

Effectiveness of Nonpharmacologic Treatments for Acute Seasonal Allergic Conjunctivitis

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Objective: To investigate whether artificial tears and cold compress alone or in combination provide a treatment benefit and whether they were as effective as or could enhance topical antiallergic medication.

Design: Randomized, masked clinical trial.

Participants: Eighteen subjects (mean age, 29.5 ± 11.0 years) allergic to grass pollen.

Intervention: Controlled exposure to grass pollen using an environmental chamber to stimulate an ocular allergic reaction followed by application of artificial tears (ATs), 5 minutes of cold compress (CC), ATs combined with CC, or no treatment applied at each separate visit in random order. A subset of 11 subjects also had epinastine hydrochloride (EH) applied alone and combined with CC in random order or instillation of a volume-matched saline control.

Main Outcome Measures: Bulbar conjunctival hyperemia, ocular surface temperature, and ocular symptoms repeated before and every 10 minutes after treatment for 1 hour.

Results: Bulbar conjunctival hyperemia and ocular symptoms decreased and temperature recovered to baseline faster with nonpharmaceutical treatments compared with no treatment ($P < 0.05$). Artificial tears combined with CC reduced hyperemia more than other treatments ($P < 0.05$). The treatment effect of EH was enhanced by combining it with a CC ($P < 0.001$). Cold compress combined with ATs or EH lowered the antigen-raised ocular surface temperature to less than the pre-exposure baseline. Artificial tear instillation alone or CC combined with ATs or EH significantly reduced the temperature ($P < 0.05$). Cold compress combined with ATs or EH had a similar cooling effect ($P > 0.05$). At all measurement intervals, symptoms were reduced for both EH and EH combined with CC than CC or ATs alone or in combination ($P < 0.014$).

Conclusions: After controlled exposure to grass pollen, CC and AT treatment showed a therapeutic effect on the signs and symptoms of allergic conjunctivitis. A CC enhanced the use of EH alone and was the only treatment to reduce symptoms to baseline within 1 hour of antigenic challenge. Signs of allergic conjunctivitis generally were reduced most by a combination of a CC in combination with ATs or EH.

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Ocular allergy represents a group of hypersensitivity disorders that primarily affect the conjunctiva. The most common form of ocular allergy is seasonal allergic conjunctivitis (SAC), accounting for 90% of cases.^{1,2} The most prevalent allergens in SAC are grass, tree, and weed pollen and outdoor molds.² In the United Kingdom, the prevalence of ocular allergy to grass pollen in patients attending optometric practice is estimated to be 8%.³ Although the signs and symptoms of SAC usually are mild, it may hinder school performance, work productivity, and everyday tasks such as driving.^{4–6}

The primary treatment strategy for SAC involves avoidance of the offending allergen to prevent the initiation of the allergic response. However, complete avoidance often is not possible, and use of topical antiallergic medications is required when signs and symptoms occur.^{7–9} It has been suggested that nonpharmacologic treatments such as artificial tears (ATs) and cold compresses (CCs) may be used in conjunction with allergen avoidance strategies and

antiallergic medications to help bring about symptomatic relief.^{9–12} However, there seems to be no evidence in the scientific literature that demonstrates the efficacy of using ATs or CCs for treating SAC. Therefore, the aim of this study was to investigate the efficacy of instillation of AT substitutes and the application of CCs alone and in combination in patients with confirmed ocular allergic sensitivity to controlled exposure to grass pollen using an environmental chamber model. In addition, the effectiveness of these treatments compared with a topical dual-action antihistamine–mast cell stabilizer licensed for the treatment of SAC alone, and in combination with CCs was investigated.

Methods

The study received ethical approval from the Aston University Research Ethics Committee and was registered as a clinical trial at ClinicalTrials.gov (identification number, NCT01569191). The

research was conducted in accordance with the tenets of the Declaration of Helsinki.

Subjects

All participants were 18 years of age or older and were volunteers from a university population with no history of asthma, without any active eye pathologic features, and who were not using ocular or systemic medications known to affect the eye. None of the participants experienced any form of allergic conjunctivitis at least 1 month before the study took place or used antiallergic medication over the 14 days before testing.

