*Original Article*

# Fat-free oral nutritional supplements for patients after acute illness: a prospective observational study

**Kensuke Nakamura,[1,2,*] Yuji Takahashi,[2] Yusuke Yanai,[3] Tomoka Miyagi,[1] Hidehiko Nakano,[2] Yasuaki Koyama,[2] and Hideki Hashimoto[2]**

[1]Department of Critical Care Medicine, Yokohama City University Hospital, 3-9 Fukuura, Kanazawa-ku, Yokohama, Kanagawa 236-0004, Japan
[2]Department of Emergency and Critical Care Medicine and [3]Nutrition Department, Hitachi General Hospital, 2-1-1, Jonan-cho, Hitachi, Ibaraki 317-0077, Japan

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**There is a lack of evidence for compliance with and the acceptability of oral nutritional supplements (ONS) by post-acute care patients. Therefore, the present study examined compliance with fat-free ONS, which are easy to drink. Patients who started oral intake in the general ward after being transferred from the Emergency Department were offered three ONS including fat-free ONS: Isocal Clear, Maybalance Mini, and Medimil, three times a day for three days. On days 1 and 3, patients evaluated each ONS using a questionnaire. Thirty-five eligible patients participated in the present study, which began a median of 10 days after their admission. Median taste ratings for Isocal Clear, Maybalance, and Medimil on day 1 were 8, 7, and 3, respectively, while median ease-to-drink ratings were 8, 7, and 5, respectively. In contrast, median taste ratings on day 3 were 5, 0, and 0, respectively, while median ease-to-drink ratings were 7, 1, and 0, respectively. Intakes of the prescribed diet during the three days had a median value as low as 30–50%. In conclusion, good compliance with fat-free ONS by post-acute care patients may be achieved.**

***Key Words*:** **oral nutrition supplement, acute illness, critical care, fat, appetite**

In critically ill patients, nutritional therapy in acute care has been recommended as it should be by a constant stream of trends.[1,2] While underfeeding is accepted during the first half of the acute phase to avoid overfeeding,[3] adequate nutrition is essential for recovery from illness in the late acute and convalescent phases.[4] However, nutritional intake after discharge from the ICU, when oral intake is initiated, may be inadequate,[5] and this shortage has been reported to persist for up to one year after discharge.[6] Oral nutritional supplements (ONS) may augment the nutritional status of patients during this time, and their aggressive use has been recommended.[1] However, this objective cannot be achieved without patient compliance.

However, the objective cannot be achieved if the ONS is prescribed, but the patient does not take it. Anorexia may develop in patients after an acute illness[7] and, together with dysphagia, is the primary cause of nutrient deprivation after the initiation of oral intake.[8] Therefore, dietitians need to actively intervene and select the ONS preferred by the patient as well as vary the prescription as the patient recovers.[9]

Energy-dense ONS were primarily developed for the recovery phase to allow for energy intake in small amounts and to accommodate occasional drinking water restrictions. Therefore, ONS contain a sufficient amount of lipids, including essential fatty acids.[10] However, since lipids take longer to digest and absorb, causing intestinal intolerance, such as diarrhea,[11] and satiety,[12] fat-free ONS may be more appropriate for patients with anorexia after an acute illness. Fat-free nutritional supplements have been developed, such as elemental diet; however, their poor taste has made it difficult to stimulate patients' appetites.[13,14]

Isocal Clear (Nestlé) is an ONS that provides 1 kcal/ml without lipids and contains 10 g of protein as whey per 200-ml bottle. Due to the absence of lipids, it is easy to drink and considered highly acceptable for patients in an anorexic state after the acute phase of illness. Therefore, we hypothesized that fat-free ONS represent an effective option after acute illness, and conducted a prospective observational study to investigate compliance with fat-free ONS by patients admitted to the Emergency and Critical Care Center.

## Materials and Methods

This clinical study was conducted after receiving approval from the Ethics Board of our hospital (2022-48). It was registered at the University Hospital Medical Information Network (UMIN) with registration number UMIN000049866 (https://center6.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000056800). We received informed consent from eligible participants. The present study was conducted in collaboration with Nestlé Japan, and the three ONS tested were provided, purchased, and used by Nestlé. Nestlé was not involved in the study design or analysis.

**Patient selection.** Patients who were admitted to the ICU at the Hitachi General Hospital Emergency and Critical Care Center, transferred to the general ward between October 2022 and September 2023, and then initiated oral intake were included. Exclusion criteria were as follows: younger than 20 years, unable to answer the questionnaire, and the designation of "do not attempt resuscitation". Since this was an exploratory study, a sample size calculation was not performed, and consecutive patients who met the inclusion criteria and agreed to participate in the study were enrolled.

