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Original Article

EFFECT OF FUCITHALMIC AND SOFINOX EYE DROPS ON EXPERIMENTAL ALLERGIC CONJUNCTIVITIS IN RATS

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ABSTRACT

Objective: To investigate the therapeutic effect of Fucithalmic 1%, Sofinox 0.5% and 1% eye drops against an IgE-mediated allergic conjunctivitis model in Wistar rats.

Methods: IgE-mediated allergic conjunctivitis was induced by ovalbumin antigen challenge. Allergic conjunctivitis induced control rats (Group I) received normal saline (0.9% NaCl; 10 µl/eye) whereas Fucithalmic 1% (Group II), Sofinox 0.5% (Group III) and 1% (Group IV) were administered as 10, 20 and 10 µl/eye respectively to the treatment group animals (n=6) for 15 days. Eye scratching behavior, hypothermia and edema was evaluated after topical antigen challenge.

Results: Sofinox 1% eye drops (10 µl/eye) significantly attenuated eye scratching behavior, hyperemia and edema in comparison with allergic conjunctivitis induced control ($p < 0.001$) and Fucithalmic 1% treated rats ($p < 0.05$). Eye scratching behavior and edema was also significantly decreased in Sofinox 0.5% eye drops (20 µl/eye) treatment group as compared to allergic conjunctivitis induced control rats ($p < 0.05$).

Conclusion: The present study revealed that the Sofinox eye drop is the potential agent that could offer a novel therapeutic opportunity against IgE-mediated allergic conjunctivitis in Wistar rats.

Keywords: Allergic conjunctivitis, Sofinox, Fucithalmic, IgE.

INTRODUCTION

Allergic eye diseases are complex inflammatory conditions of the conjunctiva with an increasing prevalence and incidence [1]. The major forms of allergic ocular diseases, seasonal and perennial allergic conjunctivitis, vernal and atopic kerato-conjunctivitis and giant papillary conjunctivitis, each have different pathophysiological and immunological components [2]. In contrast to these distinct entities, the current animal models are based on the sensitization against a small number of allergens such as ovalbumin, ragweed pollen or major cat allergens and consecutive challenge [2].

Allergic conjunctivitis is one of the inflammatory conditions of an eye with an increasing prevalence and incidence [2]. Despite the presence of disabling and prominent symptoms, this inflammatory condition is less studied and further evolutionary studies are required and more effective drugs need to be introduced. The test drug used in the present study is sodium fusidate (Sofinox) 0.5 and 1%. The steroid like structure of fusidic acid confers good anti-inflammatory property and does not possess the unwanted side effects of steroids. Hence the present study was planned to investigate the possible therapeutic role of Fucithalmic 1%, Sofinox eye drops (0.5 and 1%) in IgE-mediated rat allergic conjunctivitis model.

MATERIALS AND METHODS

Animals: 24 adult male Wistar rats weighing 150–300 g were housed in polypropylene cages, maintained under standard conditions with temperature (22–24^{0}C), 12-h light/12-h dark cycle and relative air humidity 40–60%. Rats had continuous access to norm caloric standard rat pellet diet (Hindustan Lever Ltd., Mumbai, India) and to tap water. The animals were acclimatized to the laboratory conditions for one week before the start of the experiment. The study was conducted in accordance with the Association for Research in Vision and Ophthalmology Statement for the Use of Animals in Research and Institutional Animal Ethics Committee guidelines after approval of the study protocol (Reference no. IAEC/KMC/36/2013).

Drugs

Fucithalmic 1%, Sofinox 0.5% and Sofinox 1% eye drops were obtained from Apex Laboratories Private Limited, Chennai (India).

Induction of experimetal allergic conjuctivitis:

Allergic conjunctivitis was induced in rats by the method of Minami K and Chiaki [1]. In brief, the rats were sensitized by injection of 0.6 ml of normal saline (0.9% NaCl) containing ovalbumin (1 mg), alum (2 mg) and complete Freund's adjuvant (0.1 ml) into the four footpads on the first day. Five days later, they were boosted by subcutaneous injection of 1 ml of normal saline (0.9% NaCl) containing ovalbumin (0.5 mg) at 10 sites on the back. Then, local sensitization was performed every day from day 15 to day 30 by instilling ovalbumin in normal saline (0.9% NaCl; 10 µl/site) into bilateral eyes using a micropipette.

