PharmaNutrition 4 (2016) 151–153

Contents lists available at ScienceDirect

PharmaNutrition

journal homepage: www.elsevier.com/locate/phanu

An olive polyphenol-based nutraceutical improves cutaneous manifestations of psoriasis in humans

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ARTICLE INFO

Article history:
Available online 9 November 2016

Keywords:
Psoriasis
Skin care
Olive phenols
Hydroxytyrosol
Nutraceuticals
Cosmeceuticals

ABSTRACT

Psoriasis is a chronic inflammatory disorder whose most conventional treatment includes topical agents such as corticosteroids and vitamin D analogs, phototherapy, and systemic treatments aimed at slowing down cell cycle, namely keratinocyte proliferation. Indeed, there is further need for effective yet safe remedies. We undertook a pilot, randomized, placebo-controlled, double-blind trial to evaluate the efficacy of novel olive (poly)phenol-based nutraceutical/cosmeceutical, augmented with vitamin A, riboflavin, and biotin. We recruited 30 psoriatic (mild or moderate) patients (62.5% females and 37.5% males), of which 15 were randomly allocated to a nutraceutical named Alyvium® (which contains 500 mg of an olive polyphenolic extract, 200 μg vitamin A, 0.35 mg riboflavin, and 12.5 μg of biotin per capsule; two capsules/day) and 15 patients to the placebo, i.e. two capsules/day of maltodextrins, for 12 weeks. After four weeks of treatment, the Psoriasis Area and Severity Index significantly decreased to 2.92 ± 1.52 (−27%) in those who received the supplement and to 3 ± 2.24 (−11%) in those who were administered the placebo. The amount of Body Surface Area affected also decreased. In conclusion, we provide the first evidence that a cosmeceutical/nutraceutical formulation based on olive (poly)phenols improve the cutaneous manifestations of psoriasis in patients who are moderately affected by this pathology. The use of supplements as adjuvant therapy of psoriasis could be anticipated.

1. Introduction

Psoriasis is a chronic inflammatory disorder with a relevant immunological component [1]. The prevalence of psoriasis is estimated to be around 3–4% of the world population, meaning that roughly 250 million people worldwide suffer from it [2]. Psoriasis is not just a dermatological disease: psoriatic patients are at higher risk of cardiovascular disease, likely because of increased systemic inflammation [3]. The pathogenesis of psoriasis is being elucidated and involves immune dysregulation, infection, trauma, and genetic predisposition [1]. Of note, a strong inflammatory response to immune dysregulation triggers psoriatic outbreaks in the skin and in the joints. Therefore, inflammation is one of the main target of the symptomatic treatment of psoriasis [4]. The most conventional treatment of psoriasis includes topical agents such as corticosteroids and vitamin D analogs, phototherapy, and systemic treatments aimed at slowing down cell cycle, namely keratinocyte proliferation. Side effects include phototoxicity, hypersensitivity reaction, skin irritation, tissue toxicity, and general immunosuppression [2]. Therefore, there is a need for effective yet safe remedies. From an adherence viewpoint, it should be underscored that molecules of natural origin are easily accepted by patients because they are perceived as safe as well as effective.

The biological properties of olives and their edible and non-edible derivatives, i.e. olive oil and olive mill waste water (OMWW) are being actively investigated, as recently reviewed by Bernardini and Visioli [5]. In brief, many in vitro and animal studies report the antioxidant and anti-inflammatory potential of olive (poly) phenols. Some human studies have also been performed and other ones are underway [5]. It is noteworthy that hydroxytyrosol (HT, the foremost phenolic component of extra virgin olive oil) was granted a health claim on protection of circulating lipids from oxidation by the European Food Safety Authority and it is the only (poly)phenol with such prerogative [6].

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http://dx.doi.org/10.1016/j.phanu.2016.10.002
2213-4344/

Given the current scantiness of effective treatments for psoriasis and based on the recognized antioxidant and anti-inflammatory potential of HT and associated phenolics, we undertook a randomized, placebo-controlled, double-blind pilot trial to evaluate the efficacy of novel olive (poly)phenol-based nutraceutical/cosmeceutical, augmented with vitamin A, riboflavin, and biotin.

2. Materials and methods

This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki). The study protocol was approved by the local Ethics committee and was fully explained to the participants, who provided written informed consent. The study lasted for 12 weeks.

