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Efficacy of a Dermatological Gel Based on Ozonized Sunflower Seed Oil (Oz. Or.Oil 30) on Bedsores: A Pilot Study

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Abstract

Objective: The purpose of this pilot study was to evaluate the efficacy of topical applications of a dermatological gel based on ozonized sunflower seed oil (Oz.Or.Oil 30) on bedsores of patients admitted to the "hospital-at-home" service of the Hospital "Veris Delli Ponti" in Scorrano (Lecce, Italy).

Methods: Study was made up of all patients with bedsores at stage I and II admitted to the "hospital-at-home" between September 2016 and March 2017. This pilot study was performed in randomized single blind with randomization in parallel 1:1 ratio. Sample of 22 patients was eligible, according to inclusion and exclusion criteria. They were divided into 2 groups: the experimental group treated with Oz.Or.Oil 30 and the control group treated with a common dermatological gel. To evaluate the tissue repair process, the observation period was 21 days and weekly evaluations to analyze ulcer more regularly, detect complications as soon as possible and adapt the treatment plan accordingly.

Results: 19 patients completed the study because 3 patients discontinued study participation. Every patient reported regularly for the follow-up and reported no side effects. From the evaluation score of the analyzed patients, in the observation period, it shows that the patients treated with Oz.Or.Oil 30 showed faster healing of the ulcer. In the second week, patients treated showed significant improvement ($p<0.05$) compared to the control group, with efficacy scores equal to 1.00 ± 0.00 and 0.45 ± 0.52 respectively ($p=0.014$).

Conclusion: Oz.Or.Oil 30 showed a much better efficacy than the control product, probably due to the high antibacterial and germicidal power of ozone and its capacity to stimulate tissue reparation. All patients were satisfied with the treatment whether they were in one group or the other. Further detailed studies are required with larger samples, but this study demonstrated that Oz.Or.Oil 30 can be considered as an effective medication in the treatment of bedsores.

Keywords:

Vegetables oils; Bedsores; Pressure ulcers; Ozonized oil; Dermatological gel; Randomized single blind study; Hospital-at-home

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Introduction

The treatment of the wounds is probably one of the oldest areas of medicine and represents a socio-sanitary problem in continuous growth [1-3].

Wound is defined as the loss of skin coverage, not just the skin but also subcutaneous tissues, muscles and bones, usually due to multifactorial pathogenesis, that do not spontaneously lead to a complete recovery. Indeed they can be caused by traumas that originate inside or outside the affected tissue [4].

With increased life expectancy of the population, there is increasing incidence of diseases that accompany aging (heart disease, cancer, diabetes mellitus, and hypertension) [1-3,5,6]; such conditions increase the prevalence and complexity of the wounds and delay its healing [7].

Decubitus wounds, also called pressure ulcers or bedsores, are vascular disorders that are the result of prolonged pressure, friction or shear over skin, especially at bony prominences [8,9].

Pressure ulcers can be classified according to clinical, topographical criteria and status on four different clinical stages [10-12]. Topographic classification allows for a exact correlation between the position adopted by patient and the anatomical sites of ulcerative lesions. Shall be identified anatomical areas precise where you determine with higher probability, in relation to the position maintained from the body, pressure ulcers [13]. Decubitus ulcers are wounds more likely in elderly, ill fed, or individuals who stay immobile for a long while, which include bedridden and paralyzed [9,14], with a difficult healing process due to infections and constant oxidation of the soft tissues.

Wound healing is a multiphase process involving blood clotting, inflammation, tissue proliferation, and skin repair following injury [15,16]. It is a dynamic process in which devitalized and missing cellular structures and tissue layers must be replaced. Although recent advances in antimicrobial therapy [17], wounds remain a serious problem, because treating wounds is protracted, intensive, and associated with high costs [18,19]. For these reasons, various treatment approaches have been adopted including the use of topical wound-care therapies [20,21].

Despite numerous topical and systemic agents have been used to eradicate infections, many have been eliminated because of resistance. These agents, indeed, have led to the emergence and subsequent rapid overgrowth of resistant bacterial strains, drug side effects, and organ-specific toxicity [22-24].

