Topical application of Semelil (ANGIPARSTM) in treatment of pressure ulcers: A randomized clinical trial

Article *in* DARU-JOURNAL OF FACULTY OF PHARMACY · November 2007

CITATIONS
17

READS
140

9 authors, including:

Rita Karimian
California State University, Dominguez Hills
4 PUBLICATIONS **30** CITATIONS
SEE PROFILE

Ensieh Nasli Esfahani
Tehran University of Medical Sciences
116 PUBLICATIONS **1,071** CITATIONS
SEE PROFILE

Koorosh Kamali
Zanjan University of Medical Sciences
153 PUBLICATIONS **1,030** CITATIONS
SEE PROFILE

Reza Chaman
Shahroud University of Medical Sciences
68 PUBLICATIONS **713** CITATIONS
SEE PROFILE

Topical application of Semelil (ANGIPARS™) in treatment of pressure ulcers: A randomized clinical trial

[1]Shamimi Nouri K, [1]Karimian R, [2]Nasli E, [3]Kamali K, [3]Chaman R, [4]Farhadi M, [5]Madani SH, [2]Larijani B, [*6]Khorram Khorshid HR

[1]General Surgery Department, Vali-e-Asr Hospital, Imam Khomeini Hospital Complex, [2]Endocrinology and Metabolism Research Center (EMRC), [3]Department of Epidemiology and Biostatistics, Public Health School, Tehran University of Medical Sciences, [4]ENT - Head & Neck Surgery Department and Research Center, Iran University of Medical Sciences, Tehran, [5]Department of Biotechnology, Rabe Rashidi Institute, Tabriz, [6]Genetic Research Centre, Social Welfare and Rehabilitation Sciences University, Tehran, Iran

ABSTRACT

Pressure ulcers are one of the major health care problems and results in a substantial amount of burden for both patients and health services. The aim of this study was to appraise effectiveness of topical Semelil (ANGIPARS™), a naive herbal extract, in pressure ulcers

As a randomized controlled clinical trial, 18 patients with pressure ulcers were recruited from Vali-e-Asr hospital, Medical Sciences/ University of Tehran, Iran. Nine patients received topical Semelil (ANGIPARS™) during hospitalization and nine other patients received conventional treatment.

Baseline characteristics of the topical and control groups did not differ across demographic, clinical and functional measures. The mean surface areas of the ulcers were reduced 48.2 ± 85.3 cm^2 (78.3%) and 2.8± 6.2 cm^2 (6.3%) in the treatment and control groups, respectively (p=0.000).

From the results of this study it may be concluded that the use of topical Semelil (ANGIPARS™) with conventional treatment is more effective than those of only conventional treatment for patients with pressure ulcers.

Keywords: ANGIPARS™, Pressure ulcer, Topical, Intervention

INTRODUCTION

The increased incidence of chronic and non-contagious diseases has been one of the most important problems of health systems during the past decade. Today, a remarkable amount of burden is attributed to this group of disorders. One of the most important parts in estimation of disease burden is the disability resulting from the diseases such as injuries due to trauma, car accidents, brain vessel diseases, diabetes and osteoporosis. Induced bedsore in the above mentioned diseases and due to other reasons causes major problems and disabilities.

Pressure ulcers have been associated with increase in mortality rates in both acute and long-term care settings. Death has been reported to occur during acute hospitalization in 67% of patients who develop a pressure ulcer compared with 15% of at-risk patients without pressure ulcers (1-2). Patients who develop a new pressure ulcer within 6 weeks after hospitalization are three times more likely to die as patients who do not develop a pressure ulcer (3).

In our country, in addition to above mentioned disorders, war victims bear a large amount of disabilities like spinal complications and amputation. It has been shown that bedsore is present in almost one third of war handicapped with spinal complications and most of them experience it during their life time(4).

The normal response to tissue injury is a timely and orderly reparative process that results in sustained restoration of anatomical and functional integrity (5). In chronic wounds, the healing process is prolonged and incomplete, proceeds to an uncoordinated manner and results in a poor anatomical and functional outcome (6).

There have been different methods for infection control and treatment of bedsore. Their main goal is to accelerate the wound healing and tissue

Correspondence: hrkhkh@yahoo.com

repair. All previous methods have only a partial effect on ulcer improvement and more effective therapies are essential.

A novel treatment of wound healing is an herbal extract, Semelil (ANGIPARS™) (7) which has been studied in all steps of preclinical studies (8-10). Approval of its efficacy and safety has been evaluated in three phases of clinical investigations and its capacity to accelerate ulcer healing was reported in recent studies (11-15).

