The effects of nasogastric feeding at different intervals on feeding intolerance in ICU patients: a single-blind, randomized, controlled trial

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Summary
Background. Most patients hospitalized in intensive care units (ICUs) are fed through a feeding tube. Intolerance is one of the most common complications of tube feeding, and it is observed in more than half of these patients. Each of the tube feeding methods has some advantages and disadvantages, which require more extensive research in order to confirm the proper method for nutrition.

Objectives. This study was conducted to compare nasogastric feeding at different intervals on the feeding tolerance of ICU patients.

Material and methods. Sixty-three patients hospitalized in the ICU of Besat Hospital in Hamadan, Iran who were undergoing tube feeding by the bolus method participated in this single-blind, randomized, clinical trial. The patients were randomly divided into three groups of 21 people each and were administered bolus feeding in intervals of 2, 3, and 4 hours. The feeding intolerance (regurgitation, diarrhea, and high gastric residual volume) were assessed and compared with each other according to a checklist for three consecutive days.

Results. Regurgitation accrued in 66.7% (n = 14), 38.1% (n = 8), and 23.8% (n = 5) of patients fed every 2, 3, and 4 hours, respectively; these differences were statistically significant (p = 0.017). The gastric residual volume was 61.9% (n = 13), 38.1% (n = 8), and 23.8% (n = 5) in the three groups, which was also a statistically significant difference (p = 0.04), but in the case of diarrhea, no significant difference was observed among the three groups (p = 0.14).

Conclusions. The interval of every 4 hours demonstrated a low risk of gastrointestinal complications, so it is suggested for use with patients in the ICU as the safest mode from the different intervals tested.

Key words: feeding methods, enteral nutrition, Intensive Care Unit.

Background
Nutrition is one of the basic human needs which is important for people in terms of promoting health and preventing diseases [1], such importance is more commonly highlighted for patients who are hospitalized in intensive care units (ICUs) [2]. Critically ill patients experience important metabolic changes in the course of their disease, changes which have profound effects on their nutritional status. In these patients, the metabolic response to stress and damage will increase the release of cytokines and certain hormones, such as catecholamine, glucagon, cortisol, and growth hormone. These hormones induce catabolism and overcome the anabolic effects of insulin; they cause hyper-metabolism, hyper-catabolism, and a loss of the body's energy reserves [3, 4].

Malnutrition is one of the conventional problems in acute diseases, which occurs in more than 40% of hospitalized patients and has a higher prevalence among ICU patients [5–7]. Malnutrition leads to increased rates of infection, delayed wound healing, bacteria growth in the digestive system, a loss of nutrients via the stool, a loss of respiratory muscle mass, increased dependence on mechanical ventilation, sepsis, increased length of hospital stay, increased mortality rate, and increased treatment costs [8–10]. Therefore, it is essential to support the nutritional needs of these patients.

Nutritional support is provided by tube or by intravenous methods. In patients whose gastrointestinal tract is functioning and who are simply unable to eat through their mouth, tube feeding is preferred over intravenous feeding because it is much closer to physiological conditions, prevents infection, and is cost-effective. However, there are several factors which can poten-
ially limit tube feeding, such as feeding intolerance, movement or obstruction of the feeding tube, and nutritional interference with diagnostic and therapeutic procedures and tests. Feeding intolerance, including high gastric residual volume, nausea, vomiting, and diarrhea, are the main limiting factors for food intake [11, 12]. Studies have shown that the number of hospitalization days in the ICU, the number of days with mechanical ventilation, and the mortality rate are higher in patients who experience feeding intolerance symptoms than in other patients [10, 13].

In tube feeding, the three methods which are typically used are intermittent bolus, intermittent drip, and continuous drip [14]. Studies have shown that each of these methods presents some advantages and some disadvantages. For example, Kadamani et al. examined the incidence of aspiration and gastrointestinal complications among critically ill patients undergoing tube feeding by continuous and bolus methods and concluded that there was no statistically significant difference in the incidence of vomiting, increased gastric residual volume, or pulmonary aspiration between these two feeding methods. However, the incidence of diarrhea was higher with the bolus feeding method and constipation was higher with the continuous feeding method [15]. In another study, Bowling et al. investigated the effect of nasogastric feeding using the bolus and continuous methods in gastroesophageal reflux disease (GERD) – and emptying the stomachs of healthy volunteers – and found no significant difference between the different feeding methods in terms of the incidence of complications among the healthy controls [16]. Büyükçoban et al. compared two different enteral nutrition protocols in critically ill patients and found a significant difference in the rate of gastrointestinal intolerance between two groups, reporting a lower gastrointestinal intolerance rate for a 4-hour bolus interval protocol (Group 1) than for an 8-hour protocol (Group 2) [17]. As shown by the results of these studies, there are some inconsistencies in the findings which require more extensive research in order to confirm the most appropriate nutrition method for patients hospitalized in ICUs.

