Multicenter, prospective, randomized, single-blind study comparing the efficacy and gastrointestinal complications of early jejunal feeding with early gastric feeding in critically ill patients

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Objective: To compare the incidence of enteral nutrition-related gastrointestinal complications, the efficacy of diet administration, and the incidence of nosocomial pneumonia in patients fed in the stomach or in the jejunum.

Design: Prospective, randomized multicenter study.

Setting: Intensive care units (ICUs) in 11 teaching hospitals.

Patients: Critically ill patients who could receive early enteral nutrition more than 5 days.

Interventions: Enteral nutrition was started in the first 36 hrs after admission. One group was fed with a nasogastric tube (GEN group) and the other in the jejunum through a dual-lumen naso-gastrojejunal tube (JEN group).

Measurements and Main Results: Gastrointestinal complications were previously defined. The efficacy of diet administration was calculated using the volume ratio (expressed as the ratio between administered and prescribed volumes). Nosocomial pneumonia was defined according to the Centers for Disease Control and Prevention’s definitions. One hundred ten patients were included (GEN: 51, JEN: 50). Both groups were comparable in age, gender, Acute Physiology and Chronic Health Evaluation II, and Multiple Organ Dysfunction Score. There were no differences in feeding duration, ICU length of stay, or mortality (43% vs. 38%). The JEN group had fewer gastrointestinal complications (57% vs. 24%, p < .001), mainly because of a lesser incidence of increased gastric residuals (49% vs. 2%, p < .001). Volume ratio was similar in both groups. A post hoc analysis showed that the JEN group had a higher volume ratio at day 7 than the GEN group (68% vs. 82%, p < .03) in patients from ICUs with previous experience in jejunal feeding. Both groups had a similar incidence of nosocomial pneumonia (40% vs. 32%).

Conclusions: Gastrointestinal complications are less frequent in ICU patients fed in the jejunum. Nevertheless, it seems to be a necessary learning curve to achieve better results with a postpyloric access. Early enteral nutrition using a nasojejunal route seems not to be an efficacious measure to decrease nosocomial pneumonia in critically ill patients. (Crit Care Med 2002; 30:796–800)

Key Words: enteral nutrition; critical illness; pneumonia; aspiration; intensive care units; intubation; gastrointestinal; prospective studies

Nutritional support is one of the routine therapeutic measures in critically ill patients. Some studies have advocated that enteral nutrition is better than parenteral nutrition because it maintains intestinal structure and function, it can limit bacterial translocation, it has a lesser morbidity rate and less severe complications, and it is cheaper (1–3). Also, it has been shown that early enteral nutrition administered to critically ill patients can decrease the number of infectious complications, length of stay, and mortality (4–6). Early enteral nutrition is the treatment of choice with slower weaning rates, and is most effective in patients with burned injuries (7). Enteral nutrition is the treatment of choice with slower weaning rates, and is most effective in patients with burned injuries (7).
methods to avoid the stomach and to better feed the patient (15–17). Enteral feeding through a jejunal tube could decrease the gastrointestinal complication rate, could give more volume of diet, and could decrease the incidence of bronchoaspiration and secondary pneumonia (18). This study has been designed to assess the effectiveness and gastrointestinal complications of early jejunal feeding with a double-lumen nasogastrojejunal tube (Stay-Put, Novartis Consumer Health, Barcelona, Spain) compared with early gastric feeding in critically ill patients. The primary objectives have been the gastrointestinal complication rate and the incidence of nosocomial pneumonia.

**MATERIALS AND METHODS**

**Protocol.** A prospective, multicenter, randomized, single-blind study was performed in 14 intensive care units (ICUs) during 6 months. Patients >18 yrs were enrolled if they would need enteral feeding for >5 days and there were no contraindications for it. The institutional review board of each participating hospital approved the study. Informed consent was obtained from the patients or their relatives.

**Patients.** Adult patients were eligible if they would need enteral nutrition for >5 days in ICU. Patients entered in the study were followed up prospectively until ICU discharge or after 28 days follow-up during the study period. Age, sex, weight, primary diagnosis, Acute Physiology and Chronic Health Evaluation II (APACHE II) score (19) and multiple Organ Dysfunction Score (MODS) (20) were recorded at admission. Exclusion criteria were anatomical disruptions of the gastrointestinal tract, previous gastrointestinal surgery, or contraindication for enteral nutrition or gastroendoscopy.

