Enteral Nutrition In Critically Ill Patients

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ABSTRACT

Critical illness, stress, and surgery place increased demands on the body's nutritional requirements. These conditions promote a catabolic state and negative nitrogen balance. Nutritional problems are common in critically ill patients. Nutritional supplementation affords the opportunity of slowing down or stopping the catabolic process, restoring nitrogen balance, and preventing malnutrition. Enteral nutrition preserve the integrity of the gastrointestinal mucosa and enhance immune function. Early enteral nutrition administration to critically ill patients can decrease the number of infectious complications, length of stay and mortality. However, early enteral nutrition in the critically ill is often limited by gastroparesis, which impairs gastric emptying, thereby promoting gastroesophageal reflux and aspiration pneumonia. However, Early enteral nutrition is the treatment of choice with an A level of recommendation for some authors.

A total of two hundred critically ill adult patients were enrolled in the study. Daily 18-hrs enteral nutrition via a 14F gastric tube was initiated either immediately after stabilization in group I, or later than 48hrs after admition in group II. Residual gastric volume was measured every 6hrs, and enteral nutrition was discontinued if exceed 300ml or vomiting occurred. Nutritional outcome measures included the percentage of the goal rate achieved during the study period, volume ratio, and gastrointestinal complications rate. Clinical outcomes included the incidence of ventilator associated pneumonia, multiple organ failure score, the duration of mechanical ventilation, and the length of ICU stay.

Conclusion: Overall, the evidence suggests that early enteral feeding is beneficial to critically ill patients. In our study early intervention was associated with shorter duration of mechanical ventilation and ICU stay. Patients in the early feeding group had less sever form of MOF, and decreased infectious complications and mortality. The early institution of nutritional support and the use of enteral nutrition optimize nutritional status of the patient and reduce complications associated with bowel rest resulting in improved clinical outcomes in critically ill patients.

INTRODUCTION

In the care of the critically ill patient, the first line of therapy is directed towards stabilization of the patient, optimizing haemodynamics and perfusion, and ensuring life-sustaining gas exchange (1). The initial management generally does not involve assessment of underlying nutritional status. Acute illness is associated with prolonged hyper metabolism, hyper catabolism and nitrogen loss. Negative energy and nitrogen balance are attributed to the combined effect of increased resting energy expenditure, catabolism, immobilization and inadequate nutritional delivery (2).

Malnutrition is a common problem in critically ill patients due to, inadequate nutritional support during ICU stay, because physician underestimates the nutritional needs of patients and the initiation of nutritional therapy is often delayed (3). Malnutrition in ICU patients is associated with increased morbidity, mortality and length of ICU stay due to increased ventilator dependency, higher rates of infection and impaired wound healing (4). Recent studies demonstrated that, critical illness result in local release of inflammatory cytokines such as tumor necrosis factor (TNF), interleukin-1 (IL-1) and interleukin-6 (IL-6) and in systemic release of such counter-regulatory hormones such as adrenocorticotropic hormone (ACTH), antiuretic hormone (ADH), catecholamines and cortisol. Cytokines along with systemic hormones induce hyper catabolism (5). Reperfusion may compound the effect of the original injury by causing a massive systemic release of cytokines from the bowel and...
sometimes the lung. Changes in the enteral flora coupled with increased intestinal permeability result in a predictable flooding of the liver with endotoxin and possibly translocated bacteria which may amplify the cytokine response, promote sepsis or multorgan failure and potentiate hyper catabolism and protein-caloric malnutrition\(^5\).

