

ACTA VULNOLOGICA

Vol. 10 - N. 2 - GIUGNO 2012

ORGANO UFFICIALE
DELL'ASSOCIAZIONE ITALIANA ULCERE CUTANEE

AIUC



PUBBLICAZIONE PERIODICA TRIMESTRALE - SPED. IN A.P.D.L. 381/2005 (CONV. INT. 27/02/2004 N. 46) ART. 1, COMMA 1, LETT. C) - BSN 1721/2000 - TAXE PERC/P

EDIZIONI MINERVA MEDICA

Nutraceutical supplementation in the treatment of pressure ulcers: short-term study

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Aim. The aim of the paper was to verify the short-term effectiveness of nutraceutical supplementation in the treatment of pressure ulcers (PUs) in cancer patients assisted at home by the ANT Foundation.

Methods. Seven patients (4M and 3F) were treated, 2 with double PUs, for a total of 9 PUs. 4 lesions were at stage II, 3 at stage III and 2 at stage IV. A nutraceutical product (W-care) containing specific nutrients for the treatment of PUs was used. Doses: stage II-III, 2 packages/die; stage IV, 3 packages/die. At admission to the study clinical, nutritional and nursing parameters were measured with description and photos of the PUs at T₀, T₇, T₁₄, T₂₁, T₂₈. Duration of the treatment: 4 weeks.

Results. At T₀ the PUs had been under treatment for from 63±72 days (range: 20-240). The nutritional state was normal in 5 patients, all with PUs at stage II and III. The 2 patients with PUs at stage IV presented a slight-moderate state of malnutrition. At T₂₈, the 7 lesions at stage II and III had cured. The 2 PUs at stage IV in the 2 malnourished patients had improved markedly but were not cured.

Conclusion. The cure at T₂₈ of the PUs at stage II and III shows the effectiveness of the nutraceutical product in short-term treatment. The presence of malnutrition in the 2 patients with PUs at stage IV confirms the importance of the nutritional state as a risk factor in patients with pressure ulcers.

Key words: Pressure ulcer - Dietary supplements - Medical oncology.

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One of the most important complications in elderly advanced cancer patients is the pressure ulcer (PU). By PU we mean a necrotically evolving tissue lesion involving the cutis, derma and subcutaneous tissues which, in the most severe cases, can affect the muscle, cartilage and bone. The phenomenon is caused by prolonged and/or excessive pressure exerted between the resting surface and bone surface such as to provoke mechanical stress on the tissues and a change in local blood circulation. This brings ischemia, hypoxiemia and reduced nutritional supply, with rapid formation of necrosis in the tissue.

The presence of concomitant systemic diseases such as diabetes mellitus, renal failure, immunodepression, circulatory disturbances, cancer etc. constitutes an aggravating risk factor.

The factors favouring the onset of PU and which impede cicatrisation may be split schematically into two groups:

1. extrinsic or local factors. These act directly on the pressure ulcer and consist of:
 - dry environment: this provokes dehydration and consequent cell death with eschar formation or a dry scab above the lesion which prevents cicatrisation;
 - pressure: this provokes circulatory

insufficiency in the capillaries with consequent tissue ischemia;

— stretching and chafing: slipping of the soft layers with respect to the skeletal surfaces creates circulatory failure with consequent ischemia and superficial and deep tissue necrosis; in addition the negative effects of the two surfaces chafing together are reinforced by the production of heat and prolonged exposure of the skin to humidity;

— infection: exudate, that may be purulent, consequent on cell destruction slows down curing processes;

— necrosis: prevents proliferative processes and favours infection.

