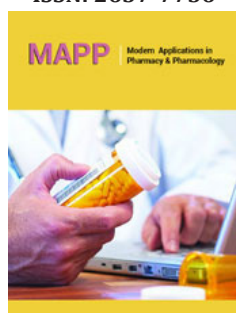


Treatment of Psoriasis: A Review on All Therapies

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Abstract

The Psoriasis is a noncontagious, chronic, immune-inflammatory, non-communicable, painful disease which affects the cutaneous parts of the body. Psoriasis affects the skin and nails and is associated with a number of comorbidities. Psoriasis is characterized by periodic episodes of red and scaly skin plaques that are sharply differentiated from adjacent normal skin. Near about 1-3% of the world population is affected by psoriasis, corresponding to about 125 million individuals. It affects the men and women of all ages, regardless of ethnic origin, in all countries. Psoriasis will also affect socioeconomic status of the people. In this we discuss the current treatment options of psoriasis. Finally, we will discuss the safety and efficacy of the complementary and alternative medicine in treatment of patients with psoriasis.

Introduction

What is psoriasis?

The Psoriasis is a noncontagious, chronic, immune-inflammatory, non-communicable, painful, disfiguring and disabling disease which affects the cutaneous parts of the body. Psoriasis involves the skin and nails and is associated with a number of comorbidities. Psoriasis is characterized by recurrent episodes of red and scaly skin plaques that are sharply demarcated from adjacent normal skin [1,2]. Psoriasis occurs worldwide. It can occur at any age and is mostly occurs in the age of 50-69 [3]. The most common type of psoriasis is chronic plaque psoriasis or psoriasis vulgaris [4,5]. However, the disease can also be classified into 4 different classes such as guttate, pustular, erythrodermic, and inverse psoriasis [6]. Near about 1-3% of the world population is affected, [7] corresponding to about 125 million individuals [8]. It affects men and women of all ages, regardless of ethnic origin, in all countries. In Spain, the estimated value of psoriasis cases was 1.4-2.7% by two telephonic surveys [9]. The word 'Psora' derived from Greek word which means 'to itch'. Psoriasis, a term which has been in use since 133AD, was originally grouped with leprosy until the 19th century. Psoriasis causes great physical, emotional and social burden. Quality of life, in general, is often significantly impaired. Additionally, it has a major impact on self-respect and quality of patient's life, and patients with moderate to severe psoriasis report a same quality of life to breast cancer or heart failure [10]. A notable proportion of the studies are performed to estimate the prevalence of diseases such as estimation of psoriasis have been conducted by means of surveys, studying only a group of the population that is good enough. Additionally, the geographic zone may alter psoriasis prevalence [11] and there are not many population-based studies of psoriasis epidemiology in gulf of sidra, where population diet and their habits could play a major role [12]. The estimated prevalence of psoriasis in countries extended between 0.09% [13] and 11.4% [14], making psoriasis a serious global problem.

The use of complementary and alternative medicine has an estimated prevalence of about 51% in patients with chronic psoriasis. Interest in alternative therapies for psoriasis stems from the high cost and side effects of topical and systemic treatments. Furthermore, Treatment of psoriasis is still based on controlling the symptoms. Topical and systemic therapies as well as, phototherapy is available which required more time, a combination of these methods is often used. So far, there is no known therapy that would give hope for a complete cure of psoriasis. The use of Herbs and Minerals in treatments as possible adjuvants to standard psoriasis treatments to achieve a long-term control [15]. In this review, we mainly discussed the clinical trials and briefly mention a few case studies which look into the use of dietary supplements, herbs, minerals, gluten-free diet, psychotherapy, meditation, and hypnosis for the treatment of psoriasis. The knowledge can help dermatologists to aware their patients who are interested in alternative remedies for psoriasis.

Current treatment options

Psoriasis can be treated by various traditional therapies such as topical, oral, biological and parenteral therapies. Phototherapy has also been used to provide symptomatic relief. But phototherapy is time consuming process.

Topical therapy: Topical therapy is easiest and more patient compliance treatment for psoriasis. The topical treatment of psoriasis is associated with irritation at site of application and generally provides moderately to unsatisfied therapy [16]. The majority of these patients have mild-to-moderate psoriasis which can be treated with topical agents which provide higher therapeutic efficacy with lower adverse effects as like systemic treatment. to the target tissue. However, in some cases, systemic delivery accompanied by topical treatment can prove to be beneficiary. There may be unwanted skin interactions due to topical applications such as irritation and burning at site of action, which may lead to patient non-compliance [17]. Anthralin is used in the treatment of psoriasis which act by lowers the keratinocyte proliferation, restores cell differentiation, prevents T-cell activation and probably through a mitochondrial dysfunction [18]. Additionally, production of free radicals may contribute to its effect. Salicylic acid also used as is a topical keratolytic agent and also been used topically for many years in the treatment of psoriasis. It can be used with TCS and calcineurin inhibitors to enhance the absorption of the latter in the psoriatic plaques. Calcineurin inhibitors are the substance which are approved for use in mild-to-moderate atopic dermatitis.

