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[FEATURES: ORIGINAL INVESTIGATION]

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Abstract

OBJECTIVE: To compare Pressure Ulcer Scale for Healing (PUSH) scores at 8 weeks in long-term-care residents with pressure ulcers who were given standard care plus a concentrated, fortified, collagen protein hydrolysate supplement vs. residents who were given standard care plus placebo.

DESIGN: Randomized, prospective, controlled, multicenter trial at 23 long-term-care facilities in 4 states.

SUBJECTS: A total of 89 residents with Stage II, III, or IV pressure ulcers were entered into the trial; 71 residents completed the study.

INTERVENTION: Residents were randomized to receive standard care plus a concentrated, fortified, collagen protein hydrolysate supplement (n = 56) or standard care plus placebo (n = 33) 3 times daily for 8 weeks. Wound healing was assessed biweekly using the PUSH tool, version 3.0. This tool categorizes pressure ulcers by surface area, exudate, and type of wound tissue.

PRIMARY OUTCOME MEASURE: Change in PUSH tool scores in each group at 8 weeks.

RESULTS: After 8 weeks of treatment, residents who received standard care plus the concentrated, fortified, collagen protein hydrolysate supplement had significantly better PUSH tool scores compared with those who received standard care plus placebo (3.55 ± 4.66 vs 3.22 ± 4.11 , respectively; $P < .05$).

CONCLUSION: By week 8, PUSH tool scores—a measurement of pressure ulcer healing—showed approximately twice the rate of pressure ulcer healing in the treatment group compared with

the control group. A concentrated, fortified, collagen protein hydrolysate supplement may be of benefit to residents of long-term-care facilities who have pressure ulcers.

The National Pressure Ulcer Advisory Panel (NPUAP) has reported pressure ulcer (PrU) incidence rates ranging from 10% to 18% in the United States.¹ Substantial costs have been estimated for PrU treatment,² with an American study calculating mean excess charges of \$10,845 for treatment of PrUs.³ The same study found an excess mortality rate of 7.2% when patients were matched for diagnosis-related group, sex, white or nonwhite race, and age within 10 years.³ A Healthy People 2010 ⁴ objective is to reduce the proportion of long-term-care (LTC) residents with a diagnosis of PrUs to no more than 8/1000 (0.8%) from a 1997 baseline of 16/1000 (1.6%).

Nutritional supplements are often used as an intervention to prevent or treat PrUs.⁵ Data suggest that high-protein diets improve healing of PrUs.^{6,7} A review of nutritional interventions for preventing and treating PrUs ⁵ identified only 1 randomized controlled trial on the effect of very high protein supplementation for the treatment of PrUs;⁸ the evidence was considered weak.⁵

The present randomized controlled trial compared the efficacy of a concentrated, fortified, collagen protein hydrolysate supplement versus placebo in the healing of Stage II, III, and IV PrUs.⁹ Outcomes from prior observational studies showed positive results in patients treated for PrUs; therefore, the investigators' goal was to evaluate the effect of this concentrated, fortified, collagen protein hydrolysate supplement on PrU healing rates over the study period.

METHODS

Subjects

Eighty-nine residents of LTC facilities with a total of 132 Stage II, III, or IV PrUs were enrolled in a double-blinded, placebo-controlled, randomized, multicenter trial. The study was designed to evaluate the efficacy of a concentrated, fortified, collagen protein hydrolysate supplement (Pro-Stat; Medical Nutrition USA, Inc, Englewood, NJ; referred to in this article as 'the study product').

Subjects were selected from a convenience sample of male and female residents of 23 LTC facilities in New York, New Jersey, Ohio, and Indiana. Residents or their legally appointed representatives gave written informed consent to participate in the study. Exclusion criteria were as follows: (a) terminal diagnosis; (b) hospice care; (c) a protein-restricted diet due to renal insufficiency; (d) active metabolic or gastrointestinal diseases that might interfere with nutrient absorption, distribution, metabolism, or excretion (eg, Crohn's disease, bowel resection, ileus, or dumping syndrome); (e) food allergies; or (f) use of corticosteroids or antibiotics for wound infection.

Study design

This double-blinded study was conducted in accordance with the Good Clinical Practice regulations of the Food and Drug Administration. The Western Institutional Review Board reviewed and approved the study protocol and its amendments for those facilities requiring such approval. Trained research assistants were available on-site or via telephone to facilitate adherence to the study protocol.

Residents with Stage II, III, or IV PrUs were randomized to receive standard care with a

placebo or standard care plus the study product. The placebo was a noncaloric liquid indistinguishable from the study product in terms of color, taste, and texture. The placebo and the study product were each packaged in identical opaque white, unit-dose bottles differentiated by a numeric code and a red dot or no dot on the label. Subjects and staff were unaware of the numeric code or the meaning of the colors. The first patient in each building was randomized to the 'red' or 'white' group by the research assistant using the flip of a coin. Ensuing assignments were made by alternating between the 2 groups.