Screening Protocol

Subjects underwent skin prick and bilateral conjunctival challenge tests to confirm systemic and ocular allergic sensitivity to grass pollen.^{13–15} The skin prick test was performed on the forearm using grass pollen solution (10 HEP, Soluprick SQ; Alk-Abello, Horsholm, Denmark) and positive (histamine solution) and negative (saline) controls. After 20 minutes, the size of the wheal response was measured, and a positive result was recorded for diameters of 3 mm or more. The conjunctival challenge test was performed by applying 20 μ l of grass pollen (Soluprick SQ) solution in 2-fold increasing concentrations from 3 to 100 IR/ml to 1 eye (selected at random to be the experimental eye) and saline solution to the contralateral (control) eye every 10 minutes until a composite score of 5 or more was reached using a standardized scoring method.^{13,14,16} Eligible subjects who had positive skin prick test and conjunctival challenge test results and proven sensitivity to grass pollen were enrolled into the study after giving written informed consent.

Eighteen subjects (one third of whom were men) with a mean age of 29.5 ± 11.0 years (range, 20–65 years) took part in the study. At each visit, subjects underwent slit-lamp biomicroscopy to ensure that signs and symptoms of SAC were not present before testing. This was followed by a series of measurements in both eyes that included slit-lamp examination and grading of nasal and temporal bulbar conjunctival hyperemia using a grading scale (Jenvis Research Institute, Jena, Germany) and ocular surface temperature of the cornea and temporal and nasal bulbar conjunctiva (5-mm² area, 2 seconds after blink) using an infrared camera (Thermo Tracer TH7102; NEC Corporation, Tokyo, Japan), where a series of digital markers were used to ensure the temperature was measured at the same location for each subject.¹⁷ Ocular allergy symptoms also were measured using the eye symptom section from the Rhinoconjunctivitis Quality of Life Questionnaire on a 0-to-6 scale, with the summed score for itching, watering, swelling, and soreness resulting in a score between 0 and 24.¹⁸

Subjects were exposed to between 251 and 500 grains/m³ of Timothy grass pollen (*Phleum pratense*; equivalent to a very high pollen count classification; concentration monitored using a Burkard continuous air sampler) in a computer-controlled environmental chamber (Design Environmental; Ebbw Vale, United Kingdom) at a temperature of 20° C and 70% ambient humidity (average local conditions in June in the United Kingdom) on separate visits. We used the concentration that caused ocular itching graded 3 or more (Rhinoconjunctivitis Quality of Life Questionnaire grade) and a 0.5-unit or more change (Jenvis scale) in nasal and temporal bulbar conjunctival hyperemia occurring in both eyes after 5 minutes of exposure.

After the concentration of pollen for each individual had been established, on separate occasions separated by at least 1 week and out of the allergy season, the subjects underwent baseline measurements and then were exposed to pollen at this concentration for 5 minutes; 5 minutes after exposure, the same measurements

were repeated. This was followed by application bilaterally of either ATs applied to the temporal conjunctiva (Blink Refreshing Eye Drops 0.5 ml single-use vial; Abbott Medical Optics, Ettlingen, Germany), a CC applied to the closed eye lid for 5 minutes (frozen gel-pack; Boots Pharmaceuticals, Nottingham, United Kingdom), ATs combined with a CC (for 5 minutes, 5 minutes after AT instillation), or no treatment to the eyes in random order (computer generated) at each visit (examiner masked). The same measures then were repeated every 10 minutes for 1 hour at each visit.

A subgroup of 11 randomly selected subjects (mean age, 29.1 ± 12.9 years; range, 20–65 years) attended 3 further identical visits, receiving 1 drop of epinastine hydrochloride (EH; Relestat 0.5 mg/ml; Allergan), 1 drop of EH combined with CC (for 5 minutes, 5 minutes after instillation of EH), or a single drop of saline (the vehicle, equivalent to the same volume as the drug, but without the active ingredients to determine how much of the effect was lubrication compared with pharmaceutical treatment) in random order to assess the efficacy of nonpharmaceutical agents against a dual-action antihistamine—mast cell stabilizer licensed for seasonal allergic conjunctivitis.