**Tube Placement.** Patients were randomly assigned to be fed through a standard nasogastric tube (GEN group) or through a dual-lumen nasogastrojejunal tube (JEN group) (Stay-Put, Novartis). The nasogastric tube was placed at admission. In the JEN group, the nasogastrojejunal tube was placed in the first 36 hrs after admission by endoscopy, fluoroscopic guidance, blind technique, or by echography. A plain film of the abdomen before diet administration was done to check correct enteral tube placement. Complications related to tube placement were defined previously and registered. Blockage was considered when it was impossible to administer the diet through the tube. Accidental withdrawal was defined as when the tube was removed partially or totally by the patient or during routine care. Dislodgment was considered if there was any radiologic evidence of misplacement of the tubes. If one of these complications was not resolved in the following 24 hrs after detection, the patient was withdrawn from the study.

**Diet Administration.** Caloric requirements and the type of enteral feeding formula were selected by each investigator. Feedings were started in the first 36 hrs after admission and delivered continuously to achieve half of the estimated caloric needs in 24 hrs. The goal was to achieve the calculated caloric requirements in the first 48 hrs of enteral nutrition. Feedings were infused at a constant rate by an infusion pump, and the containers and delivery systems were changed after 24 hrs use. The following data were recorded in accordance with the management protocol: estimated caloric needs, time of first feeding, type of enteral feeding, and duration of their use. The volume ratio, expressed as the ratio between administered and prescribed volumes, was calculated daily as an administration efficacy index. All gastrointestinal complications were recorded prospectively including the number of episodes, day of presentation, and duration according to an established protocol (11). In the JEN group, increased gastric residual was considered when the volume of the gastric aspirated was ≥300 mL. When detected, the diet was stopped in the next 6 hrs. Reasons for enteral withdrawal were also registered.

**Outcome Assessment.** Primary end points were gastrointestinal complications rate, volume ratio, and ventilator associated pneumonia incidence. Pneumonia was diagnosed according to Centers for Disease Control and Prevention (CDC) criteria (21). MODS at day 5 and at discharge, length of stay, and mortality were also registered.

**Statistical Analysis.** Random numbers were generated by computer for group assignment. Each hospital was the unit of randomization. Sample size was calculated to decrease the nosocomial pneumonia from the 48% infection rate in the GEN group, using the previous data of our group, to 20% in the JEN group. The calculated sample size was 152 patients, with 80% power and 5% significance. An intermediate analysis was done after recruiting 60% of the patients. Statistical analysis was done by intent-to-treat. Continuous data were assessed for normality, and the tests used were two-tailed Student’s t-test for normal data and Mann-Whitney for nonnormal distributions. The chi-square test with Yates’ correction was applied for proportions. Relative risk was calculated for the outcome end points. Data are expressed as mean ± so if not quoted otherwise. Statistical analysis was performed by a specialized independent institution.

**RESULTS**

A total number of 101 patients (51 GEN group, 50 JEN group) were enrolled during the 1-yr study period (Table 1). Both groups were homogeneous in demographic data and admission severity scores (Table 2).

The GEN tube was placed 5.3 ± 7.9 hrs after admission by spontaneous passage. The JEN tube was placed 21.0 ± 9.8 hrs after admission using the blinded technique in 15 patients or using endoscopy (18 patients), fluoroscopic guidance (12 patients), or echography (5 patients). One patient in the GEN group and seven in the JEN group had placement-related complications (p < .06). The JEN group had more complications related to tube maintenance (28 vs. 8 patients; p < .001).

Enteral feeding characteristics are indicated in Table 3. Enteral tube-related complications were responsible for en-
teral nutrition withdrawal in nine patients in the JEN group.

Enteral nutrition-related gastrointestinal complications were less frequent in the JEN group, with a significant decrease in the incidence of high gastric residuals and a similar rate of the other gastrointestinal complications (Table 4).

There were no differences in the caloric intake or in the volume ratio between groups during the complete follow-up (Table 5). Some ICUs had previous experience with the JEN tube used in the study. A post hoc analysis limited to data from the six ICUs with previous experience showed that the JEN group received significantly more calories and had a better volume ratio at day 7 (Table 6).

