TREATMENT OF PSORIASIS - NEWER CONCEPTS

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Summary

Various old and new modalities available for the treatment of Psoriasis are discussed. Advantages and disadvantages of various preparations are highlighted to help the treating dermatologist in making a choice from among these. Experience with various dilutions of dithranol in treating rather resistant disease is presented. Advantages of dithranol over other forms of treatment in selected patients are convincing.

KEY WORDS: Psoriasis, Dithranol, Coal tar, PUVA, Methotrexate.

Psoriasis is a chronic inflammatory disease of the skin, characterised by well defined erythematous plaques covered with silvery scales. Estimated 1-2% Caucasians suffer from psoriasis. Onset may be at any age but is rare before the age of 3 with a peak incidence in the 15 to 40 years age group. Both sexes are equally affected. Aetiology of psoriasis is multifactorial. In some patients there is a genetic predisposition to the disease though generally the disease appears following some additional assault, like infection, trauma, ingestion of drugs, endocrine, metabolic or emotional factors. The genetic susceptibility is suggested by a significant increase in the frequency of HL-A antigens in B_{13}, BW_{16}, BW_{17}, CT_7 and DMA in patients with psoriasis[1,2]. The basic abnormality in psoriasis is increased epidermal cell proliferation, nearly 10 times more than in the normal epidermis. Voorhees et al 1973[3] found low levels of cyclic AMP and high levels of cyclic GMP in psoriatic epidermis and proposed that enhanced cellular proliferation is the result of altered ratio of the two enzymes.

Immunological studies in psoriasis have shown inconsistent results among the various workers in this field. However most studies have shown decrease in circulating T-lymphocytes. Antibodies directed against the stratum corneum have been found with complement in psoriatic lesions in vivo[4]. A significant rise in the mean serum level of IgG and IgA have also been documented.

Many morphological variants of psoriasis are recognised, such as plaque, flexural, guttate, palmo-plantar, erythrodermic, arthropathic and pustular (localised and generalised). The erythrodermic, arthropathic and pustular forms of psoriasis require careful and intensive management. Other skin and systemic diseases may co-exist or alternate with psoriasis e.g. seborrhoeic dermatitis, lichen planus, lichen

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simplex chronicus, eczema, arthritis, gout, diabetes mellitus, hypocalcaemia, intestinal disease and malabsorption.

The course and prognosis of psoriasis remain as unpredictable as it was a century ago. All forms of psoriasis are troublesome and often the disease is intractable but it is rarely fatal.

In the management of the disease reassurance that it is not infectious and not related to malignancy is often helpful. It is worth emphasizing that spontaneous resolution does occur and that treatment can do a lot to improve the disease although cure is not possible. Fear for the future of children may be allayed and the patient may be enlightened with available knowledge related to genetic predisposition.

Treatment must always be appropriate to the severity of the disease and the extent of importance the individual attaches to it. Treatment should not be unpleasant or dangerous than the psoriasis itself and its complexity must be appropriate to the patients' intelligence, occupation, social and economic background. Evaluation of the daily routine of the patient and suggestions regarding reducing stresses and a holiday in sunshine often helps both the skin and the psyche. Diet is irrelevant. In all forms of unstable, pustular and erythrodermic psoriasis, rest in bed, preferably in a hospital is imperative. Elimination of obvious infection or correction of metabolic disorders is necessarily of value.

Topical Therapy

Various preparations used include the following :-

1. Bland preparations
2. Salicylic acid
3. Coal tar derivatives
4. Dithranol
5. Topical corticosteroids
6. Short wave ultraviolet light (UVB).

Choice of topical agents depends on the site, size and thickness of the psoriatic plaques. Dithranol is feasible and appropriate where large and few plaques need to be treated. For smaller and numerous lesions tar or corticosteroids are good options. UVB is often used as an adjunct to other therapy but can also benefit some patients when used alone. Coal tar preparations containing extracts of coal tar have a weak antipsoriatic action though the mode of action of this traditional therapy is not entirely clear. Tar is extremely safe; allergic contact sensitization even with repeated applications being rare and primary irritation being unusual except if used on very inflammed lesions. Tar may be incorporated in soaps, shampoos or baths and can be dispensed in the form of creams, ointments, lotions and pastes. A crude coal tar (2-5%) and salicylic acid ointment is rubbed well into the lesions. It may be combined with UVB therapy as in Goeckerman Regimen. This is easier to carry out for inpatients than outpatients and is cheap. Tar should be the first choice for majority of mild to moderate cases.

