Journal of Research in Medical and Dental Science
2022, Volume 10, Issue 8, Page No: 196-200

Available Online at: www.jrmds.in
eISSN No. 2347-2367: pISSN No. 2347-2545

Therapeutic Role of Methotrexate in Effective Treatment of Psoriasis: A Review

Shruti Udawant, Sarju Zilate*

Department of Pharmacology, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi, Wardha, India

ABSTRACT

Psoriasis is a prevalent autoimmune skin and joint disease that is chronic and recurrent. Plaque, guttate, inverted, pustular, and erythrodermic psoriasis are the five kinds of psoriasis. Psoriasis is ordinarily assumed to be an innate sickness welcomed on by environmental factors. If one of the twins has psoriasis, the other twin is more likely to be tormented than if the twins are identical. This shows that psoriasis is brought about by genetic variables. Side effects are bound to escalate in the colder time of year and when taking explicit prescriptions, like beta blockers or Nonsteroidal mitigating drugs (NSAIDs). Contaminations and mental pressure can likewise add to the condition. There have been many therapeutic approaches towards the treatment of psoriasis. But on review of various articles on psoriasis treatment we can depict that methotrexate is most prescribed first-line treatment for the condition psoriasis. Methotrexate (MTX), can also be called as amethopterin, is a chemotherapeutic medicine that suppresses immune system. In addition to other things, it's utilized to treat malignancy, immune system sicknesses, ectopic pregnancies, and clinical fetus removals. It is utilized to treat bosom malignancy, leukemia, and cellular breakdown in the lungs, lymphoma, pre-birth trophoblastic infection, and osteosarcoma, among different tumors. It is utilized to treat immune system infections like psoriasis, rheumatoid joint pain, and Crohn's illness. Methotrexate is normally used to treat severe psoriasis that has debilitating side effects. Additionally used to treat psoriasis that hasn't reacted to different medicines. It's normally recommended for a short amount of time, although it can be used for up to a year.

Key words: Psoriasis, Hyperproliferative, Skin disease

HOW TO CITE THIS ARTICLE: Shruti Udawant, Sarju Zilate, Therapeutic Role of Methotrexate in Effective Treatment of Psoriasis: A Review, J Res Med Dent Sci, 2022, 10(8):196-200.

Corresponding author: Sarju Zilate

e-mail✉: drsarjuzilate007@gmail.com

Received: 23-July-2022, Manuscript No. JRMDS-22-70053;

Editor assigned: 25-July-2022, **PreQC No.** JRMDS-22-70053(PQ);

Reviewed: 09-August-2022, QC No. JRMDS-22-70053(Q);

Revised: 13-August-2022, Manuscript No. JRMDS-22-70053(R);

Published: 22-August-2022

INTRODUCTION

What is psoriasis? Psoriasis is an ongoing, incendiary and hyper proliferative skin infection with a hereditary premise. Psoriasis has a variety of clinical cutaneous symptoms, although the most frequent are chronic, symmetrical, erythematous, scaling papules and plaques [1]. While epidermal hyperplasia and modified keratinocyte separation are conspicuous elements, extensive proof demonstrates that psoriasis is immunologically intervened [2]. Plaque, guttate, upset, pustular, and erythrodermic psoriasis are the five essential sorts. Psoriasis vulgaris, frequently known as plaque psoriasis, have approximately more than 90% of cases till date. The most well-known indications of this hyper proliferative skin disease are red patches with white scales on top. The backs of the lower arms, shins, navel region, and scalp are the most normally burdened spaces of the body. The injuries of guttate psoriasis are drop-formed. Little, noninfectious discharge filled rankles describe pustular psoriasis. Opposite psoriasis causes red regions in the folds of the skin. Erythrodermic psoriasis creates from any of different sorts of psoriasis when the hypersensitivity reactions like skin rashes becomes incredibly voluminous. Most people with psoriasis have fingernails and toenails that are affected eventually. There has been a great history of treatment of psoriasis. The great Hippocrates was the first medical practitioners to treat psoriasis with coal tar, also supported the use of topical arsenic. In 1920's arsenic became established as a popular treatment for psoriasis. Then in 1950's corticosteroids (a topical steroids) were found effective; Prednisolone and triamcinolone were both shown to be moderately effective when taken orally. Also methotrexate was used as first line of treatment

in early 1950's.In 1960's hydrocarbamide , in 1970's cyclosporine and PUVA, in 1980's Topical Vitamin D and Retinoids, and in 2000's T-cell targeted biologics and Tumour necrosis factor-α inhibitors are subsequently been used in treatment of psoriasis [3].