Statistical Analysis

The randomization code was held by a nonmasked researcher and was broken after data entry by the statistician. Statistical analysis was performed using SPSS software for Microsoft Windows (SPSS, v20, IBM, Chicago, IL). Because ocular surface temperature and conjunctival hyperemia were found to be normally distributed ($P > 0.05$, Kolmogorov-Smirnov test), their changes over time were evaluated by repeated measures analysis of variance, and where statistical significance was identified, post hoc analysis was performed using paired t tests. This approach limited the number of statistical comparisons to minimize the chance of type I statistical errors. Changes in ocular symptoms were evaluated by the Friedman test, and where statistical significance was identified post hoc analysis was performed using Wilcoxon signed-rank tests. Statistical significance was taken as $P < 0.05$. Sample size, even of the pharmaceutical comparison subgroup, met the requirements for sufficient replicates for a repeated-measures design.¹⁹

Results

Nonpharmaceutical Treatment Efficacy versus No Treatment

Ocular Symptoms. Although the symptoms differed in overall magnitude, with itching rated as the most severe symptom and swelling as the least, the profile with time after treatment and recovery was similar for each of the symptoms, so they were averaged for analysis. The global ocular symptom scores were similar at baseline at each visit ($X = 6.091$, $P = 0.107$), as was the postexposure effect ($X = 2.729$, $P = 0.435$). They decreased with time after treatment (CC, $X = 88.489$, $P < 0.001$; ATs, $X = 88.258$, $P < 0.001$; ATs+CC, $X = 87.639$, $P < 0.001$; Fig 1), with all treatments reducing symptoms more than no treatment ($P < 0.001$), but none of the treatments returned global ocular symptom scores to baseline levels within 1 hour after antigen exposure (no treatment, 58.6% relative return to baseline; CC, 71.6%; ATs, 84.8%; ATs+CC, 86.9%; $P < 0.001$).

Bulbar Conjunctival Hyperemia. Hyperemia was similar at baseline at each visit ($F = 0.955$, $P = 0.438$), as was the post-exposure effect ($F = 0.267$, $P = 0.898$). There was no difference in conjunctival hyperemia between the eyes ($F = 0.112$, $P = 0.742$); however, the nasal conjunctiva was more red than the temporal conjunctiva over the measurement period (1.71 ± 0.62 versus

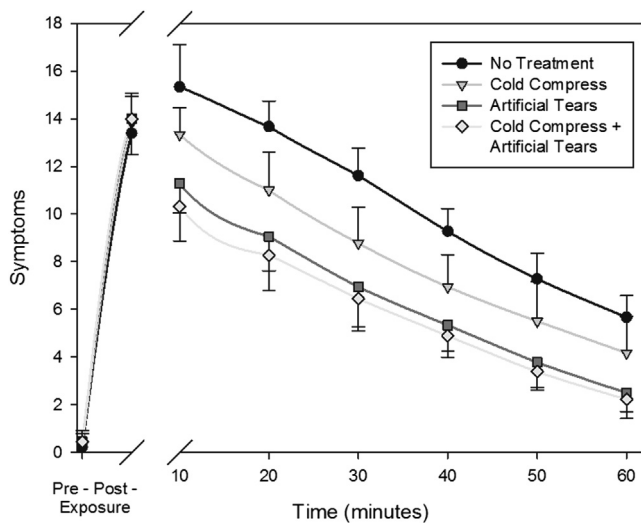


Figure 1. Graph showing ocular symptoms before and after pollen exposure and every 10 minutes thereafter up to 60 minutes for no treatment, cold compress, artificial tears, and artificial tears combined with cold compress ($n = 18$). Although the symptoms differed in overall magnitude, the profile with time after treatment and recovery was similar for each of the symptoms, so they were averaged for analysis. Error bars represent ± 1 standard deviation.

1.47 ± 0.56 Jenvis units; $F = 33.711$, $P < 0.001$). There was a significant difference in conjunctival hyperemia after each of the treatments ($F = 68.211$, $P < 0.001$; Fig 2), with a reduction in redness with time ($F = 302.764$, $P < 0.001$), although this recovery differed with treatment ($F = 9.469$, $P < 0.001$). None of the treatments achieved complete recovery to baseline within 60 minutes (no treatment, 16.5% relative return to baseline; CC, 57.9%; ATs, 73.3%; ATs+CC, 76.5%; $P < 0.001$). However, all treatments produced a significant improvement in hyperemia over time both nasally and temporally compared with no treatment ($P < 0.05$).