Oral therapy: Oral therapy used for the treatment of psoriasis generally contains drugs, which can be effectively delivered via the oral drug P system. The oral therapy is unsafe as compare to

topical treatment. Therefore, it is not widely used. In this drug is administered in monotherapy or in combination with biologics and also as phototherapy to reduce its side effects and to enhance the efficiency of drug substance. Oral therapy is mostly used in cases where topical therapy fails to exhibit improvement in symptoms. Some commonly used drugs in oral therapy are

a) Fumaric acid esters: Fumaric acid esters were first reported in treatment of psoriasis in 1959. It is a combined product of mono ethyl fumarate and dimethyl fumarate. These esters give mainly anti-inflammatory, antioxidative and antiproliferative property. Fumaric Acid Esters (FAE), also known as fumarates, these are the esters derived from fumaric acid. Fumaric acid is an intermediate in the Tricarboxylic Acid (TCA) cycle, which is a basic cellular process that occurs in mitochondria [19]. In 1959, the German chemist Walter Schweckendiek, who suffered from psoriasis himself, postulated that psoriasis occurred because of a deficiency in fumaric acid levels leading to defects in the citric acid cycle, and that oral supplementation of fumaric acid might overcome these defects [20].

b) Methotrexate: Dihydrofolate reductase enzyme is responsible for the synthesis of purines and pyrimidines at the time of DNA production, Methotrexate is an inhibitor of dihydrofolate reductase enzyme which inhibit the DNA synthesis. It is the traditional and a low-cost systemic drug for the treatment of mild to moderate psoriasis. It's active metabolite is polyglutamate analogs which exerts its anti-inflammatory effect, which in turn increase the level of adenosine, which has anti-inflammatory activity [21]. It reduces the hypertrophy of epithelial layers and enhanced apoptosis of T-cells [22]. It also acts as an anti-proliferating agent and immunosuppressive drug. Folic acid supplements are generally prescribed along with methotrexate to reduce it's side effects associated with the use. It causes liver toxicity on chronic use. Methotrexate has interactions with other drugs like, salicylates and antibiotics. Therefore, care should be taken while use in combination.

c) Biological therapy and parenteral therapy: In the last two decades, biological medications have become an important tool for care in treating moderate to severe psoriasis. Biologics are also given parentally to give a systemic effect. Generally, Biologics are glycoproteins and the living organisms are the source of biologics. These have an ability to interact with specified targets of the immunity system. Biologics are known to include antisense oligonucleotides, monoclonal antibodies, cytokines, fusion proteins, and RNA. The generally used monoclonal antibodies in treatment of psoriasis are ixekizumab, etanercept, infliximab, secukinumab, guselkumab, adalimumab, ustekinumab, and tildrakizumab. These biologically acting medications target various cytokines which is

responsible for psoriasis manifestations such as Tumor Necrosis Factor (TNF- α), interleukin-12, interleukin-23, and interleukin-17. It is a PEGylated TNF- α antibody, used in the treatment of moderate to severe plaque psoriasis and psoriatic arthritis. Another commonly used biologics are Ixekizumab and Brodalumab which are IL-17 Inhibitors.

d) Phototherapy: Long time ago, Phototherapy has been used for the treatment of skin disease. In ancient times, Egyptians were use sunlight in treatments of varieties of skin ailments, As well as the Romans and Greeks also used sunlight for therapeutic benefit [23]. Highly advanced uses of phototherapy, specifically for the treatment of psoriasis, have only occurred recently with remarkable developments in the early 20th century. In 1925, Dr. William Goeckerman described the advantages of using ultraviolet radiation in combination with crude coal tar in treatment of psoriasis [24]. Furthermore, In the 1950s, Dr. John Ingram developed a treatment schedule by using Ultraviolet B (UVB) radiation in combination with coal tar and anthralin paste [25]. In the 1970s, broadband UVB was discovered to be more effective in clearing mild forms of psoriasis when administered in doses, [26,27] while Ultraviolet A(UVA) radiation in combination with either oral [28] or topical application [29] of psoralen, was found to be highly effective in treatment of psoriasis. In 1980s, a more defined wavelength of UVB was discovered by researchers to be specifically effective in treatment of psoriasis and it was known to be narrowband UVB (nbUVB) [30,31]. Phototherapy becomes a one of the most common treatment options for psoriasis with narrowband UVB(nbUVB)and Psoralen Ultraviolet A (PUVA) as the most widely used [32]. Clinical studies have also demonstrated the effectiveness of phototherapy as one of the most effective treatment options, especially for patients with widespread disease which have moderate to severe psoriasis [33].

e) Complementary and alternative medicine: The use of complementary and alternative medicine has an estimated prevalence of about 51% in patients with chronic psoriasis. Interest in alternative therapies for psoriasis stems from the high cost and side effects of topical and systemic treatments. Forevermore, many traditional psoriasis treatments, such as phototherapy, required more time. The use of Herbs and Minerals in treatments as possible adjuvants to standard psoriasis treatments to achieve long-term control [34].

