RESEARCH
Original Research

Increased Efficacy and Safety of Enteral Nutrition Support with a Protocol (ASNET) in Noncritical Patients: A Randomized Controlled Trial

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ABSTRACT

Background Unintentional underfeeding is common in patients receiving enteral nutrition (EN), and is associated with increased risk of malnutrition complications. Protocols for EN in critically ill patients have been shown to enhance adequacy, resulting in better clinical outcomes; however, outside of intensive care unit (ICU) settings, the influence of a protocol for EN is unknown.

Objective To evaluate the efficacy and safety of implementing an EN protocol in a noncritical setting.

Design Randomized controlled clinical trial.

Participants and settings This trial was conducted from 2014 to 2016 in 90 adult hospitalized patients (non-ICU) receiving exclusively EN. Patients with carcinomatosis, ICU admission, or <72 hours of EN were excluded.

Intervention The intervention group received EN according to a protocol, whereas the control group was fed according to standard practice.

Main outcome measures The proportion of patients receiving ≥80% of their caloric target at Day 4 after EN initiation.

Statistical analyses performed Student *t* test or Wilcoxon rank-sum test were used for continuous variables and the difference between the groups in the time to receipt of the optimal amount of nutrition was analyzed using Kaplan-Meier curves.

Results Forty-five patients were randomized to each group. At Day 4 after EN initiation, 61% of patients in the intervention arm had achieved the primary end point compared with 23% in the control group (P=0.001). In malnourished patients, 63% achieved the primary end point in the intervention group compared with 16% in the control group (P=0.003). The cumulative deficit on Day 4 was lower in the intervention arm compared with the control arm: 2,507 kcal (interquartile range [IQR]=1,262 to 2,908 kcal) vs 3,844 kcal (IQR=2,620 to 4,808 kcal) (P<0.001) and 116 g (IQR=69 to 151 g) vs 191 g (IQR=147 to 244 g) protein (P<0.001), respectively. The rates of gastrointestinal complications were not significantly different between groups.

Conclusions Implementation of an EN protocol outside the ICU significantly improved the delivery of calories and protein when compared with current standard practice without increasing gastrointestinal complications.
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ENTERAL NUTRITION (EN) IS THE PREFERRED MODALITY to provide nutrition to patients with an accessible and functional gut who cannot attain their calorie and protein requirements by oral intake alone.[1-3] Early and sufficient calories and protein (≥80% of requirements) is believed to contribute to the maintenance of the epithelial and functional integrity of the intestinal barrier, decrease oxidative stress, and temper the systemic inflammatory response syndrome.[4-10]

The gap between the amount of calories and proteins prescribed and delivered through EN is large. It has been

associated with malnutrition, resulting in longer hospital stay, higher hospital costs, and worse clinical outcomes.[11-15] This has been addressed by protocols that have been developed and implemented in intensive care units (ICUs) to enhance delivery.[16-21] The protocols are often designed as bundles comprising multiple different interventions such as initiation at goal rate instead of gradual increase (ramp-up), prophylactic use of prokinetic medications, and provision of compensatory feeding when EN is interrupted. However, evidence-based EN protocols have been reported only for critically ill patients.[16,17,19,22-24]

It has been reported that 71% of noncritically ill Mexican patients receiving EN are underfed, receiving on average only 61% of their calorie requirements during hospitalization.[25] Only 28% of patients received ≥80% of their prescribed nutrition by the fourth day after EN initiation.[26] The aim of the present study was to evaluate implementation of an EN protocol in a noncritical setting. We hypothesized that, compared with standard practice, an EN protocol would increase the caloric and protein adequacy in a shorter period of time.

MATERIALS AND METHODS

Project Design and Sample Description

This was a randomized study with one active intervention arm and one control group. The trial was conducted at the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico, from October 2014 to July 2016. This work was carried out in accordance with The Code of Ethics of the World Medical Association. The Clinical Research and Bioethics Committee approved this study. The Algoritmo para el Soporte Nutricional Enteral Total (ASNET) trial was recorded at the National Institutes of Health (ClinicalTrials.gov identifier: NCT02740205).

