

CLINICAL EFFICACY AND SAFETY OF A COMBINED FORMULATION OF ZINC PYRITHIONE 0.25% AND BETAMETHASONE DIPROPIONATE MICRONIZED 0.05% IN THE TREATMENT OF MILD TO MODERATE PLAQUE PSORIASIS.

Abstract

Background Psoriasis is a common chronic inflammatory skin disease characterized by erythematous and scaling plaques. The ongoing understanding of its pathogenesis has led to new therapeutic options and new areas of research which aimed at reducing keratinocyte proliferation and suppressing T-cell activation.

Objectives To evaluate the efficacy and safety of topical use of a combined formulation of zinc pyrithione 0.25% and betamethasone dipropionate micronized 0.05% in a base of isopropyl myristate used in mild to moderate plaque psoriasis.

Methods A total of 32 patients were enrolled into a prospective open clinical trial. Patients were first treated with the combined formulation of zinc pyrithione and betamethasone dipropionate, which was topically administered twice daily for two weeks. After the 2nd week of therapy, zinc pyrithione emulsion alone was applied twice daily for two weeks and twice daily two to three times a week for the following two weeks. Efficacy and safety were assessed.

Results Our results showed that the combination of zinc pyrithione 0.25% and betamethasone dipropionate micronized 0.05% in a base of isopropyl myristate rapidly reduced erythema, thickness and scaling. Clinical improvement and Psoriasis Area and Severity Index (PASI) reduction occurred in less than two weeks of therapy. The maintenance product, zinc pyrithione alone, was able to complete the clinical remission, reduce the frequency of recurrences and avoid a long term use of topical corticosteroids.

Adverse reactions, such as lesional/perilesional dryness and mild itching, occurred in 12.5% of all patients (4/32), but improved throughout therapy by applying an emollient once daily when needed.

Conclusions Our findings suggest that a combined formulation of zinc pyrithione 0.25% and betamethasone dipropionate micronized 0.05% in a base of isopropyl myristate is an effective and well tolerated topical treatment worthy of consideration for patients with mild to moderate plaque psoriasis.

Keywords: *Psoriasis vulgaris – Zinc pyrithione – Betamethasone dipropionate*

Introduction

Psoriasis is a chronic cell-mediated inflammatory skin disease. It is one of the most common chronic dermatoses in the world with a prevalence that varies widely among different populations, up to a 5% in some areas of the world.^{1,2} Its histopathology is characterized by abnormal keratinocyte differentiation and proliferation, a high number of type 1 T cytotoxic CD-8-positive T lymphocytes (T_C1) is present in the epidermis, whereas activated type 1 helper CD-4-positive T lymphocytes (T_H1) predominate in the dermis. T_H1 and T_C1 lymphocytes release the inflammatory cytokines interferon- γ (IFN- γ), interleukin-2 (IL-2), tumor necrosis factor- α (TNF- α) upon activation, and both these cell types are considered to be effector cell populations (rather than regulatory T cells, which are chiefly type 2 cells). Also neutrophils are found in increased amounts in psoriatic skin; they leave the dermal vasculature and are directed to the site of inflammation by chemokines, such as leukotriene- B_4 (LTB-4) and interleukin-8 (IL-8).^{3,4,5}

In recent years, a variety of topical and systemic treatments for psoriasis are available including retinoids, photochemotherapy with psoralens and ultraviolet A (PUVA), phototherapy with ultraviolet B (UVB), methotrexate and cyclosporine A, however these therapies may cause side effects in the long term and/or do not always give acceptable responses.⁶ In general, the therapeutic approach to treating this life altering disease will be dependant on its clinical type and severity, which is linked to how it alters the quality of life in terms of percentage of body surface area (BSA) involved, location of the plaques, symptoms, patient's attitude about the disease, impact on daily physical and social activities.⁸

Topical corticosteroids are the most frequently used medications for treating mild to moderate plaque psoriasis. Betamethasone dipropionate is a synthetic fluorinated corticosteroid classified as a potent WHO Group III steroid. This drug is available on prescription for a once or twice daily topical use to treat plaque psoriasis on a short-term basis.

