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Original Article

Clinical efficacy and quality of life under micronutrients in combination with methotrexate therapy in chronic plaque of psoriatic patients

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ABSTRACT

Background/objectives: Psoriasis is a common dermatologic disorder, with fluctuating response to treatments. We aimed to investigate the efficacy of methotrexate (MTX) plus micronutrient supplement (MM) compare to MTX only on Psoriasis Area and Severity Index (PASI) and Dermatology Life Quality Index (DLQI) in psoriasis patients in a double-blinded clinical trial study.

Materials and methods: A total number of 30 psoriasis patients who had lesions up to 20 percent of body skin involvement were divided randomly into two groups. Group A were treated by oral methotrexate and group B were received the MTX plus one tablet of micronutrient supplement daily for 12 weeks. Clinical response (scaling, erythema, involvement and thickness of patient's lesion), PASI score and DLQI index were recorded baseline and after 12 weeks. PASI-50, PASI-75, and PASI-90 evaluated as indicators of clinical improvements.

Results: PASI 50/75/90 response rates were 100%, 73.3%, 40% in group B and they were 66.6%, 40%, 20% in group A respectively. Both treatments were effective and caused significant improvements in PASI score and DLQI ($P < 0.05$). Group B showed a noticeable and more rapid reduction of PASI score, scaling and involvement of lesions compared to group A ($P = 0.04$; $P = 0.01$; $P = 0.03$, respectively). The decline of DLQI in group B (6.80 ± 2.33) was higher than that in group A (5.40 ± 2.84).

Conclusion: Daily usage of supplements along with methotrexate is safe and concomitant with the significant reduction of PASI score and improvement of DLQI compared to the usage of MTX alone.

Introduction

Psoriasis is a common chronic inflammatory skin disease that has a significant impact on affected person's health-related quality of life (HRQoL).[1] Among widespread dissatisfaction of existing anti-psoriasis therapy,[2] Methotrexate (MTX) as a derivative of aminopterin, an analog, and antimetabolite of folic acid, was first used in the treatment of psoriasis in 1951.[3] Today, MTX shows promises for the treatment of practically all forms of moderate or severe psoriasis.[4] Due to the excellent efficacy of MTX for psoriasis treatment, MTX-based therapy of psoriasis patients could be conducted, as long as all recommendations concerning dosage and safety of treatment are considered.[5,6] After all, MTX is a relatively inexpensive drug and thereby it is available easily to low-income patients.

For decades, the effects of dietary and vitamin supplements in the management of psoriasis have been neglected. The oral 1,25 dihydroxy vitamin D3 [1,25(OH)2-D3] in the treatment of psoriasis is known to have some beneficial effects.[7] Moreover, the combined use of calcipotriol (1,25-(OH)2-D3) with MTX treatment increased the relapse time of psoriasis patients following discontinuation of MTX.[8] Various topical and systemic vitamin A derivatives were highly effective in the treatment of psoriasis and had potential benefits related to decreasing psoriasis area and severity index (PASI).[9] The potential efficacies of intramuscular and systemic

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vitamin B12 in the treatment of psoriasis have been demonstrated previously.[10] A recent randomized, controlled trial study revealed the role of supplementation containing selenium, coenzyme Q10, and vitamin E in hastening the clinical improvement in psoriasis patients compared the patients who were received placebo.[11] Furthermore, statistically significant decrease in the mean PSAI score of chronic plaque psoriatic patients was recorded under high-pressure shower regimen and selenium-rich spa water daily for three weeks.[12] Furthermore, improvement of PASI score by receiving inositol[13] and zinc supplementation[14] were demonstrated previously. Today, due to the increase in the number of recent studies on psoriasis, interests in the field of examining nutrition and functional ailments on milder flare-ups and reduction of scales and erythema have been increased accordingly.[15]

In psoriasis, physical measures of disease severity such as the affected body surface area or PASI score do not always correspond with the impact of psoriasis on the patient's HRQoL.[16] Therefore, both physical and HRQoL measurements are necessary to assess disease severity when decisions are made over psoriasis treatment and when assessing the outcome of such decisions.[17,18] In the majority of trials the Dermatology Life Quality Index (DLQI) has been used as the dermatology-specific HRQoL outcome.[19,20] In present study for the first time, we aimed to investigate the impact of consumption of micronutrient supplementation (MM) along with MTX compared to MTX only on the clinical efficacy and DLQI in psoriasis patients.

