Treatment of Psoriasis: An Update
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Introduction
Psoriasis is one of the oldest disease of mankind, history goes as hack as 500 B.C. was known as psoralepra and in 19th Century named as Psoriasis as a separate entity.

Psoriasis is a chronic relapsing disease with dull silvery scales on the lesion which usually involve extensors and complicated type are pustular and erythodermic and psoriatic arthritis.

Recently much has been learned about the pathophysiology of psoriasis, and as a result, traditional treatments such as coal tar have been joined by immunosuppressive.

Once considered a hyperproliferative disorder, psoriasis is now recognized as an autoimmune disease involving activation of T cells. As a result, new immunosuppressive agents have significant role in treatment.

During the past decade, investigators have demonstrated that the immune system plays an integral role in the pathogenesis of psoriasis. Activation of T cells, specifically CD4 cells, induces the release of interleukin-2 and alpha interferon, which induce hyperproliferation of keratinocytes.

Although there is no clear inheritance pattern, patients with psoriasis often have a family history of the disease.

Exogenous factors may also play a role. Human papilloma virus and streptococcus can evoke a psoriatic response,

A few medications can trigger the onset of psoriasis, including beta-blockers, lithium, nonsteroidal anti-inflammatory agents, and also corticosteroid withdrawal rebound can provoke Psoriasis.

Management of Psoriasis
Patient should have a total idea about his illness including line of treatment and prognosis of the disease. Treatment planned and prognosis should be explained to the patient.

Psoriasis has got multiple modalities of treatment are widely practiced now topical, systemic, phototherapy, climate therapy and few unusual treatment are practiced.

Topical therapy is generally indicated when psoriasis is limited to less than 20% of the body surface. Agents used include emollients, keratolytics, corticosteroid ointments or creams, coal tar, anthralin, calcipotriene-taza-rotene. and tarcolimus these are used either single and combination.

White petrolatum jelly used as a emolient till the date for its soothing and mild keratolytic properties.
Coal tar has been used to treat psoriasis for very long time though; its mechanism of action is still not well understood. Some studies have shown that coal tars inhibit DNA synthesis, thus acting as a cytostatic and immunomodulator. It is used in combination with ultraviolet B (UVB), 1% crude coal tar in a hydrophilic ointment is applied to the skin before daily phototherapy with minimal erythemal doses of UVB.

Combination reduces the total dose of ultraviolet radiation needed to clear psoriasis; still, the therapeutic effectiveness of this regimen is not significantly superior to that of ultraviolet radiation or tar alone.

Anthralin in paraffin is used for short-contact therapy to minimize irritation of normal skin. This method involves progressive concentrations ranging from 0.05% to 0.5%; dosage is increased according to patient response. The preparation is applied once or twice a day for 10 to 20 minutes. It should be removed using cotton wool soaked in oil or a mild detergent, followed by showering or bathing. Treatment with anthralin can clear psoriasis leaves a deep brown stain. Topical corticosteroids are the most widely used treatment for psoriasis, because of their short-term efficacy, high degree of patient acceptability, and relatively low cost. Patient compliance is better than with other topical agents since steroids do not irritate or stain the skin.

Usually potent steroidal agents, are used although milder used for intertiginous areas, such as the axilla or groin. The efficacy topical steroids can be improved by applying a plastic occlusive film over the ointment. A preparation of 0.12% betamethasone valerate was recently approved for the treatment of scalp psoriasis. It has foam base that liquefies on contact with the skin, depositing the steroid on the scalp. Long-term therapy with topical corticosteroids can cause thinning of the skin, striae, telangactasia, purpura, masking of local infections, hypo pigmentation and tachyphylaxis, prolonged use of topical corticosteroids may result in hypothalamic-pituitary adrenal suppression, particularly in children.

Calcipotinol a vitamine D analogue, Ointment does not stain clothes, but it is mildly irritating especially on the face and hypercalcemia has been reported after application of twice the recommended maximal weekly dose of 100 gm. Calcipotinol should he used with caution in the elderly and in patients with impaired renal function.

Tazarotene, available in 0.5% and 0.1% gels, is topical retinoid that was recently introduced for treatment of psoriasis. Although tazarotene has the advantage of not being a corticosteroid, it can irritate normal skin, causing purpura and erythematous. Comparison of tazarotene with the corticosteroid fluocinonide has
shown that tazarotene induces longer remission. Among patients with initially successful treatment (50% or greater clearing of psoriasis), relapse occurred within three months of discontinuing treatment in 55% of patients treated with flucinonide, 37% of those treated with tazarotene 0.05% gel, and 18% of the.

**Combined Topical Therapy**
A mixture of 10% salicylic acid and clobetasol ointment has been found to be highly effective; salicylic acid enhances penetration of medication. The combination of calcipotriene and the steroid applied once a day appears to be superior to either agent applied twice a day. Sequential use of topical corticosteroids and tazarotene may decrease the skin irritation commonly seen with the latter agent may prevent steroid-induced cutaneous atrophy. Some agents should not be combined, Mixing salicylic acid with calcipotriene results in complete inactivation of calcipotriene; combined clobetasol and hydrocortisone valerate results in marked deterioration of calcipotriene within a few days.

