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Issues and Answers

Topical therapy for psoriasis

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Psoriasis

Psoriasis is a condition caused by abnormal activity of the immune system whereby the cells, blood vessels and nerves in the skin grow faster than usual.[1] Unlike normal skin where the cells take about a month to mature and are shed unnoticed, in patients with psoriasis cells mature within five days, causing them to heap up into characteristic patches or 'plaques'.[2,3] Histologically, there is marked thickening of the epidermis, cutaneous infiltration of inflammatory cells and an increase in the number of dilated blood vessels in the upper dermis.[3]

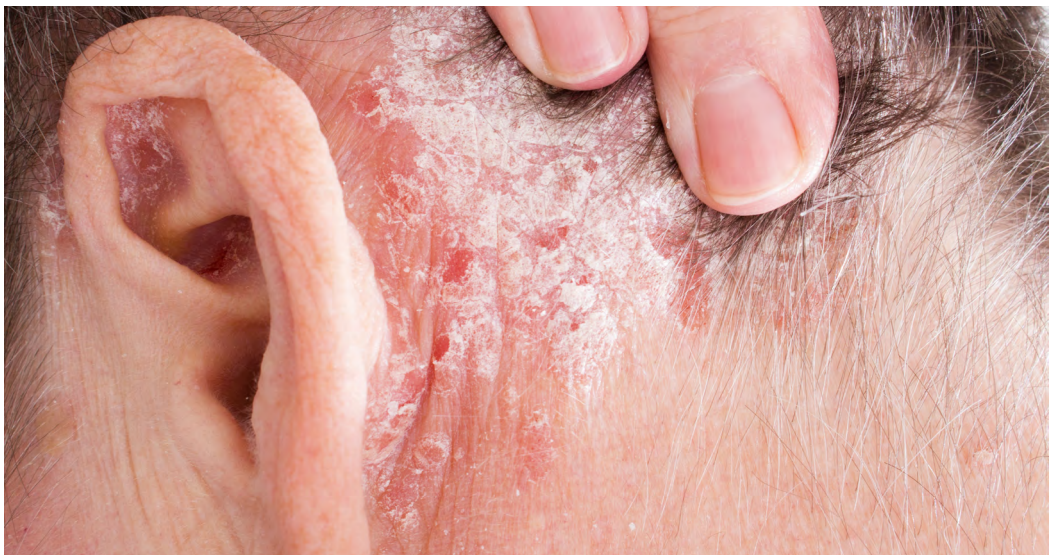
Although there are various forms of psoriasis, the most common form, occurring in around nine out of 10 cases, is plaque psoriasis. This is characterised by clearly demarcated patches or 'plaques' of thick, red skin, covered with white or silver scales, usually occurring on both sides of the body over the back of the elbows, front of the knees, on the lower back and around the umbilicus.[4] The skin lesions can cause significant discomfort, including itching, burning, bleeding and pain from irritation.[5] There may also be messy flaking of the scalp and involvement of the finger and toe nails, which may be discoloured, pitted and lift from the nail bed. Up to 50% of patients with psoriasis will demonstrate nail changes.[4]

Q How common is psoriasis?

A We have a special interest in psoriasis and are involved in various research projects at the academic hospitals in Gauteng, so we see a lot of patients who are referred, especially those who are difficult to treat. However, in private practice I would estimate we see around 50 patients with psoriasis every month.

Although it is often reported that psoriasis affects 1-2% of the population, our research suggests that the prevalence in South Africa is approximately 3%. It occurs in all population groups. However, psoriasis is an inherited condition and is especially common in the South African Indian population, with an estimated prevalence of 8-10%.

It is common in all ages, including children, but the incidence peaks around the late 30s and early 40s.