Methods

Study participants

This randomized double-blind trial was conducted on patients with psoriasis vulgaris who were referred to our Dermatology Department with the approval of the Ethics Committee of Mashhad University of Medical Sciences, Mashhad, Iran. This trial was registered on Iranian Registry of Clinical Trials (IRCT) under the registry number: IRCT 2014012016275N1. The considered cases of psoriasis patients had ages between 20 and 50 years old and lesions with up to 20% of body skin involvement. Exclusions were patients under 20 years old, patients who wanted to leave the study for any reason, patients who had type one diabetes mellitus, patients with cardiovascular disease, pregnant or lactating women, patients with familial hyperlipidemia, history of liver disease, consumption of alcohol or alcoholic beverages during study, and variations in hepatic enzymes (more than 2.5 times of normal level). Furthermore, patients who previously were taking Methotrexate, phototherapy and any systemic therapy during last two months for psoriasis treatment were also excluded. Diagnosis of plaque-type psoriasis was made by punch biopsy after taking the separate written informed consent.

Sample size

According to previous investigations on psoriasis treatment protocols, PASI-75 is considered as a benchmark for severity of disease evaluation.[21–23] Therefore, we considered PASI-75 score as defined reduction in PASI by 75% from baseline, during 12 weeks therapy. Thus, with 75% cure rate, 85% power and a 5% two-sided type I error, 11 subjects were required in each group. Moreover, considering a loss to follow-up of 20%, this number raised to 15 patients for each group. Initially, fifty psoriasis patients were enrolled according to the inclusion criteria. Then, 16 cases were excluded due to lack of eligible criteria or consent withdrawn (Fig. 1). Therefore, 34 psoriasis patients have entered the study. However, four patients were excluded due to their absence in follow-up periods. Hence, we completed our treatment protocol on 30 psoriasis patients.

Study protocol

Demographic profile including gender, age and age onset of disease and weight of patients were collected. Moreover, past medical history of all patients was also noted. First, patients were divided randomly into two different modalities of treatment (group A and group B) based on random table numbers and referral date of patients. The patients who were referred in odd days were considered as group A and those who were referred in even days were considered as group B. Patients were blind about treatment groups due to receiving their therapies with masked trademarks and as mentioned above their referring into different days. Moreover, they did not have any contact with each other.

Two studied groups (group A and group B) received 7.5–15 mg per week oral methotrexate (0.2–0.3 mg/kg/week) for 12 weeks according to the standard protocol of MTX consumption.[24] Folic acid was given to the patients at 5 mg once daily except on the day of MTX consumption.[24] In addition, patients of group B were received one tablet daily of micronutrient (Immunace, Vitabiotics Ltd, London, UK). The composition of this micronutrient supplement (see supplementary file), was higher than the recommended daily allowances (RDA) for healthy individuals due to the greater need of psoriasis patients to micronutrients.[25] Patients were advised to report to the dermatologist any occurrence of unwilling adverse effects including redness, burning, itching and erosion during 12 weeks of therapy. Baseline and weekly complete blood count (CBC) and liver function test (LFT) including measuring of alanine aminotransferase (SGOT), aspartate aminotransferase (SGPT), and alkaline phosphatase (ALP) enzymes were carried out to monitor the side effects of methotrexate.

Furthermore, the factors including the site of involvement, the size of plaques, and skin examination (erythema, thickness, and scaling of lesions), at baseline and after 12 weeks' therapy, were evaluated by three independent investigators. These investigators were not aware of treatment groups and types of patient's therapies. Moreover, they calculated independently the efficacy of treatment under Psoriasis Area and Severity Index (PASI) system (Table 1).[26] The index combines the area of affected skin (head (10%); upper extremities (20%); lower extremities (40%); trunk (30%) of whole body surface) and the grade of erythema, thickness and scaling of lesion (scored for each criterion from 0 to 4). We calculated the score of erythema, thickness, and scaling of the lesion based on the sum of their related rating score for each patient's (0–4, Table 1) head, upper limbs, trunk and lower limbs. Besides, the degree of involvement was considered as the sum of related rating score for each patient's (0–6, Table 1) head, upper limbs, trunk and lower limbs.

Then effectiveness indicator targets of our study process were evaluated with three cut points as a reduction in PASI by 50%, 75% and 90% (remission point) from baseline (PASI -50, PASI-75 and PASI-90).

The Dermatology Life Quality Index

DLQI questionnaire was selected as a widely used dermatology-specific questionnaire[27] to evaluate health-related quality of life. This questionnaire included 10 questions concerning HRQoL related to the last week, before patient admission, which ranged from 0 (no impairment of HRQoL) to 30 (maximum impairment of HRQoL). DLQI is subdivided into six areas related to different features of a person's HRQoL consisting of symptoms and feelings (questions 1, 2), daily activities (3, 4), leisure (5, 6), work/school (7),

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