Nutrition support is an accepted standard of care in intensive care units. Recent consensus conferences recommended that appropriate caloric intake should be provided to critically ill patients as a major component of therapy\(^6\). Nutrition support can result in improved wound healing, a decreased catabolic response to injury, enhanced immune system function, improved gastrointestinal structure and function and improved clinical outcome\(^7\). The primary goal of nutrition support for the critically ill patients is to provide adequate nutrients that are appropriate for the patients underling medical condition, nutritional status and available route of nutrient delivery, and to avoid complications related to the technique of providing nutrition support. Enteral nutrition is generally preferred over parenteral nutrition as it is more physiologic, is less likely to be associated with hepatobiliary dysfunction and metabolic derangement and is substantially less expensive\(^8\). However, infectious hazards, tissue injury and aspiration associated with placement and maintenance of orogastric and nasogastric tubes used for delivery of enteral nutrition suggest that not all patients benefits from this treatment. Recent data demonstrated that, enteral feeding reduce the metabolic response to stress, decrease bacterial translocation and maintain gut mucosal integrity, so nutritional intake through the digestive tract has been strongly recommended\(^9\). If enteral nutrition is preferable, starting sooner may be better. Recent data suggest that gut barrier dysfunction (mucosal atrophy and altered permeability) in critically ill patients occur very quickly\(^10\). The so called gut hypothesis of multiple organ failure suggests that, failure of the gut barrier and the consequent increased bacterial and endotoxin translocation play an important role in the pathogenesis of this syndrome\(^11\). The early use of enteral nutrition in the setting of acute illness improve immune function, augments the cellular antioxidant system, decrease the hyper metabolic response to tissue injury, preserves intestinal integrity and improves nitrogen balance and wound healing\(^12,13\). Although there are clear evidence that early gastric feeding provides the most normal route for enteral nutrition, the routine practice of instituting early enteral nutritional support is not widespread\(^14\). Observational studies documented low rates of optimal use of enteral nutrition in the critical care setting\(^15,16\). The use of this technique is limited by several technical problems and their related complications. Enteral nutrition is often started several days after admission due to, the lack of reliable access, the risk of regurgitation, aspiration pneumonia and gastrointestinal intolerance. Another important barrier in the application of early enteral nutrition is the physician practice pattern\(^17,18\). This study has been desiend to determine whether the implementation of early enteral nutrition management protocol in the critically ill patients while minimizing risks and maximizing benefits of nutrition support was associated with beneficial or detrimental outcomes compared with delayed enteral feeding. As a secondary end point, we studied the occurrence of hospital acquired infection among patients receiving early enteral nutrition. We also evaluated the impact of the protocol on tolerance of early enteral nutrition, the duration of mechanical ventilation, incidence of ventilator associated pneumonia, the length of ICU stay and in hospital mortality rates in these patients.

**PATIENTS AND METHODS**

**Patients**

The study was performed in the adult ICU of Elmenoufia university hospital (14 beds), and Dammanhour teaching hospital (17 beds) during 12 consecutive month. Subjects were recruited from the medical and surgical intensive care units (ICU). The following inclusion criteria were used: men and women \(\geq 18\) years of age, stay in ICU of 3 days or more, required enteral feeding for \(\geq 5\) days, and no do-no-resuscitate order at the time of admission. Exclusion criteria were pregnancy, current acute pancreatitis, bleeding from the stomach or esophageal varices, facial trauma, a history of esophageal or gastric surgery, burns and sever head trauma. The study protocol was
approved by the medical ethics committee in our institute, and informed consent was obtained from all patients relatives before study inclusion. No antacids, H₂-antagonists, or proton pump inhibitors were given for stress ulcer prophylaxis. The following characteristics were evaluated for each patient at the time of admission: age, gender, weight, simplified acute physiology score II (APACHE II), primary diagnosis, underlying disease and multiple organ dysfunction score (MODS). Vital signs, medication, clinical and laboratory values were monitored daily. Function of organ system were evaluated by determining serum aspartate, alanine aminotransferase, total bilirubine, creatinine, leucocytes and platelet counts and respiratory gases in arterial blood. Patients were followed until they were discharged from the ICU or until death.

Tube placement
Patients were randomly assigned to be feed through a standard nasogastric tube. A 14-Fr nasogastric tube was placed at time of admission. A plain film of the abdomen before diet administration was done to check correct enteral tube placement. Complications related to tube placement were defined and registered. Blockage was considered when it was impossible to administer the diet through the tube. Accidental withdrawal was defined as when the tube removed partially or totally by the patient or during routine care. Dislodgement was considered if there was any radiographic evidence of misplacement of the tube. If one of these complications was not resolved in the following 24 hrs after detection, the patient was withdrawn from the study.