2. Intrinsic or systemic factors. They act on the entire organism and consist of:

— age: elderly patients are more at risk of PU due to skin changes related to aging (reduction in the subcutaneous adipose tissue, thinning of the epidermis and reduction in cutaneous elasticity, reduction in perception of pain and sensitivity, reduced local immune response, modification to the cutaneous microcirculation, reduction in cell proliferative capacity);

— reduction in mobility caused by pathological states;

— body structure: in obese patients the blood supply to the fatty tissue is poor while in thin patients there may be a shortage of oxygen and nutritional substances, and protruding bones are less protected from traumas and pressure and traction forces;

— chronic diseases: diabetes, cardiovascular diseases, renal failure, cancer;

— vascular insufficiency: leads to reduced tissue perfusion;

— incontinence: urinary and/or fecal incontinence may impair the skin provoking softening and fostering the onset of infection;

— immunosuppression and radiotherapy;

— nutritional state: malnourished patients are more at risk of developing PUs.

The state of nutrition is one of the most important risk factors in the onset and maintenance of PUs. Up to the present, studies point to the presence of a biunivo-

cal relationship between nutritional state and PUs: on the one hand the presence of protein-calorie malnutrition in elderly patients increases the risk of their formation, on the other 50% of patients with PU are also malnourished.¹ A recent study by Cereda² highlights the presence of a reduced protein-calorie intake in patients with PU which, in association with the increased energy need and the protein dispersion caused by the lesion, could be the cause of the onset of a picture of malnutrition. The implementation of nutritional screening programmes is fundamental from the very moment the elderly patient is admitted for treatment,³ particular attention being paid to patients at risk of developing a PU or with ongoing impairment of skin integrity. The latter require a more careful assessment of their nutritional state through examination of specific clinical, metabolic and laboratory parameters.

The state of malnutrition in patients with PU must always be remedied with protein-calorie supplementation,⁴ by means of:

— improving oral ingestion of food with personalised diets and meal assistance if necessary;

— the use of hypercaloric and hyperproteinic nutritional integrators, enriched specific - nutraceutic - nutrients able to induce a better cicatrisation process (Table I);

— possibly setting up artificial nutrition (enteral or parenteral),⁵ in particularly critical patients.

In spite of the fact that at the present time there is no certain proof of the role and effectiveness of nutraceutics in the prevention and treatment of PUs,⁶ the literature contains comforting data regarding the effectiveness of specific aminoacids^{7,8} (arginine, glutamine, β -hydroxy- β -methylbutyrate). An experimental study by Cereda⁹ showed a significant increase in cure of PUs in patients with protein, arginine, zinc and vitamin C enriched nutritional support as opposed to a standard diet. Further studies have shown a positive effect on the prevention and cure of PUs in patients receiving oral supplementation of arginine, omega-3, vitamins A and C and zinc.¹⁰⁻¹²

TABELLA I.—*Nutraceutici coinvolti nella prevenzione e nel trattamento delle lesioni da decubito.*

Nutraceutico	Azione specifica
HMB <i>β-idrossi-β-metilbutirrato</i>	Stimola la costruzione delle proteine ed ha un effetto antinfiammatorio
Glutamina	Stimola la sintesi del collagene e delle proteine in toto
Prolina	Stimola la sintesi del collagene
L-Arginina	Stimola la sintesi del collagene e del sistema immunitario
Vitamina A	Controlla la guarigione delle lesioni ed è antiossidante
Vitamina E	Stimola il sistema immunitario ed è antiossidante
Vitamina C	Agisce nella sintesi del collagene ed è antiossidante
Vitamine del gruppo B	Proteggono le strutture cellulari
Vitamina K	Ha un ruolo importante nel controllo dell'emostasi
Omega-3	Stimola il sistema immunitario ed ha proprietà antinfiammatorie
Zinco	Stimola il turn-over del connettivo e le difese immunitarie
Selenio	Stimola il sistema immunitario ed è antiossidante
Collagene	Conferisce proprietà strutturali ed elastiche al connettivo

The Italian Skin Ulcer Association (AIUC), alongside the necessary prevention and treatment of malnutrition, recommends that nutraceutical supplementation should always form an integral part of the holistic approach to patients with Pus.¹³

The purpose of our observational study was to verify the short-term effectiveness of nutraceutical supplementation using a product based on specific nutrients (W-care) in the treatment of PUs in oncological patients assisted at home by the ANT Foundation of Bologna.