There were no differences in the incidence of nosocomial pneumonia between both groups (Table 7). Also, we were unable to find any differences in ICU length of stay, multiple organ failure score, or mortality (Table 7).

**DISCUSSION**

Studies that have assessed the gastric emptying in critically ill patients undergoing mechanical ventilation show that these patients had a marked alteration of normal gastric emptying (22–25). The impaired gastric emptying explains the gastric intolerance to enteral feedings and can justify the use of a double-lumen gastroenteric tube for enteral nutrition.

The hypothesis that early enteral nutrition would be more effective when using the transpyloric route if compared with the gastric access is confirmed in this study if we look at the different rate of enteral nutrition-related gastrointestinal complications that we have found. Nevertheless, the absence of increased gastric residuals in the patients who received feedings through the jejunal tube did not result in higher volumes of the administered diet or an increased caloric intake. The potential reasons are the increased frequency of tube-related complications (occlusion, accidental withdrawal, and dislodgment) found in the jejunal group. These complications make it difficult to maintain the caloric intake and are the cause of definitive enteral nutrition withdrawal. This assumption seems to be confirmed by the results coming from the centers with previous experience in the use of this kind of nasogastrojejunal tubes, where we found a higher caloric intake in the jejunal group compared with the gastric one.

We have been unable to demonstrate that jejunal feedings combined with gastric suction can decrease the incidence of nosocomial pneumonia in critically ill patients compared with the gastric route. Other studies have shown similar results. Montecalvo et al. (26) compared the incidence of nosocomial pneumonia in 38 critically patients randomly assigned to be fed via a gastric tube or a jejunal one placed by gastroscopy. In their study, the group fed by the jejunal route received more calories than the group fed by the gastric route but there were no differences in the incidence of nosocomial pneumonia. A similar study (27) with 44 patients showed also that the transpyloric access led to more caloric intake but the nosocomial pneumonia incidence was similar in both groups. In trauma patients, Kortbeeck et al. (28) studied also the efficacy of the transpyloric route to deliver nutrients compared with the gastric one. By using the transpyloric access, patients achieved the caloric goal earlier than patients fed by the gastric route, but, again, the authors were unable to find any differences in the incidence of pneumonia, ICU length of stay, or mortality. According to the similar incidence in

**Table 3. Enteral nutrition characteristics**

<table>
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<tr>
<th>All (%), GEN Group (%), JEN Group (%), p Value</th>
<th>Time of initiation, hrs</th>
<th>Duration, days</th>
<th>Reasons for withdrawal (%)</th>
<th>ICU discharge</th>
<th>Oral</th>
<th>Enteral nutrition complications</th>
<th>Enteral tube complications</th>
<th>Other complications</th>
<th>Terminal illness</th>
<th>Death</th>
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<td>24 ± 10</td>
<td>12 ± 9</td>
<td>20 (20)</td>
<td>14 (28)</td>
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<td>24 ± 10</td>
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<td>18 (36)</td>
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<td>24 ± 9</td>
<td>11 ± 8</td>
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**Table 4. Gastrointestinal complications of enteral feeding: Patients with one or more complications**

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<thead>
<tr>
<th>All (%), GEN Group (%), JEN Group (%), p Value</th>
<th>Abdominal distention</th>
<th>Vomiting</th>
<th>Diarrhea</th>
<th>Constipation</th>
<th>High gastric residuals</th>
<th>One of these complications</th>
<th>Death</th>
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<tr>
<td></td>
<td>9 (9)</td>
<td>6 (6)</td>
<td>14 (14)</td>
<td>5 (5)</td>
<td>26 (25)</td>
<td>35 (35)</td>
<td>32 (32)</td>
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<td>4 (8)</td>
<td>2 (4)</td>
<td>7 (14)</td>
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<td>20 (67)</td>
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<td>5 (10)</td>
<td>4 (8)</td>
<td>7 (14)</td>
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<td>12 (24)</td>
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**Table 5. Planned and administered caloric intake**

