Clinical Pharmacology & Biopharmaceutics

Kryczka and Grieb, Clin Pharmacol Biopharm 2014, 4:1
DOI: 10.4172/2167-065X.1000130

Review Article Open Access

Supportive Treatment of Pressure Ulcers with Dietary Supplementation

Tomasz Kryczka* and Paweł Grieb

Department of Experimental Pharmacology, Mossakowski Medical Research Centre, Polish Academy of Sciences, 5 Pawińskiego Str., 02-106 Warsaw, Poland

Abstract

Pressure ulcers remain a major health problem in immobilized patients, both hospitalized and staying at nursing or private homes. Malnutrition is a significant risk factor for their development and dietary supplementation is a potentially valuable method of supportive treatment. However, clinical data showing specific efficacy of supplements in pressure ulcers are scanty. The present short review compares effects of two dietary supplements which have been tested as an addition to standard treatment of pressure ulcers in non-malnourished patients: Cubitan (Nutricia) which is a complex protein and vitamin formulation, and carnosine, a dipeptide naturally present in meat, which may exert significant pharmacologic effects.

Keywords: Pressure ulcers; Dietary supplementation; Carnosine; Cubitan

Abbreviations: PU: Pressure Ulcer

Pressure Ulcers – Frequent and Dangerous Medical Condition

The term *decubitus* (pressure ulcer), derived from the Latin word *decumbre* meaning 'lying flat', started to be used in medicine in the fifteenth century. According to the current definition, a pressure ulcer (PU) is a localized injury to the skin and/or underlying tissue that usually occurs over a bony prominence as a result of pressure, or pressure in combination with shear and/or friction. The most common sites are the sacrum, coccyx, heels or the hips, but other sites such as the elbows, knees, ankles or the back of the cranium can also be affected. Depending on the severity, PUs is classified as wounds of the 1-st to 4-th stage [1].

Pressure ulcers constitute a vexing and distressingly common problem in immobilized patients, both hospitalized residents of long-term care facilities such as nursing homes, and those who are treated at home. According to the recent report, wounds of this type affect one per one hundred adults in the U.S. [2]. PU can develop in patients of any age, but the most threatened ones are elderly patients in whom they often became chronic, non-healing wounds, frequently bothering until the death.

The analysis of the population comprising more than fifty thousand patients hospitalized in the U.S. revealed that the appearance of PU doubled the mean time of patients' hospitalization and approx. tripled their in-hospital mortality [3]. This report clearly demonstrates the severity of this medical problem.

Role of Dietary Supplements in the Treatment of Pressure Ulcers

The symptoms of malnutrition, such as undesired weight loss, insufficient nutritional intake and low serum albumin level, are significant but potentially reversible risk factors for the development of PU [4,5]. Not unexpectedly, the guidelines of the international advisory bodies dealing with the issues related to PU (European EPUAP and American NPUAP) recommend an administration of amino acid, protein and vitamin supplements to patients with pressure ulcers [6]. However, these recommendations are based on the theoretical reasoning and non-clinical data from animal experiments, while clinical studies have been few, and their results often ambiguous.

The complex analysis of the safety and efficacy of various methods of PU management, published in 2013 by AHRQ (the U.S. Governmental Agency which conducts assessments of the quality, safety, efficiency, and effectiveness of health care) contains the following summary of the situation: 'Studies of nutritional support evaluated protein-containing nutritional supplementation and specific nutrient supplementation with vitamins or minerals, such as ascorbic acid (vitamin C) or zinc. Studies provided moderate strength of evidence that protein supplementation resulted in wound improvement. There was low strength of evidence indicating similar results with vitamin C compared with placebo. Evidence about zinc supplementation was insufficient to draw conclusions' ([2], pp. ES-20-21).

Further, the following statement is found ([2], pp. ES-24-25): 'nutritional supplementation may provide benefit in terms of wound improvement, although the effects of nutritional supplementation were not dramatic and it was not clear from the studies in our review whether nutritional supplementation was beneficial to all patients or only those with evidence of nutritional deficiencies'. Also, it is strongly underlined that the nutritional support was always considered as an addition to the local treatment of the pressure ulcers.

