original article

Ingestion of honey improves the symptoms of allergic rhinitis: evidence from a randomized placebo-controlled trial in the East Coast of Peninsular Malaysia

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BACKGROUND AND OBJECTIVES: The role of honey in the treatment of allergic rhinitis (AR) is controversial. We studied the complementary effect of ingestion of a high dose of honey, in addition to standard medications, on AR.

DESIGN AND SETTINGS: Prospective randomized placebo-controlled study. Subjects were recruited from an otolaryngology clinic in 2 tertiary referral centers in the East coast of Peninsular Malaysia. The study period ranged from April 2010-April 2011.

METHODS: Forty AR patients were divided equally into a case group and a control group. All the subjects received a daily dose of 10 mg of loratadine for 4 weeks. The case group ingested 1 g/kg body weight of honey daily in separate doses for the 4-week period. The control group ingested the same dose of honey-flavored corn syrup as placebo. AR symptoms were scored at the start, week 4, and week 8 of the study.

RESULTS: There were no significant differences between the mean total symptom score of the case and the control groups at the start of the study. At week 4, both groups showed progressive improvement in the symptoms; at week 8, only the case group showed a continuous improvement in the symptom score. Only the group that ingested honey showed a significant improvement in individual AR symptoms. The improvement persisted for a month after the cessation of the treatment.

CONCLUSION: Honey ingestion at a high dose improves the overall and individual symptoms of AR, and it could serve as a complementary therapy for AR.

Honey is a common supplement widely believed to alleviate symptoms of allergic rhinitis (AR). Yet, evidence for this phenomenon is scarce. To our knowledge, only 2 previous studies have investigated the effect of ingestion of honey on symptoms of AR, and they have reported contradictory results.[1,2] The first, a case-control study found no significant improvement in allergic rhinoconjunctivitis symptoms between participants who ingested a tablespoon a day of honey for a period of 30 weeks compared with a placebo group.[1] The second study found a strong correlation between oral presensitization with local honey and improvement in rhinoconjuctival and other allergy symptoms in pollen allergy patients during the subsequent pollen season.[2] Both studies were conducted in countries with a seasonal climate. In many cultures and religions in Asia, honey has been utilized for healing purposes since ancient times.[3-6] Despite being the largest continental producer of honey worldwide,[7] thus far, no study has been conducted in Asia's tropical climate.

We studied the complementary effect of ingestion of honey on AR, in addition to standard medication, in a randomized clinical setting. The study was conducted

in a multiracial tropical Asian population. In contrast to the previous published reports, this study utilized a different study methodology and different sets of study criteria, with much higher dosages of ingested honey. The reason for the higher dosages was because positive health effects of honey are only reportedly achieved if it is consumed at higher doses of 50 to 80 g per intake.[8]

METHODS

Subjects were recruited from an otolaryngology clinic in 2 tertiary referral centres in the East coast of Peninsular Malaysia. The data were collected over a 1-year period. The inclusion criteria comprised subjects aged above 18 years, a diagnosis of AR using clinical history and positive skin prick test, and a willingness to consume a considerable amount of honey daily for the study period. Subjects with known hypersensitivity to honey; a history of asthma, diabetes, or other chronic medical illnesses that require constant medical attention; a history of allergy desensitization for the past 5 years; and pregnancy were excluded from the study. The subjects' demographic data were collected, together with their clinical history of allergy. All subjects underwent a skin prick test (ALK–Abello skin prick test kit, Bege Alle, 2970 Horsholm, Denmark). The following 5 common allergens in the local community were used for the skin prick test: Dermatophagoides pteronyssinus (house dust mite), Felis domesticus (domestic cat), Mucor mucedo (fungi), wheat flour, and peanut. Histamine (as a positive control) and normal saline (as a negative control) were also included. The technique of the skin test followed previously described steps.[9] The presence of a wheal and flare of at least 3 mm and 10 mm larger than the negative control after 15 minutes was regarded as a positive reaction. The subjects with a negative skin prick test to any of the allergens were further excluded from the study. All the subjects were then graded according to the Allergic Rhinitis and Its Impact on Asthma (ARIA) classification.[10]

The subjects were randomly divided into 2 equal sized groups by a random number generator. All subjects were treated with a second-generation antihistamine (loratidine, 10 mg once daily) from the beginning of the study until 4 weeks. The case group was given honey and the control group received honey-flavored corn syrup as placebo. They were instructed to ingest this at 1 g per kg of body weight per day in separate doses for 4 weeks (1 tablespoon=20 g). The type of honey used in this study was Tualang honey, a raw, unprocessed, multifloral honey harvested from beehives of the giant honey bee (Apis dorsata) built on the branches of giant trees named Tualang in the Malaysian rainforest. The corn syrup had the texture, color, and taste similar to the honey used. All subjects received the honey and the placebo in the same container, in a double-blinded manner, whereby neither the research assistants nor the subjects knew what they were receiving. All subjects were instructed not to take any other honey or its products during the course of the study. Compliance was assessed by giving the subjects a diary in 4 stamped envelopes to record the dosage taken and possible side effects experienced in a week. The subjects were supposed to post the envelopes together with the diary each week. The research assistants followed up with the participants through a telephone call when the envelopes were not received each week.