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<tr>
<th>All, GEN Group, JEN Group, p Value</th>
<th>Caloric requirements</th>
<th>Planned caloric intake at day 3</th>
<th>Administered calories at day 3</th>
<th>Planned caloric intake at day 7</th>
<th>Administered calories at day 7</th>
<th>Volume ratio at day 3, %</th>
<th>Volume ratio at day 7, %</th>
<th>Mean planned caloric intake</th>
<th>Mean administered calories</th>
<th>Difference between planned and administered calories</th>
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<td></td>
<td>1831 ± 354</td>
<td>1588 ± 412</td>
<td>1337 ± 482</td>
<td>1604 ± 426</td>
<td>1248 ± 582</td>
<td>84 ± 24</td>
<td>77 ± 29</td>
<td>1491 ± 346</td>
<td>1261 ± 342</td>
<td>217 ± 177</td>
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<td>1797 ± 311</td>
<td>1576 ± 393</td>
<td>1339 ± 443</td>
<td>1566 ± 403</td>
<td>1181 ± 564</td>
<td>86 ± 23</td>
<td>75 ± 30</td>
<td>1461 ± 301</td>
<td>1237 ± 342</td>
<td>225 ± 173</td>
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<td>1864 ± 394</td>
<td>1601 ± 435</td>
<td>1335 ± 523</td>
<td>1643 ± 451</td>
<td>1317 ± 598</td>
<td>83 ± 25</td>
<td>80 ± 28</td>
<td>1523 ± 388</td>
<td>1286 ± 344</td>
<td>211 ± 183</td>
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*p Patients fed through a standard nasogastric tube; **Patients fed through a dual-lumen nasogastric-jejunal tube.
pneumonia indicated in the above-mentioned studies, Epsparza et al. (29), in a recent study, reported, with an isotopic method, that aspiration rates were no different between gastrically or transpylorically fed critically ill patients.

Other studies have not shown the above-indicated superiority of the transpyloric route over the gastric access in terms of caloric intake. In a prospective, randomized study done in 32 critically ill patients, Strong et al. (30) did not show any advantage in time needed to achieve the caloric requirements or in the incidence of nosocomial pneumonia. Another retrospective study (31) also failed in demonstrating advantages in nutritional efficacy (time needed to achieve caloric goals) or in the incidence of nosocomial pneumonia with the transpyloric route.

Despite the fact that enteral nutrition is considered to be a risk factor for the development of nosocomial pneumonia in critically ill patients (32, 33), it has not been established whether gastric infusion of feeding formula is accompanied by a greater incidence of pneumonia in comparison with transpyloric infusion of nutrients. Our study does not support the use of any of the two routes, gastric or transpyloric, to decrease the incidence of pneumonia. The trend toward a decreased incidence of pneumonia that we have found in our patients fed by a transpyloric tube is not significant. This would be a problem because of the number of patients studied. As the study by Kortbeeck et al. (28) points out, the number of patients needed to demonstrate a difference of 10% or more in the frequency of nosocomial pneumonia is 400 patients, or even more if we look at our results.

Another question to be solved is the criteria used for the diagnosis of mechanical ventilation associated pneumonia. The CDC criteria used in this study could have overestimated the true pneumonia incidence. Nevertheless, these criteria have been applied equally to both groups, and, therefore, it should not be a confounding factor. Other techniques, such as the quantitative cultures of tracheal aspirates or the use of protected brush catheters, could improve the results but, as other authors have pointed out (34), there are difficulties in unifying the diagnostic criteria of the ventilator-associated pneumonia in multicenter studies. Because the proposed solutions are not implemented in the clinical setting, we thought that clinical diagnoses using objective criteria, such as the CDC recommendations used in our study, are adequate.

We can conclude that early placement of a transpyloric tube for enteral nutrition in a nonselected population of critically ill patients is not useful in terms of reducing the incidence of nosocomial pneumonia or increasing nutritional efficacy. Perhaps further studies using other diagnostic criteria of ventilator-associated pneumonia with more patients would demonstrate any difference. Our results support the hypothesis, advanced by other authors (35), that the transpyloric tube is as useful as a nasogastric tube for early enteral nutrition in critically ill patients. Nevertheless, it remains to be established if the transpyloric approach could be effective in selected groups of patients, such as patients who develop high gastric residuals while receiving a diet using the gastric approach. Switching to a transpyloric access when the gastric route fails will be the only way to maintain the enteral nutrition in these cases.

Results such as these also indicate that parenteral nutrition must be needed in patients in whom nasogastric or nasojejunal feeding is partially or completely ineffective.

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