Ocular Surface Temperature. Ocular surface temperature was similar at baseline at each visit ($F = 0.685$, $P = 0.605$), as was the postexposure effect ($F = 0.636$, $P = 0.639$). There was no difference in temperature between the eyes ($F = 0.017$, $P = 0.897$); however, there were significant differences in temperature

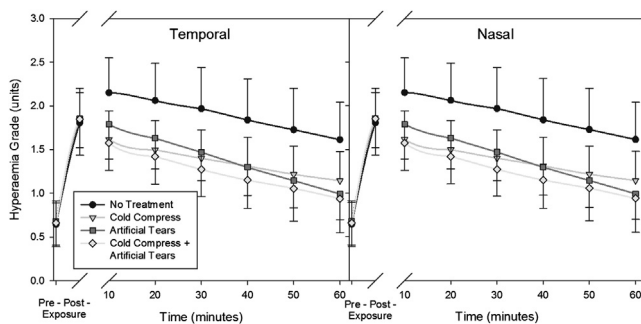


Figure 2. Graphs showing hyperemia grade before and after pollen exposure and every 10 minutes thereafter up to 60 minutes for no treatment, cold compress, artificial tears, and artificial tears combined with cold compress on the temporal (left) and nasal bulbar conjunctiva (right). Data from right and left eyes were similar and so were averaged ($n = 18$ subjects and 36 eyes). Error bars represent ± 1 standard deviation.

between corneal, nasal, and temporal locations ($F = 97.899$, $P < 0.001$). There was a significant difference in temperature after each of the treatments ($F = 19.684$, $P < 0.001$; Fig 3), with the temperature converging toward baseline over time ($F = 32.955$, $P < 0.001$), although this recovery differed with treatment ($F = 122.796$, $P < 0.001$). Temporal bulbar conjunctival and corneal temperatures returned to baseline levels (were no longer significantly different; $P > 0.05$) with the application of CCs (within 50 minutes), ATs (within 40 minutes), and ATs combined with CCs (within 40 minutes), whereas for the nasal bulbar conjunctiva, the return to baseline temperature generally was faster (40, 30, and 40 minutes, respectively). Ocular surface temperature did not return to baseline levels without treatment at any location (relative return to baseline, 57.0%; $P < 0.05$).

Relative Efficacy of Nonpharmaceutical Treatments versus a Dual-Action Pharmaceutical

Ocular Symptoms. All ocular symptom changes with time were similar, so they have been averaged for presentation and analysis. At all measurement intervals, symptoms were reduced for both EH and EH in combination with a CC compared with a CC or ATs alone or in combination ($P < 0.01$; Fig 4). Only EH alone and in combination with a CC reduced global ocular symptom scores to baseline levels within the hour after antigen exposure during which subjects were monitored (after 60 minutes: $P = 0.414$, $P = 0.705$, respectively). A CC enhanced the pharmaceutical benefit of EH alone for up to 20 minutes ($P < 0.05$); thereafter, they were similarly efficacious ($P > 0.05$). A CC also further reduced symptoms up to 20 minutes when combined with ATs compared with AT use alone ($P < 0.05$). The drug effect was from the active ingredients, rather than the saline vehicle control ($P < 0.001$).

Bulbar Conjunctival Hyperemia. There was a significant difference in conjunctival hyperemia between each of the treatments ($F = 11.728$, $P < 0.001$; Table 1), with a reduction in redness with time ($F = 581.320$, $P < 0.001$), although this recovery differed with treatment ($F = 9.463$, $P < 0.001$). Artificial tears combined with CCs outperformed ATs, CCs, and EH alone and EH combined with CCs nasally. The treatment effect of EH was enhanced by combining it with a CC. The saline volume control (vehicle) showed that the action of EH was principally from the active pharmaceutical ingredients. Artificial tear instillation had similar effectiveness to a CC application used in isolation (Table 1).

Ocular Surface Temperature. There was a significant difference in ocular surface temperature between each of the treatments ($F = 11.680$, $P < 0.001$; Table 2), with a change in temperature toward baseline with time ($F = 17.952$, $P < 0.001$), although this recovery differed for each treatment ($F = 144.816$, $P < 0.001$). A CC in combination with ATs or EH lowered the antigen-raised ocular surface temperature below the pre-exposure baseline. Artificial tear instillation alone or in combination with a CC or EH significantly, but only slightly ($< 0.5^\circ\text{C}$), reduced the temperature ($P < 0.05$; Table 2). A CC combined with either ATs or EH had a similar cooling effect. The saline vehicle volume control to EH had a similar cooling effect as ATs and no beneficial cooling effect over EH of the same volume, but containing active pharmaceutical agents.

