Effect of ingestion of honey on symptoms of rhinoconjunctivitis

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Background: Allergic rhinoconjunctivitis is a common disorder, affecting >20% of people of all socioeconomic strata. Despite this high prevalence, relatively few sufferers seek professional medical help, presumably because of a widespread reliance on complementary remedies.

Objective: We investigated the widely held belief among allergy-sufferers that regular ingestion of honey ameliorates the symptoms of allergic rhinoconjunctivitis.

Methods: The study was conducted at the University of Connecticut Health Center's Lowell P. Weicker General Clinical Research Center. Thirty-six participants who complained of allergic rhinoconjunctivitis were recruited. All recruits were scratch-tested at entry for common aeroallergens. The cohort was randomly assigned to one of three groups, with one receiving locally collected, unpasteurized, unfiltered honey, the second nationally collected, filtered, and pasteurized honey, and the third, corn syrup with synthetic honey flavoring. They were asked to consume one tablespoonful a day of the honey or substitute and to follow their usual standard care for the management of their symptoms. All participants were instructed to maintain a diary tracking 10 subjective allergy symptoms, and noting the days on which their symptoms were severe enough to require their usual antiallergy medication.

Results: Neither honey group experienced relief from their symptoms in excess of that seen in the placebo group.

Conclusions: This study does not confirm the widely held belief that honey relieves the symptoms of allergic rhinoconjunctivitis.

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INTRODUCTION

Recent studies suggest that allergic rhinoconjunctivitis is widespread, and increasing in western urbanized countries. It afflicts >20% of people of all ages and socioeconomic groups.[1–5] However, only 1 in approximately 8 patients with allergic rhinoconjunctivitis seeks professional medical help for this condition.[6] Many seem to use complementary or alternative medical strategies instead. There have been several recent reviews of the use of nontraditional remedies for allergic disorders and asthma.[7–9] There is a widespread belief, held with great conviction by many people, that honey has value in the control of allergic symptoms[10] (eg, http://www.marshallshoney.com/hallergy.html).

We reasoned that this purported efficacy of honey could be explained in terms of our understanding of the principles of immunology. It has been known for almost 100 years that oral ingestion of allergens causes immunomodulation and the development of tolerance to systemic administration of the same antigens.[11,12] High-dose oral allergy desensitization has been reported to have some success in double-blinded studies.[13–15] Various tree and grass pollens are important allergens in eliciting spring allergies. Although bees do not seem to deliberately collect these nonfloral pollens, data in the literature suggest that they do accidentally collect non-ornamental floral pollens.[16] We reasoned that the purported efficacy of honey consumption on allergies might be through the mechanism of oral low-dose tolerance to these allergens. An alternative hypothesis, which does not invoke immunologic principles, is that honey may contain antihistamine or anti-inflammatory activities. Honey is a complex biologic material with many components. It has been used in wound dressings to reduce infection and has been reported to possess anti-inflammatory properties.[17–20] This manuscript details a study that was performed to evaluate the effect of honey consumption on the symptoms of rhinoconjunctivitis. The data do not support the belief that local honey provides relief to allergy sufferers.

MATERIALS AND METHODS

Patient Recruitment

We used pilot data from a previous (unpublished) study to carry out a power analysis for the current study. Our null hypothesis was that there would be no difference in the number of symptom-free days in the honey group(s) in comparison to the placebo control group. Calculations were based on the frequency of symptom-free days for a cohort of patients not taking honey (corresponding to the placebo group). We estimated that it would require approximately 1,600 days to detect a 10% increase in the frequency of symptom-free days in the intervention group, with the power of 0.8, assuming a two-tailed *t* test carried out at the

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Table 1. Inclusion and Exclusion Criteria

Inclusion criteria	Exclusion criteria
History of allergic rhinoconjunctivitis	Participation in the previous honey study
Willingness to consume 1 tsp of honey or placebo once a day	Currently being desensitized for allergic disorder
Willingness to record allergy symptoms daily in a diary	Desensitization for allergic disorders within the past 5 years
Willingness to mail 7 pages of the diary every week in prepaid envelopes	Asthma
Willingness to suspend taking usual antihistamines for 2 days before the first visit for accurate skin tests	Any chronic ailment that requires constant medical attention

0.05 level of significance. This would correspond to a cohort of nine patients, as the patient data cover a 195-day period. As a result, we targeted at least nine participants per group for this study.