Protocol of early enteral nutrition
All patients were evaluated for the need for nutritional support at the time of admission. Energy requirement for each patient was calculated by using Harris-Benedict formula¹⁹, adjusted with a stress factor of 1.2 or 1.5 according to the patients condition²⁰. Patients were randomly allocated into two groups, 100 patients each as follow, patients on group I were placed on immediate intragatric tube feeding, while patients on group II were started on enteral nutrition later than 48 hrs after admission. Feeding was initiated with Fresubin® original (1.0 kcal/ml) (Fersenius kabi). The goal rate was determined to be the rate of the prescribed formula that provides an average of 30 kcal/kg/day. Enteral nutrition was delivered into the stomach using bolus feeds of 30 ml/hr run in by gravity. Increasing up to the target rate in the increments 30, 60, and 90 ml/hr as tolerated from 6:00 am to 12:00 pm. The goal was to administer 500ml on the first day, 1000ml on the second day, 1500ml on the third day, and 2000ml on the fourth and fifth days. Patients were not feed from 12:00 pm to 6:00 am. Erythromycin 200 mg IV, was given every 8 hours as a prokinetic, for 96hrs and continued or repeated when needed according to gastrointestinal dysfunction management protocol. Head of each patients bed was elevated to greater than 30 degree except during the performance of specific procedure, so long as their medical condition tolerating this position.

The following data were recorded: estimated caloric need, time of first feeding, time to goal, the volume ratio and change in albumin and pre-albumin. The beginning time of the study was the time that tube insertion began. Time to goal was the time from the beginning of the study to the time the goal rate was obtained and successfully continued for 4hrs. The volume ratio, considered as an index of efficiency of nutrient delivery, was calculated as follows:

VR% = administered volume of diet ÷ prescribed volume of diet × 100.

The volume ratio was calculated daily as an administration efficacy index. All difference between caloric prescription and caloric delivery were recorded by the bedside nurses and classified as one of the following: A) gastrointestinal dysfunction, B) interruption attributable to airway management, C) interruption attributable to diagnostic procedure, D) mechanical problems (gastric tube malposition or occlusion).

Tolerance to early enteral nutrition
We defined tolerance to early enteral nutrition as receiving more than 90% of the required volume of feed to meet daily energy requirement for 48 hrs, in the absence of gastrointestinal dysfunction. GI dysfunction were defined as follow: A) Abdominal distension, abdominal changes on the daily
physical examination, with tympani or the absence of bowel sounds. B) High gastric residual, refer to the volume of gastric content aspirate via a nasogastric tube at episodic check. C) Vomiting, enteral formula ejected from the mouth. D) Diet regurgitation, enteral formula found in the oral or nasal cavities. E) Diarrhea, as more than 6 watery bowel movement within 24 hrs. F) Constipation, need for treatment with laxative or enema. Residual gastric volume was measured at 6 hrs, intervals by aspirating the nasogastric tube with 50ml syringe. The aspirate returned to the patients unless exceed 300ml. All GICs were recorded including, the number of episodes, days of presentation and duration.

GI dysfunction management protocol

The following management protocol for each GIC was applied, a) abdominal distention, if bowel sounds were present despite abdominal distention, feeding rate was decreased to half dose and the patient was reevaluated in the following 12hrs, if distention disappear, the previous feeding rate was resumed, if distention persist enteral nutrition was definitively withdrawn. B) high gastric residuals, enteral nutrition was discontinued if a 6-hrs residual gastric volume exceeds 300ml. After discontinuation, prokinetic treatment (erythromycin, 250mg intravenously, every 6 hours) was reinstituted, and enteral nutrition was resumed 6hrs later at the slower rat well tolerated before discontinuation. c) vomiting and diet regurgitation, the diet was stooped, the abdomen was examined and a plain film of the abdomen cheeked the tube position. Enteral feeding was resumed after correction of the detected alteration. D) diarrhea, feeding rate was decreased, patient had rectal swab culture for vancomycin-resistant enterococci and C-difficile, and appropriate antimicrobial medications was given. E) constipation, enema and laxative were used without feeding rate change. Definitive withdrawal of enteral nutrition was considered if the previously described management protocol was not able to control the GICs in a period of 3 days. Patients from whom the enteral nutrition was stopped withdrawn from the study.