Research assistants collected medical history, medication, and anthropometric data, including height, weight, body mass index, and ulcer stage, at the initial screening from patients who met the study criteria. Site dietitians or assistants used a 24-hour dietary intake form to record amounts and types of all foods consumed by residents for 3 days before the start of the study. Food intake records were analyzed centrally by a registered dietitian utilizing nutrition analysis software (The Food Processor; ESHA Research, Salem, OR) and a standardized base for specific foods. The data were then used to estimate each resident's kilocalorie and protein intake per 24-hour period. Facility staff tracked consumption of the product and placebo on medication administration records; this was also monitored by study investigators. Blood urea nitrogen and creatinine were measured at weeks 3 to 4 and 7 to 8 to monitor renal function secondary to increased protein intake.

Study treatment in controlled facility environments was provided for 8 weeks (a total of 168 treatments: 3 times daily, starting at week 1, then up to and including week 8). Site physicians prescribed the study product or the placebo as identified by the label on the individual dose for nutritional supplementation. Site nurses, trained by the study investigators, administered individual 1.5 fluid ounce-dose units of the study product or placebo orally or via feeding tubes during routine medication distribution periods. These nurses tracked and documented administration and acceptance of the study product or placebo daily. Each unit of the study product contained 15 g of fully hydrolyzed protein in a 45-mL unit dose.

Selected LTC facilities used facility-specific standardized care procedures for Stage II, III, or IV PrUs. Protocols for standard PrU care included patient-appropriate topical and pressure-relief treatments, as well as enhanced foods, commercial supplements, and supplements formulated for wound healing. The study was designed to measure the effect on PrU healing of adding supplementation with the study product to standard care. Research assistants measured efficacy parameters at baseline and at each biweekly visit with the Pressure Ulcer Scale for Healing (PUSH), version 3.0.¹⁰ The PUSH tool provides numeric scores for the parameters of exudate, wound surface area, and tissue type, which are pertinent to wound healing. As such, it offers a complete summary of data shown over time for the study product group (treatment) and placebo group (control) ([Table 2](#)). PUSH tool scores were calculated for all subjects at baseline; these data were included in total results over time.

Week	PUSH Tool Score	
	Treatment Group (n = 44) Mean (SD)	Control Group (n = 27) Mean (SD)
0	9.11 (4.15)	6.07 (2.65)
2	7.59 (4.85)*	5.3 (4.2)
4	6.55 (5.19)	3.96 (4.42)
6	4.55 (5.28)*	3.78 (4.66)
8	3.55 (4.66)*	3.22 (4.11)

SD = standard deviation

*Rate of healing was significant in both groups over time; however, rate of healing was significantly higher for the treatment group across 2-, 6-, and 8-week periods.

Table 2. WOUND HEALING OVER TIME AS MEASURED BY MEAN PUSH TOOL SCORE

The primary end point with respect to efficacy in PrU healing was the change in PUSH tool scores in each group at 8 weeks, as measured by wound care nurses trained in use of the tool. Additional analyses were done on mean supplement intake and frequency of PrU stage by group. Safety measurements consisted of significant but not serious adverse events or serious adverse events. Adverse events were monitored from screening through 48 hours after final intake of the study product or placebo.

Statistical analysis

All data analyses were conducted according to a pre-established analysis plan, using the Statistical Package for the Social Sciences (version 13.0 for Windows, 2004; SPSS Inc, Chicago, IL). PUSH tool scores were used to characterize PrU healing in the treatment and control groups. Chi-square analysis was conducted to compare the frequency of PrU stage by groups. The t test was used to compare the mean supplement intake per group. Analysis of variance with repeated measures was calculated to compare PrU healing in the treatment and control groups.

RESULTS

Between October 2003 and October 2004, the investigators screened a total of 295 residents; 89 were randomized and treated. Thirty-three residents were assigned to standard care plus placebo and 56 were assigned to standard care plus the study product. Overall, 224 residents were excluded from the trial or dropped out before trial completion. Failure to provide informed consent was the most common reason for exclusion. A total of 71 residents completed the 8-week study. The primary analysis involved all randomly assigned patients

who completed the study. There were no significant differences in mean supplement intake between the treatment and control groups; both had consumed more than 80% of either the placebo or the study product served during the study period.

[Table 1](#) summarizes the descriptive data of the total cohort (89 residents). The 71 residents who completed the study had a total of 108 PrUs. There were 75 PrUs in the treatment group (n = 44) and 33 in the control group (n = 27). In the treatment group, 65% of the PrUs were Stage II; 17.2% were Stage IV. In the control group, 51% of the PrUs were Stage II; 22.8% were Stage IV. PUSH tool scores over time are shown in [Table 2](#). The 8-week change in PUSH tool scores in the control group was 3.22 ± 4.11 versus 3.55 ± 4.66 ($P < .05$) in the treatment group. PUSH tool scores decreased for all patients over the 8-week study; however, the treatment group showed approximately twice the rate of PrU healing compared with the control group.

