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EFFICACY AND SAFETY OF A DEXAMETHASONE INTRACANALICULAR INSERT IN PATIENTS WITH ALLERGIC CONJUNCTIVITIS: A RANDOMIZED CONTROL STUDY

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ABSTRACT

Allergic conjunctivitis affects up to 40% of the general population1, and it is linked to a reduction in patients' quality of life. Allergens can be seasonal (like pollen) or perennial (like dust mites and pet dander), but allergic conjunctivitis symptoms include ocular irritation, tearing, burning, stinging, photophobia, redness, conjunctival swelling, and nasal problems. Allergic conjunctivitis is produced by an allergic reaction to an allergen that binds to immunoglobulin E on the surface of mast cells, resulting in inflammation. Mast cell activation and subsequent cellular release of histamine, tryptase, prostaglandins, and leukotrienes, which are responsible for the early phase of the allergic response, are induced by this binding (20-30 minutes after exposure). The aim of this research was to see how effective and safe a dexamethasone intracanalicular insert was at treating allergic conjunctivitis. The dexamethasone insert is used to alleviate itching caused by allergic conjunctivitis in the short term. Patients cannot abuse this insert because it is supplied by a physician and the dexamethasone is released for up to 30 days. The hydrogel implant biodegrades fully without the need for removal over time. Patients will need to be re-evaluated by the clinician if they require retreatment during the course of their disease..

Key words: Dexamethasone, Intracanalicular, Allergic Conjunctivitis.

INTRODUCTION

Allergic conjunctivitis affects up to 40% of the general population1, and it is linked to a reduction in patients' quality of life. Allergens can be seasonal (like pollen) or perennial (like dust mites and pet dander), but allergic conjunctivitis symptoms include ocular irritation, tearing, burning, stinging, photophobia, redness, conjunctival swelling, and nasal problems [1, 2]. Allergic conjunctivitis is produced by an allergic reaction to an allergen that binds to immunoglobulin E on the surface of mast cells, resulting in inflammation [3, 4]. Mast cell activation and subsequent cellular release of histamine, tryptase, prostaglandins, and leukotrienes, which are responsible for the early phase of the allergic response, are induced by this binding (20-30 minutes after exposure) [5, 6]. In addition, mast cell degranulation activates vascular endothelial cells, which recruit inflammatory cells to the conjunctival mucosa, resulting in the late phase of the allergic response, which occurs 4-8 hours after allergen contact [7, 8]. Topical antihistamines, which block histamine receptors competitively and reversibly, are often used to treat allergic conjunctivitis. They have a quick onset but a short duration of effect, necessitating multiple instillations throughout the day [9].

Antihistamines are often effective against the early stages of the allergic response due to their mode of action.

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Antihistamines can cause dizziness, sedation, blurred vision, poor cognition, ocular burning, and ocular dryness, among other side effects.

Topical mast cell stabilizers are another type of pharmacologic agent used to treat allergic conjunctivitis; they work by inhibiting mast cell degranulation, potentially preventing the release of histamine and other allergic mediators, but they require a long loading period, which means they must be used regularly for weeks prior to expected allergen exposure [10, 11]. Preservatives are used in most eye drops, including all antihistamines and mast cell stabilizers permitted in the United States, and can induce ocular irritation, corneal toxicity, and ocular surface damage. As a result, a modified Ora-CAC model has been established, in which a series of repeated allergen challenges (four challenges over a two-day interval) generates the inflammatory component of allergic conjunctivitis, including an increase in cellular infiltrates [12].

Aim and Objective:

The aim of this research was to see how effective and safe a dexamethasone intracanalicular insert was at treating allergic conjunctivitis.

Material and Methods:

