

Effects of enteral nutrition on patients with pressure lesions: a single center, pilot study

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Abstract. – OBJECTIVE: Protein-energetic malnutrition (PEM) affects prognosis and mortality in elderly patients as an inadequate nutritional status is a risk factor for the development and worsening of pressure sores (PS). We aimed to evaluate the incidence of PEM in outpatients with PS and to study the impact of nutritional support on the stage of PS.

PATIENTS AND METHODS: PS patients, divided in a group treated with artificial nutrition (group A) and those fed orally (group B) at home, were consecutively enrolled in the Integrated Home Care program of Ascoli Piceno between June and September 2015. At T0 the patients underwent medical history, nutritional, anthropometric/biochemical parameters assessment, and the staging of the PS. The same assessments and staging of the pressure lesions were performed three months later (T1).

RESULTS: Group A (n=25) started from a better nutritional status vs. group B (n=25) at T0, according to MNA assessment. Group A showed a significant improvement of nutritional status correlating with detailed control of nutrients intake and improvement of PS stage (T0 vs. T1, $p<0.05$). On the other hand, group B showed a significant difference between nutrients intake and nutritional needs that correlated with both malnutrition state increase and worsening of the PS staging (T0 vs. T1, $p<0.05$).

CONCLUSIONS: The present study shows that PEM has a significant prevalence in the elder, in general, and in older people with PS, in particular. A targeted nutritional intake can prevent and help the healing of PS.

Key Words:

Pressure sores, Malnutrition, Personalized medicine, Integrated Home Care program.

Introduction

Nutritional value of food is a crucial element for the maintenance of health status. Several scientific evidence support the hypothesis that nutritional balance plays a central role in the treatment and prevention of many diseases like diabetes mellitus, chronic renal failure, hypertension, and osteoporosis¹.

As the nutritional status of patients' needs continuous monitoring, there is a well-known issue about the lack of continuity in the management of in-patients and out-patients' malnutrition. More interestingly, treatment of protein-energy malnutrition (PEM) is very often related to other diseases and should be one of the main targets of clinical nutrition programs^{1,2}.

However, PEM remains a misunderstood and underestimated problem, especially in hospitalized patients: during the hospitalization, PEM tends to increase very often, especially in elderly and long-term admitted patients. Recent data from literature show that over half of the patients are at risk of malnutrition, and over a third were malnourished at the time of hospital admission³. More interestingly, in the 70% of cases, nutritional status worsens during the first 10 days of hospitalization⁴.

PEM is a reversible risk factor for the development also of pressure lesions: a targeted nutritional intake is an important component that contributes to the prevention and care of this pathologic condition. In fact, the European Pressure Ulcer Advisory Panel guidelines (EPUAP) recommend an adequate dietary regimen to prevent PEM and establish the need for nutritional support plans in case of reduced intake of nutrients⁵. Several studies show that malnourished patients with pressure sores (PS) need an increase in caloric and protein intake because of the higher consume from inflammation and cell synthesis in new tissues healing process⁶⁻⁹.

In particular, the energetic requirement increases of about 200-600 kcal/day and the protein one of 20-60 g/day. Indeed, PS healing is quicker and more effective in patients fed with a protein intake of 1-2 g/day per kg of body weight and with an energetic one of 30-40 kcal/day per kg of body weight⁵. The specificity of nutrients used is also crucial for healing pressure lesions: arginine stimulates production and deposition of collagen, the flow of blood to and from the injured area, the cellular immune activity and the retention of nitrogen. Moreover, antioxidants agents (e.g., selenium, flavonoids, vitamins C, A, and E and carotenoids) promote tissue regeneration¹⁰.

The way of nutrients administration is another crucial point in the treatment of this subset of patients: according to the guidelines, the oral way of administration is the best and more suitable in order to preserve the capacity to swallow of the patient^{11,12}. Furthermore, nutritional support should cover the needs of both macro-nutrients and micro-nutrients through oral supplementation. However, both enteral and parenteral artificial nutrition are very often necessary when the oral intake is inadequate or not feasible (e.g., neurological dysphagia, oral cancers)¹¹⁻¹³.