Current scenario of psoriasis treatment

Biologicals, small molecule inhibitors, enzyme inhibitors, and other innovative therapeutic approaches for psoriasis treatment are currently available. The FDA has recently approved Denilukin diftitox, Efalizumab, Alefacept, Ustekinumab, secukimab, and Etanercept [4]. Methotrexate is the highest prescribed drugas primary treatment of psoriatic arthritis (PsA) around the world, as well as psoriasis [5]. On review of various articles we assume that methotrexate can be a good option to treat psoriasis.

Objective

To review all the therapeutic approaches for the medication of psoriasis and the efficyivity of methotrexate in the complete therapy of psoriasis though being most potent anticancer drug.

Pharmakokinetic data of methotrexate

Bioavailability: 60% in smaller amounts, 40% in greater parts. Because of gastrointestinal ingestion restrictions, the bioavailability of MTX in greater oral dosages is reduced. Higher doses have been demonstrated to be controlled by either a considerable percentage of the oral component or parenteral administration. Both will result in improved bioavailability as compared to a single more conspicuous oral portion. 35-50 percent protein restriction (parent medication), 91-93 percent (7-hydroxymethotrexate). Hepatic and intracellular digestion Half-life of disposal: 3-10 hrs (smaller dosage), 8-15 hrs. (larger dosage) (higher portions) Urine output (80-100%) and fauces discharge (limited quantities) [6].

Role of methotrexate in other disorders

Methotrexate has been shown to help patients with psoriasis, atopic dermatitis, chronic urticaria, pemphigus vulgaris, bullous pemphigoid, cutaneous lupus erythematosus, cutaneous sarcoidosis, and mycosis fungoides [7]. Methotrexate is drug of choice in treatment of Rheumatoid arthritis [8]. Methotrexate is a form of antimetabolite which represses the ingestion of folate. Two particular pathways are viewed as engaged with malignancy and rheumatoid joint inflammation. Methotrexate represses dihydrofolate reductase (DHFR), a protein associated with tetrahydrofolate creation, as is compelling against disease. Methotrexate has a 1000-crease liking for the DHFR quality contrasted with folate. Dihydrofolate is changed over to dynamic tetrahydrofolate by the protein DHFR. Folic corrosive is vital for the all over again creation of thymidine, a nucleoside fundamental for DNA blend. Moreover, on the grounds that folate is needed for the assembling of purine and pyrimidine bases, blend will be eased back. Methotrexate, subsequently, stifles DNA union [9]. Methotrexate, a folic acid enemy, which is utilized for the therapy of different kinds of malignancy and is basically a well-known anticancer drug [10].

Role of methotrexate in psoriasis

Methotrexate has clinical benefits in the medication of some disorders because of its cytotoxic, anti-inflammatory, and immunological modulatory properties [11]. In psoriasis, innovative colloidal drug delivery methods of MTX, with a focus on the benefits of liposomal formulation, niosomal gel, hydrogel, albumin conjugates, nanoparticles, and nanostructured substances transporting lipids are reviewed [11]. Methotrexate, a traditional anti-psoriatic medicine, is still effective as single agent, in aggregation with few different systemic medications, especially as a rescue treatment or in combination with medicine.[12] According to study in some articles , Prior to methotrexate prescription, the normal length of psoriasis was 10 years, and the extent of absolute body covering before methotrexate treatment was 67.2 percent, and 5.2 percent after methotrexate treatment. While getting methotrexate, 61% of patients (118 people) acquired full psoriasis freedom [13].