With an increasing frequency of antibiotic-resistant pathogens, modern medicine directs attention to natural products with antimicrobial activity for clinical practice [21,25-27]. Archaeological evidence indicates that even in prehistoric times extracts of plants, fruits, mud, water and ice were applied to wounds. Vegetables oils may alter skin permeation through increasing occlusion, widening the polar pathway and widening the non-polar pathway and in addition, they in general produce no skin irritation or sensitization problems [28].

Some herbal oils such as sunflower oil were suggested to use for bedsore prevention and treatment as well as some lotions for lubrificating the skin [29-31].

The oils of vegetable origin are also an ideal vehicle for the local therapy of ozone, in the form of ozonized oil. Several studies [32-34] have demonstrated that ozonated vegetable oil is effective on cutaneous wound healing.

Ozone reacts with the carbon-carbon double bonds of unsaturated fatty acids from vegetable oils giving rise to the formation of chemical species, such as ozonides and peroxides that are responsible for the germicidal action, as well as the properties of stimulating tissue repair and regeneration [35,36].

The ozone (O_3) and ozonated oil first of all eliminates the pathogens and then, by releasing oxygen (O_2), activates the proliferation of fibroblasts, hence the building of intercellular matrix with consequent proliferation of keratin oblasts and successive healing [37].

The purpose of this single blind randomised pilot study was to evaluate the effects of topical applications of a dermatological gel, Oz.Or.Oil 30, on bedsores in patients admitted to the "hospital-at-home" service.

Hospital-at-home is defined as a service that provides active treatment by health care professionals, in the patient's home, of a condition that otherwise would require acute hospital in-patient care, always for a limited period [38,39].

We hypothesized that a hospital-at-home service could be a practical alternative to the traditional hospital setting for the care of selected elderly patients with this type of wounds.

Methodology Applied

Description of the sample

The study was conducted with a medical preparation: Oz.Or.Oil 30. It is a dermatological gel commercialy containing 30% ozonated sunflower seed oil (acidity as oleic acid 1.60%, peroxide value 335 meqO_2/kg and viscosity 193 mPas) with alpha-lipoic acid, a potent scavenger with anti-inflammatory properties [40] and Vitamin E (α-tocopherol), a lipid-soluble essential antioxidant, scavenging hydroperoxyl radicals in a lipid milieu [41].

The various tests performed with Oz.Or.Oil 30 by Serio et al. [27] showed the safety of this kind of product. It showed antibacterial activity against Gram positive and Gram negative bacteria and it is not cytotoxic. This formulation is easily applied directly to the skin, thanks to a dispenser which allows spreading a thin layer of gel uniformly.

Patients

Study was made up of all patients with bedsores admitted to the "hospital-at-home" of the Hospital "Veris Delli Ponti" in Scorrano (Lecce, Italy) in a period of six months, between September 2016 and March 2017.

Sample eligible, according inclusion and exclusion criteria were of 22 patients. They were divided into 2 groups: 11 patients in the experimental group treated with Oz.Or.Oil 30 dermatological gel and 11 patients in the control group treated with a common dermatological gel commercially.

Were included in this study, patients of both sexes, affected by bedsores with the following features:

- Bedsores at stage I and II;
- Low presence of variable colouring slough and/or eschar on bed of the wound;
- no history of sensitivity to olive and its by-products;

Were excluded from the study, patients with:

- Bedsores at stage III, IV and unstageable;
- Presence of slough and/or eschar on bed of the wound;
- Presence of vesicles containing blood;

Study design

The study was performed in randomized single blind. Randomization has been carried out in parallel with a 1 : 1 ratio. To patients enrolled in the study, were administered a questionnaire CRF (Case Report Form) which allowed to collect the personal information to have a complete a comprehensive initial assessment of the individual with a bedsore (health/medical and social history, factors that may affect healing, psychological health, behavior, and cognition).

Assessment of the individual, his or her ability to heal, the risk for development of additional pressure ulcers, and the ulcer itself are important.

Then, the patients were subjected to medical check to evaluate physical characteristic for each ulcer (location, stage, tissue type, color, exudate and odor).

