis

Statistical analysis was performed by using SPSS 18.0 software package. Data are expressed as mean ± standard deviation (SD). Categorical data were compared by chi-squared test. Continuous data were analyzed by t-test. A *p* value of less than 0.05 was considered statistically significant.

Results

Clinical characteristics

The baseline demographic and clinical characteristics were compared between early and late EN groups **(Table 1)**. In general, there were no significant differences in baseline demographic and clinical characteristics between the two groups.

The levels of albumin and hemoglobin

The admission albumin and hemoglobin level did not differ significantly between the two groups (p = 0.848). The level of albumin of the late EN group decreased on 7 and 30 days compared to the early EN group (p = 0.006; p = 0.013, respectively). There was a trend of decrease in hemoglobin on 7 and 30 days in the late EN group. However, it was not statistically significantly lower than those of the early EN group (p = 0.648; p = 0.452, respectively) **(Table 2)**.

Nosocomial infection outcome

A total of 11 patients (50.0%) had sepsis or infections of the lung and urinary tract in the early EN group within 30 days after onset of stroke. However, 16 patients (80.0%) had this complication in

Table 1 Clinical characteristics of the two groups.

	Early EN group	Late EN group	P
Age [mean (range)]	(n=22)	(n=20)	0.302
Male/female [n(%)]	66.4 (50-83)	69.1 (49-81)	0.808
Disorder of consciousness [n (%)]	14/8 (63.6%/36.4%) 17 (77.3%)	12/8 (60.0%/40.0%) 16 (80)	0.830

Table 2 The levels of albumin and hemoglobin on day 1,7,30 after stroke.

	Early EN group	Late EN group	P
Albumin (g/L)			
Day 1 (mean ± SD)	44.1 ± 5.2	44.5 ± 5.4	0.848
Day 7 (mean ± SD)	41.4 ± 4.6	37.7 ± 3.6	0.006
Day 30 (mean ± SD)	41.6 ± 4.0	38.7 ± 3.0	0.013
Hemoglobin (g/L)			
Day 1 (mean ± SD)	132.9 ± 10.2	134.6 ± 11.7	0.619
Day 7 (mean ± SD)	130.0 ± 8.8	128.7 ± 9.5	0.648
Day 30 (mean ± SD)	128.2 ± 7.7	126.2 ± 9.6	0.452

the late EN group. The rate of nosocomial infection in the early EN group was significantly lower than that in the late EN group (p=0.043) **(Table 3)**.

NIHSS scores

There was no significant difference in baseline admission NIHSS scores between the two groups (p = 0.690). The NIHSS score of the late EN group was higher than that of the early EN group on 7 and 30 days (p = 0.027; p = 0.030, respectively). However, this phenomenon was no longer on 90 days between the two groups (p = 0.104) **(Table 4)**.

The length of ICU stay

The ICU days of the early EN group and the late EN group were 8.6 ± 2.7 and 11.2 ± 4.5, respectively. The early EN group showed a better result than that of the late EN group, which means the difference in ICU stay was statistically significant between the two groups (p = 0.026) **(Figure 1)**.

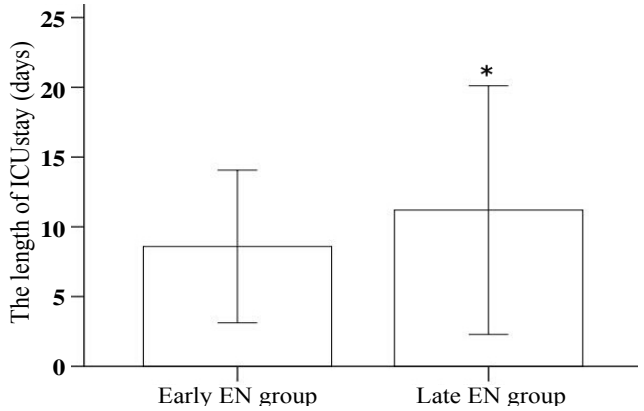

Figure 1 The length of ICU stay in the two groups. Results are expressed as the mean ± SD. *, p < 0.05, compared with the early EN group.