Objective Assessment of Efficacy of Pressure Ulcers Treatment

The current studies on the effectiveness of treatment of the patients with PU are usually based on quantitative description of the rate of wounds healing in a prospective controlled design. Patients are randomly assigned to groups comprising PUs of the comparable severity; then, patients from the study group(s) receive treatment(s) tested, while the patients from the control group either do not receive

***Corresponding author:** Dr Tomasz Kryczka, Mossakowski Medical Research Centre, Polish Academy of Sciences, Department of Experimental Pharmacology, 5 Pawińskiego Str. 02-106 Warsaw, Poland, Tel: +48 604315103; Fax: +48 226086474; E-mail: kryczka.tomasz@gmail.com.

Received January 07, 2014; **Accepted** January 23, 2015; **Published** March 16, 2015

Citation: Kryczka T, Grieb P (2015) Supportive Treatment of Pressure Ulcers with Dietary Supplementation. Clin Pharmacol Biopharm 4: 130. doi: 10.4172/2167-065X.1000130

any treatment, or take a placebo. One frequently used tool for the quantitative description of PUs is the so-called PUSH scale (*Pressure Ulcer Scale for Healing)* developed by the personnel of the nursing school at Californian University of San Francisco [7]. The starting point for the development of PUSH were the observations indicating that the changes of the size of the wound within the first two weeks of the treatment and some features of the pressure ulcer allowed to predict a chance of complete healing. The scoring in the PUSH scale is based on the sum of the three counts:

PUSH score = (a) + (b) + (c),

Where (a) is the product of the length and width of the biggest wound, (b) is the score (0 to 3) based on the estimation of the amount of exudates in the wound, and (c) is the score based on the type of tissue in the wound. The authors named the PUSH scale 'the tool for the estimation of healing of the pressure ulcers'. The use of this tool should not replace a clinical evaluation but allows an evidence-based assessment and comparison of efficiency of various methods of management of the pressure ulcers applied by independent research groups.

Comparison of the Effects of Two Dietary Supplements on Pressure Ulcer Healing

The proprietary nutridrink Cubitan (N.V. Nutricia, Netherlands) is an example of a multicomponent dietary supplement containing proteins, vitamins and minerals, recommended for patients with PU. It is advertised as a special preparation intended for medical nourishment, which contains all the necessary nutrients in the correct proportions and also a high energy dose. There are 20 g of proteins and 256 kcal per one 200 ml serving. In addition, Cubitan contains arginine, zinc and vitamins A, C and E. This dietary supplement is available in various flavors and its recommended dosage for patients with PU is between 1-3 servings (bottles) per day for two or more weeks.

The effects of Cubitan in patients with PU were tested in two dedicated clinical studies. In the first one, the elderly patients (mean age: 82 yrs.) with pressure ulcers grade II-IV and the symptoms of malnutrition were supplemented with 2-3 servings of Cubitan daily for nine weeks. The treatment resulted in the significant decrease of the surface size of the wounds and the improvement of wound appearance [8]. The number of patients observed in this study was relatively large (245), however there was no control group, and for this reason the result could not be considered of the high quality. In the other study [9] 43 patients with pressure ulcers of grade III or IV, aged 70-80 years, and with no symptoms of malnutrition were divided into two groups. One (22 patients) were receiving Cubitan three times a day for 8 weeks while the other (21 patients) were receiving a placebo. Several semiquantitative tools were used to estimate the efficiency of treatment in both groups, one of them being the PUSH scale mentioned above. The effects of Cubitan supplementation were beneficial; the between-groups differences were statistically significant. However, the effect was not particularly impressive (Figure 1).

