Journal of Clinical & Experimental Dermatology Research

Milani et al., J Clin Exp Dermatol Res 2016, 7:4
DOI: 10.4172/2155-9554.1000365

Research Article Open Access

Purified Omental Lipids (P.O.L) in the Treatment of Skin Dryness in Type 2 Diabetic Subjects with or without Vascular or Neurological Complications: A Prospective, Controlled, Assessor-Blinded Trial

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Received date: June 27, 2016; **Accepted date:** July 14, 2016; **Published date:** July 20, 2016

Abstract

Background: Skin dryness is commonly observed in diabetic patients. Purified Omental lipids (POL) are considered an effective emollient and hydrating topical product in subjects at risk of skin fissuring and damage. In addition, topical POL could express a wound-healing and skin regenerative effect.

Aim: We evaluated the efficacy of topical 25% concentrated POL product (P.O.L. cream; Difa Cooper, Italy) (POL-C) in Type 2 diabetic patients with (YES-C) or without (NO-C) vascular or neurological complications in comparison with non-treated healthy volunteers. Presence of vascular or neurological ulcers was an exclusion criterion.

Methods: We assessed the efficacy of POL-C on skin hydration and skin integrity in a prospective, evaluator-blinded controlled study in 30 type II diabetic patients (**YES-C:** n=15) (**NO-C:** n=15), aged 40–75 years, treated with POL-C twice daily for 3 months. Ten subjects, matched for age and sex, without diabetes, formed the control group. Primary outcomes were the Dryness Area Severity Index (DASI) Score evaluating xerosis, erythema, scaling and skin fissuration (**minimum-maximum score values:** 4-20) and Patient-Assessed Skin Score (PASS) evaluating dryness, itching and irritation (**minimum-maximum score values:** 3-15). DASI score was evaluated at baseline, after 1 and 3 months by an investigator unaware of treatment allocation (patients or controls) and unaware of the type of diabetes (with or without complications). PASS scores were collected at the same study times in YES-C and NO-C only groups.

Results: One subject (YES-C group) dropped out prematurely from the trial. At baseline mean(SD) DASI score was 7.4 (2.5) in YES-C group, 4.9 (0.7) in NO-C group and 5.0 (0.7) in control subjects. DASI score in YES-C was significantly higher in comparison with NO-C and control groups. POL induced significantly DASI score reductions in both diabetic patients' groups at month 1 and month 3 ($p < 0.001$) in comparison with baseline values. At month 3, DASI score was 4.5 (1.5) in YES-C and 4.1 (0.3) in NO-C. PASS score was significant reduced in comparison with baseline in YES-C group (from 5.2 to 3.5; p=0.02) and in NO-C group (from 3.7 to 3.0; p=0-05). The product was well tolerated.

Conclusion: In diabetic subjects, skin xerosis is significantly worse in the presence of vascular or neuropathy in comparison with diabetic subjects without complication and in comparison with matched healthy control subjects. The use of POL cream improves and normalizes skin xerosis both assessed by the investigator or by the subject with a clinical effect correlated with the baseline level of skin dryness severity. Application of Purified Omental Lipids cream increases skin hydration and relieves the condition of skin dryness in Type 2 diabetic patients with or without complications.

Keywords: Purified omental lipids; Diabetic dermopathy; Skin xerosis

Background

Skin complications are frequent in diabetes, with 30% of patients presenting some skin involvement during the progression of their disease and these may also be an early mark of undiagnosed diabetes [1]. Common foot changes observed in diabetic subjects include dryness of skin, fissuring, callus formation, and tinea pedis [2]. In particular xerosis is a common skin pathological condition in diabetic patients [3]. Skin dryness and callous formation are considered risk factors for the development of diabetic ulcers [4]. Effective foot skin hydration is a relevant preventive strategy in order to maintain a healthy foot [5] in diabetic subjects. Topical products with emollient and moisturizing activity are very effective in restoring the epidermal barrier function and in correcting xerosis [6]. So far, however, few studies have been performed in diabetic patients assessing whether this therapeutic approach can help correcting xerosis of the diabetic skin. Purified omental lipids (POL) extract is considered an effective topical [7] product with emollient and moisturizing actions. P.O.L. Cream is formulated to carry lipids components into the skin offering long