If tar fails, dithranol should be tried. It is more effective and faster in action than tar. It is useful for both outpatients and inpatients. Dithranol in a stiff vehicle e.g. dithranol paste (BP) is very effective in concentrations ranging from 0.05% to 2% and will clear most psoriatic lesions within 3 weeks.

In the psoriasis clinic at the PGI, graded concentrations of Derobin ointment are used as pure dithranol powder is not available in the country. Derobin ointment (Allenburys) is a

compound dithranol proprietory preparation consisting of:

Dithranol 1.1.% W/W

Salicyclic acid 1.15% W/W

Coal tar solution 5.3% W/W in soft paraffin base.

Graded concentrations are required for avoiding irritant reaction. The minimum concentration used initially is 0.025%. Concentrations of 0.05%, 0.075%, 0.1%, 0.25%, 0.5%, 0.75% and 1% can be used. The vehicle used is yellow soft paraffin. In most instances clearance of lesions occur with 0.25%-0.5% dithranol in 3-4 weeks' time. Only few patients require 0.75% and 1% concentration.

Dithranol is antimitotic in action, irritates normal skin and stains the skin and linen brown. It must be used carefully, and precisely over the lesions, usually overnight and covered with dressings. After ultra violet exposure the following day, the preparation must be thoroughly rubbed off by a tar or plain water bath before treatment is repeated. Dithranol is not applied to lesions on head, neck, body folds and genitalia. The combination of UVB, tar baths and dithranol applications is known as Ingram Regimen.

A derivative of dithranol – Triacetoxyanthracene (Exolan) - lacks the burning and staining effects of dithranol but is less effective.

There is no doubt that topical corticosteroids can produce rapid and considerable improvement of psoriasis lesions; the improvement being, however, usually incomplete and short lasting and often followed by relapse, earlier than in the case of tar and dithranol. Prolonged use of potent steroids can cause local atrophy. Weak steroid preparation like hydrocortisone ointment and vioforms or hydrocortisone cream should be reserved for areas like the face, ears, neck, flexures and genitalia. Stronger steroid preparations such as Betnovate cream may be used for short periods in treating resistant psoriasis of hands and feet. The effect of steroid can be enhanced by polythene occlusion. It is reasonable to initiate treatment with Ingram technique.

UVB and natural sunlight have long been used as an adjunct to tar and dithranol therapy. The eyes should be protected from exposure to the injurious rays Excessive use over many years is theoretically carcinogenic to the skin and tends to accelerate aging of the skin.

In acute or unstable phase of the disease, injudicious treatment with irritant and potent preparations can precipitate erythroderma. Bland preparations such as calamine lotion with or without oil, soft white paraffin or 1% ichthamol in zinc paste should be used for such cases.

Scalp is difficult to treat. For mild cases a tar - spirit lotion such as liquor picis carb 5% plus bland oil may suffice. Thorough and vigorous daily shampooing is necessary to remove scales and medicament. Salicyclic acid 3% in emulsifying ointment should be rubbed well into the scalp and washed out 4-6 hours later with a shampoo.

No effective treatment for psoriasis of nails exists. Intralesional injection of triamcinolone may be effective in the treatment of nail lesions, but is painful[6]. Methotrexate has been used locally without much success. Systemic methotrexate helps as part of a general effect Other local cytostatic agents are of no value except for a caustic effect obtained with 5-fluorouracil ointment. The addition of Vit. A, 100,000 units/ml, to triamcinolone and the use of retinoic acid ointment, are

still to be evaluated. PUVA treatment may help.

Systemic Therapy :

There is no entirely safe long term systemic treatment for psoriasis and this must be reserved for truly disabling or life threatening psoriasis resistant to topical therapy.

In the routine treatment of psoriasis corticosteroids have no place, since the disease always relapses on withdrawal of the drug or reduction of the dose. Erythrodermic or pustular psoriasis may also be precipitated on withdrawal of steroids. Corticosteroids in routine dosages may be used initially in controlling severe erythrodermic or pustular psoriasis for 4–6 weeks till more effective therapy such as methotrexate starts to act.

