ORIGINAL RESEARCH

Nutrafoods (2017) 9-12
DOI 10.17470/NF-017-1031-1

Received: November 11, 2016
Accepted: February 03, 2017

Improved wound healing after oral application of specific bioactive collagen peptides

Hans-Christoph Knefeli[1], Benjamin Durani[2]

Correspondence to: Hans-Christoph Knefeli - hans-christoph.knefeli@gelita.com

ABSTRACT

Wound healing is very important after surgery and undisturbed closure of wounds is sometimes a major problem. Intensive efforts are made to improve wound healing using numerous approaches. In recent years, the oral application of specific bioactive collagen peptides has demonstrated positive effects on matrix synthesis and skin physiology. In this observational trial, their impact on wound healing was investigated in a group of 22 (12 verum/10 placebo) patients with postsurgical wounds and a second group of 20 (10 verum/10 placebo) patients with badly healing wounds. In both groups, the patients treated with bioactive collagen peptides had a clearly better outcome regarding wound healing compared to the placebo groups who showed suboptimal or bad results in the majority of cases. No side effects or intolerance to the product were reported. The results of this investigation confirm the positive impact of collagen peptides on wound healing. These data suggest this product can be used to improve wound healing, even in cases where normal wound healing is expected, and to achieve a better aesthetic outcome.

Keywords

Bioactive collagen peptides
Nutritional supplement
Skin
Wound healing

Introduction

After surgical intervention, the primary focus of the surgeon and patient is efficient wound healing, particularly as regards the aesthetic result. Undisturbed closure of wounds is also important medically.

Wound healing is often prolonged or extremely difficult in patients with comorbidity (e.g., diabetes or vascular disease) and poses a challenge for the treating physician. There is also overall agreement in the surgical world that there is room for improvement in the general area of wound healing, for example as regards keloid.

In cases of initially normal wound healing, a change in the progress of wound closure is sometimes observed and often depends on individual circumstances. Topical applications are commonly used to treat badly healing wounds, with oral therapies also employed in recent years.

Animal studies have confirmed the positive effects of orally administered collagen peptides resulting in accelerated epithelialization and shortened wound healing time with improved angiogenesis, as well as enhanced wound healing in patients with diabetes [1, 2]. Recently, the favourable influence of specific bioactive collagen peptides on matrix synthesis and skin physiology has been demonstrated in several preclinical and clinical studies at a high scientific level. Experimental studies have also shown that collagen peptides are chemotactic for skin fibroblasts [3], increase the migration and growth of mouse skin fibroblasts [4], and enhance cell proliferation and hyaluronic acid synthesis [5].

Collagen peptides are absorbed in the gut, distributed by the blood stream, and accumulate in the skin where they stimulate fibroblasts to produce dermal extracellular matrix components. Clinical trials have demonstrated their positive effect on skin physiology [6, 7].

Clinical evidence on the efficacy of orally administered collagen peptides for wound healing has not been available to date. Therefore, the impact of specific bioactive collagen peptides on normal and disturbed wound healing was investigated in the current study.

Material and methods

VERISOL® (GELITA AG, Germany) is a special collagen product for oral application and consists of pure bioactive

[1]Surgery, emergency medicine, sport medicine.
GELITA AG, Uferstrasse 7, D-69412 Eberbach, Germany
[2]Derma- and Laser Center Heidelberg, Germany

collagen peptides optimized for skin health. It is composed of different specific collagen peptides of porcine or bovine type I collagen obtained using a special hydrolysis method. The product is clearly defined by numerous specific collagen peptides with an average molecular weight of 2.0 kDa and a specific amino acid profile. It is absolutely safe and has been certified as GRAS (generally recognized as safe) by the FDA.

The present trial was divided into two parts. Enrolled patients were separated into a group which was due to undergo a surgical intervention and did not have any conditions that could affect wound healing (normal group, NG) and a second group which had undergone a surgical intervention and had conditions that could affect wound healing and a minimum of one badly healing wound (disturbed group, DG). Patients in both groups were then randomly assigned to a placebo or a verum group. A daily dose of either placebo or verum was taken by the patients for the entire healing period. The NG group received a maximum of 45 daily doses of 5.0 g VERISOL®, while the DG group received a maximum of 90 daily doses of a higher dose of 10.0 g VERISOL® on account of their worse tissue conditions. The placebo groups received equivalent doses of maltodextrin (5.0 g and 10.0 g). All patients provided informed consent to this study.