**Protocol and measurements.** Patients who met the selection criteria and consented to participate in the present study received three ONS: Isocal Clear (Isocal Clear; Nestlé Japan Co., Ltd., Kobe, Japan), Maybalance Mini (Maybalance; Meiji Co., Ltd., Tokyo, Japan), and Medimil (Medimil; Ajinomoto Co., Ltd., Tokyo, Japan). ONS were consumed three times per day for three days and were provided free of charge. The ingredients in each formulation were as follows: Isocal Clear; 200 kcal, 10 g protein (whey), 0 g lipids, and 40 g carbohydrates per 200-ml bottle; Maybalance; 200 kcal, 7.5 g protein (milk protein), 5.6 g lipids, and 31.8 g carbohydrates per 200-ml bottle; Medimil;

*To whom correspondence should be addressed.
E-mail: knakamura-tky@umin.ac.jp

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200 kcal, 8 g protein (milk protein), 10.3 g lipids, and 20.4 g carbohydrates per 200-ml bottle. Two flavors were offered per formulation, and patients were asked to drink whichever they preferred: Isocal Clear was available in peach and lemon tea flavors, Maybalance in coffee and strawberry flavors, and Medimil in coffee milk and banana milk flavors.

Once oral intake was started in the general ward and patients were considered to be able to take nutrition on their own without dysphagia. On day 1, all ONS were tasted, and a questionnaire was completed for each ONS. In the next three days, in addition to the prescribed food menu, participants were allowed to freely select and drink one of the ONS provided and completed the questionnaire again on day 3. On days 1 and 3, respondents were asked to rate the ease of drinking each ONS on a scale of 0 to 10 (10 for very easy to drink, 0 for very hard to drink, and 5 for neither) and 0 to 10 for taste (10 for very good, 0 for very bad, and 5 for neither). Two different tastes were offered for each ONS, and respondents were asked to select the one with the higher score. On day 1, participants were asked to select what they considered to be important for ONS from the following factors, with multiple responses being allowed: taste, variety of flavors, ease of drinking, smell, high quantity, low quantity of food, and nutritional composition.

Regarding clinical information, we evaluated the following basic characteristics and outcomes: age, sex, body mass index, sequential organ failure assessment (SOFA), and acute physiology and chronic health evaluation (APACHE II) scores on admission, main disease category; sepsis, endocrine/metabolism disorder, trauma, respiratory failure, and others, date of the questionnaire from hospital admission, in-hospital mortality, length of ICU and hospital stays, mechanical ventilation during the ICU stay, and the Barthel index at discharge. The Barthel index was evaluated by nurses in the general ward who were blinded to answers in the questionnaire. In addition, nurses calculated the amount of each prescribed meal consumed on each of the three days of the study as a percentage and obtained the average for each day. Nurses also confirmed that the ONS provided were consumed during the three days of the study and identified the preferred ONS. No active intervention by dietitians or nurses was performed during the three days, and food intake and ONS selection were left entirely up to patients.

**Statistical analysis.** Isocal Clear on day 3; fat-free ONS acceptance was divided into two groups based on whether a patient responded with an ease-to-drink rating ≥7, and the characteristics of patients in both groups were compared. Continuous variables were expressed as the mean ± SD and compared using the Student's *t* test when the Shapiro–Wilk test did not reject the null hypothesis. Continuous variables were expressed as medians (interquartile ranges) and compared using the Mann–Whitney *U* test when the Shapiro–Wilk test rejected the null hypothesis. Regarding categorical variables, the percentages of patients in each category were calculated. Groups were then compared using the chi-square test. Taste and drinkability scores for the three ONS on days 1 and 3, expressed as violin plots and medians and interquartile range error bars, were tested with the Kruskal–Wallis and Bonferroni tests for each pair. All statistical analyses were conducted using JMP 14 software (SAS Institute Inc.).

## Results

Thirty-five patients who were admitted to the Emergency Department, transferred to the general ward, and met the study criteria consented and participated in the present study. The basic characteristics of patients are shown in Table 1. The median age of patients was 78.2 years, 50% were male, the median body mass index was 23.5 kg/m$^2$, the median SOFA score was 5, and the median APACHE II score was 16 after acute illness. The most common primary illness was sepsis (40.0%), followed by endocrine and metabolic disorders and trauma. Patients with coronavirus infection were not included. The median study day from admission was 10 days, and clinical outcomes were an in-hospital mortality rate of 5.7%, a median ICU stay of 3 days, length of hospital stay of 22 days, and a median Barthel index of 60 at final discharge. The mean% oral intake of the prescribed diet for the 3 days of the study period was low, with a median of 30~45% each day.

