Commentary

Fumarates in dermatology

Dermatology, like many other medical specialties today is expanding rapidly with the understanding of immunology and molecular biology on a better, adaptable footing. This is more applicable in dermatology as the challenges to treat diseases successfully are more. While there is a search for new drug for old diseases which frustrate, the dermatologist is also exploring existing drugs to be used in a better, rational manner for these existing diseases.

Psoriasis is a chronic disabling disease affecting around 2% of the world population. Various treatments have been tried with varying success rates and toxicity. The disease relapses promptly on discontinuation of the drugs and this is a major limiting factor in choosing a drug. The disease is primarily immunological in nature, though the exact triggers are not yet known. However, the emphasis today is on targeting the immunological events in psoriasis.

Fumarates or fumaric acid esters have been available for than half a century, but have not yet found their rightful place in the armamentarium for treating psoriasis as the drug is not freely available. This poses another restriction on the validity of the drug, in that adequate, large multicenter trials cannot be conducted. Prof. Uwe Wollina has cited a trials in this issue of the IDOJ, but the psoriasis researcher may want to see more work in this area, especially in comparison to other standard agents and studies of fumarates in combination with conventional drugs available elsewhere.

The need for these studies is exemplified by the relatively high incidence of adverse effects to fumarates citied in this article by Prof. Wollina. We need to see if these can be minimized or dosage modifications can help.

Any drug being evaluated for therapeutic use is evaluated on the basis of safety and efficacy. There does not seem to any doubt that the drug is highly efficacious, even over a prolonged period of time and many patients have been maintained in remission by this drug. This is probably because the drug acts at multiple levels. Prof. Wollina has highlighted the specific effects on psoriasis pathogenesis—starting at epidermal proliferation down to T cell regulation, T- and B-cell interactions and the effect of fumarates on angiogenesis. The varied effects of this drug have therefore made it useful in other diseases too.

The use of the drug in Necrobiosis lipoidica and granuloma annulare has been elaborated upon. The possible use in melanoma has been discussed. There are other works where fumarates are being explored in dermatology.

Novack *et al*.[1] explored the use of fumarates in recalcitrant Sarcoidosis.

Sarcoidosis is a multisystem disease of unknown origin characterized by the formation of noncaseating granulomas, in particular in the lungs, lymph nodes, eyes, and skin. 3 patients were treated with fumarates for 4 to 12 months with complete clearance. Side effects related to GI system, lymphopenia and flushing were observed. Fumarates worked probably because of their effect on T cells and the results seen in disseminated granuloma annulare encouraged the authors to use the drug.

We need more studies to look at the effect of fumarates in dermatology. The effect on antigen presenting T-cells led to the use in Granulomatous disease. The effect on T cells has led to the use in psoriasis. This is a drug with pluripotent actions and needs to be made available for further study.

Some areas we need to study in this respect are methods to minimize dropouts due to side effects, mechanism of renal damage, genetic variability in response to fumarates and effects of fumarates in a population which is exposed to Granulomatous disease like Hansen's disease and tuberculosis.

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REFERENCE

1. Ute Nowack, Thilo Gambichler, Christoph Hanefeld *et al*.: BMC Dermatology 2002;2:15.