The NG group consisted of 22 female patients aged between 24 and 67. All had dermal alterations such as papillary dermal naevus or epidermal keratosis, mostly on the upper part of the body (head, neck, chest and abdomen), which were removed at a dermatological practice by a physician using excision or a scraping technique. Excisions were sutured while scraped wounds were left to secondary wound healing. No wound was larger than 5×2 cm. Photographs were taken before the intervention, directly after the procedure, and after 4–6 weeks (Figs. 1 and 2). The NG patients were then randomized to either a verum (n=12) or placebo (n=10) group. Intake of the daily dose of verum or placebo started on the day of surgery.

The DG group consisted of both male and female patients aged between 28 and 82. All had badly healing wounds after surgical interventions, injuries or vascular problems associated with common conditions such as diabetes or arterial occlusive disease (AOD), and were randomized to a verum (n=10) or placebo (n=10) group at a surgical practice. The wounds were located mostly on the lower body (abdomen, legs and lower back). Successful healing required a germ-free wound and constant dressing changes for a dry wound. Thus, the first step was debridement and decontamination of the wound surface by the physician. In case of accompanying inflammation, oral antibiotic therapy was initiated and continued until all signs of inflammation had resolved. Photographs were taken before debridement and at the end of the healing period (6–12 weeks) (Figs. 3 and 4). Intake of the daily dose of verum or placebo started at the first visit.

Referring to the photographs, four physicians experienced in the field of wound healing evaluated aesthetic outcome and wound healing in the NG and DG groups as very good, good, suboptimal or bad according to:

- Signs of inflammation (redness, hyperthermia and purulence)
- Surface condition (waviness, roughness, rosy or pale skin colour, elasticity and moisture)
- Scarring or keloid
- Haematoma
- Skin perfusion
- Internal skin discoloration.

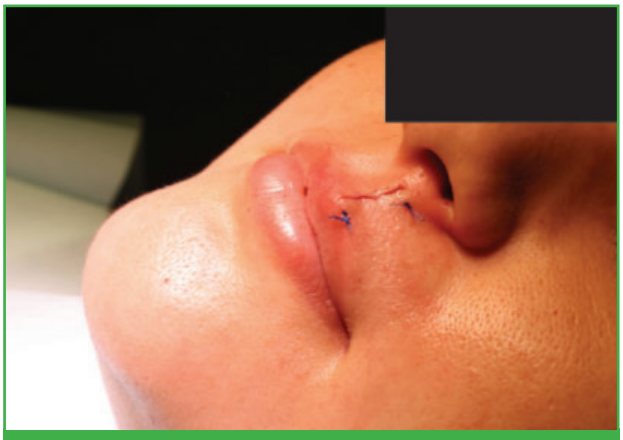

Figure 1 - Upper lip after naevus removal in a patient in the NG group

Figure 2 - Excellent result following naevus removal after 4 weeks of VERISOL® treatment in the patient shown in Fig. 1

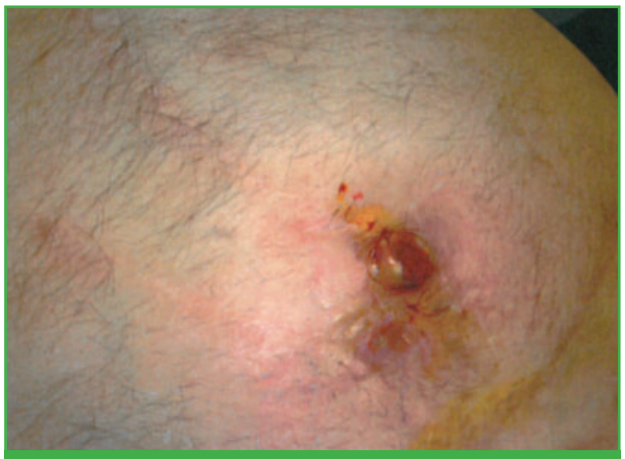

Figure 3 - Dehiscence after hernia operation in a patient in the DG group

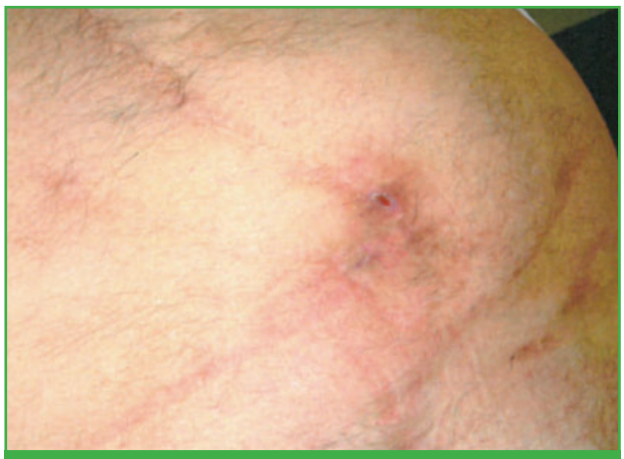

Figure 4 - Very good result following hernia operation after 6 weeks of VERISOL® treatment in the patient shown in Fig. 3

Results

No side effects or intolerance to the collagen product were reported. Patients complied with the physician instructions given at the first visit before the intervention or wound debridement.