**Table 1.** Basic characteristics

| *n* | 35 |
|---|---|
| Age, year | 78.2 ± 11.8 |
| Male sex, *n* (%) | 17 (48.6) |
| Body mass index, kg/m$^2$ | 23.5 ± 3.1 |
| SOFA score | 5 (2, 9) |
| APACHE II score | 16 (11, 28) |
| Main disease, *n* (%) | |
| Sepsis | 14 (40.0) |
| Endocrine/metabolism disorder | 7 (20.0) |
| Trauma | 6 (17.1) |
| Respiratory failure | 3 (8.6) |
| Others | 5 (14.3) |
| Survey date from hospital admission, days | 10 (3, 12) |
| In-hospital mortality, *n* (%) | 2 (5.7) |
| Length of ICU stay, days | 3 (3, 6) |
| Length of hospital stay, days | 22 (11, 31) |
| Mechanical ventilation, *n* (%) | 5 (14.3) |
| Barthel Index at discharge | 60 (20, 80) |
| Oral food intake on day 1,%* | 35 (15, 61.7) |
| Oral food intake on day 2,%* | 45 (20, 66.7) |
| Oral food intake on day 3,%* | 30 (16.7, 75) |

**Table 2.** Important factors of ONS for the patients after acute illness

| *n* (%) | *n* = 35 |
|---|---|
| Good taste | 25 (71.4) |
| Ease of drinking | 16 (45.7) |
| Small quantity/serve | 9 (25.7) |
| Large quantity/serve | 5 (14.3) |
| Composition of nutrients | 7 (20.0) |
| Smell | 3 (8.6) |
| Rich variety of flavors | 2 (5.7) |

Table 2 shows the results obtained on responses to the questionnaire on day 1. With duplicate responses, good taste was the most common (71.4%), followed by drinkability (45.7%). Regarding quantity, 25.7% of patients indicated a preference for less and 14.3% for more. Only a small number of other responses was given.

The distributions of taste and ease-to-drink ratings for each ONS on days 1 and 3 are shown in Fig. 1. On day 1, the Bonferroni test showed that median taste and ease-to-drink ratings were significantly lower for Medimil (3 and 5, respectively) than for Isocal Clear (8 and 8, respectively) and Maybalance (7 and 7, respectively), while no significant difference was observed between Isocal Clear and Maybalance. However, on day 3, scores were slightly lower for Maybalance; the median taste rating for Maybalance was 0 and that for Isocal Clear was 5, which was not significantly different. However, the Bonferroni test showed that Isocal Clear had the highest ease-to-drink rating on day 3, with a median of 7, which was significantly higher


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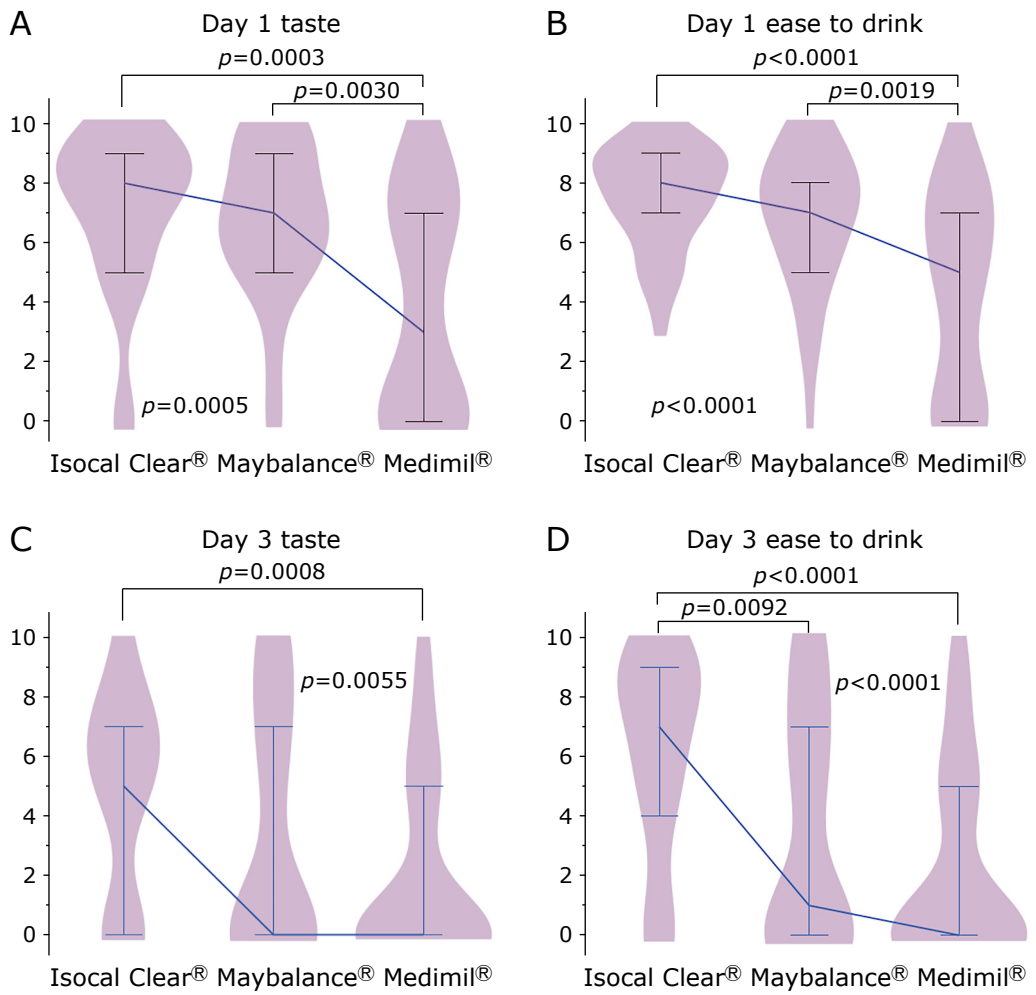