In this single secondary-centre prospective comparative study, we aimed to evaluate both nutritional status and dietary intake (the incidence of PEM and the adequacy of the daily protein and caloric intake) of outpatients with PS under Integrated Home Care (IHC) program in our countryside area. We aimed also to verify a possible relationship between the improvement or worsening of the injury and any alteration of the nutritional status.

Patients and Methods

Study Design

Patients registered for IHC program of Ascoli Piceno, who had access to the complex dressings

for PS between June and September 2015, were considered. Patients underwent two nutritional assessments, at time 0 and three months later, namely time 1, by the Dietetic and Clinical Nutrition Service of the AV5 ASUR Marche. The study was approved by ASUR Marche Regional Ethical Committee (Ancona, Italy).

Patients Evaluation

The nutritional assessment of patients was performed at T₀ using a nutritional evaluation board that included several parameters for the identification of the patient's nutritional status. These parameters included anthropometric values (current and usual weight, percentage of weight lost or gained in the last three months, height, body mass index (BMI), basal, and total energy expenditure and protein requirement), medical history (diseases, nutritional diagnosis, comorbidities, neuropsychological problems, ability to move, etc.), risk of malnutrition [calculated using the Mini Nutritional Assessment (MNA)]¹³, feeding history (nutrition's way, presence/absence of dysphagia, consistency of meals, autonomy in the execution of the meal, 24-hour recall, energetic, and protein intake), staging of PS¹⁴ and biochemical nutritional indexes [albumin and lymphocytes and the relative Onodera PNI prognostic nutritional index, namely: $10 \times \text{serum albumin (g/dl)} + 0.005 \times \text{total lymphocyte count (per mm}^3\text{)]}^{15,16}$. The caloric and protein intakes were calculated from the recall of 24 hours, using the Metadieta® software¹⁷, and then, compared with the respective requirements, in order to establish if there was a match/mismatch between them. After three months, namely T1, weight, BMI, anthropometric values, the nutritional status, and the stage of the pressure lesions were reassessed.

Patient's data were obtained by telephonic interview (with the concerned person or his family or caregiver) and by access to the Home Care program of Ascoli Piceno (Italy) in order to consult personal data, anthropometric measurements, biochemical analyses, and staging of lesions.

MNA Test

The Mini Nutritional Assessment is a multidimensional screening tool, validated in many clinical settings. More specifically, it is an integrated nutrition index that evaluates different nutritional parameters in order "to obtain synthetic information and a more accurate nutritional diagnosis"¹³. According to a metanalysis, MNA has 96% sensitivity, 98% specificity, and 97% predictive val-

ue to describe the nutritional status of patients. Moreover, MNA is easily repeatable even by non-trained nutrition professionals¹³.

The European Society for Clinical Nutrition and Metabolism (ESPEN) recommends its use both as a first-level screening and for successive follow-ups among the elderly¹³.

MNA test consists of 18 items divided into three sections: one about anthropometry and weight changes; one that considers the quality and quantity of food intake; one about disabilities and cognitive status¹³.

MNA consists of two steps:

- Screening (with a maximum score of 14 over six variables): the story of weight loss in the previous three months, food intake, motility, acute stress, cognitive status, BMI assessment. A score of 0-7 is predictive of malnutrition, a score of 8-11 suggests that patients are at risk of malnutrition, a score of 12-14 indicates that the person is well-nourished and needs no further investigation. If the score is less than 11 it is strongly recommended to continue with the remaining questions; this is necessary to obtain additional information on factors that may impact nutritional status. An MNA score higher than 24 indicates that the patient is well-nourished, a score between 17-23.5 suggests a risk of malnutrition and scores lower than 17 clearly pinpoints malnutrition.
- Self Global assessment (drugs assumption, food habits, fluid intake, residence place, patient's considerations on personal health status and on nutritional status).

Patients Population

The present study took into account 50 patients, 25 subjects fed artificially through enteral nutrition (group A) and the other 25 fed orally (group B).

Group A was composed of 8 males and 17 females, with an average age of 82.5 ± 1.3 years. These patients were all characterized by the presence of severe dementia and totally bedridden; they were fed by artificial enteral nutrition because of severe dysphagia. The enteral formula administered had a high-protein content and was enriched with arginine, zinc, C vitamin, and selenium (Cubison advanced®, Nutricia Italia, Milan, Italy).