Discussion

In the first phase of the study, the efficacy of ATs, CCs, and in combination (ATs+CC) was investigated by measuring conjunctival hyperemia, ocular surface temperature, and

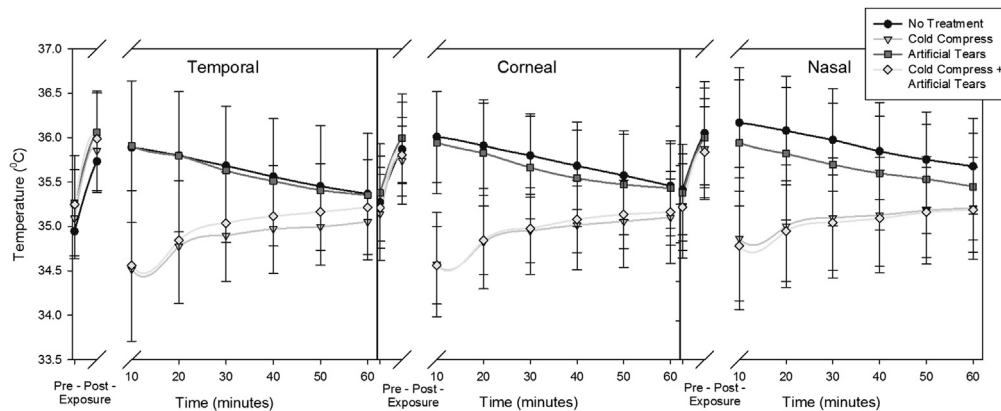


Figure 3. Graphs showing ocular surface temperature before and after pollen exposure and every 10 minutes thereafter up to 60 minutes for no treatment, cold compress, artificial tears, and artificial tears combined with cold compress on the temporal (left), corneal (middle), and nasal bulbar conjunctival surfaces (right). Data from right and left eyes were similar and so were averaged ($n = 18$ subjects and 36 eyes). Error bars represent ± 1 standard deviation.

ocular symptoms after exposure to grass pollen in an environmental chamber model to produce the response signs and symptoms of an acute ocular seasonal allergic conjunctivitis. Subjects were exposed over a 5-minute interval in the environmental chamber to a predetermined threshold of reactivity to ensure that subjects had sufficient signs and symptoms to detect any treatment effect. There was no significant difference in hyperemia, ocular surface temperature, or ocular symptoms at each visit after the multiple exposures separated by at least 1 week (and between each eye for hyperemia and ocular surface temperature), demonstrating that the environmental chamber model produces a bilaterally homogenous and reproducible ocular

allergic reaction. The data show that all treatments provided benefit in relieving hyperemia, restoring physiologic ocular temperature, and reducing ocular symptoms during an acute episode of stimulated SAC compared with no treatment.

Although ATs principally are formulated to relieve ocular surface signs and symptoms in dry eye, they have been advocated to have a beneficial effect in SAC.^{11,12} The reduction in signs (conjunctival hyperemia) and symptoms of SAC in this study are likely to have been caused principally by diluting and washing away the allergen from the eye and by the AT acting as a barrier to further exposure by preventing the allergen from binding to the ocular surface.^{7,8,11,12} This barrier effect to allergens also has been observed in contact lens wear, where patients wearing soft contact lenses exhibited reduced signs and symptoms of ocular allergy compared with controls who do not wear contact lenses after exposure in an allergen chamber, with a further benefit from using contact lenses with sustained release of a lubricating agent from within the material matrix.²⁰ Artificial tears generally are stored at room temperature, which could give them an additional soothing effect, but this study demonstrated that any benefit from the temperature change from AT is minor compared with its other properties such as lubrication, with the temperature reduction and consistency over time higher in the nasal region, compared with the cornea and lower still temporally, following the excretion pathway of the tear film.

In environmental studies of antiallergy drug efficacy, the use of ATs as a control has been shown to have a drug effect of up 50% to 70%, and this is considered to be a placebo effect.^{13,21–23} However, because ATs may produce a real physical effect on the binding of allergens to the ocular surface, this mechanism cannot be considered purely as placebo and therefore should not be considered as an effective control in studies of acute SAC, whereas their use is warranted in investigating the prophylactic effect of an ocular antiallergy drugs.²³

The use of CCs previously was recommended as supportive therapy in ocular allergy,^{11,24,25} but no studies relating to the efficacy of CC treatment has been reported in the scientific literature. Therefore, this study has