**Fig. 1.** Evaluation of each oral nutritional supplement on days 1 and 3 in the questionnaire. Isocal Clear, Maybalance Mini, and Medimil were rated by 35 patients (0–10, with 10 being the best), with violin plots and error bars by medians and interquartile ranges. The overall test was performed using the Kruskal–Wallace test. The general test was performed using the Kruskal–Wallis test. Those that were significant by the Bonferroni test for each pair are shown with *p* values: (A) Day 1 taste, (B) Day 1 ease to drink, (C) Day 3 taste, (D) Day 3 ease to drink.

than that of Maybalance (1) and Medimil (0). A small number of patients rated Maybalance and Medimil highly on day 3. These scores were significantly different in the Kruskal–Wallis test.

The characteristics of the 20 patients who found Isocal Clear acceptable and responded with an ease-to-drink rating ≥7 and <7 were compared in Table 3. The more severe the disease, the smaller the number of patients who responded that ONS were acceptable to drink, with no significant difference being observed among the 3 ONS tested. Patients with trauma responded with a higher ease-to-drink rating and patients with respiratory failure with a lower rating.

Table 3 shows that the prescribed food intake by both groups was low and was expected to be reinforced or added by ONS; however, intakes of the prescribed diet during the three days were Isocal Clear (12/35, 34.3%), Maybalance (2/35, 5.7%), Medimil (1/35, 2.9%), and almost none (20/35, 57.1%).

## Discussion

A 3-day prospective observational study was conducted to investigate the acceptance of ONS, including fat-free ONS, by patients after an acute illness. Fat-free ONS were accepted well by post-acute care patients for both their taste and drinkability, particularly after 3 days, with higher ratings than other ONS. A small number of patients preferred other ONS. On the other hand, due to the lack of active interventions by a dietitian, the amount of ONS consumed by more than 50% of patients was low despite their limited dietary intake.

To the best of our knowledge, this is the first study to examine the acceptability of and compliance with fat-free ONS in post-acute care patients. No studies have investigated fat-free ONS other than elemental diet; however, the ease of ingestion of fat-free ONS may achieve the highest compliance in this study. Although many types of ONS are marketed and recommended for use after acute care,[1] few studies have compared compliance and preferences between ONS after acute illness. A systematic review reported that compliance with ONS in healthcare settings ranged from 37–100%, with an average of 78%, and was 67% in inpatients. In post-acute care patients, anorexia and taste disorders[15] may combine to further reduce compliance,[8] making the selection of an easy-to-drink acceptable ONS critical.

