An Effective Treatment for Allergy Sufferers

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Homeopathy, a form of medicine based on the theory, "like cures like," has found its way into the ophthalmic community. However, since it's difficult to determine the mechanism of action of most homeopathic remedies due to the minute concentration of active ingredients, many physicians feel they lack scientific merit. In the following study, we evaluated the efficacy of Similasan Eye Drops #2, a homeopathic treatment containing extracts of honey bee, eyebright, and cevadillas, in order to prove that it significantly reduces the signs and symptoms of allergic conjunctivitis as induced by allergen challenge.

Materials and Methods

Before beginning the study, we performed a baseline slit lamp exam to insure that all subjects' ocular health was within normal limits. Subjects who exhibited greater than 1+ hyperemia, reported any ocular itching, or did not meet the entry criteria were not admitted into the study. To continue in this study, subjects had to agree to refrain from using any nonsteroidal anti-inflammatories (NSAIDS), antihistamines or steroids during the study. Contact lens wear was also prohibited for the study duration.

Antigen Challenge

We challenged 47 subjects with increasing doses of a solubilized antigen (short ragweed, cat dander, or timothy grass), to which they were sensitized, until each subject responded with at least 2+ itching and ciliary, conjunctival and episcleral hyperemia bilaterally, as graded by a standard scale (Table 1). We excused any subjects who failed to manifest 2+ itching and 2+ hyperemia.

Table 1: Scoring system to measure the signs and symptoms of allergic conjunctivitis.

Eyelid swelling, chemosis and hyperemia (ciliary, conjunctival, and episcleral with accompanying photographic standards). All graded separately.

0 = none

1 = mild

2 = moderate

3 = severe

4 = unusually severe

Tearing

0 = none

1 = mild (eyes feel slightly watery)

2 = moderate (blows nose occasionally)

3 = severe (tears rolling down cheeks)

Mucous discharge

0 = none

1 = present

Itching, as graded by the subject

0 = none

1 = an intermittent tickle sensation in the inner corner

2 = a mild continuous itch not requiring rubbing

3 = a definite itch; you would like to be able to rub

4 = an incapacitating itch that requires eye rubbing

0.5 increments are allowed.

At day seven, we confirmed the reproducibility of the initial response by instilling the final dose of antigen. Ten minutes after challenge, we evaluated conjunctival, episcleral and ciliary hyperemia, chemosis, lid swelling, tearing and itching.

Subjects who responded with 2+ itching and hyperemia (n=33) were given masked bottles marked "1" and "2" containing either drug or saline as control. We randomly assigned the masked bottles to each eye according to a predetermined randomization code (contralateral control within each individual). We instructed the subject to administer 1-2 drops of the appropriate liquid into the assigned eye q.i.d. for 14 days.

At day 21, we performed a baseline ophthalmic examination and administered the final dose of the appropriate medication into each assigned eye. Within five minutes of installation, we examined the eye to assess comfort and safety. Ten minutes after installation, we challenged each subject with the final dose and evaluated conjunctival, episcleral, and ciliary hyperemia, chemosis, lid swelling, tearing and itching at 3, 10, and 30 minutes following the antigen challenge.

Results

We compared the means ±S.E.M. from the drug treated group at the 10-minute examination on visit 3 (after treatment installation) to the means ±S.E.M. from the drug treated group at the 10-minute exams in visits 1 and 2 (preceding treatment installation). We also made the same comparisons within the placebo-treated group.

These analyses revealed that both the ciliary hyperemia and the conjunctival hyperemia scores were significantly less at visit 3, after administration of the respective treatments, than at comparable time points at visit 1 and 2. The differences between the means were similar for ciliary and conjunctival hyperemia in both groups (Table 2).

When we added the ciliary, conjunctival, and episcleral hyperemia scores, the comparison means ±S.E.M. showed significant differences between visits 1 and 3, and visits 2 and 3 in both groups (Table 3).

Itching was significantly less at visit 3 following treatment, than at visits 1 and 2 preceding treatment in both groups (table 4). The differences between the means are again similar for the placebo- and the drug-treated groups.