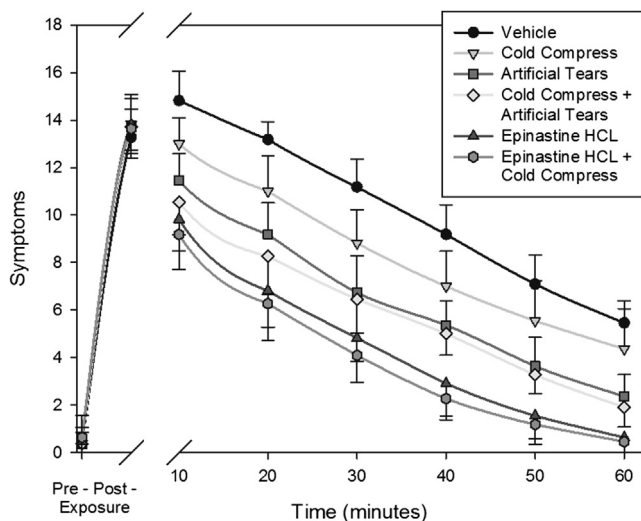


Figure 4. Graph showing ocular symptoms before and after pollen exposure and every 10 minutes thereafter up to 60 minutes for the saline vehicle volume control, cold compress, artificial tears, artificial tears combined with cold compress, epinastine hydrochloride (HCL), and epinastine HCL combined with a cold compress ($n = 11$). Although the symptoms differed in overall magnitude, the profile with time after treatment and recovery was similar for each of the symptoms, so they were averaged for analysis. Error bars represent ± 1 standard deviation.

Table 1. Statistical Comparison of Nasal and Temporal Hyperemia between the Nonpharmaceutical and Pharmaceutical Treatments

Treatment	Mean*	Significance (P Value)					
		Epinastine Hydrochloride	Epinastine Hydrochloride+Cold Compress	Cold Compress	Artificial Tears	Artificial Tears+Cold Compress	Vehicle
EH							
Nasal	1.46±0.43	X	<0.001	0.378	0.045	0.042	<0.001
Temporal	1.35±0.40	X	<0.001	<0.001	<0.001	<0.001	<0.001
EH+CC							
Nasal	1.33±0.41		X	0.002	<0.001	0.559	<0.001
Temporal	1.19±0.37		X	0.929	0.220	0.014	<0.001
CC							
Nasal	1.51±0.30			X	0.349	<0.001	<0.001
Temporal	1.19±0.29			X	0.162	<0.001	<0.001
AT							
Nasal	1.55±0.38				X	<0.001	<0.001
Temporal	1.24±0.35				X	<0.001	<0.001
AT+CC							
Nasal	1.36±0.31					X	<0.001
Temporal	1.08±0.37					X	<0.001
Vehicle							
Nasal	2.00±0.39						X
Temporal	1.65±0.38						X

AT = artificial tears; AT+CC = artificial tears combined with cold compress; CC = cold compress; EH = epinastine hydrochloride; EH+CC = epinastine hydrochloride combined with cold compress.

Nasal and temporal regions interacted significantly with treatment and so are presented separately.

*Mean hyperemia grade (Jenvis units) of right and left eyes averaged (n = 11 and 22 eyes, respectively) over 60 minutes.

demonstrated the beneficial effects of CC therapy in ocular disease for the first time. The application of CCs may reduce hyperemia and relieve signs and symptoms by causing vasoconstriction of conjunctival blood vessels, and they subsequently may prevent or minimize swelling and leakage of and inflammatory mediators involved in the allergic response.^{7,10,26} A potential limitation of the CC data was the ability to control the application to the closed eyelids, although the gel mask was held in place over the eyes with an attached elastic headband. This, however, mimicked the clinical reality where the exact area and location of contact of the compress with the eyelid varies between patients owing to differences in facial structure.

In the second phase of the study, the effectiveness of nonpharmaceutical treatments was compared with a dual action antihistamine—mast cell stabilizer pharmaceutical (EH), with or without the addition of a CC, in a randomly selected subgroup of subjects using the same acute induced-SAC methodology. Comparison over the 60-minute observation period showed that the combination of ATs and CCs was superior to all other treatments, including the pharmaceutical agent, in reducing hyperemia, although the antigen-induced ocular redness could be improved to an equivalent effectiveness by combining EH with a CC. Artificial tears or a CC used alone were more effective than the pharmaceutical used in isolation. The pharmaceutical agent effect,

Table 2. Statistical Comparison of Ocular Surface Temperature between the Nonpharmaceutical and Pharmaceutical Treatments