The aim of this clinical trial was to assess the therapeutic effects of topical Semelil (ANGIPARS™) in treatment of bedsore.

MATERIAL AND METHODS

We assigned a randomized, controlled trial over a period of one year (August 2006- August 2007) in Vali-e-Asr hospital, Medical Sciences/ University of Tehran (Iran). Eighteen patients were recruited according to the aforementioned criteria. All relevant data including patient age and weight, the longevity of the ulcer before our intervention, and the size, stage and location of the ulcer, were collected. Next, all the patients were examined to confirm their eligibility for the study. The eligibility criteria were: A) Inclusion Criteria: adult male and female subjects (with age more than 18 years) with bedsores. All patients with ulcers resulted from spinal complications (accidental or congenital), amputation of the lower limbs, chronic diseases like brain vessel disorders or fractures due to osteoporosis are included. Their ulcers sizes must be at least 1 cm^2 (measure of the longest length in longest width) with occurrence within the 2 last weeks in order to be enrolled in trial. After inclusion of each volunteer, complete information explained about the goal of the study, probable benefits and harms of the therapies and patients' rights during the research; and written informed consent was obtained. Patients voluntarily were enrolled the study.

Exclusion criteria: All patients with acute infection of ulcer or any ulcer with bone exposure excluded. Other exclusion criteria was as follows: any other disease or situation that impairs ulcer improvement (such as malignancies, vasculitis, diabetes, connective tissue diseases, Immunity system disorders, *etc.*) alcohol and drug abuse, dialysis and renal failure, corticosteroid consumption, the use of immune suppressive agents, radiotherapy, chemotherapy and any known drug hypersensitivity.

After patient enrolment, primary assessments in addition to evaluation for inclusion and exclusion criteria were as follows: Exact inspection of the ulcer, measurement of its diameters and complete explanation of the ulcer features; photography, mapping and planimetry.

Patients in intervention group received topical Semelil (ANGIPARS™) 3% gel daily and in control group received conventional treatment.

Other procedures which carried out during the study were as follows: daily wound examination before drug administration renewal of the dressing by a physician, physical examination and taking history from patients, wound debridement between therapies according to physicians' diagnosis, photography and measurement of the ulcer diameters to assess any improvement, steadiness or regression per 2 weeks till 2 months, weekly documentation of patients' compliance and their acceptance, probable side effects.

RESULTS

Eighteen patients were treated via one of two methods. The mean age of the patients were 47.9 ± 21.2 years in intervention group and 46.6 ± 22.7 years in control group. There were no significant differences among the two therapeutic groups in baseline demographic characteristics (Table 1).

The alterations of ulcers surface areas and the degree of improvement in the two therapeutic groups are shown in (Table 2)

Ulcer surface area in topical group was 56.1 ± 93.3 at the first visit and after completion of the trial reduced to 7.8 ± 8.3 (p=0.008). On the other hand, in control group, ulcer surface area was 19.5 ± 16.1 at the beginning and after completing the trial decreased to 16.7 ± 13.6 (p=0.144). The mean percentages of reduction in surface comparing to the baseline size among intervention and control groups were: 78.3 ± 12.5 vs. 6.3 ± 22.7, respectively (p=0.000).

The improvement of healing, regardless of the location and stage, was better in the topical Semelil (ANGIPARS™) treatment group than in the conventional treatment (p=0.000). In the intervention group, 6 patients out of 9 (66.7%) had complete improvement in ulcer size and 3 others (33.3%) had an acceptable healing of ulcers (Table 2).

All patients completed the study and there were no losses to follow-up, no treatment withdrawals, no changes in trial group and no adverse events.

Table 1. Baseline characteristics of study subjects

	ANGIPARS™ (n=9)	Control (n=9)	P- value
Age (year)	47.9 ± 21.2	46.0 ± 22.7	0.899
Sex (M/F)	7/2	7/2	1.000
Area of ulcer (cm^2)	56.1 ± 93.3	19.5 ± 16.1	0.264
Number of ulcer	1.2 ± 0.4	1.2 ± 0.7	1.000

Table 2. Ulcer healing status in patients who used topical Semelil (ANGIPARS™) and control groups

