Oral Antihistamines

Primary Literature

Torkildsen G, Gomes P, Welch D, et. al (2009) Evaluation of desloratadine on conjunctival allergen challenge-induced ocular symptoms. Clinical & Experimental Allergy. 39: 1052 – 1059.

Study Objective

- To evalute the impact of administering oral desloratadine 5 mg daily for 7 days on ocular symptoms in conjunctival allergen-challenged subjects.

Methods

- Design: Double-blind, randomized, placebo-controlled, cross-over study investigating the impact of 7 days of desloratadine 5 mg once daily or placebo on allergen-provoked symptoms of allergic conjunctivitis in adults with a $\geq$ 2-year history of allergic conjunctivitis associated with seasonal allergic rhinitis.
- Allocation: Subjects with a qualifying response to an ocular symptom severity erythema score $\leq$ 1 at baseline, as well as a response of bilateral ocular pruritus score $\geq$ 2 and a bilateral ocular redness score $\geq$ 2 within 10 minutes post allergen-challenge were randomized in a 1:1 to receive either desloratadine 5mg once daily or placebo at visit 3. After a 2-week washout period, subjects crossed over to the other treatment.
- Blinding: This study utilized a computer-generated code to randomize the groups.
- Follow-up period: Bilateral ocular redness, chemosis, eyelid swelling, and tearing were assessed at 10, 15, and 20 minutes post-challenge. Bilateral ocular pruritus scores were analysed at 3, 5, and 7 minutes. These values were measured after a 7-day therapy of the treatment.
- Setting: The study was conducted according to the Declaration of Helsinki and subsequent revisions and in compliance with Good Clinical Practice. The study protocol and consent forms were reviewed and approved by the Independent Ethics Committee or Institutional Review Board at each study centre.
- Participants: Seventy-six subjects were screened and 41 subjects with a confirmed qualifying allergen challenge response were included in the study. Exclusion criteria were pregnant or nursing women, abnormal physical examination, treatment with inhaled or oral corticosteroids, beta-2-agonists, cromones, theophylline, or leukotriene inhibitors who could not go through the washout periods and the entire study without using these medications, history of intranasal drug abuse, known hypersensitivity, allergy or idiosyncratic reaction to the study drug, use of the study drug within 30 days before enrollment, immunotherapy within 24 hours before any visit, unwilling to discontinue use of contact lenses during study, and dependence

upon nasal, oral, or ocular decongestants; nasal topical antihistamines; or nasal steroids.

- Intervention: Patients were administered oral desloratadine 5 mg daily for 7 days.
- Outcomes: The mean composite ocular redness score was reduced at 10, 15, and 20 minutes post-challenge with desloratadine treatment compared with placebo, though these differences were not statistically significant. Desloratadine was significantly more effective than placebo in preventing post-challenge ocular pruritus ($P < 0.001$). There was also significant improvements in ciliary and episcleral redness, chemosis, eyelid swelling, and tearing in the treatment group ($P<0.05$ vs. placebo for all comparisons).
- Patient Follow-Up: Subjects receiving desloratadine reported six (14.6%) treatment-emergent adverse effects compared with four (10.5%) in the placebo group. All adverse effects were mild or moderate and no subject discontinued because of an adverse effect. Subjects were not re-assessed after the 7 days post medication and post placebo.

Main Results:

- The change from baseline in mean composite ocular redness scores at 10, 15 and 20 minutes post-challenge was lower with desloratadine compared with placebo: 5.18, 5.43, and 5.30 vs. 5.84, 6.06, and 5.89 at 10, 15, and 20 minutes, respectively. These differences however, were not statistically significant ($P = 0.07$, 0.08, and 0.09, respectively).
- Desloratidine treatment was significantly more effective than placebo at all post-challenge time-points in preventing ocular pruritis, chemosis, eyelid swelling, and tearing. At 3, 5, and 7 minutes post-challenge, the mean change from baseline in pruritus scores for desloratadine (1.45, 1.66, and 1.41, respectively) was significantly less ($P<0.001$ for all comparisons) than those for placebo (2.24, 2.44, and 2.31, respectively).