In addition to coal tar, other topical agents can be combined with phototherapy. When topical calcipotriene is applied after treatment with psoralen methoxalen plus ultraviolet A (PUVA) or UVB, psoriatic lesions are cleared more rapidly and a lower total dose of radiation is needed. The effects of tazarotene are also enhanced when combined with UVB or UVA. Pulse therapy with calcipotriene twice a day on weekdays in conjunction with clobetasol propionate twice a day on weekends may be used to maintain remission after psoriasis has been brought under control.

**Phototherapy and Systemic Treatments**
Systemic treatment should be reserved for patients with physically, socially, or economically disabling psoriasis that has not responded to topical treatment. Approximately 20% of psoriasis disabling psoriasis that has not responded to topical treatment, either drug or phototherapy more aggressive therapy may be indicated when the disease involves more than 20% of the body surface. The risk: benefit ration for systemic treatment should be determined in each patient. Broad-band-UVB (wavelengths of 290 to 320 nm) phototherapy has ion had a major role in the management of moderate-to-severe generalized psoriasis. UVB irradiation may be used alone or in combination with coal tar UVB immunotherapy is effective for moderate psoriasis (<10% of body surface) that has not responded well to topical therapy. It clears 60% to 80% of lesions.

Narrow-band UVB (TIL-01) phototherapy, which requires a 311 nm irradiation ultraviolet bulb, is seeing increased use in the United States. Studies have shown that narrow-band UVB phototherapy is more effective than broad-band UVB, although narrow-band therapy requires longer exposure time. Narrow-band therapy is less effective than PUVA. prospective follow-up studies are required to assess the long-term risks of narrow-band UVB radiation.

PUVA combines ultraviolet A phototherapy (wavelengths of 320 to 400 nm) with psoralen methoxalen, Methoxsalen, which causes photosensitization, si taken orally two
hours before UVA exposure. PUVA’s proposed mechanisms of action include
1) intercalation of methoxsalen into DNA, forming cross-links between DNA strands that interfere with DNA synthesis and block cell proliferation, and 2) suppression of cell-mediated immune responses in involved skin. Candidates for PUVA include patients who have not responded adequately to topical therapies or UVB, and those in whom the disease effects at least 20% of the body surface. PUVA is highly effective, inducing remission for approximately one year compared with the six months typically seen after broad-band UVB. In more than 85% of patients, skin lesions disappear after 20 to 30 photochemotherapy treatments.

PUVA therapy is usually administered two to three times per week. Maintenance therapy is less rigorous, often involving only one treatment every two to four weeks, with eventual discontinuation of treatment.

The short-term side effects of PUVA include nausea in 15% of patients. Burning or severe pruritus may problems and depend on the cumulative UVA dose. In one study, one or more squamous cell carcinoma developed in 8% of patients who received 2,000 to 4,000 joules and in 15% of those who received 4,000 joules. There are no data regarding the number of PUVA treatments at which the risk of melanoma begins to increase substantially. To reduce the risk of genital skin cancer in men, it is important to shield unaffected parts of the genitalia during treatment and to minimize UVA exposure to the affected areas. After 150 PUVA treatments, patients should be switched to oral therapy.

Bath PUVA therapy has been suggested as a potentially safer alternative to conventional PUVA. In this method, a lotion or emulsion containing trimethylpsoralen or 8-methoxypsoralen is applied to the skin five minutes to two hours before UVA radiation. The treatment protocol is otherwise similar to conventional PUVA. Bath PUVA may avoid the nausea associated with systemic psoralen; it is preferred for localized psoriasis, especially on the palms and soles. Disadvantages include the risk of severe local phototoxic reactions and patchy pigmentation.

Retinoids, vitamin A metabolites have proven themselves in the treatment of psoriasis. Acitretin has become the retinoid of choice. Acitretin has more favorable pharmacokinetic properties,
including a significantly shorter elimination half-life. The optimal dose range for monotherapy is 25 to 50 mg a day, starting at 10 to 25 mg a day and escalating as needed to enhance efficacy. The overall rate of complete remission is generally less than 50%. Higher doses (50 to 75 mg/day) result in more rapid and possibly more complete responses but are associated with significantly more frequent side effects.

Acitretin monotherapy is most effective for pustular and erythrodermic psoriasis. Combination regimens with other systemic agents or UV radiation are generally preferred for plaque psoriasis; in these cases, it is even more advantageous to start with lower doses of acitretin (10-25 mg/day).