In different comparisons between the active treated group and the placebo treated group on visit 3, we did not obtain significant differences at any time following antigen challenge in any parameter.

Safety and Comfort

Similasan #2 appears to be a safe and comfortable product. Following two weeks of q.i.d. dosing, there were no adverse events reported. Following installation of the medication, we noted no significant changes in any of the safety parameters.

Discussion

These data suggest that Similasan Eye Drops #2, a homeopathic remedy, significantly reduces hyperemia and itching, the hallmark parameters of ocular hayfever. Ciliary and conjunctival hyperemia decreased by approximately a 0.5 unit in the scoring system, while itching was decreased by 1.0 unit. This 1.0 unit of itching is statistically significant. In addition, according to the FDA's general dictate defining products of efficacy, 1.0 unit of difference indicates clinical relevance as well.

These significant differences were found in both the placebo-treated and the drug-treated groups, however, this

Table 2: Hyperemia sum means +S.E.M. for all visits

Eye	Comparison of visits (A vs. B)	Mean ± S.E.M. A	Mean ± S.E.M. B	Mean Diff. (A-B)	pValue paired	pValue nonpaired
Drug	1 vs. 2	7.25±0.28	7.38±0.31	-0.13	0.99	0.77
	2 vs. 3	7.38±0.31	6.11±0.43	1.27	0.0008	0.02
	1 vs. 3	7.25±0.28	6.11±0.43	1.14	0.004	0.03
Placebo	1 vs. 2	7.25±0.27	7.27±0.29	-0.02	0.96	0.97
	2 vs. 3	7.27±0.29	6.13±0.42	1.15	0.003	0.03
	1 vs. 3	7.25±0.27	6.13±0.42	1.12	0.009	0.03

Visits 1 & 2: Prior to treatment instillation
Visit 3: Following treatment instillation
Significant p values indicated in bold

Table 3: Itching means ±S.E.M. for visits 1,2,3

Eye	Comparison of visits (A vs. B)	Mean ± S.E.M. A	Mean ± S.E.M. B	Mean Diff. (A-B)	pValue paired	pValue nonpaired
Placebo	1 vs. 2	2.98± 0.11	3.05± 3.10	-0.07	-	-
	2 vs. 3	3.05± 0.10	1.89± 0.16	1.16	0.0001	0.0001
	1 vs. 3	2.98± .011	1.89± .016	1.09	0.0001	0.0001
Drug	1 vs. 2	2.97± 0.10	3.05± 0.10	-0.08	0.9999	-
	2 vs. 3	3.05± 0.10	2.00± 0.20	1.05	0.0001	0.0001
	1 vs. 3	2.97± 0.10	2.00± 0.20	0.97	0.0002	0.0001

Visits 1 & 2: Prior to treatment instillation
Visit 3: Following treatment instillation
Significant p values indicated in bold
- = analysis unable to be applied to data

Table 4: Means ±S.E.M. and p values:
TIME RESPONSE OF DRUG DURING VISIT 3

Time (min)		Ciliary Hyperemia	Conjunctival Hyperemia	Episcleral Hyperemia	Itching paired
	Placebo	1.50±0.16	1.52±0.15	1.42±0.17	2.22±0.17
3	Drug	1.45±0.16	1.50±0.15	1.41±0.17	2.20±0.17
	p Value (paired)	0.54	0.84	0.99	-
	(nonpaired)	0.83	0.94	0.95	0.95
	Placebo	2.08±0.13	2.06±0.14	1.98±0.15	1.89±0.16
10	Drug	2.08±.013	2.05±0.14	1.98±0.15	2.00±0.20
	p Value (paired)	0.99	0.87	0.99	-
	(nonpaired)	0.99	0.94	0.95	0.67
	Placebo	1.98±0.15	1.98±0.15	1.97±0.16	0.92±0.18
30	Drug	2.08±0.16	2.08±0.16	2.08±0.16	0.86±0.18
	p Value (paired)	0.44	0.45	0.37	-
	(nonpaired)	0.67	0.67	0.62	0.32

Significant p values indicated in bold - = analysis unable to be applied to data

Traditional Treatments for Allergic Conjunctivitis

Allergic ocular diseases comprise a number of conditions ranging from the mild seasonal hayfever conjunctivitis elicited by airborne allergens (e.g. ragweed or other pollens) to the most severe forms of vernal conjunctivitis.