Treatment	Mean*	Significance (P Value)					
		Epinastine Hydrochloride	Epinastine Hydrochloride+Cold Compress	Cold Compress	Artificial Tears	Artificial Tears+Cold Compress	Vehicle
EH	35.31±0.48	X	<0.001	<0.001	<0.001	<0.001	0.057
EH+CC	34.72±0.63		X	0.228	<0.001	0.089	<0.001
CC	34.81±0.55			X	<0.001	<0.001	<0.001
AT	35.52±0.67				X	<0.001	0.319
AT+CC	34.57±0.34					X	<0.001
Vehicle	35.44±0.41						X

AT = artificial tears; AT+CC = artificial tears combined with cold compress; CC = cold compress; EH = epinastine hydrochloride; EH+CC = epinastine hydrochloride combined with cold compress.

Ocular temperature was similar between eyes and did not interact with ocular surface region, so average data are presented.

*Mean ocular surface temperature of right and left eyes and region combined (n = 11 and 22 eyes, respectively) over 60 minutes.

however, was confirmed as being derived from the active ingredients, rather than by any ocular lubricating effect of its fluid vehicle, and this also was the case for the pharmaceutical effect on ocular comfort.

A CC alone or in combination with ATs or EH pharmaceutical lowered the ocular surface temperature below baseline from the increased level caused by exposure to the antigen, whereas ATs alone had relatively little effect over ocular temperature, particularly over the temporal conjunctiva. Because this treatment result differed from that of conjunctival hyperemia and ocular symptoms, it may suggest that the inflammatory events causing increased ocular surface temperature after antigen exposure differ from those driving other signs and symptoms, or the results could be confounded by tear film thickness variations across the ocular surface and with time, because this would have affected the radiated heat imaged by the thermal camera.

Ocular symptoms improved faster with EH compared with all other treatments, reducing symptoms to baseline levels after 60 minutes, and the recovery profile was enhanced initially by the application of a CC. Although none of the nonpharmaceutical treatments reduced symptoms to baseline levels, the mean scores were low, falling within the “hardly troubled at all” category. These data suggest that ATs and CCs, either alone or in combination, are effective methods of relieving the signs and symptoms of SAC during the active phase of the condition.

Epinastine hydrochloride displays antihistamine, anti-inflammatory, and mast cell stabilizing properties in animal and in vitro studies.^{27,28} Conjunctival allergen challenge-model clinical trials of EH have shown that it is significantly more effective in preventing the signs and symptoms of allergic conjunctivitis compared with its vehicle, as confirmed in this study.^{29,30} The efficacy of EH also has been demonstrated to be effective in an environmental clinical trial,³¹ but these study designs are subject to variations in exposure, and therefore limit their ability to detect the efficacy of drugs. Thus, there has been a lack of studies investigating the efficacy of EH in acute SAC. In this study, the combination of EH combined with CCs was superior to EH alone in reducing ocular surface temperature ($P < 0.001$), was superior to EH in reducing hyperemia both nasally ($P < 0.001$) and temporally ($P < 0.001$), and enhanced the symptom recovery profile within the first 20 minutes. This suggests that, clinically, EH should be prescribed together with advice on applying CCs during acute episodes. Epinastine hydrochloride mast cell stabilizing properties are likely to enhance the pharmaceutical effect only after a few days of use, which should be considered if the patient is likely to be exposed to multiple episodes of acute pollen exposure over a short period.

The results of this study are applicable only on the ability of the treatments to relieve the signs and symptoms of simulated SAC during the acute phase of the ocular allergic response; thus they have no bearing on the ability of these treatments ability to prevent signs and symptoms from developing through prophylactic treatment. It is not expected that the application of CCs or ATs will have any effect before the ocular allergic response develops, unless

they are applied frequently. These data suggest that although EH resolves symptoms of SAC earlier, it seems to be less efficacious in resolving ocular signs of inflammation such as conjunctival hyperemia and ocular surface temperature increases compared with ATs or CCs alone, or better, in combination, during an acute episode of SAC. Therefore, for occasional sufferers, such self-management, with reduced risks of drug interactions and patient expense, should be considered. For more frequent SAC sufferers, the benefits of a CC in addition to prophylactic pharmaceuticals should be considered as part of patient management when symptoms still occur. Further study is required to measure the immunologic response to ocular signs and symptoms induced by the environmental chamber and treatment strategies.

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