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Q Please tell us more about the inherited nature of psoriasis

A The aetiology of psoriasis is multifactorial. It is an inherited autoimmune inflammatory condition that is exacerbated by environmental factors. Various gene loci (known as Psoriasis Susceptibility (PSORS) loci) associated with the disease have been identified, including at least two genes that are probably involved in the pathogenesis of psoriasis. However, it is likely that other genes may also play a role. The most important environmental risk factors are stress, alcohol consumption and smoking, and others include consumption of red meat and overweight. However, the exact nature of the association between psoriasis and overweight is unclear - whether overweight leads to flaring of the disease, or whether psoriasis itself causes overweight. Nevertheless, we have observed a definite association between psoriasis and features of the metabolic syndrome, including increased visceral fat (especially fat deposits around the liver and the heart), raised blood pressure and type 2 diabetes mellitus. In comparison to people without psoriasis, the prevalence of hypertension and metabolic syndrome is nearly doubled in those with the disease, the prevalence of type 2 diabetes is increased more than five times and, in Indian females with psoriasis, the risk of obesity is increased approximately 100-fold.

The genetic basis for psoriasis means that it is passed on within families. Children have an approximately 14% risk of developing psoriasis if one parent has the disease and a 44% risk if both parents suffer from psoriasis.

Q What is the nature of psoriasis and how does it affect the person with the condition?

A Psoriasis is a chronic inflammatory skin disease, characterised by hyperkeratosis and suprapapillary thinning. The capillaries in the upper half of the dermis become dilated, which causes bleeding. The unsightly lesions and bleeding are a cause of considerable embarrassment, shame and reduced self-esteem, so patients might avoid going out and exclude themselves from social gatherings. Psoriasis is commonly associated with depression, and there is a lot of ignorance and misinformation about the disease, causing patients to feel isolated, excluded and stigmatised. They may stay home from work and school. Other people are often afraid that the condition is contagious and avoid getting too close to someone with psoriasis. In some communities, psoriasis may be regarded as a 'curse' or sign of evil.

It is very important to understand that psoriasis is a systemic condition that does not only affect the skin. The scalp is involved in one-quarter to one-third of cases. Scalp involvement is usually a sign of chronic disease and increased risk of complications. The joints may also be involved (psoriatic arthritis), causing persistent joint pain, early morning stiffness, and inflammation of the fingers and insertions of ligaments and tendons into bone. Involvement of the cardiovascular system is common. There are also reports that people with psoriasis may be at increased risk of developing various cancers.

Types of psoriasis[1,4]	
Plaque psoriasis	This is the most common form (90%), usually occurring over the back of the elbows, front of the knees, on the lower back and around the umbilicus
Inverse psoriasis	Lesions occur on the joint creases and skin folds and tend not to scale
Guttate psoriasis	Widely distributed small red, scaly, 'tear-drop' skin lesions
Generalised pustular psoriasis	The person is very unwell with rapidly progressing tender pustules and widespread inflammation.

Q What is your approach to treatment?

A Firstly, it is important to assess the severity of the disease and the impact on the patient's quality of life. We use the Dermatology Life Quality Index Score (DLQI) to assess quality of life. It is a simple self-rated questionnaire

that takes the patient around two minutes to complete, and it gives me an indication of the patient's perspective of how psoriasis affects them. It asks about symptoms, psychological impact and impact on normal daily activities.

We use the Psoriasis Area and Severity Index (PASI) to measure disease severity. PASI combines assessment of the severity of lesions (redness, thickness and scaling) and the area affected into a single score, so that we can classify the disease as mild, mild-moderate, moderate-severe or severe. The majority of patients that I see have moderately severe psoriasis. All patients should be advised, as far as possible, to avoid or manage triggers, including stress, alcohol and red meat consumption.

For mild to moderate psoriasis, we recommend topical treatment, such as calcipotriol/betamethasone dipropionate combination gel. Topical treatment has minimal impact on quality of life, systemic absorption is minimal and the risk of systemic side effects is low. Phototherapy can also be used. If the psoriasis is chronic and/or responds poorly to topical treatment, then we would escalate treatment to oral options, including cyclosporine, methotrexate or acitretin. About three-quarters of patients with psoriasis will eventually need oral treatment. For severe psoriasis, biological agents can be extremely effective. The new biologics that target interleukins (IL-23, IL-12 or IL-17) can achieve 100% clearance of psoriatic lesions. However, they are unfortunately not available to all patients and reimbursement is not covered by medical aids.

Q How would you treat scalp psoriasis?