Materials and methods

Case series and PU characteristics

Seven oncological patients (4 male, 3 female, age 81 ± 7.3) with PUs were observed. The cancer locations were: the lung in 2 patients, melanoma in 2, the stomach, colon and prostate in 1 respectively. Two patients had double PUs for a total of 9 PUs treated. The pathogenesis of the lesion was prolonged compression in all patients to which chafing could be added in three. The localisation of the PU was: the sacral region in 4 cases, the heel in 3, the tronchanter and leg in one case respectively. The stage of the PU according to N.P.U.A.P. classification (Figure 1), was: stage II in 4, stage III in 3 and stage IV in 2.

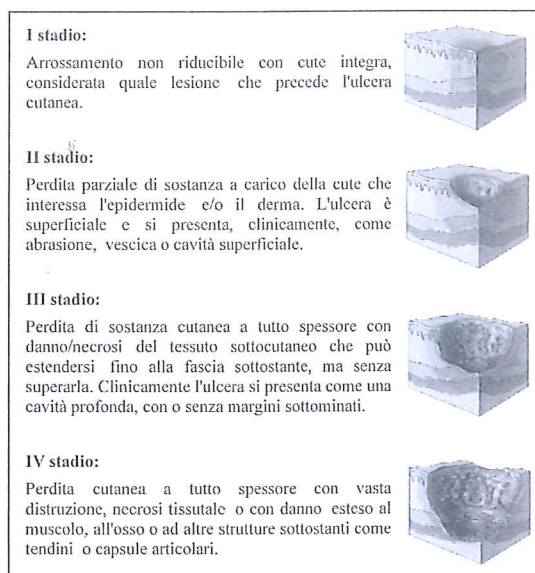


Figure 1.—PU stage according to the classification of the National Pressure Ulcer Advisory Panel (N.P.U.A.P.).

Clinical-nutritional admission form

The nutritionist physician filled out an admission form for each patient where the following clinical and nutritional parameters were recorded:

- site and propagation of the cancer;
- main clinical symptoms, Karnofsky Index (KI), state of motility and period in bed, presence or otherwise of a care-giver;
- pharmacological therapy and ongoing supplementary or artificial nutrition;

- where the patient had come from when admitted to ANT home care;
- serum and urinary analyses (hemochrome, total and fractionated, metabolic-nutritional parameters);
- dietary questionnaire and calculation of food intake per os;
- Body Mass Index ($BMI=kg/h^2$) and clinical signs of malnutrition.

The patient was considered malnourished when BMI was <18.5 , food intake per os was $<50\%$ of energy needs with consequent weight loss in the last week, albuminemia was <3.5 g/dL and the total lymphocyte count was $<1500/mm^3$. Albuminemia and total lymphocytopenia were considered relative nutritional indicators because both values are substantially affected by cancer and by the PU.

Nursing records

At the first examination (T_0), the nurse filled out a form on which the following parameters were recorded:

- typology, number of contemporaneous ulcers, site and pathogenesis of the PU;
- risk evaluation according to the Norton index (the patient was considered high risk if the Norton index was <14);
- stage of the lesion according to the classification of the National Pressure Ulcer Advisory Panel (N.P.U.A.P.) (Figure 1);
- procedures and materials used for external medication of PU;
- duration and frequency of medication in the period prior to admission to the study;
- detailed description of the lesion and any local complications, with measurement of PU dimensions;
- photo of the lesion;
- dosage scheme and patient compliance with oral intake of the product.

Every week for the next 4 weeks (T_7 - T_{14} - T_{21} - T_{28}) the nurse compiled a new form for the patient annotating any modifications to the parameters recorded in the initial form, with particular reference to the description of the lesion and its photo. Any dosage variations and patient compliance were also monitored.

