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PSORIASIS

SUMMARY

The aim of treatment is to induce a remission or to reduce symptoms to an acceptable level
The choice of treatment depends on the type and location of the psoriasis and on patient acceptability
Topical treatment is used first line in mild and moderate cases
Severe cases are referred for specialist treatment with phototherapy and / or systemic therapy (acitretin, methotrexate, cyclosporin)

INTRODUCTION

Psoriasis is a chronic inflammatory skin condition characterised by clearly defined raised red plaques with dry silvery scales that are the result of excessive proliferation of epithelial cells. Exacerbations and remissions are typical.[1-3] This condition occurs in 1-3% of the population and affects all age groups, most commonly presenting during the mid 20 's. There is an equal sex incidence for chronic plaque psoriasis.[2,4-6]

AETIOLOGY & CLASSIFICATION

The cause of psoriasis is unknown, however there is a significant genetic component involved, with approximately 30% of patients having one immediate relative with the disease. An immunological component of the disease has also been postulated.[2,5,6] Environmental risk factors include physical injury, emotional stress, streptococcal throat infection, certain drugs e.g. lithium, chloroquine, beta-blockers, excess alcohol, and possibly smoking. Sunshine can exacerbate psoriasis in a small number of patients but is beneficial in the majority of sufferers.[3,5-7] There are several types of psoriasis. Chronic plaque psoriasis is the most common form occurring in about 90% of patients, other types include guttate and the more severe pustular and erythrodermic psoriasis.[2,5,7,8]

Plaque psoriasis (psoriasis vulgaris) presents with small papules which increase in size and unite to form red plaques with a silvery surface.[2] The most common sites affected are the knees, elbows, scalp, and nails. The face is usuallyunaffected.[3]

Guttate (drop-like) psoriasis often develops suddenly with many lesions of around 1cm in diameter appearing on the trunk and limbs.[3] It occurs more commonly in children and young adults often following a streptococcal throat infection. This type of psoriasis often resolves over several months without treatment.[2,3,6]

Erythrodermic psoriasis is a severe variant characterised by redness of the skin (over 95%of body surface area), excessive protein and fluid loss, and consequent loss of body temperature, which warrants specialist management and systemic therapy.[2,5,7,9,10] It may arise alone or present as an exacerbation of another form of psoriasis.[2] Withdrawal of systemic steroid treatment is often a precipitating factor.[11]

Palmar pustular psoriasis is localised to the palms and soles. This tends to be a relapsing, remitting disorder and can be difficult to treat. **Generalised pustular psoriasis** is a more severe form which can be life-threatening. It may resultfrom the withdrawal of oral steroids and presents with fever, malaise and widespread erythema. There may be loss of fluid and concurrent infection which warrants systemic treatment.[2,5,11]

Psoriatic nail changes are see up to 50% of cases, or more if there is comcomitant psoriatic arthritis. Nail changes include thimble-like pitting and onycholysis (separation of the nail from the nail bed), accumulation of debris under the nails and colour changes. This can be indistinguishable from a fungal nail infection. Nail clippings may be cultured to make a definitive diagnosis.[2,5,6]

Psoriatic arthritis is seen in about 6% of psoriatic patients.[3] It has many of the clinical features of rheumatoid arthritis. Unlike rheumatoid arthritis, serum levels of rheumatoid factor are not elevated.[2]

TREATMENT

Psoriasis can be treated with topical agents, phototherapy, systemic agents or with a combination of these treatments. The choice of treatment depends on the type of psoriasis and patient acceptability. Mild to moderate psoriasis is usually effectively managed by topical therapy and a 6 -12 week trial is recommended.[2,3,7] Phototherapy and/or systemic therapy is reserved for patients who fail to respond to topical treatment and for moderate to severe psoriasis (20%or more of the body surface area). Combination treatments may be used to effectively manage severe cases and to minimise the toxicity of systemic agents.[5,11-16]