The other example of the dietary supplement that appears to be beneficial in non-malnourished patients with PU is carnosine, a dipeptide built of of β-alanine and l-histidine and naturally present in meat. The efficiency of carnosine and the complex of carnosine with zinc (Polaprezinc), as an addition to the standard care of patients with PU was the subject of a clinical study performed in Japan [10]. Forty-two patients (age: 60-70 yrs.), most of them suffering from psychiatric conditions, with stage II–IV PU were allocated into three groups. The patients in the control group (n = 14) received no oral treatment, the patients in the PLZ group (n = 10) received 150 mg/d Polaprezinc (containing 116 mg of carnosine and 34 mg of zinc), and the patients in the CAR group (n = 18) received orally 116 mg/d of carnosine. PU severity was assessed weekly using the PUSH score (Figure 2). The significant difference in favor of the patients receiving either carnosine or the complex of carnosine and zinc was evident. Importantly, the patients taking Polaprezinc encountered a decrease in the serum copper level, which may adversely influence wound healing, but no such effect has been noted in the patients taking carnosine.

It should be stressed that, even though in both aforementioned studies PU healing dynamics was assessed with the PUSH scale, for several reasons their results may not be fully comparable. The members of the control group in the Cubitan study were receiving the placebo, while the members of the control group in the carnosine study did not receive any oral treatment; the patients treated with Cubitan were markedly older that those receiving carnosine; the Cubitan study was carried out mostly in the European countries, whereas the carnosine

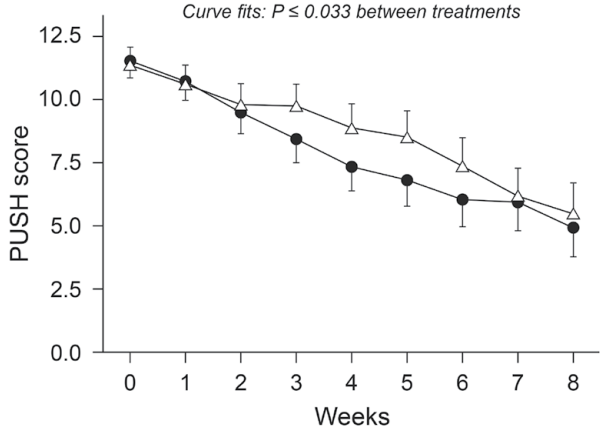

Figure 1: Mean PUSH scores. The group receiving the specific oral nutritional supplement is represented by closed symbols and the control group by open symbols. Reproduced from the article by van Anholt RD, Sobotka L, Meijer EP, Heyman H, Groen HW [9] with the acknowledgement of the publisher.

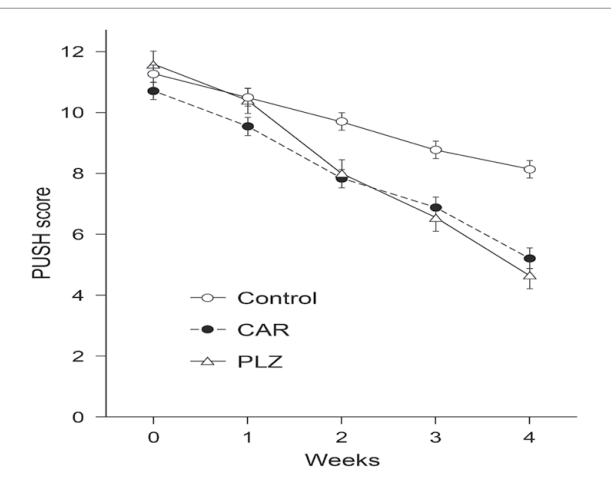

Figure 2: Changes in PUSH scores over the study period for all patients. Data represents squares mean+/- SEM. CAR, l-carnosine; PLZ, polaprezinc. Reproduced from the article by Sakae K, Agata T, Kamide R, Yanagisawa H [10] with the acknowledgement of the publisher.

study was performed in Japan, the country of different dietary customs. It is worth noting that the ingestion of Cubitan most likely influences the treatment of PU through the wide-ranging reinforcement of the nutritional status of the patients, and may not be particularly effective if the patients are not malnourished. On the other hand, carnosine or its parent aminoacids may influence PU healing through more specific mechanisms.