Dietetic supplementation

As from T_0 patients were given a daily dose of a product per os based on specific nutrients for the treatment of PU (W-care - *Nutritional Care Technology*), consisting of 8 g packages containing L-Arginine 2 g, Omega-3 500 mg, vitamin C 100 mg, type II collagen 100 mg, zinc 4 mg, vitamin E 4 mg, vitamin A 400 mcg, vitamin B6 0.4 mg, vitamin B1 0.25 mg, vitamin K 15 mcg, vitamin B12 0.05 mcg.

Posology was modulated on the basis of the stage of the lesion: 2 packages/die for patients with PU at stage II-III and 3 packages/die for those with PU at stage IV.

During the period of observation no protein-calorie supplementation was undertaken either with dietary integrators or with artificial nutrition and no significant modifications were made to the patients' daily diet. The study lasted 4 weeks.

Results

At admission to the study (T_0) (Table II), 5 patients with lesions at stages II and III presented a nutritional state within normal limits with calorie intake per os $>50\%$ of their energy need and a positive protein-calorie balance. The 2 patients with PUs at stage IV presented a picture of slight-moderate malnutrition with calories providing $<50\%$ of energy need and weight drop in the last week.

At the moment of entering the study the lesions had been under treatment with external medication for an average of 63 ± 74 days, for a period of time varying from 20 to 240 days. The medications were carried out on average 4 times a week for 20 minutes a day. The products employed were principally: physiological solution, polyurethane foam, hyaluronic acid, calcium alginate, vaselined gauze and connectivine.

After 4 weeks of treatment with a nutraceutical product per os (T_{28}), the PUs at stage II and III were completely cured (Figure 2). The two lesions at stage IV had improved with a reduction in stage and dimensions (Figure 3).

TABELLA II.—Parametri clinici e nutrizionali dei pazienti con LDD a T₀ (in corsivo e grassetto i 2 pazienti malnutriti).

Paziente (Sede LDD)	Indice Norton	Stadio LDD	Giorni di medicazione pre-T ₀	Indice Karnofsky	Body Mass Index	Intake os 50% fabb. energetico	Albumina	Linfociti
<i>U.A. (sacro)</i>	12	4	30	30	17,5	<	2,6	1120
<i>U.A. (tallone)</i>	12	3	30					
<i>M.M. (sacro)</i>	9	2	20	40	21,6	>	3,8	1870
<i>M.M. (tallone)</i>	9	3	20					
<i>P.C. (sacro)</i>	16	2	30	50	24,6	>	3,3	1829
<i>R.E. (tallone)</i>	8	4	90	30	18,0	<	2,8	890
<i>G.A. (sacro)</i>	11	2	90	40	25,7	>	3,3	2214
<i>D.G. (gamba)</i>	7	3	240	40	26,7	>	2,6	5790
<i>F.B. (trocantere)</i>	15	2	20	50	18,7	>	3,1	2200