We recruited 30 patients (62.5% females and 37.5% males; none of them suffering from psoriatic arthritis or other arthropathies), of which 15 were randomly allocated to a nutraceutical named Alyvium® (which contains 500 mg of an olive polyphenolic extract, 200 μg vitamin A, 0.35 mg riboflavin, and 12.5 μg of biotin per capsule; two capsules/day) and 15 patients to the placebo, i.e. two capsules/day of maltodextrins. Both groups also received topical methylprednisolone aceponate (0.1% cream), to be applied at bedtime for seven days followed by three break days. All patients were diagnosed with mild or moderate plaque psoriasis and have been free of topical or systemic drug for ≥ 28 days before the trial started. The affected areas were mostly arms, back and legs, followed by scalp, hands and feet. Pregnant women or women who planned to get pregnant were not included. Psoriatic arthritis patients were also not included in the study. Blood was drawn at the beginning and at the end of the study for routine analyses.

Patients were assessed by physicians who were blinded to the treatments. We appraised efficacy by evaluating the Psoriasis Area and Severity Index (PASI), the Physician's Global Assessment (PGA), and the amount of Body Surface Area (BSA) affected.

Photographs were also taken to evaluate plaque size, erythema, and degree of infiltration (see Supplementary Data).

2.1. Statistical analysis

Data were analyzed with the SPSS software (version 17.0). Normal distribution was assessed by the Kolmogorov Smirnov test. In case of normal distributions, a Student's *t*-test for paired data was used, otherwise we employed the Wilcoxon test. A $p < 0.05$ was considered as statistically significant.

3. Results

Two (13.3%) patients in the treatment group and four (26.6%) in the placebo one did not complete the study for personal reasons. The remaining patients' characteristics are shown in Table 1. No side effects were reported in either arm. The evolution of PASI is shown in Fig. 1. The average basal PASI in patients receiving Alyvium® was 4 and in those who received the placebo 3.36 (Table 1). After four weeks of treatment, PASI significantly decreased to 2.92 ± 1.52 (−27%) in those who received the supplement and to 3 ± 2.24 (−11%) in those who were administered the placebo ($p < 0.5$ between treatments; Table 2). At the end of the experimental period, this index remained stable, i.e. 3 ± 1.47 in treated patients and increased to 3.27 ± 2.57 in placebo subjects (Table 2). In terms of percentage, a three-month use of the nutraceutical resulted in a 25% decrease in PASI, whereas the use of placebo led to a 3% decrease of this indicator.

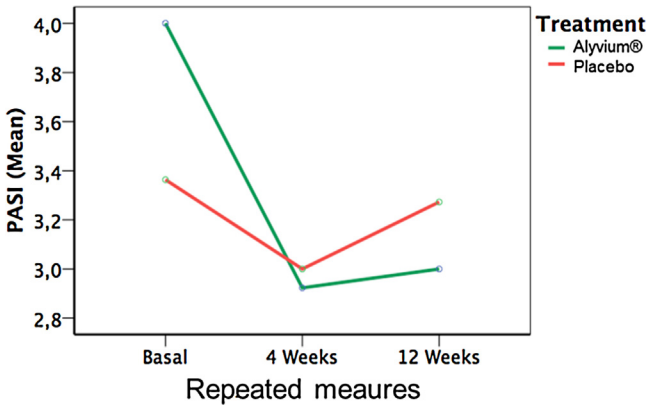

Fig. 1. Evolution of PASI throughout the study.

Fig. 2 illustrates the evolution of BSA. The initial BSA values (Table 2) were 2.08 ± 1.32 in the Alyvium® group and 1.45 ± 0.52 in the placebo one. After four weeks, these values decreased to 1.69 ± 0.65 and 1.36 ± 0.92, respectively. At the end of the study, treated patients showed a BSA of 1.77 ± 0.93 whereas the placebo ones exhibited values of 1.18 ± 0.87. The difference between treatment and placebo was not statistically significant.

We did not record notable differences in PGA (data not shown).

4. Discussion

The results of this pilot study show that a cosmeceutical/nutraceutical preparation based on olive (poly)phenols is able to lessen the cutaneous manifestations of moderate-psoriasis patients. In particular, administration of Alyvium® significantly decreased PASI as compared with placebo (Fig. 1), throughout the experiment. The treatment was well tolerated and no side effects were recorded. As far as we know this is the first time that a nutraceutical – added to conventional topical treatment – successfully ameliorates psoriatic manifestations in humans.

From a mechanistic viewpoint, several hypotheses can be formulated. The first one is that olive (poly)phenols are endowed with anti-inflammatory activities, some of which have been demonstrated in humans [5]. Even though we did not record a

Table 1
Patients' characteristics.

	Control	Alyvium®
Smoking (yes/no)	11	2/11
Weight (Kg)	75.09 ± 17.95	67.72 ± 13.37
Height (cm)	167.73 ± 6.48	165.92 ± 7.94
BMI	26,48 ± 4,81	24,64 ± 5,58
Familiarity		
Father (n of relatives affected by psoriasis)	1	3
Mother	0	2
Uncle	0	1
None	10	6

BMI, body mass index. Data are means ± S.D.