TOPICAL TREATMENT

The liberal use of emollients is one of the mainstays of treatment and may be the sole treatment used to manage mild conditions.[8,11,17] **Emollients** e.g emulsifying ointment or aqueous cream are safe,inexpensive and can reduce scaling and associated itching.[11] **Salicylic acid** ,a keratolytic,is useful for removing scale and to enhance the penetration of other topically applied products. It is usually applied in concentrations of 2-5%. Skin irritation may occur, especially at higher concentrations. Extensive application of salicylic acid to the body is not advisable due to the risk of systemic adverse effects such as tinnitus, nausea and vomiting.[2,6,18]

Coal tar has anti-proliferative,anti-inflammatory and keratolytic properties. It is more effective than salicylic acid.[5,9,18,19] The formulation and strength chosen depends on patient acceptability, the severity of the condition and the site affected. Tar-containing shampoos are effective in the management of psoriasis of the scalp and coal tar baths can be useful for extensive body lesions. Tar creams and ointments are generally applied twice daily.[5,18,19] The use of these preparations is limited by odour, staining of clothing and skin irritation.[2,5,11,14,18,20] There is no evidence to date that coal tar products are carcinogenic but chemical gloves should be worn when preparing coal tar ointments.[3,5,14,17]

Topical corticosteroids have anti-inflammatory, antiproliferative and immunosuppressive actions.[2,11,17] Mild potency agents e.g. hydrocortisone 1% may be used for psoriasis on the face, genitals and flexures for a short period of time e.g. up to 4 weeks. Potent corticosteroids e.g. betamethasone valerate 0.1% should be reserved for use on recalcitrant plaques, acute flares, lesions on palms, soles and the scalp and should only be used under strict medical supervision.[10,17,18,22] Withdrawal may precipitate a relapse or rebound psoriasis and can precipitate severe pustular

psoriasis.[3,11,17,18] Tachyphylaxis or tolerance to treatment may develop.[9,14] Side effects of corticosteroids include thinning of the skin, telangiectasiae, striae and potential systemic absorption with adrenal suppression.[2,3,14,20,22,23]

Dithranol (e.g.Dithrocream®,Micanol®) is more effective than coal tar especially if the plaques are large, well defined and few in number.[10,18] It acts by inhibiting mitotic activity and a variety of enzymes crucial to reducing epidermal proliferation, it also reduces the binding of growth factors to epidermal cells.[11] Dithranol is applied only to the lesions and it is customary to start at the lowest concentration 0.1% and gradually increase to the maximum concentration which produces a therapeutic effect without irritation.[18] The highest concentration available is 3%. A short contact time of 30-60 mins is generally allowed before washing off (hands should be washed after application).[14,18,20] A response should be seen within 3-6 weeks.[5] Traditional dithranol preparations discolour skin and stain clothing. A cream containing microencapsulated dithranol avoids this problem.[20,22] Irritation and mild burning of the skin are the main side effects.[10,18]

Calcipotriol (Dovonex®) is a vitamin D analogue used for mild to moderate psoriasis. It acts by inhibiting keratinocyte proliferation and by promoting cellular differentiation.[5,17,23] A recent review of controlled trials has shown that calcipotriol appears to be more effective than coal tar and short contact dithranol.[25] Calcipotriol is available as a non-staining, odourless cream, ointment or scalp solution. An improvement is usually seen after 2 weeks and a significant reduction in the severity of psoriasis occurs within 6-8 weeks.[6,24] Transient skin irritation and hypercalcaemia can occur.[2,3,7] To avoid hypercalcaemia the weekly dose is limited to 100g per week of cream or ointment or 60ml per week of scalp solution. When used together, no more than 30g of the cream or ointment should be used with 60ml of scalp solution or no more than 60g of cream or ointment with 30ml of scalp solution.[3,5,7,8,9,17,18] Calcipotriol should not be used on the face and should be avoided in pregnancy.[2,7,18]

