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Reports on Scientific Meeting

Steroid-free topical immunomodulator: a new therapeutic paradigm in atopic dermatitis management

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Clinical experience of tacrolimus ointment usage in Hong Kong

Speaker: Dr. H.H.L. Chan
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Atopic eczema is associated with other atopic diseases such as asthma and allergic rhinitis. It has a genetic predisposition with early onset and is due to immunological imbalance. Atopic eczema is common in Hong Kong with prevalence rate between 5% to 28%.

According to the guideline delineated in the International Consensus Conference on Atopic Dermatitis II (ICCAD II) held in New Orleans in February 2002, first line management of atopic eczema include: avoidance of irritant or allergen, use of emollient, topical steroids, antihistamine, potassium permanganate and treatment of secondary infection. Topical steroid is, however, well known for its side effects which include pigmentary changes, skin atrophy, acne, telangiectasia and pituitary adrenal suppression. Other modalities of treatment include phototherapy, azathioprine, cyclosporin but are reserved for refractory cases. Tacrolimus and pimecrolimus are topical calcineurin inhibitors that can block the synthesis of both Th-1 and Th-2 type cytokines in target cells. They are effective in treating atopic eczema and allergic contact dermatitis without causing side effects induced by topical steroid.

A local survey on parental concern of the use of topical steroid for childhood eczema in 27 cases revealed that more than 90% were treated with steroid and around 63% of parents were worried of the side effects of topical steroid.

Tacrolimus is an effective immunomodulating agent inhibiting cytokine synthesis and T-cell activation. Previous studies elsewhere had shown its efficacy in treating atopic eczema. A local study involving 33 patients with moderately severe atopic eczema (>10% body surface area affected) was carried out. Following a wash-out period, all the subjects were prescribed topical tacrolimus 0.03% ointment for two to four weeks. Uses of oral or topical steroid, immunosuppressives or Chinese herbal medicine were prohibited whilst emollients, antihistamine were allowed during the study period. Patients were instructed to apply tacrolimus ointment twice daily and were assessed once per week. Primary outcomes were measured in terms of Global Evaluation of Clinical Response (GECR) and Eczema Area Severity Index (EASI) whilst secondary outcomes include patients' assessment on global improvement on all affected areas and an evaluation of quality of life. Twenty-nine cases

completed the four-week therapy and four withdrew. It was found that more than 65% had moderate to excellent improvement on GECR at one week and this effect was sustained till the end of the four-week therapy. A few achieved complete clearance by four weeks. A significant reduction (more than half) in EASI was also observed. For the patients' assessment of treatment effects, more than 60% felt better at one week.

In conclusion, 0.03% tacrolimus ointment is effective and well tolerated by local children with atopic eczema. Intermittent use of topical steroid to control acute flares, with long-term maintenance therapy with topical calcineurin inhibitors is recommended as treatment strategy.

Learning points:

Tacrolimus ointment is a topical immuno-modulator that functions by inhibiting calcineurin. A local study in Hong Kong showed that it is effective and well tolerated in children with atopic eczema.

Tacrolimus ointment: disease control in atopic dermatitis may become reality

Speaker: Dr. S. Reitamo

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Atopic eczema is a common skin disease especially in children. Topical steroid has long been the first line treatment for this skin disorder. Topical immunomodulators such as tacrolimus and pimecrolimus are relatively new therapeutic agents used for atopic eczema. They bind to the FK binding protein (FKBP) that in turn inhibits calcineurin. This inhibits the dephosphorylation of Nuclear Factors of Activated T-cells protein (NF-ATp) and subsequently decreased intra-nuclear transfer of dephosphorylated NF-ATp. The result is a decrease in interleukin-2 production. They also inhibit the cytokine release from T-cells such as interleukin-4, mast cells and eosinophils. Tacrolimus has a higher affinity for FKBP when compared with pimecrolimus and it is available in ointment form whilst pimecrolimus has cream preparation only. Tacrolimus is, therefore, expected to have a higher efficacy.

The treatment effect of tacrolimus is dependent on the severity of atopic eczema. Previous studies indicated that topical tacrolimus was effective in moderate to severe eczema but whether it should be regarded as first line or second line therapy for atopic eczema had not yet been determined.

In a one year comparative trial on the efficacy of pimecrolimus 1% cream versus corticosteroid (Triamcinolone acetonide 0.1% for trunk and limbs plus hydrocortisone acetate 1% for face) in the treatment of moderate to severe atopic eczema, pimecrolimus was found to be less effective than topical steroid. In another multi-centre randomised double blind study comparing the efficacy of tacrolimus ointment versus corticosteroid in the treatment of atopic eczema, topical tacrolimus was found to be more effective (more than 70% clearance achieved after twelve weeks' therapy) than topical steroid (50% clearance achieved after twelve weeks' therapy).

Topical tacrolimus, even at 0.1% has negligible systemic absorption. In a study of the pharmacokinetic profile of topical tacrolimus in patients with atopic eczema, all had blood tacrolimus level less than 5 ng/mL during therapy and tacrolimus was undetectable in more than 80% of them.

Topical tacrolimus, however, may cause a burning sensation at sites of application and this undesirable effect seems to correlate with the severity of eczema. Localised flushing at sites of tacrolimus application after alcohol consumption was reported by one of the speaker's patient.

Topical tacrolimus does not cause skin atrophy and will not lead to a decrease in skin immune function which was evidenced by a marked decrease of number of staphylococcus aureus colonies in skin lesions of eczema patients shortly after therapy in one study and it was found that such decrease was sustained by twelve months. In conclusion, topical tacrolimus should be regarded as a first line therapy for atopic eczema.

Further areas for exploration include the use of topical tacrolimus in children less than two years of age and in other dermatological problems. There were growing evidence that topical tacrolimus may be useful in the treatment of seborrhoeic dermatitis, chronic actinic dermatitis, psoriasis, oral lichen planus, graft versus host disease, vitiligo and oral and perianal Crohn's disease. There were also case reports of the use of tacrolimus ointment in treating Hailey Hailey disease, Behçet's disease, cutaneous sarcoidosis, cutaneous T-cell lymphoma, rheumatoid ulcer and pyoderma gangrenosum.

Learning points:

Topical tacrolimus is an effective treatment for atopic eczema. It functions by immunomodulation without causing immunosuppression. It is free of side effects of topical steroid and it can reduce the incidence of skin infection in eczematous lesions. Moreover, there is growing evidence that topical tacrolimus is useful in treating many other skin problems.