Experimental procedure

In the experiment, a total of 24 Wistar rats of either sex were used. The rats were divided into four groups of six rats each. Before the experiment, the animals were placed in an observation cage (32 X 22X 10 cm) for about 10 min for acclimatization. The normal saline (0.9% NaCl; 10 µl/eye) and test drugs to their corresponding treatment group were instilled 30 minutes before the antigen challenge into the bilateral eyes. Treatment was done for 15 days from 15th to 30th day as follows- *Group I:* Allergic conjunctivitis induced negative control rats; normal saline (0.9% NaCl; 10 µl/site) solution was instilled into the bilateral eyes for 15 days. *Group II:* Allergic conjunctivitis induced positive control rats; Fucithalmic eye drops 1% (10 µl/site) were instilled into the bilateral eyes for 15 days. *Group III:* Allergic conjunctivitis induced rats; Sofinox eye drops 0.5% (X-191; 20 µl/site) were instilled into the bilateral eyes for 15 days. *Group IV:* Allergic conjunctivitis induced rats; Sofinox eye drops 1% (X-192; 10µl/site) were instilled into the bilateral eyes for 15 days.

Evaluation of conjunctival symptoms

After the instillation of 10 µl/site of ovalbumin dissolved in normal saline solution (0.9% NaCl) into the bilateral eyes, rats were placed

into the observation cage (1 animal/cage), and the number of eye scratches was counted for 20 min. Eye scratching behavior was defined as fore-limb movements over two times directed to the ocular surface, Hyperemia and edema were evaluated at 5 and 20 min, respectively, after topical antigen challenge. The scoring for hyperemia and edema was done individually by two investigators who were blinded to the treatments of the animals. Thereafter, average of their given scores was considered as the final score for each symptoms- hyperemia and edema.

Allergic symptoms (hyperemia and edema of the conjunctiva) were observed using the scoring system given below (Table 1)-

Table 1: The scoring system used for estimating the severity of conjunctivitis:

Score	Symptoms	
	Hyperemia	**Edema**
0	No symptoms	No symptoms
1	Slight hyperemia in one-eye	Slight edema in one-eye
2	Slight hyperemia in bilateral eyes	Slight edema in bilateral eyes
3	Severe hyperemia in one-eye and slight hyperemia in the other eye	Severe edema in one-eye and slight edema in the other eye
4	Severe hyperemia in bilateral eyes	Severe edema in bilateral eyes

Table 2: Eye scratching behavior score (Up to 20 minutes after topical antigen challenge):

Groups	Dose	Mean ±SEM	P value	Significance
I	Allergic conjunctivitis control rats- Normal saline (0.9% NaCl, 10 µl/eye)	12.66±1.20	----	
II	Allergic conjunctivitis rats treated with Fucithalmic eye drop (1%, 10 µl/eye)	8.33±0.84	0.029[a]	**S**
III	Allergic conjunctivitis rats treated with Sofinox eye drop (X-191; 0.5%, 20 µl/eye)	8.66±1.30	0.048[a]	**S**
IV	Allergic conjunctivitis rats treated with Sofinox eye drop (X-192; 1%, 10 µl/eye)	4.16±0.40	< 0.001[a]0.038[b] 0.023[c]	**S**

[a]compared to allergic conjunctivitis induced control rats [b]compared to allergic conjunctivitis induced rats treated with Fucithalmic 1% eye drops [C]compared to allergic conjunctivitis induced rats treated with Sofinox 0.5% eye drops S- Significant

Table 3: Hyperemia score (At 5th minute after topical antigen challenge):

Groups	Dose	Mean ±SEM	P value	Significance
I	Allergic conjunctivitis control rats- Normal saline (0.9% NaCl, 10 µl/eye)	3.66±0.21	----	
II	Allergic conjunctivitis rats treated with Fucithalmic eye drop (1%, 10 µl/eye)	3.00±0.36	0.484[a]	**NS**
III	Allergic conjunctivitis rats treated with Sofinox eye drop (X-191; 0.5%, 20 µl/eye)	2.66±0.33	0.164[a]	**NS**
IV	Allergic conjunctivitis rats treated with Sofinox eye drop (X-192; 1%, 10 µl/eye)	1.00±0.36	< 0.001[a]0.002[b] 0.008[c]	**S**