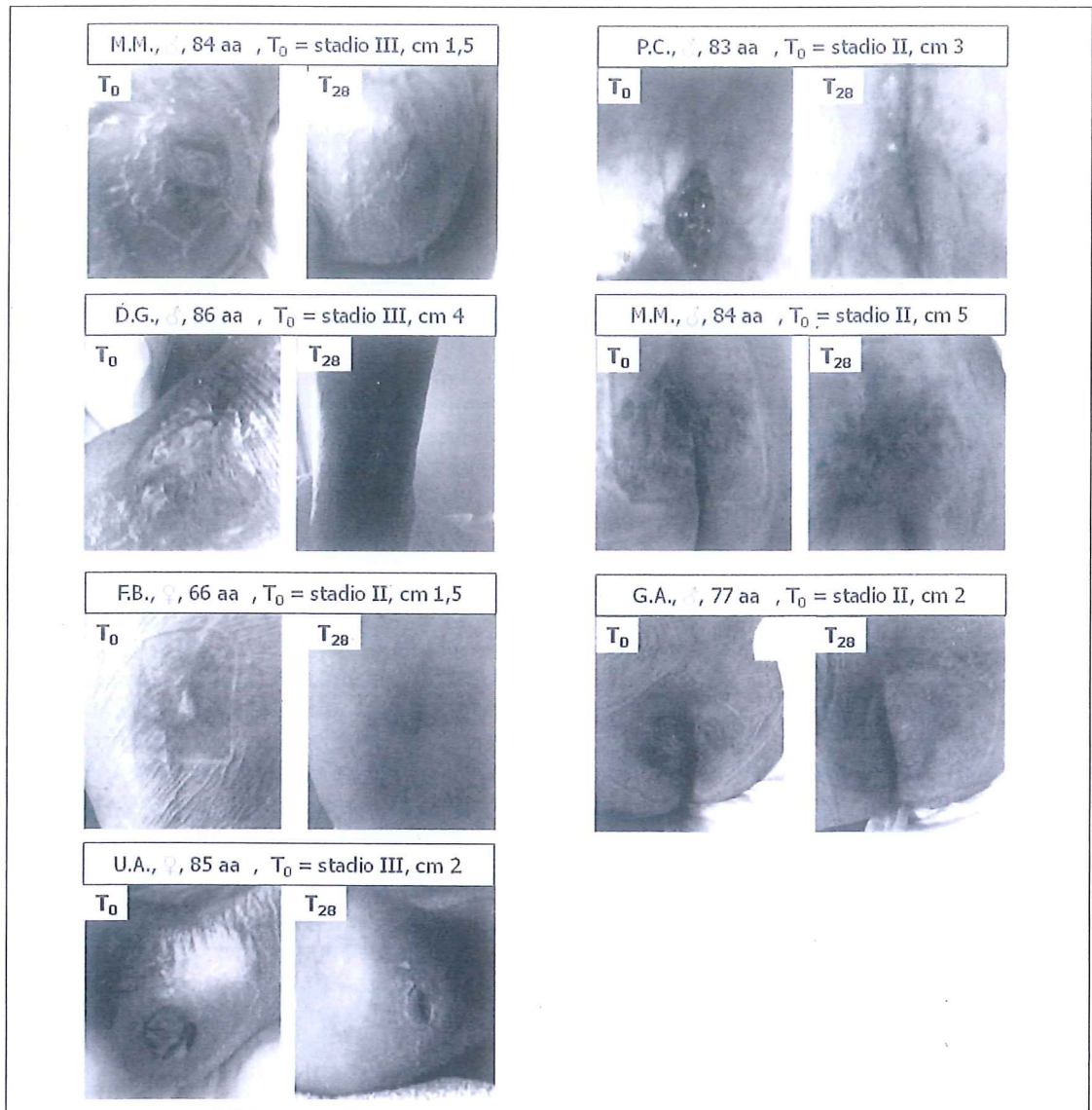


Figure 2.—II-III stage ulcers cured at T₂₈.