Ventilator-associated pneumonia

Only the first episode of ventilator associated pneumonia was evaluated. The diagnostic criteria for ventilator associated pneumonia used in this study were modified from those established by the American college of chest physicians (21). It was defined as the occurrence of new and persistent radiographic infiltrates in conjugation with 1 of the following: positive pleural / blood culture of the same organism as that received in the tracheal aspirate or sputum, radiographic cavitations, or histopathologic evidence of pneumonia, or with 2 of the following: fever (body temperature of ≥ 38.5°C), leucocytosis, or purulent tracheal aspirate. Persistence of an infiltrate was defined as having the infiltrate present radio graphically for at least 72hrs. Leucocytosis was defined as a 25% increase in circulating leucocytes from the base line and a value greater than 10000/mm³. Tracheal aspirates were considered purulent if abundant neutrophiles were present per high power field using Gram's stain (> 25 neutrophiles per high power field). A clinical diagnosis of ventilator associated pneumonia also required, a clinical pulmonary infection score (CPIS) greater than 6(22). Additionally when available bronchoscopic bronchoalveolar lavage quantitative culture were used to support the diagnosis of ventilator associated pneumonia using a threshold of 104 colony.

Outcome assessment

The primary outcome were the percentage of goal rate achieved during the study period, volume ratio, gastrointestinal complications rate and ventilator associated pneumonia incidence. Secondary outcomes included the following: infection complications, defined as the occurrence of any infection (pneumonia, urinary tract infection, catheter related and blood stream infection) related or unrelated to nutrition. Microbiological studies such as sputum Gram's stained, sputum, blood and pleural culture were used for diagnosis of infection complication. All complications were recorded as number of patients experiencing complications. Other available records included, the duration of mechanical ventilation, the total number of antibiotic days in the ICU, diarrhea associated with
clostridium difficile infection, metabolic factors such as serum Ca, K, and amylase concentration, multiple organ failure score, the length of ICU stay and mortality rate were also registered.

Groups were compared by student's t-test for continuous data and by the chi-square test for categorical variables. Whitney test was used to compare the two studied groups for median daily residual gastric volume values, median enteral nutrition values and episodes of vomiting. Values were considered significant at \( P < .05 \).

**RESULTS**

A total of 200 patients were evaluated for enrollment in the study of those 17 were excluded because their underlying medical condition rapidly resolved. By the end of the study, the final analysis involved 158 patients, 77 in group \( \text{I} \) and 81 in group \( \text{II} \). The base line characteristics of the two studied groups are summarized in (table I), patients in both groups were predominantly male, moderately to severely malnourished at the time of their admission, most of them were mechanically ventilated. The most common admission diagnosis for medical patients were respiratory failure, pneumonia and sepsis. Surgical patients most frequently underwent general surgery. There were no difference between the two studied groups for age, sex rate, simplified acute physiology score II, diagnosis, weight or risk factor for gastroparesis. All patients survived their treatment in the ICU.