A randomized open-label crossover trial that compared compliance with ONS of different energy densities by patients with relatively active disease was conducted by Leon-Sanz *et al.*[16] The findings obtained showed similar compliance between energy-dense ONS (2.4 kcal/ml) and normal ONS (2.0 kcal/ml) in a crossover study of outpatients with disease-related malnutrition. Since the ONS used as a reference in this study were also

**Table 3.** Characteristics difference with/without acceptance of the fat free ONS on day 3

| *n* | Ease to drink <7 | Ease to drink ≥7 | *p* value |
|---|---|---|---|
| | 15 | 20 | |
| Age, year | 75.1 ± 9.3 | 80.6 ± 13.1 | 0.17 |
| Male sex, *n* (%) | 8 (53.3) | 9 (45.0) | 0.63 |
| Body mass index, kg/m$^2$ | 23.6 ± 2.9 | 23.3 ± 3.4 | 0.79 |
| SOFA score | 7 (4, 9) | 4.5 (2, 8) | 0.11 |
| APACHE II score | 19 (13, 30) | 13 (10, 19) | 0.089 |
| Main disease, *n* (%) | | | 0.059 |
| Sepsis | 6 (40.0) | 6 (40.0) | |
| Endocrine/metabolism disorder | 4 (26.7) | 3 (15.0) | |
| Trauma | 0 (0) | 6 (30.0) | |
| Respiratory failure | 3 (20.0) | 0 (0) | |
| Others | 2 (13.3) | 3 (15.0) | |
| Survey date from hospital admission, days | 11 (3, 15) | 9.5 (3.3, 12) | 0.67 |
| In-hospital mortality, *n* (%) | 2 (13.3) | 0 (0) | 0.093 |
| Length of ICU stay, days | 3 (2, 7) | 3 (3, 5) | 0.86 |
| Length of hospital stay, days | 24 (11, 49) | 20 (11, 29) | 0.46 |
| Mechanical ventilation, *n* (%) | 3 (20.0) | 2 (10.0) | 0.40 |
| Barthel Index at discharge | 50 (10, 80) | 62.5 (36.3, 83.8) | 0.22 |
| Oral food intake on day 1,%* | 45 (15, 63.3) | 30 (15, 55) | 0.41 |
| Oral food intake on day 2,%* | 51.7 (18.3, 66.7) | 43.3 (23.3, 71.3) | 0.99 |
| Oral food intake on day 3,%* | 30 (3.3, 75) | 33.3 (17.1, 74.2) | 0.65 |

energy-dense ONS, it is unclear how it would compare with a frequently used ONS (1 kcal/ml); however, ONS with a high or low energy density may not necessarily affect compliance, and the three major nutrient components, taste, and drinkability of individual ONS need to be considered separately.

Lipids, including essential fatty acids, are important nutrients, and a minimum of 8 g/day was previously considered to be necessary, even in the acute phase.[17] Nevertheless, temporary non-dosing is currently acceptable.[18] The usefulness of ω3 fatty acids has been examined in the acute setting[2] and they have a history of being actively formulated and tested in ONS. In patients with pancreatic cancer[19,20] and head and neck cancer,[21] ONS enhanced with ω3 fatty acids achieved good outcomes with acceptable compliance. However, these studies were randomized controlled trials (RCT) and adherence was maintained with active interventions by dietitians and others to ensure protocol compliance. To achieve good compliance without these interventions, lipid-free ONS, such as Isocal Clear, may be a good addition to a treatment regime, particularly after an acute illness.

In the present study, more than 50% of participants only drank small amounts of the ONS provided despite their low dietary intake due to the lack of an active intervention during the study period, raising concerns about overwhelming nutritional deficiencies. Therefore, it is not inadequate to merely prescribe an easy-to-drink ONS; a dietitian needs to actively intervene during this period.[9] Advice from healthcare providers and dietitians has been shown to significantly increase ONS compliance.[22,23] Since some patients in the present study preferred other nutritional supplements, it is important to select and offer supplements that best matches their preferences, and this may be achieved through interventions by a dietitian.[9]

There are several limitations that need to be addressed. The present study was not a crossover RCT; therefore, it was difficult to accurately compare individual ONS compliance. Furthermore, questionnaire items were subjective ONS patient ratings, which may have introduced some bias. Commercially available ONS may have multiple flavors in their repertoire, and flavor differences were not verified in the present study. Since there was no support from a dietitian during the study period, different results may have been obtained with an active intervention. Moreover, although fat-free ONS were highly rated in the present study, compliance in the long term has not yet been investigated and, thus, a larger prospective observational study is needed in the future.

Compliance with fat-free ONS by post-acute care patients may be attributed to its ease of administration and, thus, they may be a good addition to the prescribing repertoire.

## Author Contributions

KN: conception and interpretation of the study. KN, TM: drafting of the manuscript. YT, YY, HN, YK, HH: conduction of the study and revision of the manuscript. All authors read and approved the manuscript.


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## Ethical Approval

This clinical study was approved by the Ethics Board of Hitachi General Hospital (2022-48). We received informed consent from participants.

## Conflict of Interest

No potential conflicts of interest were disclosed.


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## Availability of Data and Materials

The dataset is available upon reasonable request.

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