We publicized that a study was being conducted under the auspices of the General Clinical Research Center at the University of Connecticut Health Center to evaluate the value of honey in the treatment of nasal and ocular allergies. Using the inclusion and exclusion criteria listed in Table 1, we recruited 36 volunteers on a first come, first served basis. Informed consent was obtained from all individuals at the time of the first visit.

History was elicited to evaluate the seasonality of their symptoms and to ensure the absence of lower respiratory tract symptoms suggestive of asthma. Nasal examination was performed to determine that they did not have nasal polyps, significant chronic sinusitis, or septal deviation. Subjects were asked to complete questionnaires to elicit demographic information and history of allergies. They were scratch tested (Table 2 for a list of allergens used) using the MultiTest applicator (Lincoln Laboratory, Decatur, IL). The reaction sizes (0 to 4+ compared with histamine and glycerin controls) were recorded at 15 minutes by trained registered nurses. The forearms were also photographed using a digital camera and stored for future blinded evaluation by an experienced allergist (LC).

Table 2. Extracts (Greer Labs, Lenoir, NC) and Controls Used to Scratch Test Subjects Using a MultiTest on the Forearm

Glycerin control
Standardized mixed mites
Cladosporium hormodendrum
Standardized 7-grass mix
White oak
Ragweed mix
11-tree mix
Histamine control

Study Design

The subjects were randomly assigned to 1 of 3 groups using a random number generator. In a double-blinded fashion, one group was provided with a 5-pound jar of a locally collected, unpasteurized honey; the second a nationally collected, filtered, and pasteurized honey; and the third group a placebo consisting of corn syrup flavored with a synthetic honey flavoring. All subjects were instructed to consume one tablespoonful of the substance every day, either at one sitting or in three doses of one teaspoon each. Participants recorded their allergy symptoms each day in diaries that were mailed to the investigators weekly. Ten symptoms (5 upper respiratory, 5 ocular; Table 3) were tracked. They were also asked to note the days when their allergy symptoms were severe enough to require any antiallergy medication.

Table 3. List of Symptoms that Were Tracked and Graded from 0 to 3 Daily

Nasal symptoms	Ocular symptoms
Runny nose	Sore eyes
Sneezing	Swollen eyes
Itchy nose	Watery eyes
Post-nasal drip	Itchy eyes
Stuffy/blocked nose	Headache

Honey and Substitute

Locally collected, unpasteurized and unfiltered honey was obtained from Honeycomb Apiaries, Bristol, CT. Nationally collected, filtered clover honey was a generous gift of Dutch Gold Honey Inc, Lancaster, PA.

To generate a placebo, we obtained several samples of corn syrup from various vendors. These were subjected to a blind taste test among volunteers in the Department of Pathology, UConn Health Center. The corn syrup that was deemed closest in texture and taste to honey (BeeHive Golden Corn Syrup, BestFoods Canada Inc, Toronto, Canada) was selected for further testing. We obtained synthetic honey flavor (www.naturalflavors.com) and made mixtures of BeeHive corn syrup with flavoring, at 50,100, and 150 μL of flavoring in 100 mL of syrup. In blind taste tests of the mixtures, 5 of 5 volunteers felt that the 50 μL/100 mL mixture was closest in taste to honey. We made a batch of "faux-honey" using 25 mL of flavoring in 13 gallons of corn syrup.

Blinding

The two honey samples and the flavored corn syrup were dispensed into standardized unlabeled 1-L Nalgene (Nalgene subsidiary of Sybron Corp, Rochester, NY) containers, such that neither the subjects nor the nurse practitioner could ascertain what the groups were receiving. Further, the principle investigator and the data analysts were not told the identity of the material that was given to the groups. The code was not broken until the analyses were completed.

Compliance

Subjects were instructed to start consuming the honey on March 15, 2000. They were given 30 stamped envelopes, one per week of the study. At the end of each week, they were instructed to mail in the most recent 7 days of their diaries. In the event that any individual did not send in a weekly envelope, he or she was contacted to alert them of the need for compliance.