Group B was composed of 25 patients, 9 males, and 16 females, with a mean age of 81.7 ± 1.5 years. Fifty-two percent of patients (13 subjects) had severe neuropsychological problems, 64% were

bedridden (16 subjects), and 84% (21 subjects) were orally nourished only (the remaining 16% of the patients used specific oral supplements). Only 28% (7 patients) was totally autonomous in consuming the meal. Forty-eight percent of subjects (12 patients) had slight neurological dysphagia and consumed a modified consistency diet prescribed by a dedicated Nutritionist.

Statistical Analysis

In this single secondary-centre prospective comparative study, the statistical analysis of the data collected was performed through InStat® program. Data are presented as mean $\pm$ SD.

The comparisons between groups were made by Mann Withney, Kruskal-Wallis, and Fisher Exact test when needed. Significant difference was considered at the 5% level, namely $p < 0.05$ ¹⁶.

Results

At the first assessment (T_0), the average weight in group A was 58.1 ± 0.8 kg, the relative BMI was 21.6 ± 1.5 kg/m², the lymphocytes were $1.7^3 \pm 0.1$ mm³ and the albumin value was 2.9 ± 0.2 g/dl (Table I). The latter, together with Onodera, were suggestive of a risk of protein-caloric malnutrition in these patients. Indeed, the study of malnutrition's risk, obtained with MNA score, showed that at T_0 68% of the subjects in group A had a normal nutrition status, 20% was at risk of malnutrition and the remaining 12% was malnourished (Table I).

In group B, the average weight was 66.8 ± 1.7 kg at T_0 , the relative BMI was 24.8 ± 1.0 kg/m², the lymphocytes were $2.3^3 \pm 0.2$ mm³, and the albumin value was 3.1 ± 0.2 g/dl. The latter, together with Onodera, were suggestive of a risk of protein-caloric malnutrition in these patients (Table I). More in detail, according to MNA test, 28% of patients had a normal nutritional status, 16% was at risk of malnutrition, and 56 % was malnourished (Table I).

After three months (T_1) biochemical and anthropometric parameters, Onodera index and MNA assessment were improved in group A, while they were worsened in group B.

In particular, in the first group, the average body weight increased from 58.1 ± 0.8 kg to 60.2 ± 0.7 kg ($p < 0.05$), such as the corresponding BMI (increasing from 21.6 ± 1.5 kg/m² to 22.5 ± 1.3 kg/m² ($p < 0.05$)) (Tables II, III). The patients in three months gained 2.1 kg; the albumin rose

Table I. Anthropometric (body weight and BMI) and biochemical parameters (albumin and lymphocytes concentration, relative Onodera index) and malnutrition risk (MNA test) at T₀ in both group A and B.

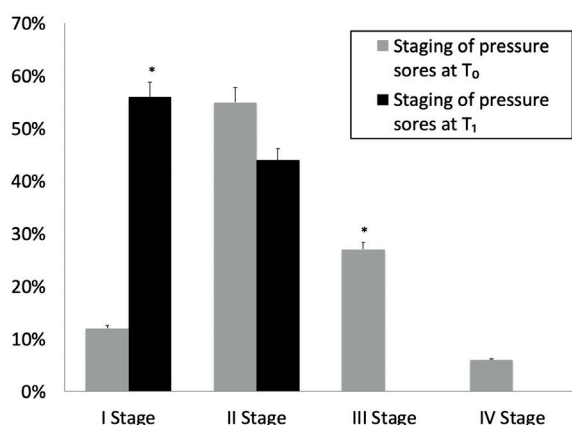
Variable	A group	B group	p-value
Weight (kg)	58.1 ± 6.8	66.8 ± 7.9	<0.05
BMI (kg/m ²)	21.6 ± 1.5	24.8 ± 0.9	<0.05
Albumin (g/dl)	2.9 ± 0.2	3.1 ± 0.4	NS
Lymphocytes (mm ³)	1.7 ³ ± 0.4	2.3 ³ ± 0.3	<0.05
Onodera index	29.0085	23.0115	<0.05
MNA normal nutritional status	68%	28%	<0.05
MNA at risk of malnutrition	20%	16%	NS
MNA malnourished	12%	56%	<0.05

from 2.9±0.2 g/dl to 3.2±0.3 g/dl ($p=NS$) and lymphocytes from 1.7³±0.1 mm³ to 1.9³±0.1 mm³ ($p=NS$) (Table III). Only 8% of patients with PS and under enteral nutrition lost weight, while the remaining gained or maintained weight.