lasting moisturizing and protection effect [8]. This product can represent an effective, safe and well tolerated treatment for the dry and cracked skin. In addition, topical POL could express a wound-healing and skin regenerative effect [9]. A topical cream product containing 25% of purified omental lipids extract (P.O.L cream, Difa Cooper, Italy) has been used for the prevention of skin fissuring and decubitus ulcers in at risk subjects [8]. This formulation could be considered an interesting product with a formula particularly suitable for the specific treatment of the dry skin in diabetic patients. However, so far, not controlled clinical data are available regarding the efficacy in subjects with diabetes with or without macrovascular or peripheral neurological complications. The aim of the present study was to evaluate the efficacy of POL cream in the treatment of xerotic skin in Type 2 diabetic patients with or without complication and to evaluate if the clinical effect is correlated with the baseline grade of skin xerosis severity.

Variable	YES-C group (n=15)	NO-C group (n=15)	Controls (n=10)	P values
Men/women	10/5	8/7	7/3	0.7
Age, years	62 (4)	61(8)	55 (7)	0.4
History of Diabetes, years	14 (6)	9 (3)	N.A	0.03
Serum glucose mg/100 mL	165 (40)#	153 (21)#	105	0.006
DASI score	7.4 (2.5)*	4.9 (0.7)	5.0 (0.7)	0.05
PASS score	5.2 (1.9)**	3.7 (0.8)	N.A	0.007
Body Mass Index	28.0 (2.8)	28.7 (2.0)	27.9 (2.5)	0.7
*: vs. NO-C and Control groups; ** vs. NO-C group. # vs. Control group				

Table 1: Patients characteristics at randomization, data presented as mean (SD).

Methods

Study design

The present trial was a mono-center prospective, controlled, assessor-blinded trial. The Institutional Review Board (Fitness Metabolic ONLUS Monterotondo) approved the study protocol. Study was performed between March 2009 and March 2012.

Patient selection

Patients and healthy control subjects were enrolled in the trial after their written informed consent according to the Declaration of Helsinki [10]. Patients enrolled in this study were men and women, aged between 50 and 75 years, with a confirmed diagnosis of type 2 diabetes and mild-to-severe foot/lower limb xerosis, who had not used any topical moisturizers on their feet for at least 2 weeks. Subjects were classified to have non complicated type 2 diabetes if Winsor Index was 0.9-1.1, ultrasound assessed of carotid arteries intimal media thickness <1 mm, Vibration Perception threshold (VPT) <25 V and Sensitive Conduction Velocity (SCV) was >49 m/s. Complicated type 2 diabetes was defined if the Winsor Index was <0.8 or >1.2, intimal medial thickness >1 mm, VPT >25 V or SCV <49 m/s. Insulin-dependent diabetes mellitus, presence of active foot lesions (both of vascular or neurological origin) were the main exclusion criteria. The treatment was applied on the feet (dorsal and plantar regions) and in the distal third of the leg twice daily for 3 consecutive months. Control subjects were instructed to not apply any topical product during the study period.

Study outcomes and methods

The principal outcome of the trial was a modified Dryness Area Severity Index (DASI) score evolution, according to Serup et al [11]. The DASI score evaluated xerosis, erythema, scaling and skin fissuration using a 5-point scale from 1 (=no sign of symptom) to 5 (=severe) with a range of minimum and maximum score values of 4 to 20. Patient-assessed Skin Score (PASS) evaluating dryness, itching and irritation using a 5-point scale from 1 (=no sign of symptom) to 5 (=severe) (minimum-maximum score values: 3-15) was also assessed. DASI score was evaluated at baseline, after 1 and 3 months by an investigator unaware of treatment allocation (GF) (patients or controls) and unaware of the type of diabetes (with or without complications). PASS scores were collected at the same study times in YES-C and NO-C groups only.