The hallmark signs and symptoms associated with allergic conjunctivitis are itching and hyperemia, although swelling, excessive lacrimation , and mucous discharge are frequently part of the symptom complex. The presence of eosinophils in conjunctival scrapings can confirm the diagnosis of allergic conjunctivitis, but their absence should not preclude an allergic diagnosis. A combination of patient and family history and a detailed evaluation of signs and symptoms lead to the final diagnosis of allergic conjunctivitis.

Therapy generally includes identification and removal of the offending allergen, if possible, and the addition of an appropriate topical ocular therapy to control acute flare-ups. Several classes of drugs are used in this capacity, including topical ophthalmic antihistamines, antihistamine/vasoconstrictor combinations, mast cell stabilizers, NSAIDS and steroids.

Levocabastine is currently the only topical ocular antihistamine that is approved for the treatment of both itching and redness associated with allergic conjunctivitis.

Antihistamines that are combined with vasoconstrictors (antezoline/naphazoline or pheniramine/naphazoline) effectively decrease the itching and hyperemia, and are now available as over-the-counter preparations.

In vivo, mast cell stabilizers such as lodoxamide have been shown to inhibit the Type 1 immediate hypersensitivity reaction.

Ketorolac is currently the only NSAID approved for the relief of the itching associated with allergic conjunctivitis.

Steroids are associated with a number of potentially serious side effects such as ocular hypertension, cataract formation and local immunosuppression. Compounds with safety profiles comparable to soft steroids but equivalent to efficacy to steroids are being developed and explored for efficacy in the treatment of allergic conjunctivitis (rimexolone and loteprednol). Keep in mind that steroids should be reserved for the most severe and recalcitrant cases.

Attempts to develop other modes of therapy such as an IgE blocker or blockers specific for arachidonic acid metabolites or enzymes have yet to yield positive results.

Clearly, a safe, comfortable treatment is still needed for ocular allergy. For many, Similasan Eye Drops #2 may be the answer.

may be indicative of a crossover effect. The lack of difference between visit 1 scores and visit 2 scores confirms the reproducibility of the model, and we would expect to record similar scores at visit 3 in the absence of a treatment effect. As the study design required dosing of 1-2 drops q.i.d. for two weeks, systemic absorption, resulting in an active effect in the placebo eye, is a possibility.

In our experience in placebo controlled trials of anti-allergic agents using this model, drug treated eyes have shown significant reductions in the signs and symptoms of acute allergic conjunctivitis, while placebo treated eyes have not. Placebo-treated eyes have generally shown negligible improvement relative to drug-treated eyes.

Thus, the values corresponding to the placebo-treated eyes posttreatment in this study are noteworthy. The highly significant p values, coupled with mean changes of 1.0 clinical unit, comparable to those in the active treated eye, are reminiscent of the crossover effects that have been observed with other compounds.

Consensual effects have been noted in previous animal studies following installation of a chemical into the eye, following experimental trauma, and following intracranial stimulation of the trigeminal nerve. One theory proposes that chemical mediators reach the fellow eye via the circulatory system. A second hypothesis suggests that centripetal neural impulses from the treated eye reach the fellow eye by either direct or antidromic neural transmission.

Conclusion

One to two drops of Similasan Eye Drops #2 administered q.i.d. for two weeks appears to significantly reduce the hyperemia and itching associated with allergic conjunctivitis. Our evaluation of safety showed this compound to be non-irritating. Recognizing the need for further investigation to elucidate these findings, we are conducting a double-masked, parallel group controlled crossover study in the same models.

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