Characteristics	Treatment Group Mean (SD) (n=56)	Control Group Mean (SD) (n=33)
Weight (lbs)	157 (39.2)	160 (55.4)
Body mass index (kg/m ²)	27 (8.8)	27 (7.9)
Kilocalories (kcal)	1381 (484.1)	1279 (520.9)
Protein (g)	55 (18)	47 (29.4)
BUN (mg/dL)	25.2 (15.81)	21 (16.36)
Creatinine (mg/dL)	0.94 (0.469)	0.88 (0.498)

SD = standard deviation; BUN = blood urea nitrogen. There were no significant differences between the 2 groups on any of the baseline characteristics (*t* test, $P > .05$).

Table 1. BASELINE CHARACTERISTICS OF THE SAMPLE (N = 89)

Eleven participants discontinued treatment because of adverse events that included hip fracture due to fall (n = 2), changes in renal lab values (n = 3), nausea or distention (n = 4), and death (n = 2). One person in each group died from causes unrelated to the study. For reasons unrelated to the study, 5 participants left their facilities before completion of the trial. There were no significant differences among groups in the rate of events (*t* test, $P > .05$).

DISCUSSION

This is the first randomized controlled trial to investigate the effect of a concentrated, fortified, collagen protein hydrolysate supplement on PUSH tool score outcomes. For the first time, data indicate that this type of nutritional supplement can promote healing of PrUs.[11,12](#) Addition of the study product to standard care significantly reduced total PUSH tool scores compared

with standard care plus placebo.[13,14](#) Residents in the present trial who received the study product showed a statistically significant mean decrease in PUSH tool scores at 8 weeks when compared with residents who received a placebo (60% reduction vs. 48% reduction, $P < .05$).

[Figure 1](#) shows the cumulative change in PUSH tool scores over time. The cumulative improvement in PUSH tool scores was approximately 96% greater in the treatment group than in the control group. These findings indicate that a concentrated, fortified, collagen protein hydrolysate supplement can be of benefit to residents of LTC facilities who have PrUs. Observational data used to design this randomized controlled trial showed similar results.

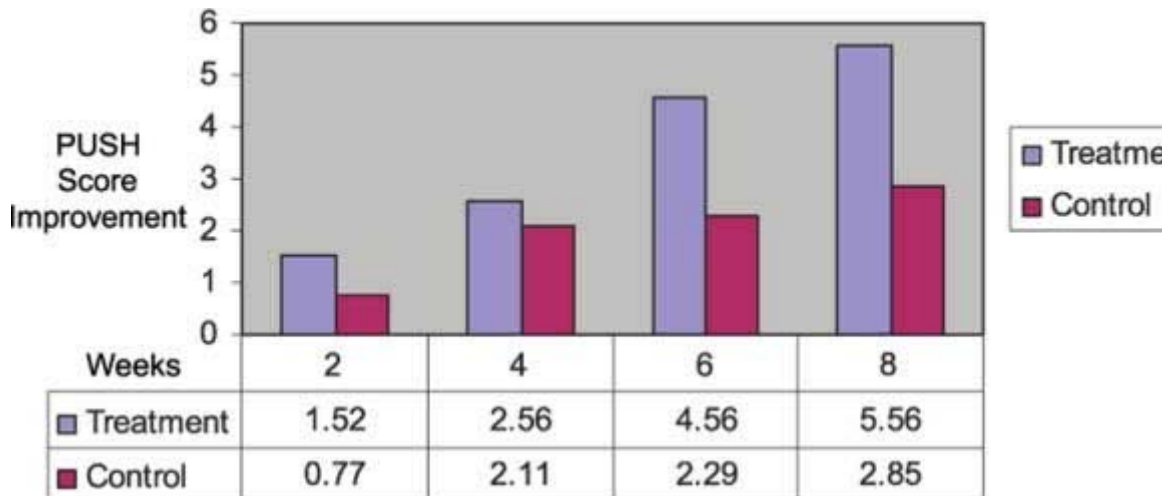


Figure 1. CUMULATIVE IMPROVEMENT IN MEAN PUSH TOOL SCORES BY SUBJECT OVER TIME (WEEKS)

The strengths of this trial include the double-blinded control, the large number of facilities, and the successful randomization to standard care plus the study product or standard care plus placebo. However, the sample size was relatively small, and, therefore, these results cannot be applied to the larger population of LTC facility residents with PrUs. Similarly, because this study included only residents of LTC facilities, the results cannot be extrapolated to patients at other sites (eg, general acute care or home care). A wide range of environmental, facility, and resident-specific characteristics may have influenced the outcomes of this study. There were no statistically significant differences between the groups. However, a limitation of this study could be that, despite randomized control, outcomes may have been biased by group differences. This study is also limited by its short duration.

To the investigators' knowledge, no studies have examined the effect of a concentrated, fortified, collagen protein hydrolysate supplement on PrU healing. Research on the use of high-protein nutritional supplements and wound healing is scarce.[5](#) The limited availability of rigorously performed clinical trials to develop evidence-based guidelines for nutritional support in wound care underscores the need for further research.[15](#)

Further study would be required to identify the extent to which the results of the present trial are attributable to the study product's amino acid profile, its hydrolyzed form, or the ease with which extra protein can be consumed in this form. Additional studies are also needed to evaluate optimal dosing and duration of treatment to achieve complete healing and to assess the benefits and costs of concentrated, fortified, collagen protein hydrolysate supplementation

in other populations.

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