ORIGINAL RESEARCH

Effects of Oral Nutritional Supplements on Mortality, Missed Dialysis Treatments, and Nutritional Markers in Hemodialysis Patients

Debbie Benner, MA, RD, CSR, [*] *Steven M. Brunelli, MD, MSCE,* [†] *Becky Brosch, RD, CSR,* [*] *Jane Wheeler, MS, RD,* [*] *and Allen R. Nissenson, MD* [*,‡]

Objective: Protein-energy wasting is common in end-stage renal disease patients undergoing dialysis and is strongly associated with mortality and adverse outcomes. Intradialytic oral nutritional supplements (ONS) reduce risk of mortality in these patients. Large studies characterizing the impact of ONS on other outcomes are lacking. We assessed the associations between administration of ONS and clinical and nutritional outcomes.

Design: Retrospective evaluation of a pilot program providing ONS to patients at a large dialysis organization in the United States. The pilot program provided ONS to in-center hemodialysis patients with serum albumin ≤3.5 g/dL at 408 facilities.

Subjects: ONS patients were compared to matched controls with serum albumin ≤3.5 g/dL, identified from facilities not participating in the ONS program (n = 3,374 per group).

Intervention: Receipt of ONS.

Main Outcome Measures: Death, missed dialysis treatments, hospitalizations, serum albumin, normalized protein catabolic rate, and postdialysis body weight were abstracted from large dialysis organization electronic medical records.

Results: There was a 69% reduction in deaths (hazard ratio = 0.31; 95% confidence interval = 0.25-0.39), and 33% fewer missed dialysis treatments (incidence rate ratio = 0.77; 95% confidence interval = 0.73-0.82) among ONS patients compared to controls ($P < .001$ for both). The effects of ONS on nutritional indices were mixed: serum albumin was lower, whereas normalized protein catabolic rate values, a surrogate for dietary protein intake, and postdialysis body weights were higher for ONS patients compared to controls during follow-up.

Conclusions: Our evaluation confirmed the beneficial effects of ONS in reducing mortality and improving some indices of nutritional status for hypoalbuminemic hemodialysis patients. We also report the novel finding that ONS can reduce the number of missed dialysis treatments. These results support the use of intradialytic ONS as an effective intervention to improve the outcomes in hemodialysis patients with low serum albumin.

Introduction

PROTEIN-ENERGY WASTING (PEW) is a complex clinical condition characterized by multiple metabolic and nutritional derangements and is highly prevalent among end-stage renal disease (ESRD) patients receiving dialysis.[1-3] Several factors contribute to the development of PEW in ESRD, including lack of uremic toxin clearance, inflammation, inadequate protein intake, and catabolic consequences of hemodialysis.[1,4] Low serum albumin concentration, which though nonspecific is by far the most commonly used marker for PEW in clinical practice, is a strong predictor of mortality and poor clinical outcomes in dialysis patients.[5-7] Targeting PEW through dietary interventions has been proposed as a strategy to improve clinical outcomes in dialysis patients.[8,9] Observational studies have shown that intradialytic administration of oral nutritional supplements (ONS) can reduce risk of mortality for patients with low serum albumin.[10,11] However, there is a lack of data from large, well-powered studies on the effects of ONS on other outcomes. Here, we report the findings from a retrospective evaluation of a pilot program to provide ONS to hypoalbuminemic hemodialysis patients at a large dialysis organization (LDO) where we assessed the effects of ONS on mortality, missed dialysis treatments, hospitalizations, and nutritional markers.

Materials and Methods

Study Design

This was a retrospective evaluation of a pilot program at 408 facilities within an LDO that provided ONS to patients with serum albumin concentrations ≤3.5 g/dL as measured

[*] *DaVita Inc, Denver, Colorado.*

[†] *DaVita Clinical Research, Minneapolis, Minnesota.*

[‡] *David Geffen School of Medicine, University of California, Los Angeles, California.*

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Address correspondence to Debbie Benner, MA, RD, CSR, 2000 16th St., Denver, CO 80202. E-mail: debbie.benner@davita.com

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by bromocresol green. We conducted our retrospective evaluation using deidentified patient data collected during the course of routine patient care; therefore, according to 45 Code of Federal Regulations (CFR) part 46 from the US Department of Health and Human Services, this study was exempt from institutional review board or ethics committee approval. We adhered to the Declaration of Helsinki, and informed consent was not required.