i. Capsaicin: Capsaicin (trans-/1-methyl-N -vanillyl-6-nonenamide)It is a active compound present in various species of Capsicum (chilli peppers) and that's a reason you feel a burning sensation when you eat food seasoned with chilies in concentrations less than 10⁻⁶M [35,36]. The ability to create a "burning" of cells might actually helps to heal the psoriasis flares. When you first time

applying capsaicin, you may experience an deep burning sensation at the site of application. But the patients in a successful treatment of psoriasis reported that the burning discomfort subsided when they kept using the capsaicin cream. It has also been reported that capsaicin affects on the microvasculature of the skin are likely associated to its depletion of substance P from local sensory nerve terminals [37-39]. Substance P is anuropeptide having a powerful vasodilating properties. Because initial vasodilation and leakiness of papillary vessels may be an important primary event in the development of psoriasis [40]. Therapeutic potential of topically applied CAP (trans-8-methyl-N-vanillyl-6-nonenamide) is attributed to the inhibition of cutaneous vasodilatation and blockade of the axon reflex vasodilatation produced by a numbers of ery the matogenic chemicals. Moreover, topical capsaicin is a powerful substance P depletory agent which act as an important factor in the pathophysiology of psoriasis [41]. However, topical use of capsaicin on human skin is restricted due to the induction of erythema assisted with sting, burning and pain sensations [42].

ii. Aloevera: Aloe vera is a plant known for its soothing and cooling properties. Aloe vera may also helps to regenerate the dead skin cells and heal the irritated skin. Aloe Vera plant has been used for array of ailments, which covers skin diseases. Current experimental research have proven the presence of biologically active components in the gel, but there are few controlled, clinical trials to rate the efficacy of aloe Vera gel. Paulsen et al. [43] performed a randomized, double-blind, placebo-controlled study on 41 individuals which suffer from stable plaque psoriasis. The study based on a 2-week wash-out period and subsequently, a 4-week treatment period with two times daily applications and check out visits after 1 and 2 months. Results of the whole study showed that the score sum of erythema, infiltration and desquamation decreased in the area which treated by Aloe Vera extract as compared with the placebo-treated areas. There is No serious side-effects were recorded. Although, 55% of the individuals records local side-effects, including drying-up of the skin on test areas. The efficiency of therapy with Aloe Vera gel was lower than treatment with placebo gel which is a substance that differed only from the Aloe Vera gel by the absence of the biologically active components [43]. The results of these trials proves that Aloe Vera can be used effectively in the treatment of a various skin disorders, such as psoriasis, vulvar lichen planus and nappy dermatitis.

iii. Curcumin: Curcumin is a polyphenol derived from the golden spice turmeric, which is broadly used as an alimentary addictive and culinary spice, make - up and, finally, as a natural product for the treatment of different diseases, particularly for the chronic inflammatory ones. Recently, curcumin has been suggested as a valid and safe therapeutic possibility for psoriasis. In the last few

years, the numbers of studies highlight the possible use of curcumin in the treatment of psoriasis. There is much evidence which underlined its therapeutic efficacy. Kurd et al. [15] Performed an analysis on 12 individuals with chronic plaque psoriasis were treated with 4.5g/d of orally administered curcumin for approximately 12 weeks. Eight individuals completed the trial. The intention to treat response rate was 16.7% and as treated response rate was 25%. After 12 weeks, the two patients who responded to treatment had a Physician Global Assessment (PGA) score of excellent (75 to 99% improvement) and experienced an 83% and 88% improvement in Psoriasis Area and Severity Index (PASI) scores, respectively [33]. The curcumin with its antioxidative properties may reduce the oxidative stress of psoriatic lesions on patients' skin [44,45]. Now, different reports shows that the therapeutic efficacy of curcumin might also be related to its ability in blocking the phosphorylase kinase enzyme, which generally increase in psoriatic patients [46,47]. Also, the result concluded by Varma et Al. [46] about the application of curcumin at the concentration of 25 and 50 μ M in the treatment of psoriatic. The authors explains that how the curcumin was capable of inhibiting the proliferation of psoriatic cell, by the downregulation of pro-inflammatory cytokines, such as tumour necrosis factor- α , interleukin-17, interferon - γ and interleukin-6. Besides, curcumin significantly stimulate the skin - barrier function by the up-regulation of Filaggrin (FLG) and Involucrum (iNV).

iv. Zinc: Zinc is a trace mineral which shows antioxidant, immunomodulatory, anti-inflammatory, and wound healing properties. The skin and appendages contain about 20% of total body zinc stores [48,49]. The concentration of zinc has been found to be decreased in the hair, serum, and urine in the patients with psoriasis. The skin scrape of psoriatic patients is cytologically similar to the scrapes experienced in the animals having inadequate amount of zinc such as parakeratosis and acanthosis [50]. There is a similarity between the patient with psoriasis and the animals having disease in zinc serum level (parakeratosis) [51]. Further it is known that by the addition of zinc in the diet of the animals the parakeratosis can be treated [50]. This observation lead us to initiate a program of trace metal treatment on these patients the preliminary results of which are presented in this communication [52]. Additionally, to this, review of the literature of past 40 years confirm our conception that the trace metals also be an important element in etiopathogenesis of psoriasis [53] and furthermore contribute significantly to the treatment of psoriasis.

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