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[Intervention Review]

Topical antihistamines and mast cell stabilisers for treating seasonal and perennial allergic conjunctivitis

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ABSTRACT

Background

Seasonal/perennial allergic conjunctivitis is the most common allergic conjunctivitis, usually with acute manifestations when a person is exposed to allergens and with typical signs and symptoms including itching, redness, and tearing. The clinical signs and symptoms of allergic conjunctivitis are mediated by the release of histamine by mast cells. Histamine antagonists (also called antihistamines) inhibit the action of histamine by blocking histamine H1 receptors, antagonising the vasoconstrictor, and to a lesser extent, the vasodilator effects of histamine. Mast cell stabilisers inhibit degranulation and consequently the release of histamine by interrupting the normal chain of intracellular signals.

Topical treatments include eye drops with antihistamines, mast cell stabilisers, non-steroidal anti-inflammatory drugs, combinations of the previous treatments, and corticosteroids. Standard treatment is based on topical antihistamines alone or topical mast cell stabilisers alone or a combination of treatments. There is clinical uncertainty about the relative efficacy and safety of topical treatment.

Objectives

The objective of this review was to assess the effects of topical antihistamines and mast cell stabilisers, alone or in combination, for use in treating seasonal and perennial allergic conjunctivitis.

Search methods

We searched CENTRAL (which contains the Cochrane Eyes and Vision Trials Register) (2014, Issue 7), Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily, Ovid OLDMEDLINE (January 1946 to July 2014), EMBASE (January 1980 to July 2014), the *metaRegister* of Controlled Trials (*mRCT*) (www.controlled-trials.com), ClinicalTrials.gov (www.clinicaltrials.gov) and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictcp/search/en). We did not use any date or language restrictions in the electronic searches for trials. We last searched the electronic databases on 17 July 2014. We also searched the reference lists of review articles and relevant trial reports for details of further relevant publications.

Selection criteria

We included randomised controlled trials (RCTs) comparing topical antihistamine and mast cell stabilisers, alone or in combination, with placebo, no treatment or to any other antihistamine or mast cell stabiliser, or both, that examined people with seasonal or perennial allergic conjunctivitis, or both. The primary outcome was any participant-reported evaluation (by questionnaire) of severity of four main

ocular symptoms: itching, irritation, watering eye (tearing), and photophobia (dislike of light), both separately and, if possible, by an overall symptom score. We considered any follow-up time between one week and one year.

Data collection and analysis

Two review authors independently extracted data and assessed risk of bias. Disagreements were resolved by discussion among review authors and the involvement of a third review author. We followed standard methodological approaches used by Cochrane.

Main results

We identified 30 trials with a total of 4344 participants randomised, with 17 different drugs or treatment comparisons. The following antihistamines and mast cell stabilisers were evaluated in at least one RCT: nedocromil sodium or sodium cromoglycate, olopatadine, ketotifen, azelastine, emedastine, levocabastine (or levocabastine), mequitazine, bepotastine besilate, combination of antazoline and tetryzoline, combination of levocabastine and pemirolast potassium. The most common comparison was azelastine versus placebo (nine studies).

We observed a large variability in reporting outcomes. The quality of the studies and reporting was variable, but overall the risk of bias was low. Trials evaluated only short-term effects, with a range of treatment of one to eight weeks. Meta-analysis was only possible in one comparison (olopatadine versus ketotifen). There was some evidence to support that topical antihistamines and mast cell stabilisers reduce symptoms and signs of seasonal allergic conjunctivitis when compared with placebo. There were no reported serious adverse events related to the use of topical antihistamine and mast cell stabilisers treatment.

Authors' conclusions

It seems that all reported topical antihistamines and mast cell stabilisers reduce symptoms and signs of seasonal allergic conjunctivitis when compared with placebo in the short term. However, there is no long-term data on their efficacy. Direct comparisons of different antihistamines and mast cell stabilisers need to be interpreted with caution. Overall, topical antihistamines and mast cell stabilisers appear to be safe and well tolerated. We observed a large variability in outcomes reported. Poor quality of reporting challenged the synthesis of evidence.

PLAIN LANGUAGE SUMMARY

Topical antihistamines and mast cell stabilisers for treating seasonal and perennial allergic conjunctivitis

Review question

Are treatments with eye drops of antihistamines and mast cell stabilisers, alone or in combination, effective and safe in people with seasonal and allergic conjunctivitis? The main outcome measure was eye symptoms reported by participants, including eye itching, irritation (burning sensation), watering eyes (tearing), and photophobia (dislike of light). We found 30 trials.

Background

Conjunctivitis refers to inflammation of the conjunctiva, which is the thin tissue that covers the sclera (white part of the eye). Seasonal and perennial allergic conjunctivitis is the most common type of allergic conjunctivitis. Although this condition does not cause sight loss, it can cause intense itching and eye watering. Eye drops with antihistamines or mast cell stabilisers, or both are commonly used.

Study characteristics

The evidence is current to July 2014. Among the 30 studies reviewed there were 17 different comparisons, including 4344 participants ranging in age between 4 and 85 years. The duration of treatment ranged from one to eight weeks. Ten out of 30 studies were funded by the drug manufacturer (8 totally and 2 partially funded); 20 studies did not report any source of funding. There was inconsistency in the way the effect of treatment was measured and reported. Overall risk of bias was low.

Key results

Topical antihistamines and mast cell stabilisers, alone or in combination, are safe and effective for reducing symptoms of seasonal and perennial allergic conjunctivitis. We found insufficient evidence to discern which topical antihistamines and mast cell stabilisers are the most effective.