Table 2
PASI in placebo and treated patients.

PASI	Time 0	4 weeks	12 weeks
Placebo	3.36 ± 1.50	3.0 ± 2.24	3.27 ± 2.57
Alyvium®	4.0 ± 1.35	2.92 ± 1.55*	3.0 ± 1.47*
BSA			
Placebo	1.45 ± 0.52	1.36 ± 0.92	1.18 ± 0.87
Alyvium®	2.08 ±1.32	1.69 ± 0.65	1.77 ± 0.93

PASI, Psoriasis Area and Severity Index; BSA, Body Surface Area. Data are means ± S.D.
* $p < 0.05$ as compared with placebo, Wilcoxon ranges test.

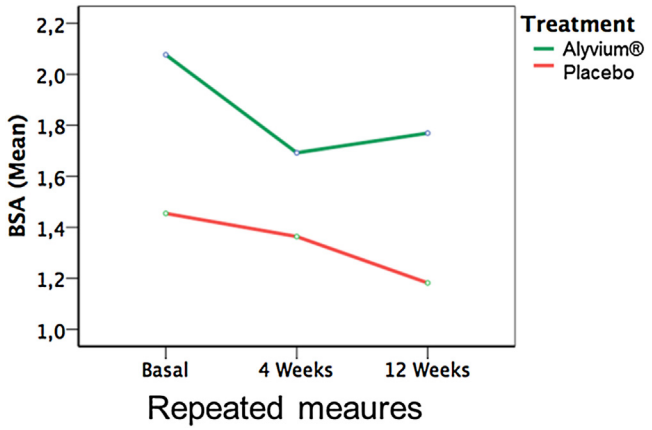

Fig. 2. Evolution of BSA throughout the study.

decrease in C-reactive protein circulating concentrations (data not shown), we can conceive that decreased cutaneous inflammation might be responsible for the observed effects. Another potentially healthful mechanism of action is direct antioxidant activity by olive phenolics, namely HT. Indeed, HT has been granted an antioxidant health claim by the European Food Safety Authority (EFSA), namely as protector of circulating lipids and low-density lipoprotein [6]. It must be underscored that direct antioxidant activity by (poly)phenols in general is still debated because of bioavailability and kinetic constraints [7–9]. Also, provision of antioxidants to humans does not result in better prognosis, thus questioning the true contribution of lipid peroxidation to human pathology [10]. In contrast, the proposed "nrf-2 hypothesis" which posits that para-hormetic responses leading to increased production of endogenous antioxidants might mediate the healthful effects of (poly)phenols is gaining traction [7]. Again, we must underline that this hypothesis has never been proven in humans [8,11] and that future, ad-hoc studies are required to eventually prove it. Yet, a marked redox-balancing effect of anti-TNFα therapy has been reported [12]. We speculate that the nutraceutical we tested might have contributed to the normalization of redox code [13] and, therefore, to the amelioration of cutaneous manifestations.

Being this supplement composed by four bioactive ingredients, it is of course impossible to ascertain their individual contributions. Biotin administration reverses alopecia in children treated with valproic acid [14]. Yet, there are no published scientific studies that support the claim that biotin supplements are effective in skin disorders.

Retinoids exhibit anti-inflammatory properties and regulate the proliferation and differentiation of skin epithelial cells, as well as the production of sebum. For these reasons, both natural and synthetic retinoids are used as pharmacologic agents to treat various skin disorders, including psoriasis [15]. Being vitamin A liposoluble and olive phenolics hydrophilic, we hypothesize synergistic effects at the cutaneous level and in the various layers of the derma.

Riboflavin, in the form of flavin adenine dinucleotide (FAD) participates in the redox cycle of glutathione, via the actions of the FAD-dependent enzymes glutathione reductase, glutathione peroxidase, and xanthine oxidase [16]. Of note, olive phenols from olive mill waste water have been shown to increase circulating glutathione concentrations in humans [17]. Accordingly, a glutathione-enhancing whey protein preparation was shown to improve psoriasis in a pilot study [18].

In conclusion, we provide the first evidence that a cosmeceutical/nutraceutical formulation based on olive (poly)phenols improve the cutaneous manifestations of psoriasis in patients who are moderately affected by this pathology. The use of supplements as adjuvant therapy of psoriasis could be envisioned, following appropriate, large-scale trials.

Acknowledgments

This study was supported by Solvitae Medica (Madrid, Spain), which also provided Alyvium® and placebo, and European FEDER Funds and the Comunidad de Madrid through the "Programa de actividades en tecnologias" (ALIBIRD-CM S2013/ABU-2728) to F.V.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.phanu.2016.10.002.

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