Statistical analysis

We performed the statistical analyses using SPSS statistical software (ver. 13.0). Data were expressed as mean (SD). All P values were two-sided. The present trial was designed as a superiority trial. The power calculation assumed a difference between baseline and the DASI score at week 12 of at least 1.1 points with an effect size of 0.7. This assumption provided 90% power at an alpha level of .05 (two-tailed test) for a sample size of at least 30 evaluable patients in total. Sample size calculation was performed using G*Power program Ver.3.03 (Kiel, Germany). Two-tailed unpaired T-test, two-tailed Mann–Whitney (unpaired) and Wilcoxon (paired) tests were applied to compare treatment with control and to compare baseline levels with values at the end of study period. The analysis was based on the intention-to-treat principle and involved all patients who were enrolled. A P value ≤ 0.05 was considered statistically significant.

Results

Fifty-four patients were screened for inclusion in the study. A total of 30 patients, fulfilling inclusion and exclusion criteria were enrolled: 15 were classified as subjects without vascular or neurological complications (NO-C) (n=15) and 15 with complications (YES-C). Table 1 shows the subjects characteristics at baseline. Main demographic characteristics at baseline were similar in the three groups. All but one patient concluded the 3 months treatment period. One subject (YES-C group) dropped out prematurely from the trial. At baseline mean (SD) DASI score was 7.4 (2.5) in YES-C group, 4.9 (0.7) in NO-C group and 5.0 (0.7) in the control group. DASI score in YES-C was significantly higher in comparison with NO-C and control groups. No differences in the baseline DASI score were observed between NO-C group and control subjects. POL induced a significant DASI score reduction in both diabetic patients' groups at month 1 and month 3 ($p<0.001$) in comparison with baseline values. At month 3, DASI score was 4.5 (1.5) in YES-C and 4.1 (0.3) in NO-C and 5.2 (0.5) in the control group (Figure 1).

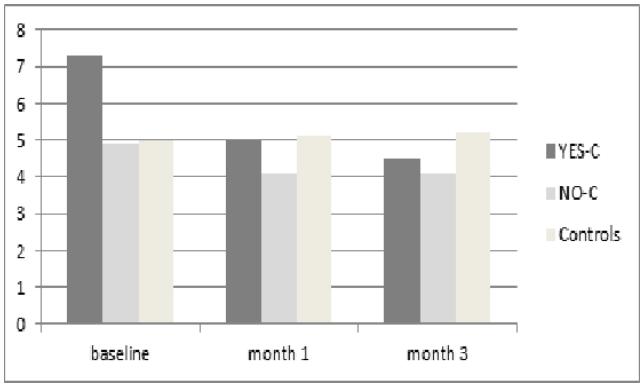

Figure 1: Evolution of DASI (Dry Area Severity Index) score; YES-C: diabetic subjects with complications; NO-C: diabetic subjects without complication; Control: Control group. For statistical significance see text).

At month 3 DASI scores in YES-C and NO-C were significantly lower (P=0.05) than DASI score value in control group, suggesting a complete normalization of skin appearance in all treated subjects (Figure 1). PASS score at baseline was 5.2 (1.9) in YES-C group and 3.7 (0.8) in NO-C group (p=0.05). PASS score was significant reduced in comparison with baseline in YES-C group (from 5.2 to 3.5; p=0.02) and in NO-C group (from 3.7 to 3.0; p=0.05) (Figure 2).

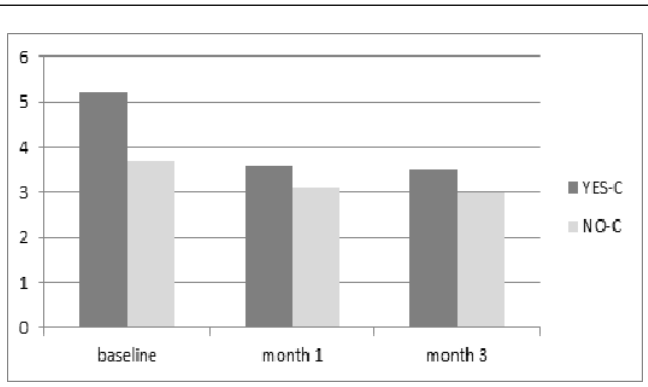

Figure 2: Evolution of PASS (Patient-Assessed Skin) score; YES-C: diabetic subjects with complications; NO-C: diabetic subjects without complication; For statistical significance see text).