This was a placebo-controlled, multicenter, randomized, control study. The study followed the Declaration of Helsinki's principles and was in compliance with the Health Insurance Portability and Accountability Act. For all participating locations, a single central Institutional Review Board was used, and both the protocol and the informed consent form received IRB clearance before the trial began. Subjects signed the Health Insurance Portability and Accountability Act of 1996 form after providing written informed permission. A Phase 3 Study Evaluating the Safety and Efficacy of OTX-DP for the Treatment of Chronic Allergic Conjunctivitis has been registered on ClinicalTrials.gov. Subjects had to be at least 18 years old, have a history of ocular allergies, and have a positive skin test reaction to both a perennial (cat or dog dander, dust mites, cockroaches) and a seasonal allergen (trees, grasses, and/or ragweed), as confirmed by the allergic skin test given at the subject's initial screening visit. A positive bilateral CAC reaction (i.e., ocular itching score 2 on the Ora Calibri itching scale, which measures ocular itching on a scale of 0-4 where 0 = none and 4 = severe, and a conjunctival redness score 2 on the Ora Calibri conjunctival redness scale, which measures ocular redness on a scale of 0-4 where a score A positive bilateral CAC reaction for at least 2 of the 3 time points following the challenge during the first confirmatory CAC (on both visits); an average itching score of 3 and a conjunctival redness score of 2.5 for both eyes at post-CAC assessments during the second confirmatory CAC; and a visual acuity of 0.7 log MAR or better in each eye during the second confirmatory CAC The primary efficacy analyses were conducted using Markov chain Monte Carlo multiple imputation methodology on an intent-to-treat (ITT) population (all randomized patients). The safety population was used to conduct all analyses (all subjects who received an ophthalmic insert). SAS version 9.2 software was used to conduct statistical analysis on the data gathered from this investigation. A total of 40 patients per treatment arm provided 91.4 percent and 98.6% power, respectively, to show a statistically significant difference in ocular itching between the dexamethasone insert and the placebo. Assuming a difference of 0.8 units at the first time point and 1.0 unit at the final two time points, an SD of 1.0 unit, and a 2-sided Type I error of 0.05, insert arms at the first and each of the last two post-CAC time points of week-1 CAC-day 8.

Table1: Disposition and demographics and baseline characteristics

Population	Dexamethasone inserts	Placebo insert
ITT	38	32
Safety	36	34
Characteristics (ITT population)	(n= 38)	(n=32)
Age in years Mean ±SD Median Min, max s	 38.1±11.62 37 19.1, 66.2	 36.2±12.14 36 18.6, 61.5
Sex Male Females	 23 (60.12%) 15 (39.46%)	 20 (62.5%) 12 (37.5%)
Ethnicity Hispanic or Latino Not Hispanic or Latino NR/ unknown	 12 (31.52%) 15 (39.47%) 11 (28.94%)	 18 (56.25%) 5(15.25%) 9 (28.15%)
Race Asian	 12 (31.57%)	 12 (31.57%)

White	10 (26.31%)	8 (21.05%)
Black/ African American	5 (13.15%)	10 (26.31%)
Multiple	11 (28.94%)	2 (5.26%)

Results and Discussion:

This trial included 70 participants, 35 of whom were randomly assigned to the dexamethasone insert arm and 38 to the placebo insert arm. 70 of the 73 subjects enrolled in the ITT population and analyzed for the primary outcome (Table 1) completed the study, while two subjects (1 in each treatment arm) dropped out due to withdrawn consent and one subject (in the dexamethasone insert arm) dropped out due to unsuccessful insert placement.

As a result, 70 people received the therapy they needed. The safety population consisted of 70 participants (minus the subject who had the dexamethasone insert placed incorrectly) (Table 1). Table 1 shows the demographics and baseline characteristics of the ITT population. The patients that received the dexamethasone insert had an average age of 38.2 years and were evenly split between Asians and Caucasians.

The dexamethasone insert arm had significantly lower scores for subject-reported ocular itching (on a scale of 0 [none] to 4 [severe]) than the placebo insert arm at the week-1 CAC-day 8 visit, with a 0.91-point difference at 3 minutes (1.71 vs. 2.62, respectively), a 0.87-point difference at 5 minutes (1.90 vs. 2.77, respectively), and a 1.00-point difference at At practically every time point (3, 5, and 7 minutes post CAC) at each visit (week-1 CAC-day 6 through week-4 CAC-days 28-31), the dexamethasone insert arm demonstrated a substantial reduction in ocular irritation compared to the placebo insert arm, for a total of 34 of 36 distinct time points.

The dexamethasone insert is used to alleviate itching caused by allergic conjunctivitis in the short term. Patients cannot abuse this insert because it is supplied by a physician and the dexamethasone is released for up to 30 days. The hydrogel implant biodegrades fully without the need for removal over time. Patients will need to be re-evaluated by the clinician if they require retreatment during the course of their disease.

Conclusion:

In conclusion, these findings show that a single, hands-free, physician-administered, preservative-free dexamethasone intracanalicular insert treatment can offer alleviation of allergic conjunctivitis signs and symptoms for up to four weeks while preserving a positive safety profile.

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