		ANGIPARS™ (n=9)	Control (n=9)	P- value
Decrease in ulcer area (cm^2)*		48.2 ± 85.3	2.8 ± 6.2	0.000
Decrease rate (%)		78.3 ± 12.5	6.3 ± 22.7	0.000
Healing†	> 80%	6 (66.7)	0	0.000
	50-80%	3 (33.3)	1 (11.1)	
	20-50%	0	0	
	< 20%	0	8 (88.9)	

* Mean ± SD; † Number (%)

DISCUSSION

Pressure ulcers are extremely difficult to heal. Once they develop, this type of chronic wound is very resistant to any known medical therapy. Estimates of complete healing for pressure ulcers are as low as 10%. As less as 13% of pressure ulcers heals by 2 weeks in acute hospital settings (16, 17). In the younger patients with traumatic paraplegia, 74% of operated pressure ulcers were healed at discharge, 76% of patients were free of pressure ulcers. Within 10.9 months, 79% of operated ulcers recurred, and 79% of patients had additional pressure ulcers. Only 21% of traumatic paraplegics and 31% of nontraumatic nonparaplegic elderly patients remained healed after muscle-flap coverage for pressure ulcers (18). A decision analysis demonstrated that myocutaneous flap procedures for stage 3 of pressure ulcers were favorable unless the success rate for surgery was less than 30% or the healing rate with medical therapy was more than 40% (19).

Lack of cellular and molecular signals required for normal wound repair processes such as resolution of inflammation, angiogenesis, deposition of extracellular matrix, contraction, epithelialization, and remodeling may be a major contributing factor to poor healing of chronic wounds such as pressure ulcers (20,21).

Several types of topical wound treatments can promote more rapid epidermal resurfacing, as shown in controlled trials. Range of acceleration in healing varies from 18% to 36 % (22).

Growth factors given topically including transforming growth factors alpha and beta, epidermal growth factor, platelet derived growth factor, fibroblast growth factor, interleukin-1, interleukin-2, and tumor necrosis factor alpha have been demonstrated to mediate the healing process. The concept of acceleration of healing in chronic wounds by using these acute wound factors is attractive. However, in trials in pressure ulcers, platelet derived growth factor failed to produce complete healing (23),although it did shorten the time to closure of wounds, as did basic fibroblast growth factor (24,25) The development of wound healing factor is still in its infancy but shows great promise

Semelil (ANGIPARS™) is an herbal extract (7) and its capacity to accelerate ulcer healing was reported in recent studies (11-15). Since then, it has been used topically for wounds of diabetic foot ulcers in humans (15). Possible mechanisms of action of topical ANGIPARS™ on wound healing are increased angiogenesis.

In this study, the therapeutic effects of topical ANGIPARS™ with usual treatment on pressure ulcers were shown to be superior to those of only usual treatment. In view of the cost of pressure ulcer management in hospitals and sanitariums and the high expenses of plastic surgery, it seems rational to shift to simpler methods that are more cost efficient and executable by the individual patients. The use of Semelil (ANGIPARS™) for treatment of pressure ulcers is less expensive and more comfortable and will ultimately increase the patients' self-confidence.

ACKNOWLEDGEMENTS

The authors want to express their gratitude to ParsRoos Co. for supporting this research and also wish to extend their thanks to Dr. R. Heshmat and Dr. M. Arzaghi for critically reading the manuscript and their helpful comments.