Mortality outcome

In this study, 3 patients were discharged in each group because family members of those patients gave up further treatment for the very serious condition of patients. We followed up those patients. Without exception, all patients died within a few days after they discharged. 5 of 22 patients (22.7%) in the early EN group died within 90 days after onset of symptoms. In the late EN group, 6 patients (30.0%) died within 90 days. However, the mortality rate of the early EN group was not significantly lower than that of the late EN group (p = 0.592).

Discussion

Previous studies suggested that approximately 40% of patients are malnourished at the time of admission to the hospital [13]. Malnutrition is often associated with impaired organ function and tissue wasting, which may lead to prolonged hospitalization and increased mortality [14]. Decreased levels of hemoglobin and albumin are important manifestations of malnutrition. In our study, we observed that the albumin level in the late EN group was more obviously decreased than the early EN group at 7 and 30 days follow-up. However, the hemoglobin level was not significantly altered between the two groups. We speculate that this phenomenon may be related to the different half-life of red blood cells and albumin.

Table 3 Incidence and type of nosocomial infection within day 30 after stroke.

Type of nosocomial infection	Early EN group (22)	Late EN group (20)	P
Pneumonia (n)	8 (36.4%)	14 (70.0%)	0.029
Urinary (n)	8 (36.4%)	10 (50.0%)	0.372
Sepsis (n)	2 (9.1%)	3 (15.0%)	0.555
Total numbers of nosocomial infection (n)	11 (50.0%)	16 (80.0%)	0.043

Table 4 NIHSS scores on day 1, 7, 30, and 90 after stroke.

	Early EN group	Late EN group	P
Day 1 (mean ± SD)	15.7 ± 3.7	`15.3 ± 4.0	0.690
Day 7 (mean ± SD)	11.7 ± 2.5	13.7 ± 3.1	0.027
Day 30 (mean ± SD)	10.0 ± 2.0	11.5 ± 2.2	0.030
Day 90 (mean ± SD)	8.2 ± 1.7	9.2 ± 2.0	0.104

In our study, nosocomial infection was defined as an infection that developed 48 hours after admission and up to 10 days after discharge from hospital [15-17]. Nosocomial infection is a major cause of death in patients with acute stroke. Dysphagia is the strongest independent predictor for in-hospital infection in acute stroke [18]. In our study, we observed a high rate of hospital infection in the early and late EN groups. We think that the high rate of hospital infection may be associated with severe illness and dysphagia in the two groups. However, there was a significant reduction in nosocomial infection in the early EN group than in the late EN group. In previous studies, early EN after acute ischemic stroke was found to reduce the serum levels of inflammatory markers, such as glutathione peroxidase (GPx), C-reactive protein (CRP), and interleukin 6 (IL-6) [19]. Early EN after acute stroke has also been reported to reduce septic morbidity [11]. Our finding suggested that prevention and treatment of malnutrition play an important role in reducing the nosocomial infection. Interestingly, in our study, we found that the early EN only prevented pneumonia in a variety of hospital infections.

The NIHSS is a 15-item impairment scale that provides reliable information for assessment of neurological deficits and predicting outcomes after stroke [20,21]. After 7 and 30 days of stroke, early EN reduced NIHSS scores compared to late EN. Interestingly, the early EN group did not show a better score than that of the late EN group on 90 days. This may be related to the active rehabilitation therapy of two groups. Rehabilitation played a pivotal role in the patient's prognosis.

Length of hospital stay is not a good parameter because the actual day of discharge is mainly dependent on the availability of social and community services than on the actual clinical condition of the patient [13]. Therefore, we assessed the length of ICU stay in this study. Compared to late EN, early EN shortened ICU days of dysphagic patients with acute severe cerebral stroke.

Stroke is one of the most common causes of disabilities and death

worldwide. In high income countries, the incidence of stroke decreased from 163-94 cases per 100,000 person years between 1970 and 2008 [22,23]. However, there is a dramatic increase in stroke prevalence during the past 20 years in China. Dennis et al., [24] found that early EN within a week of admission may substantially reduce the risk of death after stroke. In our study, we found that early EN did not decrease mortality rate of stroke patients as compared with late EN group. A possible explanation could be that the sample size of our study is too small.

Conclusion

In this study, our data suggested that the effects of early and late EN were significantly different in dysphagic patients with acute severe cerebral stroke. Early EN may reduce infection, neurological deficits, and ICU stay. However, the sample size of our present study is small. Future studies with larger sample size are needed to further validate the different role of early versus late EN on stroke outcome.

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