Tazarotene (Zorac®) is the first topical retinoid to be developed for the treatment of mild to moderate plaque psoriasis affecting up to 10%of the skin.[18,26,27,28] It modulates three key factors in psoriasis: keratinocyte proliferation, keratinocyte differentiation and inflammation.[12,26,28,29] Improvement has been demonstrated as early as one week after starting treatment and maximum benefit is seen after 12 weeks. Efficacy has persisted for up to 12 weeks after cessation of treatment which enhances cost effectiveness.[26,27] The gel is applied once daily in the evening and should be avoided in pregnancy and women of childbearing age.[9,18,28] The most common side effects are erythema, pruritus and burning. Higher doses and prolonged duration of use are associated with increased side effects.[26,27,29,30]

PHOTOTHERAPY

Since its development in 1974, phototherapy has been widely used in the outpatient setting to treat severe psoriasis that is unresponsive to conventional topical therapy .Broad band UVB, methoxypsoralen plus UVA **(PUVA)**and more recently narrow band UVB are all effective forms of treatment. **Methoxsalen** (8 methoxypsoralen,8 MOP, Deltasoralen®),a psoralen, is a photosensitiser which increases the skins reactivity to ultraviolet radiation. It is used orally or topically with UVA irradiation.[8,31,32] The oral dose depends on the patients weight and is usually administered 2 hours before UVA exposure. Patients are treated twice or three times weekly initially, until substantial improvement is achieved and then once every 2-4 weeks. Protective sunglasses should be worn during daylight for 24hrs after taking methoxsalen and patients should be advised to avoid sunlight exposure for at least 8

hrs after PUVA. Common side effects of PUVA are erythema and pruritus.[3,8,14,33] Longterm PUVA therapy increases the risk of squamous cell carcinoma of the skin which studies have found to be related to the cumulative dose of radiation.[8,32,34,35]

SYSTEMIC TREATMENT

Acitretin (Neotigason ®),a retinoid,is used under specialist supervision for the treatment of severe extensive psoriasis which is resistant to other forms of therapy. It is effective for pustular and erythrodermic psoriasis.[2,11] Retinoids normalise keratinisation, alter cell maturation, modify the immune system and they may have anti-inflammatory properties.[2,23] The initial daily dose is 25 or 30mg for 2-4 weeks .The dose is then adjusted according to response and generally maintained at 25-50mg (maximum 75mg) for a further 4-6 weeks when maximum benefit is seen. Treatment should be limited to 6-9 months with a 3-4 month rest period before repeating treatment.[18,36] Acitretin is a known human teratogen. Pregnancy must be excluded before commencing treatment and avoided for at least 2 years after stopping treatment. Other contraindications include breast-feeding and hepatic or renal impairment.[2,3,18,36] Side effects are generally dose related, involving dryness and sometimes erosion of mucous membranes and of the skin leading to scaling, erythema and pruritis. Dryness of the conjunctiva can result in conjunctivitis and intolerance of contact lenses. Reversible alopecia and hyperlipidaemia can also occur.[18,36]

Methotrexate has been used in the management of psoriasis for 40 years. It is licensed for the treatment of severe cases of uncontrolled psoriasis under specialist care and is ideally used to permit the return to conventional topical therapy.[31,36] Methotrexate inhibits dihydrofolate reductase, affecting the proliferation of rapidly dividing cells more than normal cells,and it also has immunological effects.[2,23] Improvement may be seen within 48hrs.[3] The recommended dosage is 15-25mg **once weekly** ,adjusted according to response.[18] In the elderly a reduction in dosage should be considered. Folic acid is given to minimise side effects.[2,12,22] Contraindications to the use of methotrexate include pregnancy and renal or hepatic impairment. Conception must be avoided for at least 6 months after treatment is discontinued in both males and females. Alcohol consumption should be minimised to prevent possible liver damage.[3] Side effects include abdominal pain, nausea, ulcerative stomatitis, chills, fever and fatigue. Routine monitoring of blood counts and liver function is essential due to the potential for bone marrow suppression and liver toxicity.[18,31,36]