The product was in general well tolerated.

Discussion

Diabetes mellitus causes frequently pathophysiologic changes in the skin [12]. Xerosis (with prevalence higher than 35%) with itch and scleroderma-like skin alteration are the most commonly observed cutaneous manifestations of the disease [13]. Xerosis of the foot in diabetic patients could represent the first stage of the ulceration process through the development of fissures, cracking and hyperkeratosis. Correction of skin dryness in diabetic subjects trough specific skin treatments are of great relevance and must be implemented as soon as possible. Skin xerosis is usually treated with the long-standing use of emollients and moisturizers [14]. Their use relies on the evidence-based clinical data showing the importance of maintaining the water content of the skin. The clinical efficacy of emollient products could vary in term of beneficial effects on the skin [15]. Topical use of POL in cream formulation has demonstrated that this product could be an effective emollient and moisturizing therapeutic strategy in subjects with marked xerosis and at high risk of skin damage such as pressure sore. Rinaldi et al. [16] evaluated 25 diabetic patients with neuropathic ulcers and severe skin dystrophy in a controlled left-vs-right side study design. The skin areas surrounding the necrotic tissues were treated with POL cream on the other side, used as a control, with hyaluronic acid. Both products were applied twice daily for 30 consecutive days. At the end of the study period , evaluation of TEWL (Trans epidermal water loss), sebometry, corneometry, and pH values demonstrated significant improvement on the POL cream treated sites with clinical and instrumental improvement greater than the control site where hyaluronic acid was applied. P.O.L cream treatment, in addition, improved also skin microcirculation assessed by laser-Doppler velocimetry. This improvement was not observed in the skin area treated with hyaluronic acid. POL cream was also effective in subjects at risk of pressure ulcer. A total of 210 hospitalized patients at risk of pressure ulcer were studied by Bertoli et al. [17]. At baseline 22 subjects suffered from decubitus ulcers, 45 subjects had local dystrophy and 143 with unaffected skin where the medication was applied for pressure ulcer prevention. Treatment duration lasted 2-6 weeks (average 3.5 weeks). After the utilization of P.O.L cream, 144 patients presented unaffected skin, two patients with ulcers showed remission, and 63 patients showed a marked improvement in ulcers and skin appearance. The overall improvement was evaluated statistically significant ($p<0.01$). In the present study, we demonstrated that 3 months application of P.O.L cream is associated with an improvement toward a normalization of skin xerosis in diabetic subjects with or without complications. This clinical benefit correlates with the baseline level of skin impairment: the greater the level of skin dryness the greater the reduction of the DASI score observed. Some trial limitations should be taken in account in evaluating our results. This study was not double-blind. In order to increase the internal validity of our trial, we decided to perform an assessor-blinded evaluation of the DASI and PASS score which were the primary endpoints of the study. A second limitation of our study is that we have evaluated as primary endpoint a subjective clinical assessment parameters (DASI score and the PASS) instead of an instrumental objective variable. However, the principal therapeutic goal of emollient treatment in diabetes is to increase skin hydration. Additional future studies are necessary to evaluate if the treatment with this topical product could be associated with improvement in microcirculation and/or modification of skin structure in diabetes.

Conclusion

The present study demonstrates that application of POL cream improves skin hydration and relieves the condition of skin dryness in Type 2 diabetic patients with or without complications. After 3 months of treatment POL cream completely normalize skin appearance as documented by the evolution of DASI and PASS scores.

Authors' contributions

AF and GF had the original study idea and participated in its design and coordination. MM helped regarding study design, protocol definition, data collection, and analysis. AF and GF carried out the

patients' selection and visits. All authors read and approved the final manuscript.

Competing Interests

MM is an employee of Difa Cooper. All the other authors declare that they have no competing interests.

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