All wounds closed and healed in an adequate time frame. None of the participants had any problems regarding secondary bleeding, infection or purulence. Thus, the only objective assessment criterion was the appearance of the healed wound in the photographs evaluated by an expert who was blinded to the treatment received by the patient.

In both the NG and DG groups, patients who had been treated with the specific collagen peptides showed clearly better results than those who had received placebo.

NG group

Six of the 12 patients in the NG verum group had very good results, while the other six had good results as evaluated by the physicians. The patients themselves were very satisfied with their healed wounds and none had a suboptimal or bad result. These findings demonstrate that 100% of the patients in the verum group had a good or very good outcome (Fig. 5).

In contrast, none of the 10 patients in the placebo group was rated as having a very good outcome. Five of the patients had good results (50%), while three had suboptimal results and two had bad results. These findings demonstrate that 50% of the patients in the placebo group had a bad or suboptimal aesthetic outcome (Fig. 6).

DG group

Three of the 10 patients in the DG verum group were evaluated by the physicians as having very good results, while the other 7 patients had good results. The patients in this group

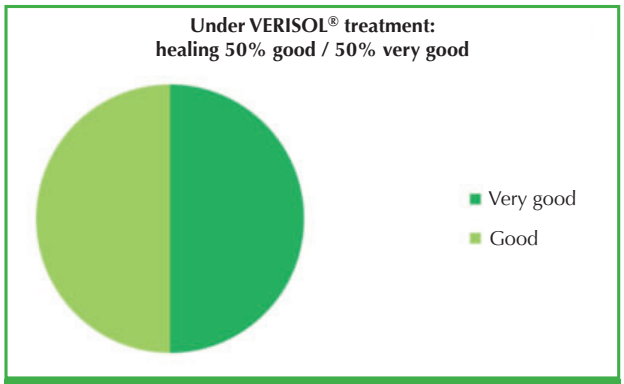

Figure 5 - Results in the NG verum group (n=12 patients)

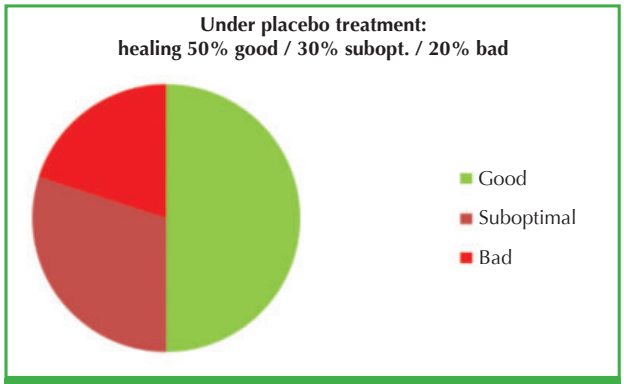

Figure 6 - Results in the NG placebo group (n=10 patients)

were very satisfied with the outcome of their wound healing and none had suboptimal or bad results. These findings show that 100% of the patients in the verum group had a good or very good outcome (Fig. 7).

In contrast, none of the 10 patients in the placebo group was rated as having a very good outcome. Two of the patients had good results (20%), while five had suboptimal results and three had bad results. These findings show that 80% of the patients receiving placebo had a bad or suboptimal outcome (Fig. 8).

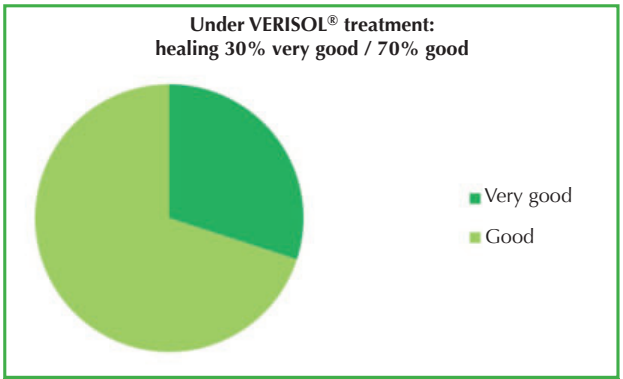

Figure 7 - Results in the DG verum group (n=10 patients)

