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Novel Regimens for Treatment of Psoriasis

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ABSTRACT

Psoriasis is a dermatological disorder consists of abnormal multiplied skin cells than normal one. It causes the thickness of skin is increased and forms a red patches and white scales in the lesion. The disease causing several adverse problems in patient's i.e. adverse physical and mental conditions that are same to malignancies, heart disorder, diabetes mellitus, and depression. This review focus on the novel therapies for psoriasis that have emerged recently. It contains different classes of drugs (local, systemic) with different mechanism of action. Psoriasis cure rate is very low, so this regimens goal is to relieve symptoms as long as possible with a good benefit/risk ratio. In this review, the new regimens that target pathways and other steps in the pathogenesis of psoriasis are discussed, including IL12/IL-23, IL-17, IL-22, TNF-∝, JAK inhibitor etc.The prevalence of disease in worldwide is 0.6 to 4.8%. Cyclosporine and methotrexate are the example of systemic treatment regimen for the management of psoriasis but their toxicity is very high, nephrotoxicity, hepatotoxicity and pulmonary fibrosis are the toxicities of methotrexate and cyclosporine. But in the case of novel regimens the toxicity is very low as compared to existing regimens. This article was designed to compare the treatment efficacy of novel regimen with already available treatment options for psoriasis.

Keywords: Cyclosporine, Methotrexate, Psoriasis, JAK inhibitor, TNF-∝, Interleukin,

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INTRODUCTION

Psoriasis is a chronic dermatological disorder produced by a hyperactive auto immune system. Flaking, inflammation of skin, thickening of skin, formation of white silvery and red patches on the skin is the symptoms of psoriasis. The prevalence of disease in worldwide is 0.6 to 4.8%. The disease causing several adverse problems in patients i.e. adverse physical and mental conditions that are same to malignancies, heart disorder, diabetes mellitus, and depression. The disease are classified into plaque, gestate, pustule, and erythrodermic psoriasis.

This common dermatitis is extremely variable in clinical manifestations by morphology and extent of involvement, ranging from innocuous lesion to widespread life threatening pustule and erythrodermic forms. It can affect any area including palms, soles and genitalia. Several treatment modalities are currently available and many guidelines have been formulated all over the world. The treatment is mainly suppressive aimed at inducing remissions and improving the patient's quality of life. [1]

Routinely for limited psoriasis, coal tar, topical corticosteroids, dithranol, calcipotriol and topical photochemotherapy are administered. For extensive psoriasis UVB, PUVA, PUVASOL, methotrexate, hydroxyurea, acitretin and cyclosporine are preferred. Disease modifying agents such as etanercept, infliximab and other biological may be required in resistant cases.

The immune system involved a major part in the development of psoriasis, this concept utilized to the discovery and development of several novel regimen for the treatment of psoriasis, i.e. which drug that target to the IL-17, IL-23 and drug that are involved in intracellular signaling pathways i.e. Janus Kinase (JAK) inhibitor and phosphodiesterase-4 (PDE-4) inhibitor.[1]

This article was designed to compare the treatment efficacy of novel regimen with already available treatment options for psoriasis.

NOVEL REGIMENS

1. JAK inhibitor JTE-052:

Janus kinases (JAKs) are involved in progression of psoriasis. They are act by included in several inflammatory cytokine signaling pathways in psoriasis. So JAK inhibitors considered as a most important therapeutic option for psoriasis. JAK inhibitor like JTE-052 inhibitsthe type 1 T helper cells, type 2 T helper cells and type17 T helper cells immune responses. These responses are involved in chronic dermal diseases. [2]

JTE-052 inhibits the skin inflammation and suppresses the inflammatory cell activation in various type of psoriasis. The efficacy of oral JTE-052 is very rapid in skin inflammation compared to oral cyclosporine and methotrexate in psoriasis.[3]

Cyclosporine and methotrexate are the example of systemic treatment regimen for the management of psoriasis, but their toxicity is very high, nephrotoxicity, hepatotoxicity and pulmonary fibrosis are the toxicities of methotrexate and cyclosporine so their usage is limited. But in the case of JAK inhibitor there have a no reports of organ toxicities. So JAK inhibitors are therefore most important systemic therapeutic option for psoriasis, with fewer side effects than other systemic therapies.[4,5]

***2. Tetherin, Type I interferon biomarker and Ustekinumab, an interleukin 12/23 p40 monoclonal antibody*:**

Tetherin is a novel type I interferon biomarker also known as bone marrow stromal antigen 2 is a protein in human it encoded by the BST2 gene. It act on the blood leukocytes and trapping interferon level and combining with Ustekinumab an interleukin 12/23 p40 monoclonal antibody, is used in the treatment of psoriasis. Ustekinumab is interfering with triggering of the inflammatory responses in psoriasis by suppression of certain cytokines in the body, i.e. it blocks the interleukin12 /23 which help in activation of certain T-cells.[5,6]

3. Human interleukin-23 monoclonal antibody – Guselkumab:

Generalized pustular psoriasis (GPP) and Erythrodermic psoriasis (EP) are rare severe types of psoriasis and their treatment is very difficult. So guselkumab is very effective in this subtype of psoriasis.