Table 4. Dropout List and Reasons

Subject ID #	Date of dropout	Reason
001	Never started	Illness, death in family
004	Never started	Husband's illness, weight issues
008	Never started	Never reported for tests
009	4/27	Regimen makes subject gag
011	3/31	Too sweet, makes subject sick
013	6/7	"Tastes awful"
021	6/29	Unable to maintain diary
022	4/14	No reasons given
023	4/28	Too sweet
028	5/22	Family reasons
029	4/00	Too sweet
034	4/00	Trouble maintaining diary
036	5/25	Did not like taste

Data Entry

Forms for the daily diaries were created using Teleform Standard version 6.2 (Cardiff Software, San Marcos, CA). As the diary pages arrived each week, they were scanned using a ScanPartner 15C scanner (Fujitsu Computer Products of America, San Jose, CA) and directly exported into a tab-delimited spreadsheet. Data in the database were imported into an Excel spreadsheet from a tabular web page output.

Data Analysis

Symptoms were recoded in binary format, to present or absent outcomes (dichotomous), and groups were compared with respect to frequency of symptom days (days symptoms were present) using a χ^2 analysis. Mean number of days with symptoms were compared across groups using a one-way analysis of variance; multiple comparison procedures were used to isolate pairwise mean differences in those cases where statistically significant results were obtained.

RESULTS

Demographics of the Study Population

The 36 individuals recruited to this study ranged in age from 20 to 72 years (X = 45.3). Twenty-four individuals were female and 12 male. The age ranges of the three groups were 28 to 71, 31 to 72, and 20 to 64, with means of 48.4, 47.2, and 40.15, respectively. There were 6 women and 5 men in the local honey group; 7 women and 5 men in the national honey group; and 11 women and 2 men in the placebo group.

Retention

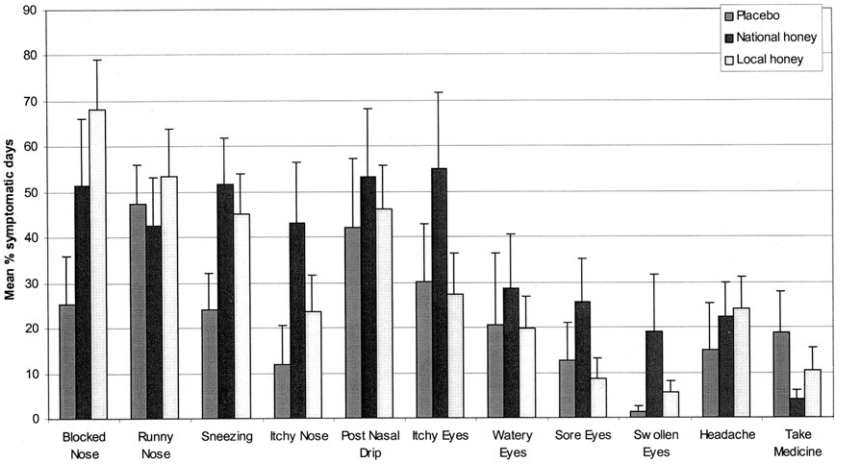
Twenty-three of the 36 patients completed the study. The dropouts were attributed almost exclusively to an inability to tolerate the extreme sweetness of the regimen or to "personal reasons" (Table 4). After blinding was removed, we found that 6 of 13 dropouts were among the group that had been asked to take the placebo, 5 of 12 from the supermarket honey group, and 2 of 12 from the local honey group.

Effect of Honey or Placebo Ingestion on Symptoms of Allergy

We divided the allergy season into four periods, corresponding to the changes in the dominant aeroallergen(s) in Connecticut. Thus, from March 15 to May 1, the predominant allergens are tree pollens; from May 1 to June 15, grass and white oak pollens; from June 15 to August 15, the pollen counts are very low; and from August 16 until the end of the study period, ragweed pollen is the major aeroallergen. The perennial aeroallergens (mold spores and dust mite excreta) are present throughout the study period.

Clinically, it would be most useful to the subjects if they experienced no symptoms typical of allergy. Therefore, we evaluated, for each group, the distributions of days into the following two categories for each symptom: 1) days with no symptoms and 2) days with symptoms. Thus, each day fell into 1 of 2 categories, either "no symptom" or "symptomatic." Figures 1 through 4 graphically represent the distributions of mean percentage of symptomatic days for the four time periods for each symptom by group.

