Auranofin Is Ineffective in Atopic Dermatitis

Sir,

Gold compounds have been extensively used as therapeutic agents in the treatment of rheumatoid arthritis. Their mechanism of action in vivo remains, however, unclear. The pharmacokinetic properties of the recently available oral compound auranofin (Ridaura®) differ greatly from parenteral gold formulations. Auranofin appears to have anti-inflammatory activity due to (a) reduction of the release of inflammatory mediators such as lysosomal enzymes (1, 2), histamine (3), prostaglandins (4) and interleukin 8 (5); (b) inhibitory effect on the first component of the complement (6); and (c) inhibitory effect on the chemotactic and phagocytic response of macrophage and PMN (7). In addition, it has specific immunomodulatory properties such as inhibition of antibody-dependent cell-mediated toxicity, complement lysis (8) and stimulation of suppressor T cells (9). Furthermore, it has anti-infectious activity.

Since auranofin may act at several levels of the inflammatory and immune response with fewer and milder side-effects than classical gold salts (10), it might be useful in the treatment of atopic dermatitis (AD), a disease with immunologic abnormalities including abnormal regulation of IgE synthesis, disturbed T cell function and altered pharmacological reactivity and releasability of vasoactive mediators. We have used it in several patients with AD during the past years. As some positive effects were noticed (subjective lesional and topographical improvement described by 4 patients after 2 months' therapy), we decided to prospectively study the effect of this compound in 4 patients with severe AD during a 6-month period.

Four patients (all male, mean age 32 years (range 26–35 years)) entered this prospective study after informed consent. All patients had severe AD fulfilling the criteria of Hanifin & Rajka (11). Patients with abnormal renal, hepatic or hematological function were excluded. The range of serum IgE value at start was 2,920–16,910 IU/ml.

Each patient was treated with a triple combination consisting of auranofin (Ridaura®) 6 mg/d, astemizole (Hismanal®) 10 mg/d and ranitidine (Zantic®) 300 mg/d taken for a period of 6 months (September 1992 to March 1993). Patients were allowed to continue using topical corticosteroids as necessary. An ophthalmologic examination was performed at the beginning and at the end of the treatment period. Standard biochemical parameters of renal and hepatic function were monitored monthly.

The response to treatment was evaluated by a monthly clinical scoring system (12). Itching sensation was reported by the patient on a classical visual analog scale, and requirements for topical steroids were recorded.

Three patients showed little or no change after 6 months of treatment and one patient had an exacerbation of the AD leading to discontinuation of the trial after 4 months. The reduction of the overall lesional score was only 10%, due to a 50% improvement of itch without significant change of other parameters such as surface involvement, erythema, scaling and excoriations. The reduction of the topical steroid consumption was insignificant (2.5 g/week).

Important fluctuation in the disease activity occurred during treatment in 3 out of the 4 patients. There was no major adverse effect including hepatic, renal, ocular or hematological function. Serum IgE levels and eosinophil blood count were unchanged.

A clinical effect of auranofin (reduction of the lesional and topographical scoring) was not detectable in this study. No patients described an improvement of their AD; none could omit or reduce significantly his topical corticosteroid treatment. The main benefit of the triple combination was the important reduction of the pruritis, which may have been due to the association of the H1 and H2 receptor antagonists given during the trial, although recent studies showed that H1 blockers had no effect regarding itch in AD.

The hypothesis of a possible benefit of auranofin in AD was based on the fact that AD, like rheumatoid arthritis and pemphigus, is a chronic disease associated with humoral and cellular immune abnormalities (13). This hypothesis was not confirmed in the present study.

REFERENCES

1. Persellin RH, Ziff M. The effect of gold salts on lysosomal enzymes of the peritonal macrophage. Arthritis Rheum 1966; 9: 57–65.
2. Finckelstein AE, Roisman FR, Ladizeski MG, Walz DT. Auranofin and lysosomal enzymes. J Rheumatol 1982 (Suppl 8); 9: 46–53.
3. Toshiaki T, Yukata M, Koichiro K, Terumasa M. Auranofin, an oral chrysotherapeutic agent, inhibits histamine release from human basophils. J Allergy Clin Immunol 1984; 74: 297–301.
4. Malo PE, Wasserman M, Parris D, Pfeiffer D. Inhibition by auranofin of pharmacologic and antigen-induced contractions of the isolated guinea pig trachea. J Allergy Clin Immunol 1986; 77: 371–376.
5. Deleuran B, Kristensen M, Paludan K, Zachariae C, Larsen CG, Zachariae E, et al. The effect of second-line antirheumatic drugs on interleukin-8 mRNA synthesis and protein secretion in human endothelial cells. Cytokine 1992; 4: 403–409.
6. Schultz DR, Volanokis JE, Arnold PL. Inactivation of C1 in rheumatoid synovial fluid purified C1 and C1 esterase by gold compounds. Clin Exp Immunol 1974; 17: 395–406.
7. Davis P, Cindy L, Milli R, Russel AS. Effects of gold compounds on the function of phagocytic cells. J Rheumatol 1982 (Suppl 8); 9: 18–24.
8. Walz DT, Dimartino MJ, Griwold DE. Mechanisms of action of auranofin: effects on humoral immune response. J Rheumatol 1982 (Suppl 8); 9: 32–36.
9. Lorber A, Jackson WH, Simon TM. Effects of chrysotherapy on cell mediated immune response. J Rheumatol 1982 (Suppl 8); 9: 37–45.
10. Chaffman M, Brogden RN, Heel RC, Speight TM, Avery GS. Auranofin. Drugs 1984; 27: 378–424.
11. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. Acta Derm Venereol (Stockh) 1980; 92: 44–47.
12. Costa C, Rilliet A, Nicolet M, Saurat JH. Scoring atopic dermatitis, the simpler the better? Acta Derm Venereol (Stockh) 1989; 69: 41–45.

13. Thomas I. Gold therapy and its indications in dermatology. J Am Acad Dermatol 1987; 16: 845–854.

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