The stages of bedsore were considered by using the European Pressure Ulcer Advisory Panel [11] grading system for pressure ulcer classification including:

Stage I: Intact skin with non-blanchable redness;

Stage II: Partial thickness loss of dermis presenting as a shallow open ulcer with a red pink wound bed, without slough. May also present as an intact or open/ruptured serum-filled or sero-sanginous filled blister;

Stage III: Full thickness tissue loss. Subcutaneous fat may be visible but bone, tendon or muscle are not exposed, may include undermining and tunnelling;

Stage IV: Full thickness tissue loss with exposed bone, tendon or muscle [42].

To evaluate the tissue repair process, the observation period was 21 days (3 weeks) with two applications a day and weekly evaluations to provide the opportunity to evaluate ulcer more regularly, detect complications as soon as possible and adapt the treatment plan accordingly.

Ulcers are monitored using digital photography and cleansing application. Cleansing is an important first step in preparing the ulcer wound bed to heal by removing surface debris and dressing remnants and allowing better wound visualization for assessment

The cleansing procedure adopted consists of:

1. application of cleansing solution (normal saline) with sufficient pressure to cleanse the wound without damaging tissue or driving any bacteria into the wound;

2. drying of the wound using an aseptic technique;
3. treatment of the wound with evenly application of a thin layer of about 1-2 mm of studied product (Oz.Or.Oil 30 dermatological gel);
4. overlay of the primary dressing so performed, with a traditional or inert absorbent secondary dressing

For the control group, the procedure adopted will be the same, with the application of the control product. As a control product, a common dermatological gel will be used, specifically indicated in the cleansing and scarring of sores and lesions of ulcerative, necrotic, post-operative or traumatic origin. It performs a healing and antiseptic action, important in promoting healthy healing, while at the same time limiting the risk of overlapping bacterial infections.

All processes of intervention, observation and recording have been done by just one person in order to control the effect of those factors weakening the results. No cream/lotion or any other oil was used on the area of being examined in both groups.

Statistical analysis

Statistical analysis was performed with SPSS (Chicago, IL) software, version 24.0, using nonparametric tests. Differences between independent groups were evaluated with Mann-Whitney tests. Significance was established at $p<0.05$. Experimental data obtained for each patient are presented as the mean ± standard deviation. Due to the small sample size of this pilot study, $p<0.05$ was considered to indicate a statistically significant difference, in order to reduce the probability of error.

Results

Distribution of patients, according to age, sex and pathology of the patient can be observed in Table 1. Finally, 19 patients completed the study because 3 patients discontinued study participation. Every patient reported regularly for the follow-up and reported no side effects. They include 8 males and 11 females, with ages ranging between 34 and 90 years.

They were distributed into two groups:

- Group 1: 11 patients in the experimental group treated with Oz.Or.Oil 30 dermatological gel;
- Group 2: 8 patients in the control group treated with control product.

In Group 1 the average age of patients enrolled was 72.55 ± 15.81 while in Group 2 was 69.75 ± 19.24.

The data for the stages of bedsore considered indicate that in Group 1, 63.6% enrolled patients had bedsores at stage I, while 62.5% in Group 2.

Results regarding patient's progress were shown in Table 2. From the evaluation score of the analyzed patients, in the observation period, it shows that the patients treated with Oz.Or.Oil 30 dermatological gel showed faster healing of the ulcer. In the second week, patients in Group 1 showed significant improvement ($p<0.05$) compared to the control group, with efficacy scores equal to 1.00 ± 0.00 and 0.45 ± 0.52 respectively ($p=0.014$).

Table 1: Clinical characteristic of patients treated with Oz.Or.Oil 30 (Group 1: patients 1 to 11) and in the control group (Group 2: patients 12 to 19).