(Table II) (Fig.1) provides information on the estimated daily caloric requirements, the nutrient intake and the percentage attainment of goal rate in the two studied groups. At the end of the first week, group \( \text{I} \) was receiving daily a larger quantity of enteral feed than group \( \text{II} \) (\( p<0.025 \)), although the protocol prescribed equal amounts of food for both groups. The actual daily calories delivered to patients during the first week after ICU admission was statistically greater among patients who had sufficient energy intake. (Table III,IV) (Fig.2) provide information on the enteral nutrition-related gastro-intestinal complications (GIC) in the two studied groups. The most common GICs were high gastric residuals and diarrhea. Enteral nutrition was discontinued during the study period in 16 patients (20.7\%) in group \( \text{I} \) and 9 patients (11.1\%) in group \( \text{II} \) (\( p<0.07 \)). Reasons for discontinuing enteral nutrition were 6 hrs high residual gastric volume of > 300ml (9 and 6 patients in group \( \text{I} \) and group \( \text{II} \) respectively), diarrhea (5 and 2 patients in group \( \text{I} \) and group \( \text{II} \) respectively), vomiting (one patient in group \( \text{I} \) and a patient in group \( \text{II} \)), and illus (only a patient in group \( \text{I} \)). In the 18 of the 25 patients who were unable to tolerate enteral nutrition, intolerance occurred during the first three study days after initiation of enteral nutrition. Of the 7 remaining patients, four were in group \( \text{I} \) and three were in group \( \text{II} \). Enteral nutrition-related GICs were less frequent in group \( \text{II} \), but without significant difference between the two studied groups. (Fig.3) display the mean length of, receiving nutritional support, receiving mechanical ventilation and ICU stay for the two studied groups. The mean duration of mechanical ventilation was 11.2 ±19.5 days in group \( \text{I} \) and 17.9±31.3 days in group \( \text{II} \). The mean ICU length of stay was 11.1±6.2 days in group \( \text{I} \), and 14.9±4.2 days in group \( \text{II} \). It was clear that, early enteral nutrition resulted in a trend towards a shorter duration of mechanical ventilation and a shorter ICU stay. Length of stay in the ICU was significantly different (\( p< 0.02 \)) between patients provided early nutrition support (SD, 6.2) and patients provided nutrition support more than 48 hrs. after ICU admission (SD, 4.2). (Table V) indicates that on the first measurement the median lactose/mannitol (L/M) ratio was 0.029 in group \( \text{I} \) and 0.045 in group \( \text{II} \). On the post ICU admission day 4, the L/M ratio in group \( \text{I} \) decreased slightly to 0.020 and increased significantly in group \( \text{II} \) to 0.060. The median L/M ratio for group \( \text{I} \) and group \( \text{II} \) was 0.024 and 0.045, respectively; the difference between the two studied groups was statistically significant (\( p< 0.02 \)). (Fig.4) provide information on the incidence of ventilator associated pneumonia and infection complications in the two studied groups. The development of ventilator associated pneumonia was greater among patients in the early feeding group compared with patients
Table I: Patients data. Values are mean ± SD

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>77</td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>75±15</td>
<td>59±18</td>
<td>NS</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>54/23</td>
<td>63/18</td>
<td>I 54/23, II 63/18</td>
</tr>
<tr>
<td>APACHE II score</td>
<td>19±7</td>
<td>17±7</td>
<td>0.4</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27</td>
<td>29</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Diagnosis at ICU admission, N**

- Trauma: 38, 34
- Respiratory failure: 16, 20
- Sepsis: 15, 20
- Acute metabolic disorders: 8, 7

**Albumin, mg/d**

- Group I: 2.1
- Group II: 2.1

**Pre-albumin, mg/dl**

- Group I: 11.5
- Group II: 10.1

APACHE II score = The acute physiology and chronic health evaluation II score.

Table II: The time of initiation, volume and percentage of enteral nutrition given after ICU admission. Values are mean ± SD or median.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>P. value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiation of EN (h)</td>
<td>4.4(3-5.7)</td>
<td>59.4(49.9-72.6)</td>
<td>0.003</td>
</tr>
<tr>
<td>Duration of EN(days)</td>
<td>11±7</td>
<td>11±8</td>
<td>0.97</td>
</tr>
<tr>
<td>Caloric req (kcal/kg)</td>
<td>1921±350</td>
<td>1189±322</td>
<td>0.02</td>
</tr>
<tr>
<td>Vol of EN on day 4(ml)</td>
<td>1340±473</td>
<td>703±701</td>
<td>0.009</td>
</tr>
<tr>
<td>VR% at day 4(%)</td>
<td>82±27</td>
<td>68±33</td>
<td>0.03</td>
</tr>
<tr>
<td>% EN/day BEFW</td>
<td>80.5±16.3</td>
<td>60.9±25.6</td>
<td>0.025</td>
</tr>
<tr>
<td>Mea adm calories(kcal)</td>
<td>1418±309</td>
<td>1179±363</td>
<td>0.01</td>
</tr>
<tr>
<td>TTGRA</td>
<td>32.2(31-35.7)</td>
<td>75.1(73.4-78.8)</td>
<td>0.001</td>
</tr>
</tbody>
</table>


**Fig 1.** The percentage attainment of goal rate for each group during the first four days of the study, the last group of bars represents percentage of goal rate attained average over the study period.
Table III: The enteral nutrition-related gastrointestinal complications in the two studied groups.