On the other hand, in group B, the average body weight decreased from 66.8±1.7 kg to 63.9±1.4 kg ($p<0.05$) (Table II), such as the average BMI (from 24.8±1.0 kg/m² to 23.6±1.1 kg/m², $p<0.05$); these

patients lost 2.7 kg in three months (about 4.6% of initial body weight); albumin fell from 3.1±0.2 g/dl to 2.9±0.1 g/dl ($p=NS$) and lymphocytes from 2.3³±0.2 mm³ to 2.0³±0.1 mm³ ($p=NS$) (Table III). Fifty-six percent of patients in group B lost weight while the remaining maintained or gained it. At T₁, 86% of the subjects in group A was well-nourished, 10% at risk of malnutrition, and the remaining 4% frankly malnourished ($p<0.05$, well-nourished, T₀ vs. T₁) (Table I, II). In group B, 10% of subjects was well-nourished, 6% at risk of malnutrition, and 84% frankly malnourished ($p<0.05$, malnourished T₀ vs. T₁) (Tables I, II). It is important to note that, although anthropometric and biochemical parameters (e.g., weight, BMI, albumin, lymphocytes, Onodera index) reveal that nutritional status of group B was better than the group A at the first assessment, MNA assessment unraveled the opposite. Moreover, at T₁ there was a further worsening of nutritional status in group B and further improvement of that of group A, according to MNA test.

At T₀, in the group with pressure lesions and under enteral nutrition (A), 12% of the sores was at 1st stage, 55% at 2nd, 27% at 3rd and 6% at 4th stage (Figure 1); in group B, 39% of PS was at the 2nd stage, 41% at the 3rd and the 20% of the 4th stage (Figure 2).

**Figure 1.** Staging of the pressure sores in group A at T₀ and T₁, respectively; * $p<0.05$ between T₀ and T₁.**Table II.** Anthropometric (body weight and BMI), biochemical parameters (albumin and lymphocytes concentration, relative Onodera index) and malnutrition risk (MNA test) at T1 in both group A and B.

Variable	A group	B group	p-value
Weight (kg)	60.2 ± 7.3	63.9 ± 7.6	NS
BMI (kg/m ²)	22.5 ± 1.1	23.6 ± 1.2	NS
Albumin (g/dl)	3.2 ± 0.3	2.9 ± 0.4	NS
Lymphocytes (mm ³)	1.9 ³ ± 0.5	2 ³ ± 0.2	NS
Onodera index	32.0095	29.01	NS
MNA normal nutritional status	86%	10%	<0.05
MNA at risk of malnutrition	10%	6%	NS
MNA malnourished	4%	84%	<0.05

Table III. Change of antropometric (body weight and BMI), biochemical parameters (albumin and lymphocytes concentration, relative Onodera index) and malnutrition risk (MNA test) between T₀ and T₁ in both group A and B.

Variable	Group	T0	T1	p-value
Weight (kg)	A	58.1 ± 6.8	60.2 ± 7.3	< 0.05
	B	66.8 ± 7.9	63.9 ± 7.6	<0.05
BMI (kg/m ²)	A	21.6 ± 0.8	22.5 ± 0.7	<0.05
	B	24.8 ± 1.1	23.6 ± 1.2	<0.05
Albumin (g/dl)	A	2.9 ± 0.2	3.2 ± 0.3	NS
	B	3.1 ± 0.4	2.9 ± 0.4	NS
Lymphocytes (mm ³)	A	1.73 ± 0.4	1.93 ± 0.5	NS
	B	2.33 ± 0.3	2.03 ± 0.2	NS
Onodera index	A	29.0085	32.0095	NS
	B	31.0115	29.01	NS

After 3 months (T₁), 48% of patients in group A had no longer injuries and 52% of patients had sores at 1st or 2nd stage only (Figure 1). In B group, conversely, all the patients still presented with PS at 1st (25%), 2nd (53%), 3rd (13%), and 4th (9%) stage (Figure 2).

