Cyclosporin: Experiences in Paediatric Patients

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Date:	24 June, 1999
Venue:	JW Marriott Hotel
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Organizer:	HKSDV; Scientific Meeting

The incidence of atopic eczema has been increasing in recent years. In 1946, 5.1% of children suffered from atopic eczema while this number had increased to 16.5% in 1997. It is known that atopic eczema is more prevalent among the higher social classes. One study reported that the prevalence of atopic eczema among children under seven years of age was 4.8% in social class one compared to 2.4% in social class five. Hence, with the increasing prevalence of atopic eczema, effective treatments are increasingly important.

Cyclosporin has a more rapid onset of action in atopic eczema than in psoriasis. A maximal effect may be seen as early as two weeks after starting the drug. A study showed that at eight weeks after starting cyclosporin, there was a significant decrease in severity, itch, extent, and sleep disburbance scores. This is important as it has been shown that atopic eczema can significantly interfere with social life,work and sleep. In a double blind, cross-over study comparing cyclosporin with placebo in reducing itch in atopic eczema, cyclosporin was significantly better than placebo.

Cyclosporin is well-tolerated. The side effect profile of cyclosporin in 422 patients with psoriasis treated with cyclosporin were studied. Only eight patients withdrew due to side effects. In this study, the most common side-effect was gastro-intestinal disturbance. The next most common side effect was parasthaesia while other side effects rarely led to cessation of treatment. Hypertrichosis is more common in children and occurs usually within three months of starting cyclosporin and is reversible. Nephrotoxicity and hypertension are two of the most important side-effects. Nephrotoxicity is dose-related and is more common in elderly patients who have pre-existing renal impairment. It is less likely to occur in young patients who have no renal disease. At a dose of <5 mg/day, functional renal impairment occurs which is reversible within three months after stopping cyclosporin. Structural abnormalities occur when the dose exceeds 7.5 mg/day. It is not known whether structural abnormalities occur when doses of <5 mg/day are used on a long term basis. However, in a study of 60 patients with rheumatoid arthritis who had taken cyclosporin for 87 months, it was found that the incidence of renal impairment was not increased.

The current recommendations for its use are that it should be reserved for severe cases of atopic eczema. It may be used as substitute of corticosteroids during the drug holiday in patients with severe atopic eczema. Regular supervision is required. Short-term, intermittent courses are recommended. It has been shown that short courses have a lasting effect. In a study of 22 patients with atopic eczema who were treated with cyclosporin 5 mg/day for eight weeks, 15 patients showed severity scores persistently better than baseline when assessed at eight weeks after stopping treatment.

However, due to the immunosuppressive effect of cyclosporin, patients are more prone to staphylococcal infections even when the eczema is in remission. It has been shown that patients with atopic eczema are at a higher risk of skin sepsis due to the higher load of staphylococcus aureus on the skin. Thus, it is important to control the staphylococcal levels before starting treatment. On the other hand, once disease activity is controlled, relapse can be controlled with antibiotics alone.

Cyclosporin acts by inhibiting the production of interleukins in CD4 T-lymphocytes. Cyclosporin inhibits calcineurin which is a calcium-dependent serine threonine phosphatase. As a result, the production of cytokines such as interleukin II and γ-interferon are impeded. As calcineurin is also involved in the regulation of ionic transport in the nephron, the function of the kidney is affected, resulting in nephrotoxicity. Cyclosporin does not lead to malignancy in normal skin but in cases with pre-existing malignancy, tumour growth is increased, that is, it is not a tumour initiator

but is a tumour promotor. This is because cyclosporin increases the level of β-transforming growth factor which has immmunosuppressive effects resulting in tumour growth. Because of the pharmacokinetics of cyclosporin is age dependent, a higher dose is required to achieve the same therapeutic effect in children.

There is also an improvement in growth in paediatric patients treated with cyclosporin. In atopic eczema, growth is reduced both due to sleep disturbance and long term topical steroids applied over a wide area. Topical steroids have a significant effect on growth especially in patients with over 50% body surface area involvement. Cyclosporin resolves both problems, thus enabling normal growth to take place.

In the discussion, questions were raised regarding the use of cyclosporin with PUVA and narrow band UVB. Dr. Allen felt that short-term cyclosporin (for example, two month courses) could be used as part of a rotatory regime. When questioned about the possibility of topical preparation for cyclosporin, Dr. Allen commented that no effective preparation could be developed at the present moment as the high molecular weight of cyclosporin posed problems when attempting to fit the drug into a vehicle cream.

Learning points:

Because of the pharmacokinetics of cyclosporin is age dependent, a higher dose is required to achieve the same therapeutic effect in children with atopic eczema.