<table>
<thead>
<tr>
<th>Complication</th>
<th>%OC</th>
<th>No OC</th>
<th>TI</th>
<th>DI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>GI</td>
<td>GII</td>
<td>GI</td>
</tr>
<tr>
<td>High RGV</td>
<td>38</td>
<td>44</td>
<td>52</td>
<td>35</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>28</td>
<td>28</td>
<td>25</td>
<td>23</td>
</tr>
<tr>
<td>Constipation</td>
<td>24</td>
<td>27</td>
<td>18</td>
<td>27</td>
</tr>
<tr>
<td>Emesis</td>
<td>14</td>
<td>14</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>Illus</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

%OC: % of complications. No OC: number of complications in each group. TI: transient interruption of enteral nutrition. DI: definitive interruption of enteral nutrition.

Table IV: Causes on interruption of enteral nutrition in the two studied groups.

<table>
<thead>
<tr>
<th>Reasons for feeding holding</th>
<th>Group I</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td>High tube residual</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Feeding tube removed, repositioned</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Haemodynamic instability</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Emesis</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Table V: Multiple organ failure score (MOF), number of patients in each group developing MOF during ICU treatment, lactose/mannitol (L/M)ratio values in patients and mortality rate in the two studied groups.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOF</td>
<td>Mean±SD</td>
<td>No</td>
<td>Mean±SD</td>
</tr>
<tr>
<td>Mortality rate%</td>
<td>2.5±0.7</td>
<td>12</td>
<td>3.1±0.8</td>
</tr>
<tr>
<td>L/M ratio</td>
<td>30</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>L/M ratio day 2</td>
<td>0.029(0.013-0.059)</td>
<td>0.045(0.02-1.07)</td>
<td>0.23</td>
</tr>
<tr>
<td>L/M ratio day 4</td>
<td>0.020(0.01-0.039)</td>
<td>0.060(0.011-0.202)</td>
<td>0.15</td>
</tr>
<tr>
<td>Median L/M value</td>
<td>0.024*(0.011-0.048)</td>
<td>0.045*(0.017-0.13)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Fig 2. Number of elevated residuals (>300ml), in each group during the first four days of the study.
Fig 3. The mean length of receiving nutritional support, mechanical ventilation and stay in ICU in the two studied groups.

Fig 4. The incidence of ventilator associated pneumonia, and infection complication in the two studied groups.

VAP: ventilator associated pneumonia incidence.
BAL: Bronchoalveolar lavage positive.
NP: No pathogen.
MP: Multiple pathogen.
CVRE: Colonization with vancomycin resistant enterococci.
HABSI: Hospital aquired blood stream infection.
UTI: Urinary tract infection.
AD: Antibiotic days.
Table VI: Average urine urea nitrogen (UUN) and prealbumin measures in the two studied groups.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UUN</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First UUN</td>
<td>+3.0 (SD, -7.26)</td>
<td>+5.0 (SD, -10.34)</td>
</tr>
<tr>
<td>Last UUN</td>
<td>-0.6 (SD, -4.18)</td>
<td>-7.0 (SD, -7.31)</td>
</tr>
<tr>
<td><strong>Average prealbumin measures</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission</td>
<td>11 (SD, -4.79)</td>
<td>11 (SD, -9.86)</td>
</tr>
<tr>
<td>Initial enteral feeding</td>
<td>10 (SD, -4.09)</td>
<td>9 (SD, -2.93)</td>
</tr>
<tr>
<td>Final enteral feeding</td>
<td>12 (SD, 6.82)</td>
<td>8 (SD, -6.75)</td>
</tr>
<tr>
<td>Discharge</td>
<td>17 (SD, -7.57)</td>
<td>17 (SD, -5.71)</td>
</tr>
</tbody>
</table>