The initial symptom scores were recorded at the start of the study and repeated at day 28 (week 4) and day 56 (week 8). Seven symptoms were assessed in the symptom score: nasal blockage, rhinorrhea, hyposmia, nasal, eye and palatal itchiness, and sneezing. The scoring was done by asking the patient to evaluate the severity of individual symptoms using a 7-point visual analog scale, published by The Joint Task Force on Practice Parameters on Allergy, Asthma, and Immunology.[11] The symptom score was marked by the same independent person at all times.

The sample size was calculated using Power Analysis and Sample Size, 11th edition (NCSS, Kaysville, Utah) software to an 80% power of study.

Data analysis

Symptoms of AR, a positive family history of AR, asthma history, and ARIA classification were recorded in binary dichotomous format (present or absent of outcomes). AR symptoms were assumed to be present when the subject reported a score of at least 3 (mild, easily tolerable symptoms) in the AR symptom score. The case and the control groups were compared with respect to the frequency of the dichotomous data using a chi-square analysis. The mean and the standard deviation were calculated for the total symptom score at the start of the study, week 4, and week 8 for the case and the control groups. Multiple comparison procedures using the repeated measures ANOVA and independent t test were used to determine the significance of differences in the total symptoms score and in the individual symptoms score between the case and the control groups at the start, week 4 and week 8 of the study.

The study protocol was approved by the Research and Ethics Committee of the hospitals where the study took place.

RESULTS

Forty AR patients were recruited in this study and were divided randomly and equally into a case and a control group. The age group of the subjects in the entire study group ranged from 20 to 50 years, with a mean age of 35.7 years. The mean age of the control group was 33.2 years, and the mean age of the case group was 38.2 years. A total of 26 female patients (65%) were included in the study, 12 of whom were in the control group. The majority of the study population was Malay, which accounted for 92.5% (37) of the subjects, followed by Chinese (5%) and one Siamese (2.5%). Most of the study subjects (25%) were teachers, followed by housewives (20%), office workers (15%), and self-employed (5%) individuals. The remainder subjects were either odd-job workers or unemployed. The average rate of honey consumption prior to the study was equal in both the case and the control groups, with the average being 1 to 2 tablespoons a week. The majority of the subjects had non-seasonal AR (persistent type) based on the ARIA classification, with most having a severe type.

The clinical demography of the subjects is summarized in **Table 1**. The prevalence of the symptoms, clinical history, severity, and positive skin prick test were equally distributed in the case and the control groups, with no significant difference between the groups ($P>.05$). **Table 2** shows that there were no significant differences between the mean total symptom score of the case group and the control group at the start of the study. No significant differences were observed at week 4 and week 8 between the case and the control groups.

One-way repeated measures ANOVA was conducted to test the effect of ingestion of honey on the AR symptoms score before, within, and after the exposure weeks. There was a significant effect of ingestion of honey on AR symptoms score, $F(2.57)=6.159$. Paired samples t tests were used to make post hoc comparisons between the weeks in the case and control groups, as shown in **Table 3**. Significant differences were observed between the mean total symptom score at week 0 and week 4, week 4 and week 8, and week 0 and week 8 within the case group. This suggests that there was progressive amelioration of the symptoms from week 0 to week 8 within the honey ingestion group. However, within the control group, the significant differences were observed at week 0 to week 4, but not from week 4 to week 8. This suggests that the improvement in the symptoms declined from week 4 onward in this group following the cessation of the antihistamine treatment.

The cardinal symptoms of AR are nasal blockage, nasal discharge, nasal itchiness, and sneezing. We found that these symptoms were the most common complaints of the subjects in both groups (**Table 1**). These 4 cardinal symptoms showed a significant improvement with time in the case group (**Table 4**). However, in the control group, no significant improvement was seen for nasal blockage and rhinorrhea at the end of the study. In the case group, all 4 symptoms showed an overall improvement from week 0 to week 4 when subjects were taking antihistamine, and the improvement in all the symptoms, except rhinorrhea, continued even after stopping the antihistamine. However, this was not evident in the control group where no significant improve-

Table 1. Clinical characteristics of the study subjects.