Because it is possible that relief was provided only during specific pollen



Figures 1–4. Mean percent symptomatic days for each symptom by group. In all four figures, the *x*-axis denotes the 10 subjective symptoms and percentage of days usual allergy medication was taken. The *y*-axis is the mean percentage symptomatic days for each symptom. The codes for the bars are indicated on the top right corner. Figures 1–4 are for the tree pollen, grass/oak pollen, the low symptom, and ragweed pollen periods, respectively.

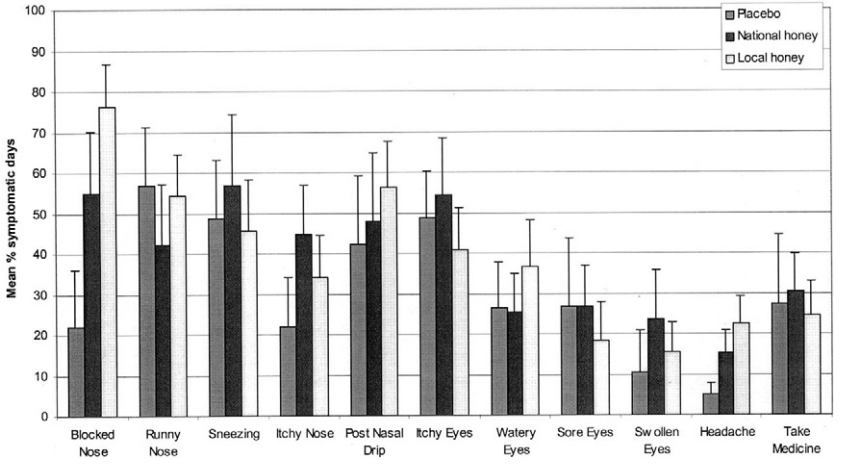


Figure 2. Grass-oak period mean % symptomatic days.

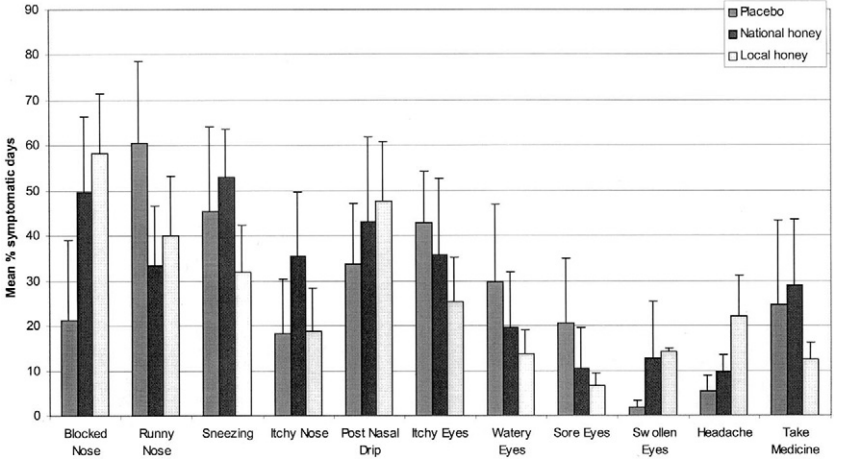


Figure 3. Low allergy period mean % symptomatic days.

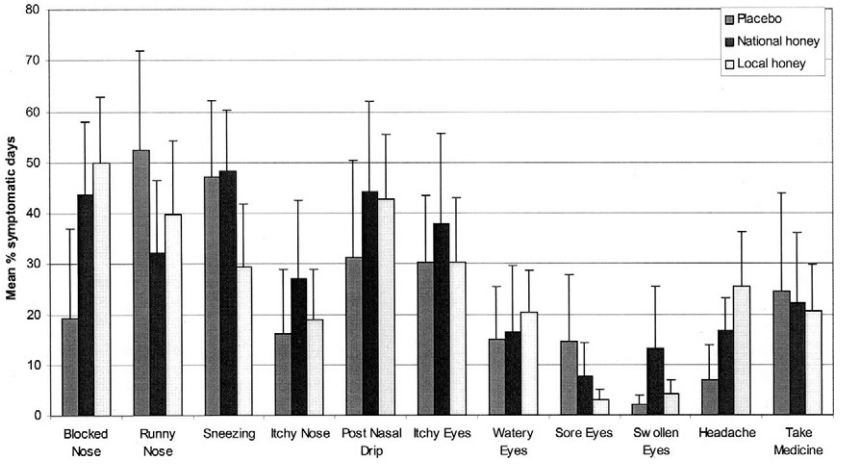


Figure 4. Ragweed period mean % symptomatic days.