At T₀, the difference between caloric intake and energetic requirement was minimal in group A: there was a negative difference of 44 kcal/day. Similarly, the difference between protein intake and demand showed a minimal non-significant negative difference of 6.4 g/day (Table IVa).

In group B, the difference between caloric intake and energetic requirement resulted significantly higher than in group A, with a negative difference of 295 kcal/day ($p<0.05$). Similarly, the difference between protein intake and needs showed a defect of 13.6 g/day, significantly higher than in group A ($p<0.05$) (Table IVa).

In group B, 88% of the subjects resulted to be malnourished and 68% had a share of protein significantly lower than the recommended daily dose.

At T₁, the difference between caloric intake and energetic requirement remained minimal in group A: there was a negative difference of 55 kcal/day. Accordingly, the difference between protein intake and demand showed a negative difference of 5.1 g/day only (Table IVb).

The difference between caloric intake and energetic requirement remained significantly higher

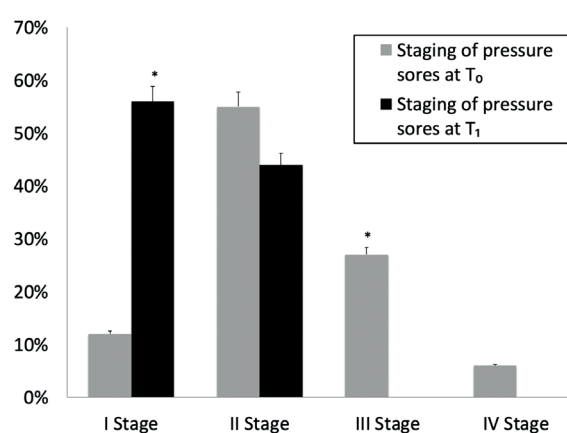


Figure 2. Staging of the pressure sores in group B at T₀ and T₁, respectively; * $p<0.05$ between T₀ and T₁.

in group B vs. group A ($p<0.05$), with a negative difference of 326 kcal/day. Also, the difference between protein intake and needs showed a defect of 12.6 g/day, statistically higher than group A ($p<0.05$) (Table IVb).

Discussion

Patients from the present study had clinical conditions that increased the risk for PEM and favoured the onset of compression lesions³⁻⁶. In

Table IVa. Difference between intakes and requests of calories and proteins in group A and B at time 0 (a) and 1 (b), respectively.

Variable	Group	Requests (R)	Intakes (I)	Delta	p-value
Energy (kcal)	A	1420 ± 146	1376 ± 183	44	NS
	B	1602 ± 154	1307 ± 196	295	<0.05
Proteins (g)	A	72.8 ± 5.9	66.4 ± 6.2	6.4	NS
	B	73 ± 11.9	59.4 ± 12.2	13.6	<0.05

Table IVb. Difference between intakes and requests of calories and proteins in group A and B at time 0 (a) and 1 (b), respectively.

Variable	Group	Requests (R)	Intakes (I)	Delta	p-value
Energy (kcal)	A	1450 ± 130	1395 ± 170	55	NS
	B	1672 ± 140	1346 ± 196	326	<0.05
Proteins (g)	A	75.8 ± 5.0	70.7 ± 5.3	5.1	NS
	B	75.7 ± 12.9	63.1 ± 11.1	12.6	<0.05

fact, several of them had severe neuropsychological problems, due to chronic disease and comorbidities that involved central and peripheral nervous system (ischemic or haemorrhagic stroke, senile dementia, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, diabetes mellitus, etc.)¹⁻³. Moreover, they were bedridden, with a feeding dependent on meal ingestion aid efficiency, because of very frequent neurologic or mechanical dysphagia^{3,18}.

According to the MNA test, in group A 32% of cases had a malnourished nutritional status while in group B 56% of subjects was malnourished.

On the other hand, it is interesting to note that the average BMI of patients from both groups at T₀ was indicative of malnutrition. Furthermore, also mean serum albumin, lymphocytes count, and Onodera index at T₀ suggested a state of malnutrition in these subjects. These biochemical parameters, such as serum albumin, may be useful to predict an incoming state of malnutrition but may bias the real state of nutrition description and should be confirmed by validated tests, such as MNA and/or Malnutrition Universal Screening Tool (MUST) assessments^{19,20}.