Physician nutrition specialists, internists, and rotating doctors of other specialties (such as gastroenterology, surgery, and geriatrics), dietitian nutritionists, and interns comprise the clinical nutrition service (CNS), members of which perform both the nutrition evaluation based on Subjective Global Assessment and the nutrition therapy prescription at admission.[27-29] Research staff performed the enrollment procedure to avoid any coercion (the physician or nutritionist who treated a patient included in the study was not part of the research staff). Adult patients admitted to the hospital for a noncritical illness (ie, not requiring immediate treatments, invasive monitoring, or vasopressor use) who were unable to maintain oral nutrition intake, but received exclusively EN, were eligible for inclusion. Patients with carcinomatosis, ICU admissions, prior hospitalization within the previous 30 days, receiving EN before hospitalization, transferred to the ICU, received EN for <72 hours, or received another form of nutritional support (oral or parenteral nutrition) were excluded. Informed consent was provided by the patient or next of kin when the patient was unable to provide consent. The prescription of the enteral formulas in both groups was dependent upon the patient's clinical status and the hospital availability of specialized and standard formulas. The principal investigator, using Stata 12,[30] performed randomization with a 1:1 allocation using random block sizes of 2 and 4.

Standard of Care

The standard of care (SOC) for EN delivery consisted of unstructured prescription of the route, estimation of requirements, and monitoring of tolerance at the discretion of the CNS. To estimate the energy and protein requirements, the CNS employed several predictive equations, as well as indirect calorimetry that was performed using QUARK-PFT equipment (COSMED). The initial rate of infusion is not standardized, but it is usually increased by >10 mL/h each 24 hours until goal. In cases where extra protein was necessary, modular protein was added with extra water. If EN was interrupted due to intolerance, procedures, or nursing care, compensatory feeding was not provided and the EN was restarted at the previous rate of infusion. Promotility agents were not routinely prescribed.

Development of the ASNET

First, CNS held conferences between July 2014 and October 2014 to achieve consensus on the protocol design and tools. Second, a systematic literature search was performed using the following Medical Subject Headings terms: *protocols*, *enteral nutrition*, *nutritional support*, and *critical care*. Studies were graded using the preferred reporting items for systematic reviews and meta-analyses or consolidated standards of reporting trials checklist. The team also reviewed international guidelines for nutrition support: American Society for Parenteral and Enteral Nutrition, Society Critical Care Medicine, Canadian Guidelines for Enteral Nutrition Support, and European Society for Clinical Nutrition and Metabolism.[2,31,32] The guidelines were discussed and integrated into the ASNET protocol design and a pocket version manual was developed. The ASNET included one protocol for gastric and postpylorics feeding and a compensatory feeding table (the summary protocol is presented in Figure 1).[16-18,21,30-33]

Study Intervention

Enrolled patients were randomly assigned to the intervention or control group. The research team provided protocol tool instructions to the dietitian and attending physician caring for the intervention patients. A research team member assessed the intervention and the CNS provided feedback (strategies to monitoring the EN tolerance according to the protocol schedule proposed) to optimize compliance in the intervention arm. All other aspects of patient care were at the discretion of the medical staff. The follow-up carried out by the research team started when the EN was prescribed and finished when the patient had adequate oral intake (ie, >60% of nutritional requirements), switched to parenteral nutrition, was discharged from the hospital (deceased/alive), or 30 days after study enrollment, whichever occurred first.

The primary outcome was the proportion of patients who received ≥80% of target calorie and protein (via the enteral route) at day 4 after EN initiation. The amount of energy and grams of protein delivered per hospital day (24 hours) were recorded. The calories from the modular protein supplements (Proteinex, Victus Laboratories) were added to the total calories. The total amount of calories and protein received per 24-hour period were divided by the amount prescribed and the patients were then dichotomized according to whether or not they had received ≥80% of target calories and protein.