Zinc pyrithione has bacteriostatic and fungistatic properties and is used at 1-2% in the control of seborrhoeic dermatitis, in which epidermal cells proliferate, dandruff, eczema, erythema and psoriasis. Several short-term studies have shown the effectiveness of 0.25%-0.5%-1% zinc pyrithione in the treatment of dandruff and seborrhoeic dermatitis. The ultimate goal of the use of zinc pyrithione in shampoo formulation (applied twice a week for 4 weeks) was to remove scales and reduce multiplication of the resident lipophilic yeast *Malassezia furfur* (formerly known to be *Pityrosporum ovale*), which is increased in the scaly epidermis of both conditions. Zinc pyrithione reduced the severity and area affected of the scaling.⁷

We report our experience with zinc pyrithione 0.25% and betamethasone dipropionate micronized 0.05%, topically administered, in 32 patients affected by mild to moderate plaque psoriasis.

Materials and Methods

32 patients (20 males and 12 females, aged 7-77 years, median age 46.3) affected by mild to moderate plaque psoriasis were enrolled in this study. Patients were affected by this disease for a minimum time frame of 2 month up to 34 years. 10/32 patients had a 1st degree familiarity with plaque psoriasis. Most of patients tried other conventional therapies, such as tacalcitol, calcipotriol, ditranol, tazarotene, PUVA among others, but achieved only temporary and unacceptable responses.

All patients gave signed consent to participate in the trial after review and approval of the present study by all ethics committees and health authorities. Furthermore, patients had no topical or systemic treatments for 2 weeks prior to the topical use of zinc pyrithione.

Patients had a Psoriasis Area and Severity Index (PASI) score of 4 to 12, 10% to 30% of body surface area (BSA) coverage involving at least 10% of one or more body regions (face, arms, legs and trunk).

All patients were treated with zinc pyrithione 0.25% and betamethasone dipropionate micronized 0.05%, topically administered twice daily for the first two weeks of treatment. After the 2nd week of therapy patients began to use zinc pyrithione 0.25% emulsion alone twice daily for other two weeks and when affected areas were clinically improved or clear, patients were recommended to continue the application of zinc pyrithione 0.25% emulsion twice a day two-three times a week.

To maintain clear skin, zinc pyrithione 0.25% emulsion was applied, as a maintenance program, once a day three times a week on the affected areas providing substantial relief.

Clinical and photographic documentation and PASI assessment were performed before treatment, and then at week 2 and 6 of therapy. Extension, severity of psoriasis (thickness, redness and scaliness) and side effects were recorded at each visit (week 0, 2 and 6).

Results

At the end of our study we evaluated 32 patients (20 men and 12 women) affected by mild to moderate plaque psoriasis.

Among 32 patients, 18 (56.3%) achieved a significant improvement of the thickness, redness and scaling already after 2 weeks of treatment with zinc pyrithione compounded with the mild steroid. 13 patients (40.6%) showed a complete clinical remission. 1 (3.1%) patient interrupted therapy after only two applications due to incoercible itching and erythema. The percentage change in PASI score from baseline to visit 2 (end of 2nd week) was significant (48.4%).

After 4 weeks of treatment with zinc pyrithione alone (from week 3 to week 6), 22/31 (64.5%) patients achieved complete clinical remission, 8/31 (32.3%) showed a partial response and 1/31 (3.2%) had mild flair-ups.

After other 4 weeks (from week 7 to week 10) of the maintenance program, zinc pyrithione alone once a day two-three times a week, only 2 patients showed recurrences.

Adverse events, lesional/perilesional dryness and mild itching occurred in 4 patients (12.5%). These side effects improved throughout therapy by applying an emollient once daily. In this study no case of skin atrophy was reported.