Cyclosporin (Neoral®), a potent immunosuppressant, is licensed for severe resistant psoriasis for patients under specialist care.[3,18] For induction of remission, the initial oral dose is 2.5mg/kg/day given in two divided doses and titrated according to response. If there is no improvement after one month, the dose may be increased gradually up to a maximum dose of 5mg/kg/day. For maintenance treatment,the lowest effective dose should be used.[2,8,10,31,36] Common side effects include hypertension, gastrointestinal disturbances, burning sensations of the hands and feet and flu-like symptoms. Careful monitoring of creatinine and urea is necessary because of the possibility of renal dysfunction. The development of malignancies, particularly of the skin has been reported with cyclosporin. Exposure to sunlight and the use of UVB radiation or PUVA should be avoided.[3,7,22,36] Cyclosporin interacts with a wide range of other drugs and should be used with caution with other nephrotoxic agents e.g. non-steroidal anti-inflammatory drugs. Grapefruit juice can increase cyclosporin toxicity and should be avoided 1 hour before administration.[16,18,36]

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COSTS

EMOLLIENTS Cost per 500g

Aqueous cream £1.80
Emulsifying ointment £2.46
Silcocks base £1.74

COAL TAR PREPARATIONS Cost per 50g /200ml

Bath Additives

Psoriderm Bath Emulsion ® ((coal tar 40%)£3.24

Creams,Lotions,Gels

Coal Tar Ointment £0.45
Gelcotar ® gel ((strong coal tar solution BPC 5%,Tar BP 5%).£3.21
Apply once or twice daily
Psoriderm ® cream((coal tar 6%,lecithin 0.4%).Apply twice daily £3.26
Cocois ® ointment((coal tar 12%,sulphur 4%,salicylic acid 2%in coconut oil)£5.71
Apply daily for 3-7 days then intermittently

CALCIPOTRIOL Cost per 30g /30ml

Dovonex ® cream,,ointment (calcipotriol 50mcg/g).Apply once or twice daily £9.82
Dovonex ® scalp application ((calcipotiol 50mcg/ml).Apply twice daily £11.59

DITHRANOL Cost per 50g

Dithrocream ® 0.1%%,0.25%,Forte 0.5%.£4.36,£4.68,£6.38
Apply once daily (30-60mins)or overnight
Dithrocream HP ® 1%%,2%.Apply once daily for 30-60mins £6.27,£7.86
Micanol ® cream 1%%,3%.Apply once daily for 10-30mins £8.10,£10.08

DITHRANOL &UREA

Psoradrate ® cream ((Dithranol 0.1%,Urea 17%)£4.50
(Dithranol 0.2%,Urea 17%)£4.98

TAZAROTENE Cost per 30g

Zorac ® gel 0.05%%,0.10%.Apply once daily £17.39,£18.49

CORTICOSTEROIDS Cost per 30g /100ml

Mild

Hydrocortisone 1%

Hydrocortisyl ® cream,,ointment.£0.64

Moderate

Betamethasone 0.025%

Betnovate RD ® cream,,ointment.£1.06

Potent

Betamethasone valerate 0.1%

Betnovate ® cream,,ointment,lotion.£1.52
Betacap ® scalp application..£4.44

Clobetasone propionate 0.05%

Dermovate ® cream,,ointment.£2.75
Dermovate ® scalp application..£10.64

ORAL PREPARATIONS Cost of 28 days treatment

Acitretin (Neotigason ®)25mg -50mg daily £32.32 -£64.64
Cyclosporin (Neoral ®)2.5mg -5mg/kg daily (70kg patient)£138.41 -272.18
Methotrexate 15mg -25mg once weekly £2.43 -3.97

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