A Treatment for scalp psoriasis depends on the severity. By the time I see patients the condition is usually quite severe, with thick scaling and hair loss, so I treat quite aggressively. Initial treatment is daily application of a combination of clobestasol (a high-potency corticosteroid) medication plus calcipotriol/betamethasone dipropionate combination gel medication. Thereafter, if the patient has responded well and does not need oral therapy, application can be reduced to twice weekly. Treatment needs to be aggressive, because when the scales are so thick it is difficult for the medications to penetrate the epidermis. You want to gain control of the scalp condition before there is more damage and hair loss.

Q What advice would you give to general practitioners who treat patients with psoriasis?

A The GP plays a vital role in the management of patients with psoriasis. It is important to remember that psoriasis is not only a skin condition and patients must be examined thoroughly and monitored for systemic manifestations of the disease and complications. It is especially important to regularly screen patients for hypertension, type 2 diabetes, other metabolic diseases and depression. I tell a patient that from the moment of their psoriasis diagnosis, they need to see their general practitioner every 4-6 months for the rest of their life.

Remember that psoriasis should never be treated with oral corticosteroids. Withdrawal of systemic corticosteroids can cause severe flaring of pustular psoriasis, which can be life threatening and requires hospitalisation.

Clinical notes

Topical treatments for psoriasis

Topical treatments include corticosteroids, vitamin D analogues, keratinolytics and coal tar preparations.[3]

Corticosteroids have anti-inflammatory and antiproliferative properties, and reduce erythema, scaling and pruritus. They are classified according to potency (mild, medium, potent and very potent) and are available in a variety of formulations including creams, emollient cream, ointment, spray, gel lotion, solution, nail lacquer, tape and foam. Disease severity, site of application and individual preference will determine which of these formulations is most appropriate for a given patient. Low-potency corticosteroids should be used in children and on sensitive skin sites, such as the face, axillae and intertriginous areas. Hyperkeratotic areas, such as the palms and soles require high-potency corticosteroids. It is usually recommended that

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use of high-potency corticosteroids be limited to 2-4 weeks, but where treatment is prolonged they may be applied intermittently. Local side effects of topical corticosteroids include skin atrophy, striae, telangiectasia, purpura, rosacea, acneiform dermatoses and rebound erythema.

Vitamin D derivatives, including calcipotriol, exert their actions through binding to the vitamin D receptor. They normalise keratinocyte proliferation and differentiation and modulate the immune response, inhibiting activation of T cells and dendritic cells and stimulating T helper cells. Topical calcipotriol has been shown to be at least as effective as betamethasone dipropionate. It is well tolerated on sensitive and irritated areas of skin and may be used in children. Although side effects are rarely severe, local effects may include erythema, burning, pruritus and oedema.[3]

Different combination products consisting of calcipotriol and betamethasone are available for use on the skin and on the scalp. They are applied once daily. Because they have distinct mechanisms of action, combining these two agents enhances the therapeutic efficacy and may allow for use of lower doses of either or both, with the potential to reduce the occurrence of adverse effects.[3] The scalp preparation is a gel formulation, which is easier and more convenient to apply than a cream or an ointment.

In clinical studies, the two-compound formulation more effectively improved both PASI and Physician Global assessment (PGA) scores than calcipotriol gel monotherapy and betamethasone dipropionate monotherapy.[6] Rapid and consistent effectiveness was associated with improved quality of life.[7] A 52-week study showed that with long-term treatment, the two-compound product was well tolerated, with a lower incidence of adverse effects than calcipotriol monotherapy.[8]

Potential benefits of combination topical therapy with betamethasone dipropionate and calcipotriol[3,6,7]

1. Combines skin cell normalising effects of calcipotriol with anti-inflammatory effects of corticosteroid;
2. Enhances treatment effectiveness - more effective than either ingredient alone;
3. Rapidly and consistently effective for mild to moderate psoriasis;
4. One daily application replaces frequent application of one or more single-ingredient products;
5. Gel formulation for scalp is easier and more convenient to apply than cream or ointment;
6. Clinically proven to improve measures of quality of life;
7. Does not share the odour or staining potential of coal tar.

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