Data Source and Study Patients

Data were derived from the electronic health records (EHRs) of the LDO. This evaluation included patients from all payors except for those who were US Veterans Affairs beneficiaries (contractual stipulation). Eligible patients were those who between September 01, 2012, and January 31, 2013: were ≥18 years; received in-center hemodialysis (ICHD) at LDO facilities; had a recorded body mass index; if treated at participating facilities, had albumin ≤3.5 and received at least 1 dose of ONS; and if treated at nonparticipating facilities, had albumin ≤3.5 g/dL. ONS was prescribed as one serving per treatment that was to be consumed in the dialysis center unless extenuating circumstances, such as nausea, prevented in-center consumption. There were 2 different ONS product formulary options Novasource Renal (21.6 g protein, 475 calories/237 mL serving) or Liquacel (16 g protein, 70 calories/30 mL serving) from which the patients could choose. ONS treatment continued until serum albumin concentrations were >3.9 g/dL for 1 month, or >3.7 g/dL for 2 consecutive months or the patient refused the supplement for 6 consecutive sessions, or ONS was discontinued by a physician. Participation in the ONS program was re-evaluated for hyporesponse by a physician and registered dietitian after 6 consecutive albumin concentrations <3.6 g/dL. Patients exhibiting contraindications, such as dysphagia or intolerance to food or supplements during dialysis, were not included in the ONS program.

Exposure

Exposure status was adjudicated as above. Date of entry was defined as the first date of the first month following initial ONS treatment (for ONS patients) or qualifying albumin measurement (for control patients). ONS patients were propensity matched to eligible controls. Propensity scores were estimated using a logistic model in which the receipt of ONS was the dependent variable and was predicted as of entry date on the basis of: qualifying albumin level, month of entry, age, sex, race, etiology of ESRD, access type, diabetes, Charlson comorbidity score, dialysis vintage, body mass index, hospitalization in the prior month, hemoglobin level, and serum phosphorus. ONS patients were matched 1:1 to controls using a nearest neighbor matching algorithm.

Outcomes

Patients were followed for 8 months starting on the date of entry. Outcomes were considered beginning on entry date and continuing until end of study or censoring due to death, transfer of care, transplant, recovery of renal function, withdrawal from dialysis or modality change. Clinical outcomes considered in this study were patient deaths and missed dialysis treatments. We also analyzed serum albumin, normalized protein catabolic rate (nPCR), and postdialysis body weight as nutritional markers.

Statistical Analysis

Baseline demographics and characteristics were considered as of date of entry and were summarized for each group as means, standard deviations, medians, interquartile ranges, counts, and proportions, as dictated by data type. Comparisons between groups were made with t-tests and chi-square tests as appropriate.

Risk of death during follow-up was compared between ONS patients and matched controls using Cox proportional hazard models. Crude incidence rates for missed dialysis treatments were calculated by dividing the sum of events by the sum of cumulative at-risk time in ONS patients and matched controls. Incidence rate ratios were estimated by negative binomial regression. Serum albumin, nPCR, and postdialysis weight were examined using mixed linear models with patient-level random intercepts. For clinical laboratory tests measured more than once in a month, the first recorded value in the month was used.

Results

Baseline Characteristics

There were 3,374 qualifying ICHD patients treated with ONS and 48,298 eligible controls. Prior to matching, there was significant imbalance between cohorts on the majority of variables (Supplementary Data, Table S1). Notably, ONS patients were older, were more likely to use arteriovenous fistulas for vascular access, and had higher Charlson comorbidity index scores. All ONS patients were successfully matched to one control patient. In the matched analytical cohort, patient characteristics were well balanced (Table 1). Subsequent results pertain to the matched analytical cohort.

Clinical Outcomes

Overall, there were 555 deaths during 2,850 patient-years of at-risk time. Survival was significantly greater among ONS patients compared to controls (Fig. 1). The mortality rate among ONS patients was 10.9 deaths per patient-year, which was significantly lower when compared to 29.1 deaths per patient-year in matched controls (hazard ratio [95% confidence interval {CI}] = 0.31 [0.25, 0.39]; $P < .001$).

The association of ONS with missed dialysis treatments is presented in Figure 2. Patients treated with ONS missed 1.35 dialysis treatments per patient-month, which was significantly lower when compared to 1.69 missed dialysis