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Reports on Scientific Meetings

Recent advances in psoriasis therapy

Reported by PT Chan 陳寶德

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Venue:	Hyatt Regency Hotel, Hong Kong
Speaker:	Prof. C. E. M. Griffiths Head of Manchester Dermatology Centre, The University of Manchester, Hope Hospital, United Kingdom
Organiser:	The Hong Kong Society of Dermatology and Venereology

Various aspects of psoriasis including recent advances in topical treatment, immune mechanism, biologic therapy and cognitive-behavioural therapy were discussed. The new vitamin D_3 analogue, calcitriol ointment 3 μg/g, has similar efficacy to calcipotriol ointment 50 μg/g in the treatment of plaque psoriasis. Calcitriol has less local irritative side effects such as erythema, oedema and stinging sensation as compared with calcipotriol ointment and hence can be used in sensitive areas such as flexure, face, hairline and retroauricular region. Good efficacy and tolerability can be demonstrated both subjectively by patients and objectively by physicians. Another new topical therapy is the use of tacrolimus ointment for thin plaque psoriasis. This drug has been approved by the US Food and Drug Administration (FDA) for atopic dermatitis in children and adults. It is not effective for thick plaque psoriasis because of limited skin penetration. Preliminary studies show that it can be used in thin plaque psoriasis over face and flexures, avoiding the side effects of glaucoma and skin atrophy associated with topical steroids.

There has been a growing interest in the use of biologic therapy in psoriasis treatment as conventional medications for severe psoriasis carry the risks of hepatotoxicity, nephrotoxicity and myelosuppression. T-lymphocytes are important in the pathogenesis of psoriasis. The majority of skin-infiltrating T-cells in psoriasis have memory effector phenotype CD45R0. In the epidermis, majority of the T-cells are CD8 positive, whereas in the dermis, CD4 lymphocytes predominate. Psoriasis is characterised by a Th1 cellular response with increased interleukin (IL)-2, IL-12 and interferon-γ.

The new biologic therapy encompasses T-cell targeted or cytokine approaches. Potential T-cell targets include adhesion molecules (anti-CD11a), activation pathway via IL-2 (cyclosporin, pimecrolimus and anti-CD25), cytotoxic proteins (IL-2 diptheria toxin fusion protein) and co-stimulatory molecules (alefacept and efalizumab). Cyclosporin, the firstly used drug in the above list, has problems of nephrotoxicity and hypertension. In severe psoriasis, combination therapy of cyclosporin and methotrexate is useful and lower doses of both drugs can be employed. Pimecrolimus is a macrolactam produced by soil fungus. It acts similarly to cyclosporin in reducing T-cell activation. Oral pimecrolimus has been tried

in moderate to severe psoriasis. Fifty percent of patients achieve a greater than 75% reduction in psoriasis area and severity index (PASI) score. Some patients experience a warm sensation over the presternal area forty minutes to one hour after administration.

Alefacept has been approved by the FDA for treatment of moderate to severe psoriasis. It blocks the interaction of CD2 and leukocyte function antigen-3 (LFA-3) and enhances the apoptosis of CD45R0 memory-effector T-cells. When the drug was given intramuscularly for 12 weeks at 15 mg/week, 24% of patients achieved complete clearance or almost complete clearance. There was no rebound or increase in infection with alefacept. Efalizumab is the second new systemic biologic therapy approved by the FDA for treatment of psoriasis. It is an antibody directed against CD11a, a component of intercellular adhesion molecule (ICAM)-1. The interaction between ICAM-1 and lymphocyte function associated antigen (LFA)-1, which is essential for activation and migration of lymphocytes, is suppressed. When it is administered subcutaneously at 1 mg/kg once weekly, 25% of patients achieve a greater than 75% PASI reduction at week twelve.

At the cytokine level, infliximab and etanercept have been used in rheumatoid arthritis and etanercept has been approved for treatment of psoriatic arthropathy. Infliximab is an antibody directed against tumour necrosis factor (TNF)-α. It is given intravenously at 5 mg/kg at zero, second and sixth week. It has quick therapeutic effect for psoriasis, but has the potential side effect of tuberculosis reactivation. Etanercept is administered subcutaneously at 25 mg twice per week. Twenty to thirty percent of patients have over 75% improvement in PASI at week twelve. There is a possible increased risk of demyelination which needs to be substantiated by further clinical experience. Recombinant IL-4, a Th2 cytokine, has also been used successfully in the treatment of psoriasis.

Stress is important in psoriasis exacerbation and up to 60% of psoriasis patients report stress as an exacerbating factor. Anxiety and pathological worry have been shown to be predictors of slower response to photochemotherapy. Cognitive-behavioural therapy, which includes introduction of coping techniques and health education on psoriasis, has been shown to enhance response to psoriatic treatment.

Learning points:

Psoriasis, being a T-cell mediated disease, is amenable to various emerging biologic therapies. On the other hand, psoriatic patients may have psychological co-morbidity which may affect treatment outcome.