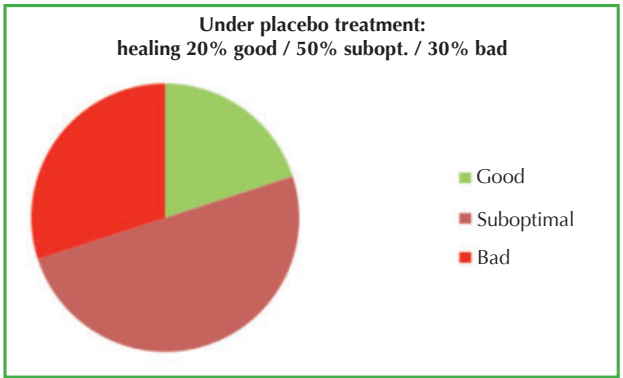

Figure 8 - Results in the DG placebo group (n=10 patients)

Conclusion

The results of this observational trial showed positive effects on wound healing after the oral application of bioactive collagen peptides. In the NG placebo group, none of the patients had a very good result, while 50% had a suboptimal or bad aesthetic outcome. Likewise, none of the patients in the DG placebo group showed a very good result, while more than 75% had a suboptimal or bad outcome.

The pronounced effect of bioactive collagen peptides on connective tissue has been demonstrated in several clinical studies. The positive effect on the skin is mainly due to a direct impact on dermal extracellular matrix turnover with a subsequent significant increase in collagen and elastin synthesis [7]. Accelerated epithelialization and shortened wound healing with improved angiogenesis, even in diabetic rats, has been observed in animal experiments [1, 2]. Other studies on humans have also confirmed stimulation of granulation tissue and proteases, a decrease in inflammation parameters, and improved perfusion especially with regard to microcirculation [8, 9]. These findings might explain the striking results for wound healing seen in this trial.

In summary, these findings show that these specific collagen peptides have a positive impact on wound healing, and suggest that these bioactive collagen peptides should be administered for better results even in cases where wound healing is expected to be normal. However, it must be noted that these results are only valid for VERISOL®, as other collagen hydrolysates or collagen peptides might show different outcomes.

Additional studies on larger populations, including patients with wound healing disorders, will be conducted and hopefully confirm these initial results.

Acknowledgements

Hans-Christoph Knefeli is an employee of GELITA AG, Uferstrasse 7, Eberbach, Germany. Benjamin Durani declares that he has no conflicts of interest.

REFERENCES

1. Dang QF, Liu H, Yan JQ, Liu CS, Liu Y, Li J *et al* (2015) Characterization of collagen from haddock skin and wound healing properties of its hydrolysates. Biomed Mater 10(1):015022
2. Zhang Z, Zhao M, Wang J, Ding Y, Dai X, Li Y (2011) Oral administration of skin gelatin isolated from Chum salmon (*Oncorhynchus keta*) enhances wound healing in diabetic rats. Mar Drugs 9(5):696-711
3. Postlethwaite AE, Seyer JM, Kang AH (1978) Chemotactic attraction of human fibroblasts to type I, II, and III collagens and collagen-derived peptides. Proc Natl Acad Sci U S A 75:871–875
4. Shigemura Y, Iwai K, Morimatsu F *et al* (2009) Effect of prolylhydroxyproline (Pro-Hyp), a food-derived collagen peptide in human blood, on growth of fibroblasts from mouse skin. J Agric Food Chem 57:444–449
5. Ohara H, Ichikawa S, Matsumoto H *et al* (2010) Collagen-derived dipeptide, proline-hydroxyproline, stimulates cell proliferation and hyaluronic acid synthesis in cultured human dermal fibroblasts. J Dermatol 37:330–338
6. Proksch E, Segger D, Degwert J, Schunck M, Zague V, Oesser S (2014) Oral supplementation of specific collagen peptides has beneficial effects on human skin physiology: a double-blind, placebo-controlled study. Skin Pharmacol Physiol 27:47–55
7. Proksch E, Schunck M, Zague V, Segger D, Degwert J, Oesser S (2014) Oral intake of specific bioactive collagen peptides reduces skin wrinkles and increases dermal matrix synthesis. Skin Pharmacol Physiol 27:113–119
8. Nonaka I, Katsuda S, Ohmon T *et al* (1997) In vitro and in vivo antiplatelet effects of enzymatic hydrolysates of collagen and collagen-related peptides. Biosci Biotechnol Biochem 61:772–775
9. Kouguchi T, Ohmon T, Shimizu M *et al* (2013) Effects of a chicken collagen hydrolysate on the circulation system in subjects with mild hypertension or high-normal blood pressure. Biosci Biotechnol Biochem 77:691–696