Discussion

The present study wanted to evaluate the efficacy and safety of a combined formulation of zinc pyrithione 0.25% with betamethasone dipropionate micronized 0.05% in a base of isopropyl myristate in the treatment of mild to moderate plaque psoriasis. Psoriasis is a chronic life-altering disease, which often requires long-term topical therapy. Although patients treated were affected by plaque psoriasis, which may be considered a mild-moderate type of this disease, with a low PASI score at the baseline and more than 10% of body surface area involved; they had a strong will to achieve a better quality of life. There are multiple factors that encompass a clinical definition of severity issue that may not be based only on BSA.⁸

Topical zinc pyrithione treatment is an effective anti-itching, anti-flaking, anti-fungal and bacteriostatic agent for chronic skin conditions, such as seborrheic dermatitis and dandruff, eczema, erythema and mild to moderate plaque psoriasis.^{7,9}

Histopathology of psoriasis treated with zinc pyrithione was described by *Rowlands C.G.* and other authors whose purpose was to examine the histological changes induced by this drug, applied twice daily, in a well developed psoriatic plaque. After 2 weeks of treatment, histological features of psoriasis resolved completely. The mechanism of this normalization was unknown. However, hypotheses include blockage of cytokine and growth factor effect, disappearance of neutrophils and induction of apoptosis.^{10,11}

In our study, 32 patients were treated with zinc pyrithione combined with a mild steroid such as betamethasone dipropionate micronized 0.05%. This topical treatment was well tolerated in 31/32 patients and showed a high number of complete clinical remission, 40.6% and 64.5% respectively at visit 2 (2nd week) and at visit 3 (6th week). Only 4 cases of lesional/perilesional dryness.

The combination of zinc pyrithione 0.25% with betamethasone dipropionate micronized 0.05% in a base of isopropyl myristate is a new formula and first of its kind that exhibits a synergistic action with anti-inflammatory, bacteriostatic and anti-fungal properties which allows a shorter time of application for the patient with maximum absorption. It is thought that the zinc may be able to reduce epidermal proliferation. Although the exact mechanism of action of the “activated” zinc pyrithione preparation is unknown it may be speculated that the possible anti-proliferative mechanism of action involves the regulation of DNA transcription factors containing “zinc fingers” binding domains. It is also recognized that many enzymes require the binding of metal ions for activation, perhaps one of these “zinc requiring” enzymes or transcription factors plays a key role in the cell proliferation. It is also well known that a deficiency of zinc produces a disease state, acrodermatitis enteropathica, that includes psoriasiform lesions.

The particular use of a micronized form of this mild steroid is fundamental to insure positive results thus reducing the amount of topical corticosteroid. Therefore, the combined formulation used twice daily shows remarkable responses in less than 14 days of therapy and accomplishes it avoiding the negative effects associated with long term corticosteroid usage. Also the maintenance formula of 0.25% zinc pyrithione without the steroid showed a better absorption rate and quicker response time than other competitive products available on the market with a higher concentration (up to 2%) and indicated to treat dandruff and mild cases of seborrhoea. This capacity may be related to the specific isopropyl myristate vehicle utilized that permits a physiologic level of zinc to be reached at the target cells, either epidermal and/or lymphocytic.

The tolerability of a drug and its safety are fundamental for the success of a therapy. We report a great acceptance of treatment and an increase of patient's compliance due to ease of administration, quick drying capability, odor and stain free characteristics. Moreover, the maintenance product without the steroid had an important psychological effect on stress reduction, peace of mind and attitude towards such chronic disease.

Our findings suggest that zinc pyrithione 0.25% with betamethasone dipropionate micronized 0.05% in a base of isopropyl myristate is a new well tolerated topical treatment worthy of consideration for patients with mild to moderate plaque psoriasis.

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Competing financial interests

The authors declare that there are no competing financial interests.

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