Mechanism of Action of methotrexate in psoriasis

In normal as well as psoriatic skin, intradermal methotrexate suppresses the formation of DNA up to the duration of 12-16 hrs.It actuates all out limitation in psoriasis however just incomplete restraint in ordinary epidermis when managed intramuscularly [14]. Methotrexate is supposed to work by inhibiting DNA formation by inhibiting dihydrofolate reductase. Dihydrofolate reductase is required for the regeneration of reduced folate, which is needed in the DNA synthesis pathway for the production of precursors [15]. Low-dose MTX has an incomplete anti-inflammatory mode of action. The long-held belief that this disease-modifying anti-rheumatic medication (DMARD) works through the folate route does not appear to be true. MTX has recently been discovered to be a JAK/STAT pathway inhibitor. Methotrexates DMARD activity is most likely mediated by its suppression of the JAK/STAT pathway, while many of its side effects are likely linked to the folate system [16].

Dose of methotrexate in psoriasis treatment

Methotrexate now prescribed at a dosage of 7.5–25 mg per week. One time a week, in three divided doses at 12hour intervals, is the optimum dosage schedule. The medicine can be given subcutaneously, intramuscularly, or intravenously in a one weekly dose of 2.5–25 mg [17]. The segment that repeats week after week might irritate some people. A professional can recommend three 2.5-mg oral doses each week for their needs. These smaller servings should be consumed throughout a 12-hour period [18].

Folic acid supplement with methotrexate

Methotrexate may be a pteroylmonoglutamic acid antagonist that has been wont to treat response and inflammatory diseases for several years. Methotrexate

can cause severe adverse effects and toxicity in certain persons. Folate supplementation is frequently used to reduce methotrexate side effects and toxicity. Some studies show that taking folate supplements while taking methotrexate decreases toxicity and side effects while maintaining efficacy [19]. Regardless of pre-treatment folate levels, the antipsoriatic effect of amethopterin during the remission-induction phase of therapy is maintained by folic acid level and may be greatly decreased if additional treatment with Folic Acid is employed [20]. Skin specialist's were every less likely to include folate to their Methotrexate regimen. Supplementing with FA has conflicting evidence. The literature confirms that MTX has fewer side effects; however there is less evidence that it has less efficacy. Folate supplementation in methotrexate-treated indivisuals should be investigated, given the possibility that folate may diminish MTX efficacy [21] .GIT symptoms occur of times with immunosuppressant medical care for skin disease and may be controlled with vitamin B6 supplementation, apparently while not compromising the therapeutic effectivity of immunosuppressant [22].

Side effects of methotrexate

In psoriasis, methotrexate is by far the most commonly utilized cytotoxic medication. Pregnancy and alcohol misuse are absolute contraindications to treatment, which needs adequate kidney, liver, and bone marrow function. Serious side effects are known, although they can be avoided if the medicine is administered carefully. Hematopoietic and hepatotoxic side effects are the most common. Long-term methotrexate has been shown to cause liver damage that can progress to severe fibrosis or cirrhosis in a many patients. MTX-induced liver cirrhosis is not aggressive, according to recent investigations. A variety of medications can interact with each other, causing major difficulties in some cases [23].

Combination therapy with methotrexate in psoriasis

Acitretin and methotrexate are both effective treatments for psoriasis. However, due of the potential hepatotoxicity of the medication interactions, their combination has only been used in the treatment of psoriasis in a few cases. The aim of the study was to look into the effectivity of such a combination the treatment for psoriasis vulgaris, as well as the potential benefits and side effects that might occur during treatment. Thirty-nine individuals with psoriasis vulgaris were given acitretin, methotrexate, or a combination of the two drugs, or were given a placebo [24]. For the past two and a half years, individuals with severe erythrodermic psoriasis and pustular episodes have been treated successfully with a combination of methotrexate and exterminate. The psoriatic lesions have cleared up to a degree on this regimen, and there have been no serious adverse effects. Hepatotoxicity has not been discovered in either patient [25].

Treatment other than methotrexate in psoriasis

Psoriasis can show up as a few stable plaques or as an unstable illness that recurs quickly after therapy. Some individuals respond well to topical therapies, while others are difficult to maintain, displaying treatment resistance even to systemic medicines. As a result, a variety of treatments are available to tailor psoriasis treatment to the patient's specific needs. Surface treatments, such as vitamin D3 analogues and topical corticoids, are used to treat the great majority of patients. If the vitamin D3 treatment fails, tazarotene can be used as a substitute. Dithranol and tar therapy may be employed in some unusual circumstances. Individuals who don't react well to topical therapy might consider phototherapy with UVB and photo chemotherapy (PUVA). Chronic exposure to photo chemotherapy, in particular, does, however, raise the risk of photo carcinogenicity. In individuals who cannot be controlled with topical or phototherapy, systemic therapies such as methotrexate, cyclosporin, acitretin, and fumarates are recommended [26].