Methotrexate is an effective agent for treatment of severe psoriasis involving 80% or more of body surface. A folic acid antagonist, it inhibits the synthesis of DNA during the S-phase of mitosis[6]. The drug is excreted largely via kidneys and to a lesser extent via liver. Before treatment, renal, hepatic and marrow functions should be assessed. Minor side effects such as nausea, malaise and headache are common, in the 48 hours after administration. The most serious side effect of prolonged therapy is hepatic fibrosis. Routine liver function tests are not of value in predicting this complication. A pretreatment liver biopsy is needed to exclude active liver disease. Regular blood tests to detect any evidence of early marrow depression should be performed before each dose. The drug is teratogenic and should be avoided during the reproductive years especially in females. Hair loss may be a problem in some patients.

The drug is given orally or parenterally in dose of 0.2–0.5 mgm/kg body weight. Three main dosage schedules are recommended :

a) Daily oral doses should be of 2.5 mgm 5 days per week.

b) Weekly single oral doses of 25–40 mgm. This is the safest and most accepted method of administration.

c) Weekly parenteral doses of 20–40 mgm.

The following regimen is followed in the psoriasis clinic of the P.G.I. An initial dose of 5 mgm oral dose is given, which is slowly increased every week by 2.5–5 mgm to a maximum of 25–40 mgm and maintained till erythema, scaling and infiltration become minimal. Thereafter the dosage is reduced very gradually till a maintenance dose of 10–20 mgm per week is reached. Haemoglobin, total and differential leucocytic and platelet count are estimated fortnightly. Liver function tests are repeated every 3 to 6 months and needle biopsy of the liver is assessed yearly. At the time of writing, ten patients are on treatment with methotrexate for 2 years. The response is very satisfactory. The patients do get mild side effects like nausea, vomiting and headache. Two patients have significant hair loss and one young unmarried female patient developed endogenous depression probably unrelated to methotrexate therapy.

Other antimetabolite drugs such as azathioprine and hydroxyurea have been used in psoriasis but they are less effective than methotrexate and tend to damage the marrow more than the liver.

Interaction of light and the photoactive drug 8-methoxypsoralen is the basis of PUVA therapy. The long wave ultra violet light (UVA) which represents wave length of 320–400nm. is

used. In the presence of UVA, psoralen molecules form photo-adducts with DNA-pyrimidine bases and cross links between complementary DNA strands. This inhibits DNA synthesis and cell division. The drug is given orally (0.6-0.7 mgm/kg body wt.) and two hours later when the concentration of the drug in the skin is maximum, the whole body is irradiated with long wave ultraviolet light in a specially made chamber emitting calculated joules of UVA.

The immediate side effects are slight. The skin remains photosensitive for 8 hours after taking psoralen and during this period exposure to sun must be avoided. The long term side effects are not known but may include premature aging of the skin, development of cutaneous malignancies and persistent chromosomal damage. PUVA therapy has other disadvantages.

Improvement takes longer than in the case of dithranol and the patient needs to come to the hospital twice or thrice a week for exposure. PUVA should be avoided in children, pregnant women and in patients with light sensitivity disease. PUVA can be combined with other modes of treatment in certain resistant cases.

Synthetic retinoids and synthetic Vit-A analogues have generated much interest in certain countries on the treatment of extensive and refractory psoriasis and palmoplantar pustular psoriasis[7]. These may be sometimes effective when other modes of treatment fail. Liver function tests and blood counts should be monitored. Since the drug is teratogenic and only slowly removed from the body, pregnancy should be avoided during therapy and for a year after stopping it. Minor side effects are usualy a dry, scaly, fissured chelitis being the commonest.

Razoxane

Razoxane is an oral antimitotic agent which has been proved effective in severe psoriasis where other modes of therapy have failed. The drug does not produce hepatotoxicity. A dose of 125 mgm 8 hourly for 2 days may be given initially and repeated after 7–14 days. Severe psoriatic arthritis is reported to give good response with this drug. Important points to note with regard to Razoxane treatment are :

1. The margin between therapeutic effect and marrow depression is narrow.

2. The dose required to clear psoriasis in individuals varies widely.

3. At least 6 weeks treatment may be required before improvement is seen.

4. Neutropenia is dose-dependent and reversible.

Treatment of psoriatic arthritis follows the general line of treatment of rheumatoid arthritis and is best supervised by a rheumatologist. Periods of rest and physiotherapy may be needed. Aspirin, paracetamol, phenylbutazone, indomethacin, ketoprofen all have a place in the control of pain and stiffness. Cytotoxic drugs azathioprine and methotrexate have been used with some success. Systemic steroids may be occasionally indicated in severe mutilating arthritis.

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