Guselkumab selectively inhibits Interleukin -23 by specifically binding with P^{19} subunit. Interleukin-23 is an inflammatory cytokines, it stimulate the CD4 and T-helper cells and involved in inflammatory processes and induces psoriasis plaque formation. Guselkumab proved symptomatic improvements in psoriasis patients. Elevated levels of IL-17A, T-helper-17 producing cells in skin lesion are reported in patients with GPP and EP. IL-23 blocking by guselkumab may result in inhibiting the level of Th17 cells and IL-cells in psoriasis patients.[7,8]

The mechanism of action of guselkumab is selectively blocking the interleukin 23. It may result in preventing the action of pathogenic T-helper cells and decreasing the level of IL-17A in skin lesion.[9,10]

4. Indirubin: A new topical traditional Chinese medicine:

Indirubin is a active constituent of Indigo naturalis, is a Chinese herb also known as Qing Dai. Recent clinical studies demonstrated that they are effective in mild to moderatepsoriasis. They are effective in psoriasis by which preventing the proliferation of cells and inducing cell differentiation. By interacting with aryl hydrocarbon receptorthey inhibit cell-cycle-related kinases and cell signalingproteins such as STAT3. It also inhibitsinterferon-γ is a pro inflammatory cytokines.[11]

Indirubin is administered as topical, and they aremore safe and effective therapy than topicalcorticosteroids in the treatment of psoriasis and not required safety concerns comparing with topically administered corticosteroids. Indirubin effective in psoriasis by different mechanism of actionand totally different from other topical therapies.[12]

5. Syl930 –A newly developed sphingosine -1-phosphate (SIP_1) modulator:

A newly developed sphingosine-1-phosphate (SIP_1) modulator Syl930 is studied and used in psoriasis patients. The orally administered Syl930 inhibits proliferation and inflammation in psoriasis patients. So we reveal that Syl930 is an important treatment option for psoriasis.

Activation of SIP_1 contributes to the immune reaction by recirculation of lymphocytes.SIP also inhibitsepidermal cells growth and it leads to keratinocytes differentiation. So SIP_1 signaling pathway is promising treatment option for psoriasis treatment.[13,14]

Syl930 is studied in various animal models for demonstrating their effects in psoriasis treatment.

i. In sodium lauryl sulphate applied mouse skin irritation model:

This animal model mimics the early skin symptoms of psoriasis. Topically applied SLS in mice increase then thickness of the skin due to inflammation. Oral administration of Syl930 decreases the thickening of skin of mice. So it's strongly supporting the Syl930 in the treatment of psoriasis.[15,16]

ii. In mouse tail assay:

In psoriasis patients changes in skin including hyperkeratosis and loss of granular layer. The orally administered Syl930 elevate the granular layer scales compared to the control group in the study.

iii. In propranolol treated Guinea pig psoriasis model:

Both ears of guinea pig were treated with 5% propranolol solution twice a day induce psoriasis, it leads to elevatedPara keratosis, acanthuses, diminished granular layer and elongation of rete ridges and dilated capillaries are seen in ears of guinea pig.so Syl930 at a dose of 1.0mg/kg reduced the Para keratosis and acanthosis, and increased granular layer and decreased thickening in the epidermis.[17]

6. Ixekizumab:

Ixekizumab (IXE) is a monoclonal antibody it selectively bindsand blocks IL-17A, and is discovered and used in the treatment of psoriasis. Ixekizumab have good safety and efficacy profile compared to other biological in the treatment of psoriasis. Itadministered as a subcutaneous injection and rapid clinical improvement in psoriasis.[18]

Ixekizumab is the humanized monoclonal immunoglobulin G(IgG) that act by specifically targetting and inhibiting IL-17A and it lead to the inhibiting inflammatory changes in psoriasis patients. Psoriasis patients have elevated levels of IL-17A.[19,20]

CONCLUSION

Treatment for psoriasis is more important in psoriasis patients, because patients are depressed due to abnormal appearance and texture of their skin, so they are less likely

to be involved in other activities due to stress and depression.These novel regimens offer patients and their caregivers the prospect of more targeted therapeutic regimens that offer enhanced clinical outcomes with more favorable side-effect profiles. As clinicians and researchers build upon this knowledge in the years to come, we can offer psoriasis patients an increasingly diverse and powerful therapeutic armamentarium.

CONFLICT OF INTEREST

Nil

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