Blocking of histamine-induced conjunctivitis by the oral antihistamine, astemizole

T.C. STOKES & G. FEINBERG

Chest Department and Department of Immunology, United Medical and Dental Schools, St Thomas' Campus, London SE1 7EH

When histamine is applied topically to the eye it produces stinging and inflammation of the caruncle and bulbar and palpebral conjunctiva. This model has been employed in the present study to assess the ability of an oral antihistamine, astemizole, to attenuate the irritation and inflammatory signs. Astemizole 30 mg, taken orally once daily for 1 week, considerably lessened the stinging and significantly lowered the signs of inflammation caused by topically applied histamines.

Keywords histamine conjunctivitis astemizole

Introduction

Challenge of the conjunctiva with allergen in allergic patients is a classical procedure. Challenge of normal conjunctiva with histamine is of more recent origin, but as early as 1951 Dannenberg and Feinberg employed conjunctival histamine challenge for the assessment of tolerance to antihistamines.

In the present study, we have used the technique of conjunctival challenge with histamine to assess the ability of the antihistamine astemizole to moderate histamine-induced conjunctivitis in human volunteers.

Methods

Histamine solution

Solutions of histamine dihydrochloride or histamine diphosphate were prepared in pH 7.2 phosphate-buffered saline to produce a neutral solution of histamine. Concentrations were made up ranging from 100 ng to 7240 µg histamine base per ml of solution.

Subjects

Twenty-one healthy volunteers over age 18 years who had no existing allergy or inflammatory eye disease, did not wear contact lenses and were taking no other medication were selected for the

trial. Pregnant or lactating women were excluded. There were no significant differences in age and sex distribution between the drug and placebo groups.

Conjunctival challenge

A wide range of histamine concentrations were tested in unmedicated volunteers to establish a scoring system for the conjunctival inflammatory response (Philips, 1984). (The response to such challenge in untreated subjects is described in the 'Results' section.)

For the purpose of the antihistamine trial, a challenge solution containing 12.5 µg histamine base per ml was selected. On a double-blind basis one eye received 25 µl of this histamine solution, the contralateral eye receiving 25 µl of phosphate-buffered saline.

The subjects were randomly allocated to receive either placebo or astemizole (30 mg) daily for 7 days. Placebo and drug were presented in identical tablets, coded and dispensed under double-blind conditions. Dosing was carried out under supervision each morning, at least 30 min before food.

Each subject was tested on day 1 of the trial prior to the start of medication and again 4 to 6 h after the final dose of medication/placebo 1 week later. Reactions were scored 15 min after histamine challenge.

	<i>Gross appearance</i>		<i>Bulbar conjunctiva</i>		<i>Palpebral conjunctiva</i>		<i>Caruncle</i>		<i>Total</i>	
<i>Total scores</i>	<i>ast</i>	<i>plac</i>	<i>ast</i>	<i>plac</i>	<i>ast</i>	<i>plac</i>	<i>ast</i>	<i>plac</i>	<i>ast</i>	<i>plac</i>
Pre-treatment score	34	36	34	36	34	35	38	36	140	143
Post-treatment score	25	32	24	32	21	31	23	34	93	128
Difference	-9	-4	-10	-4	-13	-4	-15	-2	-47	-15
P value (Wilcoxon signed rank test)	P = 0.05	NS	P = 0.05	NS	P = 0.01	NS	P = 0.01	NS	P < 0.01	NS

We found that in topical conjunctival histamine challenge with super-physiological doses (though the amount that actually penetrates the mucosa is unknown), stinging was of short duration and seemed disproportionate to the degree of inflammation observed. The stinging symptom abated long before the inflammatory signs. Nevertheless, all placebo subjects reported stinging of the histamine challenged eye, but only half the astemizole-treated subjects detected any stinging – and of a lesser degree than that experienced prior to taking the antihistamine.

Though the astemizole treatment lowered the histamine-induced inflammation to a significant degree, at the doses of astemizole and histamine used complete obliteration of inflammatory response was not achieved. To check whether oral

antihistamine treatment could effect complete suppression of conjunctival inflammatory response to a lower dose of histamine, we tested an additional five astemizole subjects with a challenge solution containing 100 ng histamine base ml^{-1} , as recommended by Abelson & Allansmith (1979), matched with five placebo controls. While the antihistamine could virtually obliterate the conjunctival inflammation, we found that the very mild inflammatory response of the placebo subjects increased the subjectivity of the scoring to an unacceptable level.

The results of our investigation support the findings in clinical studies (Howarth & Holgate, 1984) designed to assess the efficacy of astemizole treatment of allergic conjunctivitis associated with hayfever.

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