REFERENCES

1. Guralnik JM, Harris TB, White LR, et al. Occurrence and predictors of pressure ulcers in the National Health and Nutrition Examination Survey Follow-up. J Am Geriatr Soc 1988; 36:807–812
2. Baxter CR. Immunologic reactions in chronic wounds. Am J Surg 1994; 167:12S–14S.
3. Berlowitz DR, Wilking SVB. The short-term outcome of pressure sores. J Am Geriatr Soc 1990; 38:748–752.
4. Hollisaz MT, Khedmat H, Yari F. A randomized clinical trial comparing hydrocolloid, phenytoin and simple dressings for the treatment of pressure ulcers. BMC Dermatol. 2004; 4: 18
5. Lazurus GS, Cooper DM, Knighton DR, et al. Definitions and guidelines for assessment of wounds and evaluation of healing. Arch Dermatol 1994; 130:489–493
6. 6. Nwomeh BC, Yager DR, Cohen IK. Physiology of the chronic wound. Clin Plast Surg 1998; 25:341–356.
7. Larijani B, Hasani Ranjbar S. Overview of diabetic foot; novel treatments in diabetic foot ulcer. DARU 2008; 16(suppl.1): 1-6.
8. Abdollahi M, Farzamfar B, Salary P, Khorram Khorshid HR, Larijani B, Farhadi M, Madani SH. Rodent acute and sub-chronic toxicity evaluation of Semelil (ANGIPARS™), a new phytotherapeutic drug for wound healing. DARU 2008; 16(suppl.1): 7-14.
9. Farzamfar B, Abdollahi M, Ka'abinejadian S, Heshmat R, Shahhosseiny MH, Novitsky Y.A, Farhadi M. Sub-chronic toxicity study of a novel herbal-based formulation (Semelil) on dogs. DARU 2008; 16(suppl.1): 15-19.
10. Khorram Khorshid HR, Sadeghi B, Heshmat R, Abdollahi M, Salary P, Farzamfar B, Madani SH. In vivo and in vitro genotoxicity studies of Semelil (ANGIPARS™). DARU 2008; 16(suppl.1): 20-24.
11. Heshmat R, Mohammad K, Mohajeri Tehrani MR, Tabatabaie Malazy O, Keshtkar AA, Gharibdoust F, Larijani B. Assessment of maximum tolerated dose of a new herbal drug, Semelil (ANGIPARS^{TM}) in patients with diabetic foot ulcer: A Phase I clinical trial. DARU 2008; 16(suppl.1): 25-30.
12. Masoompour SM, Bagheri MH, Borhani Haghighi A, Novitsky YA, Sadeghi B, Gharibdoust F, Larijani B, Ranjbar Omrani G. Effect of ANGIPARS™, a new herbal drug on diabetic foot ulcer : A phase 2 clinical study. DARU 2008; 16(suppl.1): 31-34.
13. Larijani B, Heshmat R, Bahrami A, Delshad H, Ranjbar Omrani G, Mohammad K, Heidarpour R, Mohajeri Tehrani MR, Kamali K, Farhadi M, Gharibdoust F, Madani SH. Effects of Intravenous Semelil (ANGIPARSTM) on Diabetic Foot Ulcers Healing: A Multicenter Clinical Trial. DARU 2008; 16(suppl.1): 35-40.
14. Bahrami A, Kamali K, Ali-Asgharzadeh A, Hosseini P, Heshmat R, Khorram Khorram HR, Gharibdoust F, Madani SH, Larijani B. Clinical application of oral form of ANGIPARS™ and in combination with topical form as a new treatment for diabetic foot ulcers: A randomized clinical trial. DARU 2008; 16(suppl.1): 41-48.
15. Shamimi Nouri K, Heshmat R, Karimian R, Nasli E, Larijani B, Novitsky YA, Farhadi M, Gharibdoust F. Intravenous ANGIPARS™ as a novel therapy for pressure Ulcer: A randomized clinical trial. DARU 2008; 16(suppl.1): 49-53.
16. Allman RM, Walker JM, Hart MK, et al. Air-fluidized beds or conventional therapy for pressure sores: A randomized trial. Ann Intern Med 1987; 107:641–648
17. Michocki FJ, Lamy PP. The problem of pressure sores in a nursing home population: statistical data. J Am Geriatr Soc 1976; 24:323–328.
18. Disa JJ, Carlton JM, Goldberg NH. Efficacy of operative cure in pressure sore patients. Plast Reconstructr Surg 1992; 89:272–278.
19. Siegler EL, Lavizzo-Mourey R. Management of stage III pressure ulcers in moderately demented nursing home residents. J Gen Intern Med 1991; 6:507–513.
20. Bennett NT, Schultz GS. Growth factors and wound healing: biochemical properties of growth factors and their receptors. Am J Surg 1993; 165:728–737.
21. Bennett NT, Schultz GS. Growth factors and wound healing. Part II: role in normal and chronic wound healing. Am J Surg 1993; 166:74–81
22. Alvarez O. Moist environment for healing: matching the dressing to the wound. Ostomy Wound Manage 1988; 21:64–83
23. Robson MC, Phillips LG, Thomason A, et al. Recombinant human platelet-derived growth factor-BB for the treatment of chronic pressure ulcers. Ann Plast Surg 1992; 29:193–201.
24. Robson MC, Phillips LG, Thomason A, et al. Platelet-derived growth factor B for the treatment of chronic pressure ulcers. Lancet 1992; 339:23–25.
25. Robson MC, Phillips LG, Lawrence WT, et al. The safety and effect of topically applied recombinant basic fibroblast growth factor on the healing of chronic pressure sores. Ann Surg 1992; 216:401–408.