in the late feeding group but with no statistical significance. Broncho-alveolar culture support diagnosis of ventilator associated pneumonia in 12 patients (15.5%) in the early feeding group compared with 9 patients (11.1%) in the late feeding group. There was no growth of bacteria on respiratory tract in 5 patients in the early feeding group with ventilator associated pneumonia, multiple pathogens were identified in 3 patients in these group. In the late feeding group 3 patients with ventilator associated pneumonia had no growth of pathogens and 6 patients had multiple pathogens identified. The most common pathogens associated with ventilator associated pneumonia in both groups were pseudomonas erogenous and staphylococcus areus. It was clear that, there were no significant difference in the incidence of nosocomial pneumonia between the two studied groups. Colonization with vancomycin-resistant enterococci was identified in 20 patients (25.9%) in the early feeding group and 18 patients (22.2%) in the late feeding group (p= .570). Diarrhea associated with C-difficle infection was more common in the early feeding group, but with no statistical significance. No statistical significant difference in hospital acquired blood stream infection (12.9% versus 9.8% p= .797) or urinary tract infection (25.9% versus 32.09% p= .460) were observed between patients in the early and late feeding groups. Total antibiotic days in the ICU setting were greater in the early feeding group, but with no statistically significant difference compared with patients in the late feeding group (8.4 ±8.8 antibiotic days versus 7.5 ±6.1 antibiotic days, p= .678).

**DISCUSSION**

Nutrition support is generally accepted as an important supportive therapy for critically ill patients. Adequate nutritional support help to prevent malnutrition and is related malcomplication. The optimal timing of the initiation of enteral nutrition is still controversial. With respect to the effect of EN on splanenic haemodynamic, gut mucosa and barrier function, it has to postulated that initiation shortly after admission might be beneficial. Most of the patients that we studied were moderately to severely malnourished with a high acuity of illness on admission to the ICU, and many of them required mechanical ventilation, making them particularly vulnerable to developing malnutrition related complications. The use of EN and the institution of nutritional support as soon as possible after ICU admission increased the percentage of estimated energy and nitrogen requirement being met in the intervention patients, compared with late feeding patients, during the first week after ICU admission. Early EN improve clinical outcomes without increased mortality from aspiration pneumonia, or increased duration of dependence on EN or mechanical ventilation.

Our findings were greatly correlated with a consensus statement published by the American Colleague of Chest physicians support the initiation of EN as soon as possible after resuscitation (23). Early initiation of nutrition support, specifically enteral feeding, has been promoted to improve outcomes. Marik et al, confirmed our findings in their two large meta-analysis, they demonstrated that, early enteral feeding was beneficial compared with late enteral feeding (12). In
agreement with our study results, findings obtained by Kompan and his colleagues, they demonstrated that, the institution of EN in the first 6hrs. after admission resulted in a lower intestinal permeability compared with patients in whom EN was started later than 24hrs. after admission (24). On the other hand, Minard et al, in their small studies, found that early enteral nutrition did not appear to be advantageous compared with late enteral feeding (25). Additionally, in a study by Ibrahim et al, they found that patients feed early had more infections and longer stay in the ICU (26). Even though more infections occurred in the group feed early, Ibrahim et al, did not find any difference in mortality between the group feed early and the group fed late. However, in their clinically important study, Kudsk et al, demonstrated that, the use of early EN resulted in some improvement in the cytokines profile (27). The same findings were obtained by Manhart et al, they demonstrated significant relationship between early EN and enteral immunity, starvation itself resulted in a variable degree of mucosal atrophy, with some increase in the intestinal permeability; this lead to an increased susceptibility to respiratory and likely intestinal infection. Early enteral administration of complex diet may reverse this situation any more have the potential to modify the inflammatory response to critical illness (28). These results were confirmed by the findings of Raff et al, they found that, early EN was an effective substitute to the administration of histamine 2-(H2) antagonist as prophylaxis for gastritis and upper GIT hemorrhage (29).

