Flunisolide: A Review of its Pharmacological Properties and Therapeutic Efficacy in Rhinitis

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Summary

**Synopsis:** Flunisolide1, a derivative of fluocinolone acetonide, is advocated for intranasal inhalation for the treatment of perennial and seasonal allergic rhinitis. It is rapidly absorbed by all routes of administration, but it quickly undergoes extensive first-pass metabolism to a 6β-hydroxylated metabolite, which possesses only weak corticosteroid effects. Intranasal flunisolide relieves nasal symptoms (but not eye symptoms) in both perennial and seasonal allergic rhinitis, being most effective in patients who have an allergic component to their rhinitis; and like other intranasal corticosteroids it may reduce the need for systemic antihistamines in such patients, especially during peak pollen periods. A few well designed comparative studies have shown flunisolide to be as effective as intranasal beclomethasone, and (in a single study) more effective than intranasal sodium cromoglycate solution.

Only transient side effects have occurred, including nasal stinging and throat irritation. No Candida infections have been clinically apparent in short or longer term trials. Resting morning plasma cortisol levels have not been suppressed by usual therapeutic doses of intranasal flunisolide, but the drug's effects on hypothalamo-pituitary-adrenal (HPA) axis integrity during conditions of stress have not been evaluated.

**Pharmacology:** In animal studies flunisolide has several hundred times the anti-inflammatory, thymolitic and anti-adrenocorticotropic hormone activities of hydrocortisone. It has been shown in animal models to reduce inflammation after topical application, and in man to cause cutaneous vasoconstriction with an activity similar to beclomethasone dipropionate and triamcinolone acetonide. Inhaled flunisolide has an eosinophil suppressive potency one-third that seen with the intravenous route. Unlike systemically administered corticosteroids, inhaled flunisolide does not impair neutrophil chemotaxis.

Administration of intranasal flunisolide for several months did not produce drug related abnormalities on nasal biopsy. A small nasal septal perforation waxed in a single patient receiving flunisolide, but whether this was related to flunisolide treatment was unclear.

**Pharmacokinetic Studies:** Flunisolide is rapidly absorbed following oral ingestion and bronchial or intranasal inhalation. Systemic bioavailability is 21%, 39% and 49% when it is administered orally, by inhalation and intranasally, respectively. After intranasal inhalation, peak plasma concentrations are reached in 10 to 30 minutes. Flunisolide has a relatively large volume of distribution (about 1.8 L/kg) in man and is widely distributed to body tissues in rats. In man, it undergoes rapid and extensive first-pass metabolism to a 6β-hydroxylated metabolite, which has less than 0.01 times the potency of flunisolide, and is less than 3 times as potent as hydrocortisone. The plasma elimination half-life of flunisolide is about 1.8 hours by all routes of administration. After intravenous or oral administration flunisolide is excreted in the urine (about 50%) and faeces (about 40%), mainly as the 6β-hydroxylated metabolite and conjugates.

**Therapeutic Trials:** Flunisolide has been studied in a number of placebo controlled trials and in a few well designed comparative studies with other agents. Intranasal flunisolide (150

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1 ‘Syntaris’, ‘Rhinalar’, ‘Nasalide’ (Syntex).