periods rather than globally across the entire year and for some symptoms and not others, we analyzed the data for differences among the groups for each symptom for each allergy period. We included all 10 subjective symptoms, and, in addition, the number of days the subjects consumed medication for relief of symptoms. These analyses provided 44 parameters (11 symptoms $\times$ 4 periods). We found that the placebo group did better than the other two for 19 parameters, the local honey for 18, and supermarket honey for 7 parameters (Table 5). There was no consistent improvement for any symptom (or drug ingestion) for any group. Nor was any symptom or drug ingestion reduced for the same pollen period of any group.

When we reviewed the skin reactivity patterns, we noted that although subjects had referred themselves to the study based on their self-evaluation as sufferers of seasonal allergies, not all scratch-test reactivities were consistent with this diagnosis. Only 14 of the final cohort of 23 showed scratch-test reactivity to the seasonal allergens that were tested, whereas the rest were either unreactive or reacted to nonseasonal allergens such as mites or mold. We therefore divided the cohort into two groups, those that were reactive to seasonal aeroallergens by the scratch test and those that were not. We graphed the mean reported symptom intensity for all symptoms for each subject through the allergy season. Representative graphs are shown in Figure 5, A and B.

Using these graphs, we evaluated whether a given subject was experiencing symptoms during the period expected from his/her skin reactivity. For both these subjective analyses, two individuals (LC and TVR) matched the subjective reporting of symptoms with the skin reactivity. We assumed that a total symptom score <2 for any given day was consistent with random noise. We therefore drew a horizontal line for all symptom days at a level of 2 on the *y*-axis. A total symptom level above that was interpreted to mean a "symptomatic day." If one analyzes the dis-

Table 5. Ranks of Groups by Symptomatic Days

Groups	1st rank	2nd rank	3rd rank
Placebo	19	14	11
National honey	7	21	16
Local honey	18	9	17

For each symptom for each period, we ranked the groups by the mean number of symptomatic days reported by the groups. The group with the least number of symptomatic days was ranked 1, the next higher 2 and the group with the most symptomatic days ranked 3. There were a total of 44 categories (10 symptoms + 1 days usual allergy drugs consumed × 4 time periods). The sum of each column and row thus total 44.

tribution of total symptom score for the year for patient 12 (Fig 5A), we note that there is no increase over this noise level during the tree or grass/oak pollen seasons. However, this patient did show reactivity to tree and grass pollens by skin testing, indicating that he should have reported symptoms during the first interval. This lack of symptoms during the periods for which he/she should have been symptomatic was interpreted to mean that this patient was "helped" by his regimen. In this particular case, patient 12 was a member of the placebo group.

In contrast, patient 24 exhibited marked symptoms during the tree and grass pollen days. His skin reactivity showed that he was, in fact, allergic to both grass and tree pollens. We therefore evaluated that his symptoms were expected from his skin reactivity patterns and therefore, his regimen did not help him. The data presented in Table 6 show that these 7 subjects were distributed comparably (2, 3, 2) among the placebo, national honey, and local honey groups respectively ($P = 0.65$; Fisher's exact test).

DISCUSSION

Despite the widespread prevalence of allergic rhinoconjunctivitis, relatively few patients avail themselves of professional medical help. Significant numbers of patients presumably rely on alternative or complementary medications. One such remedy that has been widely reported to be of help is the regular ingestion of honey. We reasoned that a possible immunologic mechanism by which honey could help allergy sufferers is that local honey, by inducing oral tolerance to environmental pollens, could reduce symptom intensities. Another possible mode of action is that honey may contain antihistaminic and/or anti-inflammatory activities. We designed the study to determine whether the regular ingestion of honey will indeed help alleviate the symptoms of rhinoconjunctivitis.