Methotrexate is contraindicated in

Patients which had unfavorably susceptible reaction for methotrexate ought not take it. In light of the expanded danger of teratogenicity and discharge into bosom milk, pregnant or nursing ladies ought to try not to utilize methotrexate. Patients with previous blood issues, for example, bone marrow hypoplasia, leukopenia, thrombocytopenia, or considerable frailty should utilize methotrexate with alert. Individuals with constant liver ailment, chronic hepatic inflammation, alcoholic hepatitis, or persistent liquor abuse ought not utilize methotrexate in the event that they have rheumatoid joint pain or psoriasis. Methotrexate ought to likewise be stayed away from if you have HIV/AIDS, blood dyscrasias, or kidney infection [27].

Saftey and efficacy of methotrexate in psoriasis

Background immunosuppressant (MTX) has been accustomed treat disease of the skin for over half a century. Even so, clinical information characterizing its efficaciousness and safety area unit thin. Objective so as to boost the out there proof, we have a tendency to conducted 2 meta-analyses, one for efficaciousness and one for safety outcomes, severally, in step with PRISMA listing [28]. Patients (matured 4-18 years) with serious plaque psoriasis who didn't reacted to effective treatment were arbitrarily relegated (1:1:1) to get adalimumab 0/8 mg/kg or 04 mg/kg subcutaneously at week 0, then, at that point, each and every other week beginning at week 1, or oral MTXonce week by week (01-04 mg/kg) for a long time utilizing an intelligent voice or web-reaction framework. With a three-block size, randomization was defined by history of etanercept treatment. In the event that illness became wild, responders were taken off treatment (for as long as 36 weeks) and yet again treated with adalimumab (for an ample of time). The extent of patients who worked on by at minimum 75% from gauge was positioned as an essential adequacy result [29].

Short term methotrexate therapy in psoriasis

The review checked out individuals who had constant unmanageable, erythrodermic, summed up pustular or serious palmoplantar psoriasis and were treated with methotrexate (MTX). MTX was regulated in a solitary oral week by week portion going from 3.75 to 30 mg, contingent upon body weight. MTX was likewise utilized securely in a objective was to pull out MTX as quickly as practical, fully intent on giving a medication free time of 4-6 months that corresponded with occasional abatements in sickness action. Up to 90% of patients could be off MTX in just 25 week [30].

Routes of administration of methotrexate

In people, the pharmacokinetics of i.v. furthermore, p.o. methotrexate (MTX) are depicted. The plasma fixation profiles following the two conveyance techniques were almost indistinguishable, with a mean last half-existence of 24.9 hours. At a portion of 30 mg MTX per sq m body surface region, triturated MTX is totally retained from arrangement. In the one patient who got the more noteworthy portion of 80 mg/sq m, just 31% of the sum was ingested. At 6% of the portion, the measure of metabolites created following i.v. organization is immaterial. Conversely, 35% of the assimilated measurement is disposed of as metabolites after p.o. organization. It is recommended that p.o. MTX is processed in the gastrointestinal plot or during the initial pass through the liver [31]. Methotrexate is available in 2.5 mg tablets for oral use and in 7.5, 10, 15, 20, or 25 mg preloaded needles for parenteral administration (subcutaneous or intramuscular). 50-mg vials for intramuscular infusion are also available. These can be fractioned into smaller doses, but it's important to remember that because of its deadly nature, caring for and removing MTX can be dangerous. The Methotrexate regimen, which has been used since the medicine was first approved for the treatment of psoriasis, has a modest week by week portion. 14 The weekly dose of 7.5 to 30 mg is handled on a single day or divided into three dosages and monitored over a 12-hour period [32].

Alcohol interaction with methotrexate

Methotrexate can cause liver challenges, and utilizing it with different medications that can hurt the liver, like ethanol, can aggravate the condition. While utilizing these drugs, you ought to keep away from or limit your liquor use. Pyrexia, chills, pain or swelling in joints, unusual drainage or injuries, skin rash, loss of appetite, fatigue, queasiness, heaving, stomach pain, decreased urine output, pale faecalis excreta, and yellowing of the skin or eyes should all be reported to your PCP as soon as possible. On the off chance that you have any various forms of feedback, converse with your PCP or drug specialist. It's basic to advise your PCP about any extra remedies you're taking, including nutrient enhancements [33].