According to the literature, most of the studies carried out on tube feeding methods deal with a comparison of bolus feeding and continuous methods; not many studies have been conducted on the time interval of bolus feeding in order to reduce complications. Considering the fact that the feeding method used in most Iranian hospitals today is bolus feeding at a 3-hour interval [18], the authors hypothesize that a 2-hour or 4-hour interval may be superior to the usual 3-hour interval in reducing complications.

Objectives

The aim of this study was to assess the effect of nasogastric feeding at different intervals on feeding tolerance among ICU patients.

Material and methods

Study design

This study was a 3-group clinical trial.

Participants

The research population included all of the patients hospitalized in the ICU of Besat Hospital, Hamadan, in western Iran. The ICU has 28 beds; the patients are visited daily by general surgical, internal medicine, and critical care specialists.

From 98 patients hospitalized in the ICU who underwent nasogastric feeding, 63 patients met the inclusion criteria and were selected to participate in the study (Table 1).

The inclusion criteria were as follows: an age of 18 years or more [19]; nasogastric feeding by the bolus method for at least three days of admission in the ICU according to a physician’s or

def; a Glasgow Coma Scale (GCS) score of less than 11; no history of diabetes, liver failure, or renal failure (due to the need for a special diet); no immunosuppressive diseases or use of immunosuppressing drugs; no gastrointestinal diseases or surgery during the previous six weeks [20]; no addiction to drugs or use of drugs which increase gastrointestinal motility [19]; and no diarrhea prior to the study [21]. The exclusion criteria were use of drugs that enhance gastrointestinal motility; a residual volume greater than 200 ml [2]; gastrointestinal complications due to reasons other than the patient’s intolerance; and patient’s transfer from the ICU to another ward. The tools used in this study included a checklist for recording nutritional status and a form for recording which drugs were administered.

Sampling method

The sampling was performed using the convenience sampling method, and the patients were divided into three groups. Once the proposed study was approved, the researchers assessed the patients, and after verifying that they met the inclusion criteria, obtained written consent from the patient or their guardian/family member. The number of calories required for each patient was calculated using the formula 25 kcal/kg/day [22]. Before entering the study, disease intensity and consciousness levels were assessed by the Acute Physiology and Chronic Health Evaluation (APACHE) II and GCS scales, respectively. The food formula and feeding method used were similar in all three groups. The food formula was standard Ensure powdered formula made in Germany and the feeding method was bolus feeding with a no. 18 Nasogastric tube. The first, second, and third groups were fed a volume of 200 ml every 2 hr, 300 ml every 3 hr, and 400 ml every 4 hr, respectively, by one of the ICU staff members. The tools used in this study included a checklist for recording which drugs were administered.

\[
\begin{align*}
\alpha &= \frac{Z^2 \times (1 - \beta)}{\delta^2} + \frac{Z^2\times(1-\alpha)}{\delta^2}, \\
\beta &= 2(1.64 + 1.64) \times \frac{5.85^2}{5^2} = -21/1.64 = Z_1 - \beta, 1.96 = Z_1^2 - \alpha/2, \delta = 5 \text{ mm} = \mu = \mu_j, \delta 2 = 5.85.
\end{align*}
\]

Ethical consideration

The study was approved by the Research Ethics Committee of Hamadan University of Medical Sciences (no. p/16/35/9/6169) and recorded in the Iranian Registry of Clinical Trials (IRCT) database (no. IRCT20140817188321N1). Also, this study was conducted in accordance with the ethical principles provided by the Declaration of Helsinki and the guidelines of the Iranian Ministry of Health and Medical Education. The purpose of this study was explained to the patients while they were conscious; otherwise, the explanation was provided for their family members and relevant authorities. Then, informed written consent was obtained from them.
Statistical analysis

After collecting the data for three days, descriptive and inferential statistical methods were used for the purpose of data analysis. To show the demographic characteristics, descriptive statistics such as frequency distribution tables, means and standard deviations, and—in order to compare feeding groups—inferential statistical tests such as the Kolmogorov–Smirnov test (to determine normal distribution of the variables), the chi-squared test, and analysis of variance (ANOVA) were used in Statistical Package for the Social Sciences (SPSS version 16.0, for Windows). A p-value of less than 0.05 was considered significant.