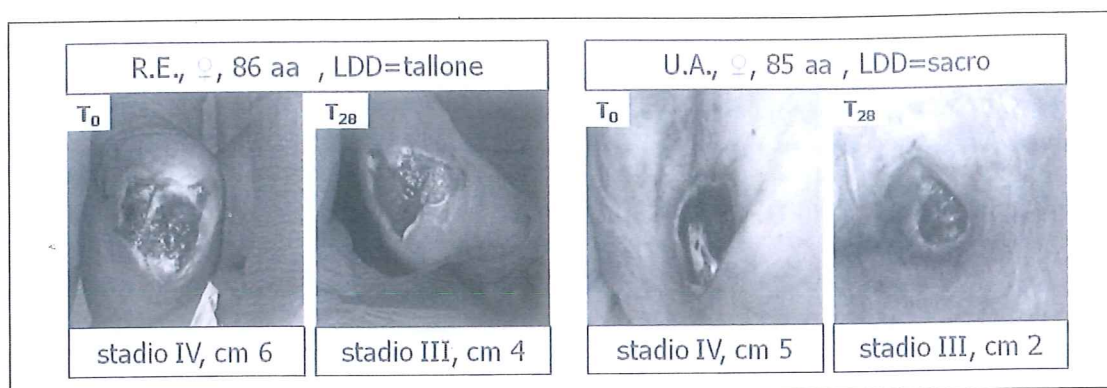


Figure 3.—IV stage ulcers improved at T₂₈.

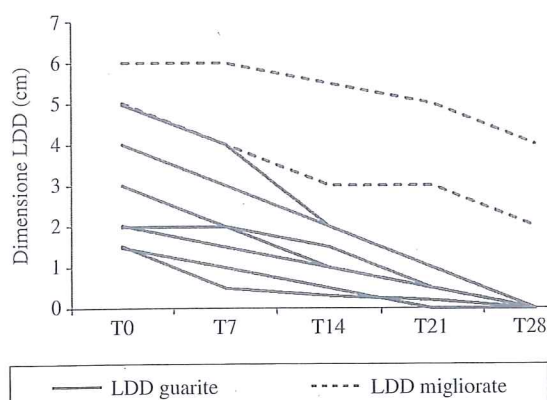


Figure 4.—Course of pressure lesion (7 patients, 9 PUs).

Patient compliance to the product was high and there were no drop-outs.

The Figure 4 graph sums up the course of the 9 pressure ulcers during the 4 weeks of the study.

Discussion

The ANT-Italia Onlus Foundation is an association set up in 1978 which assists cancer patients at home, daily and without charge.¹⁴ The ANT Nutritional Service was set up in 1990 with the aim of preventing death by cachexia and improving the quality of life of oncological patients who are unable to eat naturally and who need Artificial Home Nutrition (AHN).^{15, 16} In order to identify the state of malnutrition and/or precachexia and act in time, the ANT Nutri-

tional Service has undertaken a nutritional screening programme in all oncological patients entering ANT home assistance in Bologna and province. Within this programme an investigation has been started on the nutritional status of patients with PUs.

From the clinical, management and economic standpoints, PUs are one of the most important complications for the cancer patient. Vice versa, cancer is a multifactorial condition with a high risk of onset of PUs, combining advanced age with reduction in mobility, the presence of anaemia and fever with the state of malnutrition. Although there are no precise data in Italy on the significance of PU in cancer patients, a recent study¹⁷ shows a prevalence of 22.9% with an incidence of 6.7% in a large population of patients resident for more than 6 months in a palliative treatment centre.

Nutrition is one of the basic components for the maintenance of tissue integrity and the promotion of cicatrization processes. In addition, the gravity of pressure ulcers is closely related to the importance of the nutritional deficiency.¹² Although reported data show that only in the malnourished patient is an improvement in clinical and nutritional condition possible,¹⁸ recent data show a positive effect of nutraceutic integrator supplementation on the tissue repair of pressure ulcers even in the non-malnourished patient.^{19, 20} In addition, many studies highlight a reduction in the blood levels of anti-oxidant vitamins and zinc in patients with chronic pressure ulcers.^{21, 22}

Starting from these observations we decided to carry out a study to assess the effectiveness of dietetic supplementation with a product based on specific nutrients on the prevention and treatment of PUs. In fact, when these nutrients are taken in quantities considerably higher than that normally present in the daily diet, they become pharmaco-nutrients or nutraceuticals. These nutraceuticals permit an internal therapeutic approach to the lesions which is, obviously, flanked by external treatment with medications, so guaranteeing optimal conditions for cure.