Many critically ill patients have impaired GIT motility, resulting in poor gastric emptying and poor tolerance of early enteral nutrition (30). In our study 15.8% of the patients were intolerant to early enteral nutrition. The discrepancies between the calories prescribed and those delivered during enteral nutrition were caused by gastrointestinal intolerance. Our findings of GICs frequency of 43.6% were in consistent with the data referred by other reviews (52%) (15,31), and showed the need to establish a management protocol to treat these complications. High gastric residuals was the most frequent GICs in our study, and it is similar to that found by Heyland et al, (15). The same results reported by Mentec et al, they reported 32% occurrence of increased residual gastric volume, which compares well with our results of 38% (32). The 300ml limit used in our study nearly complies with the volume used by Line and Van, who concluded in their study that, stopping feeding for gastric residual volume (GRV) less than 400 to 500ml might not be physiologically sound or clinically appropriate (33,34). Additionally, McClav et al, in their study assured that, 80% of these patients with elevated RGV; responded with decreasing residuals as feeding continued (35). In our study prophylactic administration of erythromycin has been associated with improved tolerance of early enteral nutrition, this attitude was in consistent with data referred by many authors (36,37). Diarrhea was not the most common complication in our study. This is in sharp contrast to the reported prevalence of 50% in older studies in critically ill patients (38-40). This difference can be explained by the fact that, there are many problems with the definition and reporting of enteral feeding-related diarrhea. The 28% frequency of diarrhea in our study, one of the lowest reported with critically ill patients, could be explained by that our definition was objective and easy to use by the participating units. Our management protocol was effective in avoiding definitive withdrawal from enteral nutrition, despite the high frequency of GICs. We attributed our success to the repeated attempts applied to control these complications and to avoid EN withdrawal. For instance, 53 patients presented with diarrhea, but EN was definitively withdrawn in only two cases.

In the intensive care, mortality from a primary infective process generally arise from community acquired infections such as staphylococcal septicemias and sever pneumonia. Failure of the initial innate immune response has been to be an antecedent of acquired nosocomial infection in the critically ill (41). In our study, results demonstrated that, lower rates of infection complications, shorter length of stay in ICU and shorter duration of mechanical ventilation in the early feeding group compared with the late feeding group. This findings were in consistent with the results concluded by Gianotti et al (42). In agreement
with our work, Neumayer et al, they demonstrated that, early initiation of nutritional support in ICU patients resulted in better clinical outcomes than if nutritional support is delayed\(^{(43)}\). Moore et al, demonstrated that, the implementation of early nutritional management protocol significantly shortened the duration of mechanical ventilation\(^{(18)}\) and this finding was in consistent with the results in our study. In a clinically important study, Marik confirmed our findings, he showed that, there were significantly lower rates of infection and length of hospital stay in the early nutrition group \(^{(42)}\). Semirecumbancy was a low cost and easy to apply measure for preventing aspiration and reducing the risk of nosocomial pneumonia in our study. This finding was in consistent with the result obtained by Heyland et al, who found that, semi recumbent position was associated with significantly lower incidence of pneumonia \(^{(44)}\). Drakulovic et al, assured our results when demonstrated that, strategies that maximize the delivery of EN while minimizing the risks of gastric colonization, gastro esophageal reflux and pulmonary aspiration, have the potential to improve the outcome of critically ill patients receiving EN \(^{(45)}\).

Evidences suggest that early EN has become more and more a therapy directed towards the preservation of gut function. To date there is sufficient evidence that the gut play a pivotal role with respect to the morbidity and mortality of ICU patients. Our increasing understanding of the relationship between nutrition support and the immunologic and barrier functions of the bowel have radically altered patients care in this area. Semirecumbancy has been recommended as a key factor in pneumonia prevention in patients receiving early EN and on mechanical ventilation. However, conflicting study results and obstacles still prevent the general application of early enteral feeding. The use of prokinetics and semi recumbent position, early EN can be successfully carried out in virtually all critically ill patients.

**CONCLUSION**

Early intensive nutritional support is very important part for the management of the critically ill patients, and that paying attention to nutrition early in the patient's ICU courses will improve outcome, shorten the length of ICU stay, and facilitate more rapid rehabilitation.

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