In an earlier, open-label study, we had found that patients who consumed honey reported statistically significant lowering of symptoms, particularly ocular symptoms. The relief was sufficiently promising that we felt encouraged to conduct the current placebo-controlled trial. Volunteers for the current study were selected because of their reported rhinitis symptoms (if they otherwise met the entry criteria). Scratch testing and symptom diaries confirmed the sensitivity to perennial aeroallergens in several members of the cohort. Others were negative by

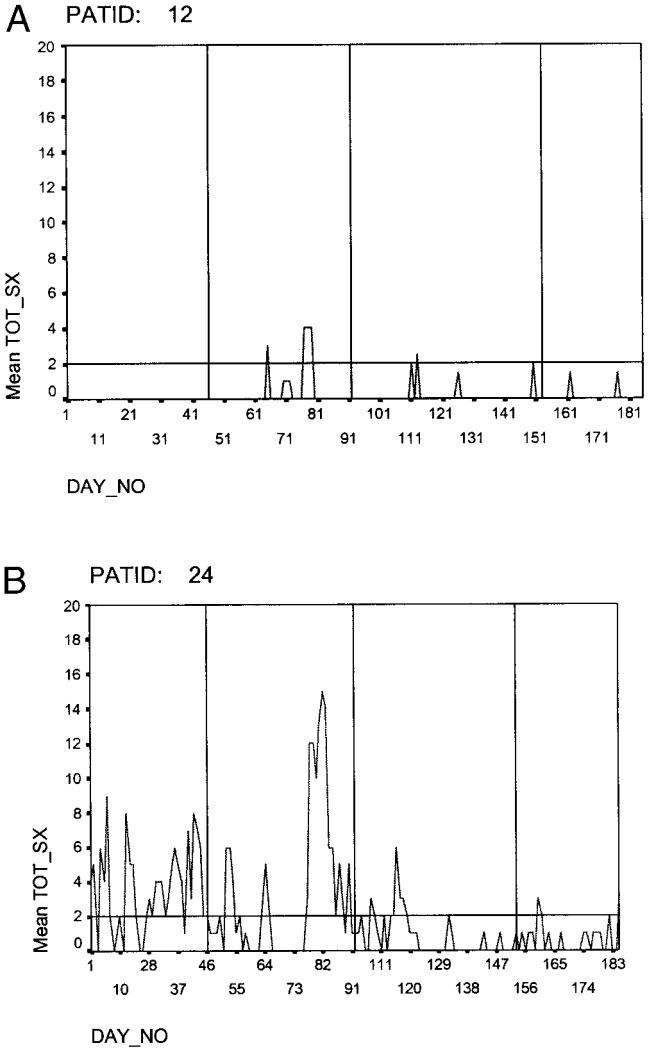


Figure 5. (A) This subject had skin scratch-test reactions to tree and grass pollens but no symptoms during the relevant periods. We interpreted the observations to mean that he did obtain relief from the treatment. (B) This subject had reactions to tree and grass pollens and reported symptoms during the relevant periods. We interpreted the data to mean that he was not helped by the treatment.

Table 6. Distribution of Subjects whose Skin Tests were Consistent with Seasonal Allergic Disorder into the Benefited and Nonbenefited Categories

Group	Benefited by treatment	Not benefited by treatment
Placebo	2	1
National honey	3	2
Local honey	2	4

scratch testing to all six antigens tested (Table 2). However, not every indigenous pollen and mold was tested and more sensitive intradermal testing was not performed.

The current study does not support the premise that honey provides relief from the symptoms of rhinoconjunctivitis, even among subjects whose skin reactivity patterns are consistent with a diagnosis of seasonal allergic disorder. It is possible that the dose we used was inadequate to control symptoms; it is also possible that more prolonged ingestion of honey, over several seasons may be required to observe the effects that are reported in the lay media. We find that neither the nationally available, commercial honey, which many honey believers around the country are consuming, nor the local honey that theoretically should have worked better are effective in controlling seasonal or perennial allergy symptoms at the dose used. It is worth noting that this dose (one tablespoonful a day) was large enough to cause 13 of 36 volunteers to drop out, because the regimen was unpleasantly sweet to consume on a daily basis for the duration of the study. A higher dose would presumably have caused more dropouts. Despite the fact that there was not even a trend toward improvement in the honey groups compared with placebo, the smallness of the cohort size in each cell mandates that further studies, using larger groups, have to be conducted to confirm unequivocally these findings.

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