Caffeine interactions with methotrexate

Restricted proof proposes that espresso utilization of in excess of 180 mg each day might decrease the adequacy of methotrexate (MTX) in rheumatoid joint pain patients. The particular technique for collaboration is obscure, but it very well may be associated with caffeine's adversarial impact on adenosine receptors, as MTX's mitigating activities are thought to be because of adenosine development. Patients with high caffeine admission (in excess of 180 mg/day) received fundamentally less effective response in morning firmness and agony of joints from standard than individuals with less coffee consumption (under 12 mg/day) in an investigation of few patients treated with methotrexate 7.5 mg per week (without folic acid supplementation) for a considerable length of time. There were no critical varieties in responses between patients who burned-through moderate measures of caffeine (120-180 mg/day) and the rest two gatherings. In a meeting of ninety-one individuals given therapy of methotrexate, 26% of individuals who stopped the medication were standard espresso consumers contrasted with just 2% of those actually getting the medication. Since treatment disappointment was the justification behind MTX end in 80% of individuals, the specialists proposed that coffee must be meddling with Methotrexate viability [34-39].

CONCLUSION

Methotrexate can be assumed as a ultimate treatment and is a protected and viable medication for the therapy of psoriasis and other chronic illness.

REFERENCES

1. Langley RG, Krueger GG, Griffiths CE. Psoriasis: Epidemiology, clinical features, and quality of life. Ann Rheum Dis 2005; 64:18-23.
2. Gudjonsson JE, Elder JT. Psoriasis: Epidemiology. Clin Dermatol 2007; 25:535946.
3. Reid C, Griffiths CEM. Psoriasis and treatment: Past, present and future aspects. Acta Derm Venereol 2020; 100:adv00032.
4. Rahman M, Alam K, Ahmad MZ, et al. Classical to current approach for treatment of psoriasis: A review. Endocr Metab Immune Disord Drug Targets 2012; 12:287-302.
5. Coates LC, Merola JF, Grieb SM, et al. Methotrexate in psoriasis and psoriatic arthritis. J Rheumatol Suppl 2020; 96:31-35.
6. Mager DR. Methotrexate. Home Healthcare Now 2015; 33:139-141.
7. Shah RA, Nwannunu CE, Limmer AL, et al. Brief update on dermatologic uses of methotrexate. Skin Therapy Lett 2019; 24:5-8.
8. Bianchi G, Caporali R, Todoerti M. Methotrexate and rheumatoid arthritis: current evidence regarding subcutaneous versus oral routes of administration. Adv Ther 2016; 33:369-378.
9. Dev S, McCallum RM, Jaffe GJ. Methotrexate treatment

for sarcoid-associated panuveitis. Ophthalmology 1999; 106:111.