Thus, there was a gap in malnutrition diagnosis between a validated test (namely MNA test) and other indexes that are suggestive of malnutrition only^{13,19,20}.

This difference in malnutrition description between validated tests and indirect indexes was present also in the comparison between T₀ and T₁. However, some index was able to describe the improvement or worsening of nutritional status. In particular, the average albumin level in group A was suggestive of a decreased percentage of risk of malnutrition from T₀ to T₁, passing from malnutrition (2.9 g/dl) to risk of malnutrition (3.2 g/dl), while in group B the change was exactly the opposite (passing from 3.1 to 2.9 g/dl)²¹. These data were confirmed by MNA test assessments.

The general improvement of the nutritional status in group A can be explained by the fact that the artificial enteral nutrition with its high protein content allowed a precise and detailed control on

the provision of micro-nutrients and macro-nutrients²². This is in agreement with a significantly lower gap between the general energetic intake and requirement both at T₀ and T₁ vs. group B. On the other hand, in group B, the significant difference between intake and nutritional need, significantly higher than group A, sensibly conditioned the deterioration of patient's nutritional status.

Indeed, subjects with PS fed orally have often mild to moderate dysphagia, due to their remote disease or other comorbidities and they must, therefore, resort to a modified consistency diet (soft, semi-solid or semi-liquid) or make use of products created for children (milk, biscuits, baby food, etc.)^{23,24}. The latter does not guarantee an adequate supply of micro-nutrients and macro-nutrients to an elder subject, perhaps with a significantly increased nutritional demand²⁵.

A non-significant percentage of patients of group B used oral food supplementation not only rich in calories and proteins, but also in micro-nutrients such as arginine, selenium, flavonoids, vitamins, and carotenoids^{22,26}. This amount is very low in comparison with the request of these patients vs. that received by group A. In fact, several national and international studies and clinical practice guidelines show that dietary supplements promote the healing of PS and the improvement of nutritional status^{5-7,9,13}.

In group A, 48% of patients did not show PS after three months of treatment with an enteral nutrition mixture specifically designed to meet the requirements in macro-nutrients and micro-nutrients of the subjects with PS. The remaining patients still presented lesions at 1st and 2nd stage only. Although these lesions did not reach total healing, they were significantly improved vs. T₀.

On the opposite, in group B 16% of patients only showed lesions completely healed, while the remaining patients had not only PS at 1st and 2nd stage but also at 3rd (13%), and 4th stage (9%). These findings can be explained by the insufficient caloric, protein, and micro-nutrients and macro-nutrients supplementation received^{22,26}. The present study shows that protein-energetic malnutrition

remains a misunderstood issue in the daily management of PS patients³⁻⁸. An adequate nutritional intake represents an important component that contributes to the prevention and/or healing of PS, as perhaps described by several revisions of literature^{27,28}. However, the present study has some limitations: the small sample size from a single center, the compared groups were not homogenous at T₀.

Further larger prospective multicentre randomized controlled trials are needed to confirm these preliminary results from this single center prospective study showing that nutritional status is strongly associated with PS staging and healing in two different groups of patients. In fact, we need more data to verify the role of enteral nutrition and nutritional supports in managing pressure ulcers and to compare the role of enteral nutrition vs. standard balanced oral diet. Finally, more similar baseline patients' characteristics are needed for future comparative trials.

Conclusions

The fight against malnutrition cannot ignore the lack of continuous standard of care for patients in the grey zone between hospital and home. It is necessary to provide the most appropriate nutritional strategies to reduce the prevalence and severity of PEM, to improve the quality of life of fragile people who have a compromised nutritional status, to reduce costs for the management of PS and to reduce PEM complications and hospitalization incidence¹⁻³.

To make this possible, it is necessary to promote integrated programs for training, retraining, and upgrading of the various professional figures involved in the prevention and treatment of PS (e.g., nurses, dieticians, and general practitioners) in the frame of the IHC program²⁹⁻³¹. This can be feasible only if there is a continuous interplay between the countryside healthcare system and the hospital-based health assistance.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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