The results of the study showed that, independently of the nutritional state, integration with specific nutraceuticals permitted rapid improvement (within the 4 weeks we identified as the minimum period necessary to assess the effectiveness of the therapeutic response) of the PUs in the 7 patients observed, up to complete cure in 5 of them. The PUs had been under treatment with external medication on the wound for an average of 63 ± 72 days. The integration of specific nutrients, particularly arginine as an aminoacid source, collagen, anti-oxidants and immune activity stimulants like omega-3, zinc and vitamins A-C-E-group B, enabled us to redress the balance of a relative shortfall of these nutrients, when related to the increased need from the organism to permit the rapid cure of the lesion.

In our experience, 2 packages/die of the nutraceutical produce used by us (W-care) were sufficient to bring complete cicatrization of the 7 stage II-III PUs after only 4 weeks. Of these patients the case of D.G. was emblematic (M, 86, myeloma, normal state of nutrition, bed-ridden, stage III PU on the leg and diameter of the lesion 4 cm), under treatment for 240 days with nursing medications 3-4 times/week for a total of 120 days of treatment without any real evidence of improvement: after 4 weeks of treatment with 2 packages/die the wound had cured completely (Figure 2). It is thus confirmed that even in patients whose nutritional state is within normal limits, it is necessary to act from within in synergy

with the external medication, so as to bring about PU cicatrization within a short time.

The study also confirmed the correlation between malnutrition and gravity of PUs. In fact the 2 patients who were not cured, although they saw a great improvement to their PUs in terms of dimensions and gravity, were the only ones with an impaired nutritional state (slight-modest degree of malnutrition). This hypothesises the need to normalise the state of nutrition by employing a personalised therapeutic plan using calorie integrators enriched with nutraceuticals, or resorting to artificial (enteral or parenteral) nutrition.

Achieving rapid cure of PUs in cancer patients makes it possible to reduce their complications and at the same time improve the patient's quality of life, an objective that comes fully within the sphere of the "global" concept of eubiosis (good life) on which the ANT-Italia Onlus Foundation's home care is based. Finally, we must not ignore the economic advantage deriving from a reduction in the nursing time and pharmaceutical expenditure necessary for external medications when these are associated with a specific nutraceutical supplementation that makes it possible to accelerate wound cure times.

Conclusions

The cure of stage II and III PUs in patients with normal nutritional status after 28 days of treatment points to the effectiveness of the product (W-care) in the short term, and confirms the need for integration with specific micronutrients even in the non-malnourished patient.

The improvement without cure in the two stage IV cases suggests the usefulness of prolonging the treatment period and/or of increasing the nutraceutical integration dose to 4 packages/die in this type of patient. The fact that the two stage IV ulcers were present in the only two malnourished patients confirms the importance of nutritional state on the cure of the lesion, and recommends the undertaking of personalised nutritional therapeutic strategies aimed

at countering malnutrition and bringing clinical and laboratory nutritional parameters back within normal limits.

The results suggest the need to pursue the study with the aim of extending the series and investigating the cost-benefit analysis of nutraceutical supplementation on the cure of pressure ulcers.

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The paper was presented at the AIUC Congress 2011 held at Ancona on 21-24 September 2011, winning on that occasion 1st prize as the best poster.

Received on June 15, 2012.

Accepted for publication on July 9, 2012.

Supplementazione nutraceutica nel trattamento delle lesioni da decubito: studio a breve termine

Una delle complicanze più importanti nel paziente anziano con neoplasia in fase avanzata è rappresentata dalle lesioni da decubito (LDD). Per LDD si intende una lesione tissutale ad evoluzione necrotica che interessa la cute, il derma e gli strati

sottocutanei, fino a raggiungere, nei casi più gravi, il muscolo, la cartilagine e l'osso. Il fenomeno è causato da una prolungata e/o eccessiva pressione esercitata tra piano d'appoggio e superficie ossea, tale da provocare uno stress meccanico sui tessuti