Findings

According to the results, the mean age of the patients in the 2-, 3-, and 4-hr groups was 51.57 ± 20.58, 59.38 ± 21.68, and 51.43 ± 19.73 years, respectively. The breakdown by gender was as follows: there were 17 male patients (81%) and 4 female patients (19%) in the 2-hr group, 14 men (66.7%) and 7 women (33.3%) in the 3-hr group, and 19 men (90.5%) and 2 women (9.5%) in the 4-hr group. In terms of reason for hospitalization, 36 patients (57.1%), 11 patients (17.5%), and 16 patients (25.4%) were hospitalized in the ICU due to trauma, neurological problems, or respiratory problems in the 2-, 3-, and 4-hr groups, respectively. The patients’ mean GCS score was 6.68 and their mean Apache score was 17.9. At the time of intervention, 90.4% and 57.1% of the patients were administered antibiotics and narcotics, respectively. Patients in all three groups had similar demographic and clinical characteristics and had received the same drugs (p > 0.05) (Table 1).

In terms of feeding complications, regurgitation was seen in a total of 27 patients (42.9%), of whom 14 (66.7%), 8 (38.1%), and 5 patients (23.8%) were fed at intervals of 2, 3, and 4 hours, respectively. The breakdown by feeding group was as follows: for the 2-hr group, 17 patients (81%) were fed a volume of 200 ml every 2 hr and 4 patients (19%) were fed a volume of 200 ml every 3 hr. For the 3-hr group, 14 patients (66.7%) were fed a volume of 200 ml every 3 hr and 7 patients (33.3%) were fed a volume of 200 ml every 4 hr. For the 4-hr group, 19 patients (90.5%) were fed a volume of 200 ml every 4 hr and 2 patients (9.5%) were fed a volume of 200 ml every 5 hr.

Table 1. Demographic and clinical details of the participants

<table>
<thead>
<tr>
<th>Variable</th>
<th>2-hr group (n = 21)</th>
<th>3-hr group (n = 21)</th>
<th>4-hr group (n = 21)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years): Mean ± SD</td>
<td>51.57 ± 20.58</td>
<td>59.38 ± 21.68</td>
<td>51.43 ± 19.73</td>
<td>0.360</td>
</tr>
<tr>
<td>Sex: n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>17 (81)</td>
<td>14 (66.7)</td>
<td>19 (90.5)</td>
<td>0.194</td>
</tr>
<tr>
<td>Female</td>
<td>4 (19)</td>
<td>7 (33.3)</td>
<td>2 (9.5)</td>
<td></td>
</tr>
<tr>
<td>GCS score Mean ± SD</td>
<td>6.62 ± 2.44</td>
<td>6.38 ± 2.27</td>
<td>7.05 ± 2.44</td>
<td>0.698</td>
</tr>
<tr>
<td>APACHE 2 score Mean ± SD</td>
<td>17.10 ± 5.19</td>
<td>18.57 ± 4.61</td>
<td>18.05 ± 5.74</td>
<td>0.649</td>
</tr>
<tr>
<td>Hospitalization causes: n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trauma</td>
<td>15 (71.4)</td>
<td>8 (38.1)</td>
<td>13 (61.9)</td>
<td>0.284</td>
</tr>
<tr>
<td>Neurological problems</td>
<td>3 (14.4)</td>
<td>5 (23.8)</td>
<td>3 (14.4)</td>
<td></td>
</tr>
<tr>
<td>Respiratory problems</td>
<td>3 (14.4)</td>
<td>8 (38.1)</td>
<td>5 (23.8)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Diagram of enrollment, allocation, follow-up, and analysis of the patients
respectively. Also, the chi-squared test revealed a statistically significant difference among the three groups (p = 0.017). Diarrhea was observed in 22 patients (34.9%), of whom 8 (38.1%), 10 (47.6%), and 4 patients (19%) were fed at intervals of 2, 3, and 4 hours, respectively; the chi-squared test did not reveal any statistically significant difference among the three groups (p = 0.194). Finally, high gastric residual volume was observed in 26 patients (41.3%), of whom 13 (61.9%), 8 (38.1%), and 5 patients (23.8%) were fed at intervals of 2, 3, and 4 hours, respectively. A chi-squared test revealed a statistically significant difference among the three groups (p = 0.04) (Table 2).

Discussion

Statistical tests for comparing the selected complications in the three feeding groups revealed a statistically significant difference between them in terms of the occurrence of regurgitation (p = 0.017) and high gastric residual volume (p = 0.04). In terms of suffering from diarrhea, however, the complication was more observed in the 3-hr group more than in the other groups, but the difference was not statistically significant (p = 0.194).