10. Wei CW, Yu YL, Chen YH, et al. Anticancer effects of methotrexate in combination with α-tocopherol and α-tocopherol succinate on triple-negative breast cancer. Oncol Rep 2019; 41:2060-2066.
11. Rajitha P, Biswas R, Sabitha M, et al. Methotrexate in the treatment of psoriasis and rheumatoid arthritis: Mechanistic insights, current issues and novel delivery approaches. Curr Pharm Des 2017; 23:3550-3566.
12. Carretero G, Puig L, Dehesa L, et al. Guidelines on the use of methotrexate in psoriasis. Actas Dermosifiliogr 2010; 101:600-613.
13. Roenigk HH, Fowler-Bergfeld W, Curtis GH. Methotrexate for psoriasis in weekly oral doses. Arch Dermatol 1969; 99:86-93.
14. Weinstein GD, Goldfaden G, Frost P. Methotrexate: Mechanism of action on DNA synthesis in psoriasis. Arch Dermatol 1971; 104:236-243.
15. Czarnecka-Operacz M, Sadowska-Przytocka A. The possibilities and principles of methotrexate treatment of psoriasis-the updated knowledge. Postepy Dermatol Alergol 2014; 31:392-400.
16. Chan ES, Cronstein BN. Methotrexate—how does it really work?. Nature Rev Rheumatol 2010; 6:175-178.
17. Newburger AE, Weinstein GD, McCullough JL. Biological and biochemical actions of methotrexate in psoriasis. J Invest Dermatol 1978; 70:183-186.
18. Van Tyle JH. Ketoconazole: Mechanism of action, spectrum of activity, pharmacokinetics, drug interactions, adverse reactions and therapeutic use. Pharmacotherapy J Human Pharmacol Drug Therapy 1984; 4:343-373.
19. Strober BE, Menon K. Folate supplementation during methotrexate therapy for patients with psoriasis. J Am Academy Dermatol 2005; 53:652-659.
20. Chládek J, Simková M, Vanecková J, et al. The effect of folic acid supplementation on the pharmacokinetics and pharmacodynamics of oral methotrexate during the remission-induction period of treatment for moderate-to-severe plaque psoriasis. Eur J Clin Pharmacol 2008; 64:347-355.
21. Al-Dabagh A, Davis SA, Kinney MA, et al. The effect of folate supplementation on methotrexate efficacy and toxicity in psoriasis patients and folic acid use by dermatologists in the USA. Am J Clin Dermatol 2013; 14:155-161.
22. Duhra P. Treatment of gastrointestinal symptoms associated with methotrexate therapy for psoriasis. J Am Academy Dermatol 1993; 28:466-469.
23. Zachariae H. Methotrexate side-effects. Br J Dermatol 1990; 122:127-133.
24. An J, Zhang D, Wu J, et al. The acitretin and methotrexate combination therapy for psoriasis vulgarisachieves higher effectiveness and less liver fibrosis. Pharmacol Res 2017; 121:158-168.
25. Tuyp E, MacKie RM. Combination therapy for psoriasis with methotrexate and etretinate. J Am Academy Dermatol 1986; 14:70-73.
26. van de Kerkhof P, Vissers WH. Established treatments of psoriasis. Curr Drug Targets Inflamm Allergy 2004; 3:145-156.
27. Hannoodee M, Mittal M. Methotrexate. StatPearls 2021.
28. West J, Ogston S, Foerster J. Safety and efficacy of methotrexate in psoriasis: A meta-analysis of published trials. PloS One 2016; 11:e0153740.
29. Papp K, Thaçi D, Marcoux D, et al. Efficacy and safety of adalimumab every other week versus methotrexate once weekly in children and adolescents with severe chronic plaque psoriasis: A randomised, double-blind, phase 3 trial. Lancet 2017; 390:40-49.
30. Kumar B, Handa S, Kaur I. Short term methotrexate therapy in psoriasis. Indian J Med Res 1994; 100:277-280.
31. Wan SH, Huffman DH, Azarnoff DL, et al. Effect of route of administration and effusions on methotrexate pharmacokinetics. Cancer Res 1974; 34:3487-3491.
32. Carretero G, Puig L, Dehesa L, et al. Guidelines on the use of methotrexate in psoriasis. Actas Dermo Sifiliográficas 2010; 101:600-613.
33. https://www.drugs.com/disease-interactions/methotrexate,methotrexate-lpf-sodium.html
34. Nesher G, Mates M, Zevin S. Effect of caffeine consumption on efficacy of methotrexate in rheumatoid arthritis. Arthritis Rheum 2003; 48:571-572.
35. Thakre PP, Deshmukh S, Ade V. A case study on plaque psoriasis with ayurvedic management. Int J Ayurvedic Med 2020; 11:342-345.
36. Kute PK, Muddeshwar MG, Sonare AR. Pro-oxidants and anti-oxidant status in patients of psoriasis with relation to smoking and alcoholism. J Evol Med Dent Sci 2019; 8:2677-2681.
37. Hirapure AS, Deshmukh S, Thakre T. Management of palmo-plantar psoriasis by classical shodhan and shaman chikitsa-A case report. Int J Ayurvedic Med 2021; 12:166–170.
38. Murray CJ, Abbafati C, Abbas KM, et al. Five insights from the global burden of disease study 2019. Lancet 2020; 396:1135-1159.
39. Vos T, Lim SS, Abbafati C, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: A systematic analysis for the global burden of disease study 2019. Lancet 2020; 396:1204-1222.