Case No.	Sex	Age	Pathology of the patient	Bedsores stage
1	F	80	Venous insufficiency	I
2	F	80	Peripheral artery disease	II
3	F	62	Rheumatoid arthritis	I
4	M	31	Degenerative stenosis	II
5	M	83	Venous insufficiency	I
6	F	73	Diabetes and venous insufficiency	I
7	F	90	Peripheral artery disease	I
8	M	73	Peripheral artery disease	I
9	F	83	Venous insufficiency	I
10	M	68	Hemiplegia	II
11	F	75	Peripheral artery disease	II
12	M	75	none	I
13	F	85	Peripheral artery disease	I
14	F	67	Chronic peripheral artery disease	I
15	F	88	Diabetes	I
16	M	74	Peripheral artery disease	II
17	M	49	Peripheral artery disease	II
18	F	86	Vascular edema	II
19	M	34	none	I

Table 2: Efficacy of treatment in patients treated with Oz.Or.Oil 30 (Group 1) and in the control group (Group 2) (*p<0.05).

Treatment week	Group 1 (n=11)	Group 2 (n=8)	p (*p<0.05)
0	1.36 ± 0.50	1.38 ± 0.52	0.961
Week 1	1.38 ± 0.52	1,00 ± 0.45	0.107
Week 2	1.00 ± 0.00	0.45 ± 0.52	0.014*
Week 3	0.13 ± 0.35	0.09 ± 0.30	0.816

Discussion

Bedsores, also known as decubitus ulcers, pressures sores, or pressure ulcers, can develop quickly and create serious skin concerns and complications. These sores result from constant pressure on a small area of skin. They can happen anywhere on your body, but they're most common on the skin covering your hips, tailbone, shoulder blades, heels, ankles, and any other area of the body. It is for many years that bedsore is not only an unsolved problem for nurses, but also for those who provide health care in global arena [43]. Given the clinical significance of these problems, there is a need to explore alternative management approaches for these difficult to treat this particular type of wounds.

The use of ozone (O_3) appears providential because eliminates the pathogens and, by releasing oxygen (O_2), activates the proliferation of fibroblasts, hence the building of intercellular matrix with consequent proliferation of keratinoblasts and successive healing [37]. Ozone exhibits wound-healing and antimicrobial properties, which may promote tissue repair and regeneration [44].

Introduction of ozone in the field of Medicine conditioned the search for new strategies, taking into consideration the properties of this gas. Its use in the form of ozonated water and ozonized oil has been accepted.

Several authors [45,46] evidence ozone's oxidant power and its application as germicide in its ozonated oil modality by means of preclinical studies which supports its use in clinical assays in medicine to control infections.

A previous study conducted by Valacchi et al. [47] has demonstrated the beneficial effects of O_3 on wound healing, may be due to decreased bacterial infection, ameliorated dermal wound healing or increased oxygen tension from O_3 exposure in the wound area. O_3, indeed, does not actively penetrate the cells but reacts instantaneously with polyunsaturated fatty acids (PUFAs) to form reactive oxygen species (ROS), such as hydrogen peroxide, which can induce the synthesis of growth factors and accelerate the cell cycle via the activation of redox transcription factors, such as nuclear factor-kappaB (NF-kB).

From this pilot study it was found that ozonized oil therapy reduced the healing duration compared to conventional approaches in bedsores.

Though both, the group treated with Oz.Or.Oil 30 as well the one treated with a control product, progressed satisfactorily.

By analysing efficacy of both medications, Oz.Or.Oil 30 showed a much better efficacy than the control product, probably due to the high antibacterial and germicidal power of Oz.Or.Oil 30 [27] and its capacity to stimulate tissue reparation [48,49]. This product accellerates the healing time.

All patients were satisfied with the treatment whether they were in one group or the other. They indicate the strong smell of Oz.Or. Oil 30, oily consistency and a slight burn on the skin at the time of application, but referring also that relief of these symptoms was so rapid that they were pleased with the treatment.

In conclusion, there is strong evidence coming from human studies and systematic reviews which supports the following health benefits of topical applied ozonized sunflower oil: antifungal treatment in adults onychomycosis, infection preventing in premature neonates, atopic dermatitis treatment in infants, anti-wrinkling and anti-ageing properties, psoriasis complementary treatment.

Further detailed studies are required in the future with larger samples to make use of beneficial effect of this dermatological gel, but this study demonstrated that Oz.Or.Oil 30 can be considered as an effective medication in the treatment of bedsores.

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