Following an oral intake carnosine undergoes an intestinal absorption and in human blood plasma is relatively quickly hydrolysed to the parent aminoacids [11]. Therefore, it may exert beneficial effects acting both as an intact compound and as products of its hydrolysis and metabolic conversion. It was suggested almost three decades ago that an enhancement by carnosine of wound healing may be ascribed to the stimulation of the early effusion by histamine derived from histidine, and of collagen biosynthesis by β-alanine [12]. More recently researchers at the Karolinska Institute in Stockholm [13] have found that in a murine model of diabetes, the administration of carnosine accelerates wound healing through a stimulation of expression and release of growth factors and cytokines in tissues flanking the wound. Also, it has been reported that low levels of the essential amino acids, tryptophan and histidine, are commonly encountered in older people with wounds [14]; the second of these deficiencies may be specifically targeted by carnosine supplementation.

Although it may be too early to recommend carnosine supplementation as compulsory adjunctive treatment of PU, the data reported by Sakae et al. [10] are certainly very promising. Some further evaluation in randomized studies of the effects of carnosine supplementation on healing of pressure ulcers is urgently needed.

References

1. Black J, Baharestani MM, Cuddigan J, Dorner B, Edsberg L, et al. (2007) National Pressure Ulcer Advisory Panel's updated pressure ulcer staging system. Adv Skin Wound Care 20: 269-274.
2. Saha S, Smith MEB, Totten A, Fu R, Wasson N, et al. (2013) Pressure Ulcer Treatment Strategies: Comparative Effectiveness. Rockville (MD): Agency for Healthcare Research and Quality (US);
3. Lyder CH, Wang Y, Metersky M, Curry M, Kliman R, et al. (2012) Hospital-acquired pressure ulcers: results from the national Medicare Patient Safety Monitoring System study. J Am Geriatr Soc 60: 1603-1608.
4. Pinchcofsky-Devin GD, Kaminski MV (1986) Correlation of pressure sores and nutritional status. J Am Geriatr Soc. 34: 435-440.
5. Shahin ES, Meijers JM, Schols JM, Tannen A, Halfens RJ, et al. (2010) The relationship between malnutrition parameters and pressure ulcers in hospitals and nursing homes. Nutrition 26: 886-889.
6. European Pressure Ulcer Advisory Panel and National Pressure Ulcer Advisory Panel (2009) Prevention and treatment of pressure ulcers: quick reference guide. Washington, DC: National Pressure Ulcer Advisory Panel.
7. Stotts NA, Rodeheaver GT, Thomas DR, Frantz RA, Bartolucci AA, et al. (2001) An instrument to measure healing in pressure ulcers: development and validation of the pressure ulcer scale for healing (PUSH). J Gerontol A Biol Sci Med Sci 56: M795-799.
8. Heyman H, Van De Looverbosch DE, Meijer EP, Schols JM (2008) Benefits of an oral nutritional supplement on pressure ulcer healing in long-term care residents. J Wound Care 17: 476-480.
9. van Anholt RD, Sobotka L, Meijer EP, Heyman H, Groen HW, et al. (2010) Specific nutritional support accelerates pressure ulcer healing and reduces wound care intensity in non-malnourished patients. Nutrition 26: 867-872.
10. Sakae K, Agata T, Kamide R, Yanagisawa H (2013) Effects of L-carnosine and its zinc complex (Polaprezinc) on pressure ulcer healing. Nutr Clin Pract 28: 609-616.
11. Gardner ML, Illingworth KM, Kelleher J, Wood D (1991) Intestinal absorption of the intact peptide carnosine in man, and comparison with intestinal permeability to lactulose. J Physiol 439: 411-422.
12. Nagai K, Suda T, Kawasaki K, Mathuura S (1986) Action of carnosine and beta-alanine on wound healing. Surgery 100: 815-821.
13. Ansurudeen I, Sunkari VG, Grünler J, Peters V, Schmitt CP, et al. (2012) Carnosine enhances diabetic wound healing in the db/db mouse model of type 2 diabetes. Amino Acids 43: 127-134.
14. Dawson B, Favaloro EJ (2009) High rate of deficiency in the amino acids tryptophan and histidine in people with wounds: implication for nutrient targeting in wound management--a pilot study. Adv Skin Wound Care 22: 79-82.