In this study, there was a statistically significant difference among the three groups in occurrence of regurgitation and high gastric residual volume. There was no significant difference in the incidence of diarrhea. In terms of feeding tolerance status, the patients fed at 4-hr intervals were at a minimal level. Nevertheless, some studies have shown that feeding intolerance is a complication which is more prevalent in bolus feeding than other methods. In Zeraatkari et al. study, patients tolerate the continuous method better than the bolus method [28]. However, the results of a study by MacLeod et al. which compared continuous and intermittent feeding in critically ill trauma patients showed that the patients receiving intermittent feeding every 4 hr reached the target caloric intake faster than the patients undergoing continuous feeding; also, this feeding method is simpler than the continuous method, therefore, the quality of training to nursing staff could be an important factor in the difference between the results of studies [35, 36].

Table 1. Demographic and clinical details of the participants

<table>
<thead>
<tr>
<th>Variable</th>
<th>2-hr group (n = 21)</th>
<th>3-hr group (n = 21)</th>
<th>4-hr group (n = 21)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug intake: n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics</td>
<td>19 (90.5)</td>
<td>19 (90.5)</td>
<td>20 (95.2)</td>
<td>1</td>
</tr>
<tr>
<td>Inotropics</td>
<td>1 (4.8)</td>
<td>3 (14.3)</td>
<td>1 (4.8)</td>
<td>0.605</td>
</tr>
<tr>
<td>Narcotics</td>
<td>14 (66.7)</td>
<td>10 (47.6)</td>
<td>12 (57.1)</td>
<td>0.459</td>
</tr>
<tr>
<td>Antacids</td>
<td>20 (95.2)</td>
<td>18 (85.8)</td>
<td>21 (100)</td>
<td>0.311</td>
</tr>
</tbody>
</table>

Table 2. Comparing feeding tolerance between the three feeding intervals

<table>
<thead>
<tr>
<th>Variables</th>
<th>2-hr group (n = 21)</th>
<th>3-hr group (n = 21)</th>
<th>4-hr group (n = 21)</th>
<th>Pearson chi-squared test value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regurgitation:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No: 36 (57.1%)</td>
<td>7 (33.3%)</td>
<td>13 (61.9%)</td>
<td>16 (76.2%)</td>
<td>8.167</td>
<td>0.017</td>
</tr>
<tr>
<td>Yes: 27 (42.9%)</td>
<td>14 (66.7%)</td>
<td>8 (38.1%)</td>
<td>5 (23.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No: 41 (65.1%)</td>
<td>13 (61.9%)</td>
<td>11 (52.4%)</td>
<td>17 (81%)</td>
<td>3.911</td>
<td>0.141</td>
</tr>
<tr>
<td>Yes: 22 (34.9%)</td>
<td>8 (38.1%)</td>
<td>10 (47.6%)</td>
<td>4 (19%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastric residual volume ≥ 150 ml:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No: 37 (58.7%)</td>
<td>8 (38.1%)</td>
<td>13 (61.9%)</td>
<td>16 (76.2%)</td>
<td>6.418</td>
<td>0.040</td>
</tr>
<tr>
<td>Yes: 26 (41.3%)</td>
<td>13 (61.9%)</td>
<td>8 (38.1%)</td>
<td>5 (23.8%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

found that there was no statistically significant difference in the feeding method in terms of the incidence of diarrhea, vomiting, or gastric residual volume (p < 0.05) [15].

In the present study, regurgitation occurred in 42% of the patients, which was consistent with the results of Reitnam et al. [31]. Also, diarrhea was found in 35% of our patients and the statistical tests showed no difference among the three feeding groups in the incidence of this complication, a finding which is consistent with studies by Montejo et al. [32] and Lee and Auyeung [33]. Serpa et al. found that high gastric residual volume occurred in 46.6% of the patients undergoing tube feeding, though there was no significant difference among the feeding groups in terms of incidence of high gastric residual volume [34]. The results of this study were consistent with our study when it comes to high gastric residual volume.

The results of these studies are sometimes consistent with our results. It seems that the cause of these differences and contradictions can be due to differences in the study groups, nutritional support, and follow-up period. Since nursing practices such as proper nutrition in ICU require adequate and appropriate training, therefore, the quality of training to nursing staff could be an important factor in the difference between the results of studies [35, 36].

Limitations of the study

The limitations of this study were the small sample size and the short follow-up period, as well as the fact that the intervention took place in a limited clinical setting, which could reduce the generalizability of the findings. Therefore, it is recommended to perform additional studies and compare different feeding methods in other wards, with a larger sample size and a longer follow-up period.

Conclusions

Our study showed that the patients in the ICU who underwent the feeding program using the bolus method at an interval of 4 hr had better feeding tolerance. Therefore, this interval can be used with patients who are fed by the bolus method but cannot tolerate it. This interval can replace the 3-hr feeding interval which is currently used in ICUs. This finding may be useful for all ICU nurses as well as patients who require tube feeding at home, including stroke and cancer patients, in order to prevent aspiration and its complications.
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References


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