Conclusions:

- The authors conclusion states that desloratadine administered 5 mg once daily for 7 days reduced ocular redness and pruritus, chemosis, eyelid swelling, and tearing following a conjunctival allergen challenge in subjects with a history of seasonal allergic conjunctivitis and demonstrated an adverse effect profile similar to that of placebo

Comments and Critical Appraisal

- Overall, this study showed only a statistically significant difference from desloratadine and placebo for its secondary endpoints, but not the primary endpoints
- This study also had a considerably small number of subjects
- Therefore, this study represents weak evidence to support oral antihistamines as a first line treatment

- Although this study was double-blinded and randomized, multiple observers who had undergone redness-standardization training measured the endpoints. This is a weakness of the study, since the endpoints were subjective.
- A strength was the fact that each subject had a trial of the placebo and desloratadine 5mg. Therefore, the results of the treatment arm of the study were compared amongst the results of the placebo arm of the study on an individual basis. This eliminates variability amongst subjects.
- In terms of external validity, the study had a very long list of exclusion criteria. In fact, 76 subjects were screened and only 41 subjects were included in the study. Furthermore, of the criteria considered as an abnormal physical examination was a history of asthma. Dependence upon nasal, oral or ocular decongestants was also an exclusion criteria of the study. Therefore, this study has a moderate external validity, since its exclusion criteria most likely eliminates many patients that would experience allergic conjunctivitis.

Schoeneich M. and R. Pecoud (1990) Effect of cetirizine in a conjunctival provocation test with allergens. Clinical and Experimental Allergy. 20: 173 – 174.

Study Objective

- To determine the effect of cetirizine on allergen-induced itching and redness of the eye

Methods:

- Design: Double-blind and placebo-controlled study
- Allocation: The subjects underwent a conjunctival provocation test (CPT). If the CPT was positive, the subjects entered the study. The subjects underwent two other CPTs, one after placebo and one after cetirizine treatment in a random order. There was a 2 week interval between two CPTs.
- Blinding: The authors state that it was a double-blinded study but did not specify as to how the treatment orders were determined.
- Follow-up Period: Between 4 and 8 hours after the CPT, the subjects were examined by the investigator.
- Setting: The study was performed in a hospital in the winter. Patients gave written consent and the study was approved by the Ethics Committee of the same hospital.
- Participants: Eleven subjects (seven males, mean age 26 $\pm$ 5 year, range 17 – 35) were studied. All suffered from seasonal rhino-conjunctivitis due to hypersensitivity in grass pollen.

- Intervention: Patients were administered oral cetirizine 10mg twice a day for four days.
- Outcomes: The mean conjunctival allergic reaction threshold, the mean allergen concentration inducing either itching or redness, and the severity of the symptoms produced by the highest allergen concentration.
- Patient follow-up: Subjects were not re-assessed after the 7 days post medication and post placebo.

Main Results

- Itching was prevented by cetirizine
- Redness was also prevented by cetirizine compared to placebo, however it was not statistically significant
- The intensity of the itching and redness was significantly milder after cetirizine compared to placebo.

Conclusions

- The authors' main conclusion was that oral cetirizine administration has a good protective effect against allergic conjunctivitis and might be useful in subjects suffering from this disease during hay fever season
- The authors' did however state that CPT may not be the best model to study allergic reactions in humans since they might be seen only when larger amounts of allergen are used, which would be uncomfortable for the subjects

Comments and Critical Appraisal

- Overall, this study had very weak evidence to support the efficacy of oral antihistamines in allergic conjunctivitis
- There were many weaknesses of this study including a small sample size, out-to-date information (study conducted in 1990), and the outcomes measured were subjective.
- A strength was the fact that each subject had a trial of the placebo and cetirizine. Therefore, the results of the treatment arm of the study were compared amongst the results of the placebo arm of the study on an individual basis. This eliminates variability amongst subjects.
- This study does not have strong external validity, since this study was conducted at a time when second-generation antihistamines were not yet created. Therefore, this information is quite obsolete, since many other alternative oral antihistamines have been manufactured.