[a]compared to allergic conjunctivitis induced control rats [b]compared to allergic conjunctivitis induced rats treated with Fucithalmic 1% eye drops [C]compared to allergic conjunctivitis induced rats treated with Sofinox 0.5% eye drops NS- Not significant S- Significant

Table 4: Edema score (At 20thminute after topical antigen challenge):

Groups	Dose	Mean ±SEM	P value	Significance
I	Allergic conjunctivitis control rats- Normal saline (0.9% NaCl, 10 µl/eye)	3.86±0.16	----	
II	Allergic conjunctivitis rats treated with Fucithalmic eye drop (1%, 10 µl/eye)	3.16±0.16	0.175[a]	**NS**
III	Allergic conjunctivitis rats treated with Sofinox eye drop (X-191; 0.5%, 20 µl/eye)	2.33±0.21	0.001[a]	**S**
IV	Allergic conjunctivitis rats treated with Sofinox eye drop (X-192; 1%, 10 µl/eye)	2.16±0.30	< 0.001[a]0.021[b]	**S**

[a]compared to allergic conjunctivitis induced control rats [b]compared to allergic conjunctivitis induced rats treated with Fucithalmic 1% eye drops NS- Not significant S- Significant

Data analysis

Using SPSS version 20.0. Data was expressed as mean ± Standard error of mean (SEM) and analyzed by one way analysis of variance (ANOVA) followed by post doc Tukey test. *P* value less than 0.05 was considered as statistically significant.

RESULTS

There were significant changes in Sofinox 1% (10 µl/eye) treated rat group for all the three conjunctival symptoms (Eye scratching behavior, hyperemia and Edema) when compared with allergic conjunctivitis induced control rats and Fucithalmic 1% eye drops treated rats. There was also the significant decrease in eye scratching behavior and hyperemia for Sofinox 1% eye drops (10 µl/eye) treated rats in comparison with Sofinox 0.5% eye drops (20 µl/eye) treatment group. Eye scratching behavior and edema was significantly reduced in Sofinox 0.5% eye drops (20 µl/eye) treatment group as compared to allergic conjunctivitis induced control rats (Table 2-4).

DISCUSSION

Allergic conjunctivitis is a common ocular disorder. The pathophysiology of allergic conjunctivitis involves primarily a type I hypersensitivity mechanism, with release of histamine and other chemical mediators from mast cells [3]. However, a type IV hypersensitivity with participation of secondary inflammatory cells, such as T helper cells, eosinophils, and their chemical mediators, also plays a role. Current therapy of allergic conjunctivitis is based

on general measures that aim at eliminating exposure to the allergen, and medical treatment. Antihistamines, mast cell stabilizers, non-steroidal anti-inflammatory agents and corticosteroids are used to treat allergic conjunctivitis [3]. The present study demonstrated that fucithalmic 1%, sofinox 0.5% and sofinox 1% eye drops reduced the symptoms of acute conjunctivitis namely eye scratching, hyperemia and edema. All three eye drops used in this study contain the antibiotic fusidic acid. Fucithalmic is a 1% microcrystalline suspension of fusidic acid in a carbomer gel. The sustained release formulation of Fucithalmic provides prolonged contact with the eye. Sofinox eye drops are 0.5% and 1% microcrystalline suspension of sodium fusidate (equivalent to fusidic acid 0.25% w/w) homogenous, white viscous liquid.

One of the in vitro studies suggested that fusidic acid has immunomodulatory effects similar to cyclosporin A [4]. In addition, the anti-inflammatory and immunosuppressive effects of fusidic acid may reduce meningeal inflammation [5]. It is also reported that fusidic acid attenuated systemic levels of the proinflammatory cytokines, tumor necrosis factor-α and IL-8 [6]. Hence the beneficial effect of these eye drops in allergic conjunctivitis may be due to its anti-inflammatory and or immunomodualtory effect.

The present study revealed the therapeutic role of Fucithalmic 1%, Sofinox 0.5 and 1% eye drops in allergic conjunctivitis. The Sofinox 1% eye drops showed a better activity than Fucithalmic 1% eye drops against allergic conjunctivitis in rats. Further, clinical evaluation has to be performed to precisely define the role of Sofinox 1% eye drops in allergic conjunctivitis conditions of human subjects.

CONFLICT OF INTERESTS

Declared None

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