Oral retinoids are highly teratogenic. Contraception is mandatory for all women of childbearing potential for one month beginning acitretin therapy, during therapy, and three years after therapy. Other potential side effects of acitretin include hair loss, pyogenic granuloma formation, thin nail plates, onychomadesis, rhinitis and cheilitis, photosensitivity reaction, xerophthalmia, and thin nail plates. Methotrexate. Dermatologists have used methotrexate in the treatment of severe cases of plaque, erythrodermic, and pustular psoriasis for more than 30 years. Methotrexate inhibits the enzyme dihydrofolate reductase, which is necessary for nucleotide and amino acid synthesis. Thus, the drug decreases DNA synthesis and so inhibits mitosis and cell proliferation in rapidly dividing cells. It also affects the immune system by altering lymphocyte and monocyte activity cytokine production, and neutrophil function.

Cyclosporine is a fairly recent addition to the psoriatic armamentarium. The immunosuppressant inhibits interleukin-2 production, thereby suppressing T cell-mediated immunity. Clearing of lesions begins as early as two weeks after the start of treatment at a dosage of 2.5 to 4 mg/kg/day given in two divided doses.
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and considerable improvement occurs in most patients by week 12. The patient should be kept on the 2.5 mg / kg / day at two-week intervals based on clinical response and tolerability.

Baseline monitoring should include a complete history, physical examination (including two measurements of blood pressure), chemistry screening, complete blood count, and two measurements of the serum creatinine level. Follow-up monitoring is performed every two weeks for the first two to three months of therapy, then monthly thereafter. The dosage should be reduced if the serum creatinine increases 30% above the baseline level.

In addition to nephrotoxicity, major side effects of cyclosporine include hypertension, hirsutism, and gingival hyperplasia. The development of lymphoma has been reported. Patients should not be treated with cyclosporine for more than one year at a time. Intermittent short courses of cyclosporine are safe and effective for clearing moderate to severe psoriasis and may induce prolonged remission in some patients.

Tacrolimus (Fk-506) has a mechanism of action similar to that of cyclosporine. In a double blind, placebo-controlled European multicenter trial, oral tacrolimus was effective in the treatment of redacitrant plaque psoriasis at a daily dose of 0.1 to 0.15 mg/kg. The most common side effects were paresthesias and diarrhea. The same monitoring guidelines used for cyclosporine apply. Topical tacrolimus is not effective for psoriasis.

Hyoxuurea, although of limited benefit as monotherapy, hydroxyurea may provide enhanced efficacy when used in combination with retinoids or phototherapy. Its major dose-limiting side effect is bone marrow suppression.

Thioguanine. The antimetabolite 6-thioguanine has reported to be efficacious in patients with severe psoriasis. Because of the risk of myelosuppression, a complete blood and platelet count should be obtained every two weeks, and every week when the dose is increased. The drug should be discontinued if the platelet count falls below 125,000 /pL or the white blood cell count below 4,000/mm³.

**Combined Systemic Therapy**

Some patients eventually require combination therapy with various agents to maintain adequate clearing of their psoriasis. Several combinations have proved effective in such cases.

**Combination Systemic Treatments for Psoriasis**

- Methotrexate + Phototherapy (PUVA or UVA)
- Methotrexate + Topical Corticosteroids
- Methotrexate + Acitretin + Phototherapy (PUVA or UVA)
- Hydrothrotrexate + Acitretin + Phototherapy (PUVA or UVB)

Unusual treatment: Antimicrobials sometimes help in remission of psoriasis:

Surgery: Tonsillectomy may help in guttate psoriasis of children. Electrogasulation, Gyotherapy and Laser also may help.
Mentioned, there is evidence that streptococcal antigens can trigger an immune cascade that leads to the development of psoriasis. Consequently, a prospective, controlled study is being conducted to determine the efficacy of oral clindamycin for the treatment of the disease. The increased expression of angiogenesis factors in psoriatic lesions has led to the investigation of angiogenesis-blocking therapy with shark cartilage extract. The treatment has shown only modest results.

Several new biotechnological therapies that target the immune system are currently being investigated for psoriasis. These include fusion proteins, monoclonal antibodies, cytokines, T-cell receptor vaccines, and gene therapy: Fusion Proteins. The fusion protein DAB 391 L-2 consists of interleukin-2 attached to diphtheria toxin. DAB 391 L-2 binds specifically to high-affinity receptors on activated T cells. After binding it enters the cell and the toxin detaches, resulting in cell death. LFA3TIP, a fusion of the protein LFA3 and Fc fragment of a human IgG antibody, blocks CD2 receptors on the surface of T cells, thereby preventing the co stimulatory signals necessary for T-cell activation. The fusion protein CTLA4-Ig also inhibits costimulatory signals but acts at CD28 receptors on T-cells. Monodonal Antibodies. A preliminary study indicates that a monoclonal antibody directed against T cells, anti-CD1 1 a, may be useful for psoriatic. Monoclonal antibodies that block activation of C 134 T cells are also being developed.

Cytokines
Various cytokines involved in the regulation of the immune process are being targeted as potential treatment for psoriasis.

Gene Therapy
Chromosomes involved in psoriasis have already been mapped, and more genes involved in the expression of psoriasis are being identified. Gene therapy promises to be one of the most important areas of treatment of psoriasis in the new millennium.

Reference
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