Symptoms	Total subjects (n=40) n (%) Positive symptoms at the start of study[b]	Case (n=20) n (%)	Control (n=20) n (%)	*P* value[a]
Nasal itchiness	40 (100)	20 (100)	20 (100)	>.05
Nasal blockage	39 (97.5)	19 (95)	20 (100)	
Rhinorrhea	39 (97.5)	19 (95)	20 (100)	
Sneezing	39 (97.5)	20 (100)	19 (95)	
Eye itchiness	38 (95)	18 (90)	20 (100)	
Palate itchiness	35 (87.5)	18 (90)	17 (85)	
Hyposmia	34 (85)	17 (85)	17 (85)	
Family history of AR	22 (55)	10 (50)	12 (60)	.520
Concurrent asthma	15 (37.5)	10 (10)	5 (25)	.102
ARIA classification				
Mild intermittent	8 (20)	3 (15)	5 (25)	df=3, *P*=.876
Moderate-severe intermittent	4 (10)	2 (10)	2 (10)	
Mild persistent	7 (17.5)	4 (20)	3 (15)	
Moderate-severe persistent	21 (52.5)	11 (55)	10 (50)	
Positive skin prick test				
House dust mite	39 (97.5)	20 (100)	19 (95)	>.05
Peanut	37 (92.5)	17 (85)	20 (100)	
Cat	36 (90)	18 (90)	18 (90)	
Wheat flour	34 (85)	19 (95)	15 (75)	
Mucor mucedo	29 (72.5)	13 (65)	16 (80)	

AR: Allergic rhinitis, df: degree of freedom, [a]Chi-square analysis of the difference between the case and control group. [b]Positive symptom is when the subject reported a score of at least 3 (mild, easily tolerable symptom).

ment was observed during the treatment (week 0–4) or after the medication was stopped (week 4–8). Nasal itchiness and sneezing were the 2 commonest symptoms expressed by our patients. The results suggest that nasal itchiness and sneezing in the case group had a more significant and sustained recovery, even after the treatment was stopped in the fourth week of the study compared with the control group.

DISCUSSION

We found that the ingestion of honey at high doses, in addition to the usual standard medication, affected the recovery of the symptoms of AR in our patients compared with the control group. Those patients who ingested a regular daily high dose of honey exhibited significant alleviation of their overall symptoms, as shown by the improvement in the mean total symptom score. The case subjects also showed a progressive, steady improvement in their overall mean symptom score throughout the study period from week 0 to week 8, whereas in the control subjects, the improvement in symptoms seemed to decline following the cessation of the antihistamine. The ingestion of honey at a high dose, together with the antihistamine, also significantly improved all 4 cardinal symptoms of AR, but the same effect was not seen in the control group. Although sneezing and nasal itchiness improved significantly from week 0 to week 8 in both groups, the improvement after the withdrawal of antihistamine was significant only in those who had ingested honey.

In our study population, the main symptom expressed by the patients was nasal itchiness, followed by sneezing, runny nose and nasal blockage. Based on the ARIA classification, the majority of our patients had moderate-to-severe persistent AR. This is consistent with the findings of a larger prevalence study on AR in the same population and geographical area.[12] We found no significant difference in the mean of the initial symptom score between the 2 groups, and this suggests satisfactory randomized sampling for subsequent comparisons. Based on the ARIA guidelines and the latest review of the safety of antihistamines, a second-generation oral antihistamine, such as loratadine, is the first treatment option for AR.[13,14] The development of subsensitivity after prolonged treatment with certain antihistamines has been reported previously but not with loratadine.[15,16] Both the case and the control groups showed a significant improvement from week 0 to week 4 when antihistamine was taken. The ingestion of honey seemed to complement and sustain the effect of loratadine, which was not seen in the control group.

Loratadine has been proven to be effective in relieving nasal itchiness, rhinorrhea, and sneezing in AR, but it provides only partial relief from nasal congestion.[17] In this study, the ingestion of honey, together with the antihistamine treatment, significantly improved all the 4 symptoms, including nasal congestion. This study also showed that all 4 cardinal symptoms of AR showed more of an improvement within the first 4 weeks in those with honey ingestion. These results may indicate that the ingestion of honey as an adjuvant to antihistamine improves the overall symptom score and individual symptoms compared with the placebo within a short period. The effect sustained at one month after withdrawing the antihistamine treatment.

We postulate several mechanisms that possibly explain the improvement in the symptoms of AR with honey ingestion. First, honey could have suppressed an IgE-mediated hypersensitivity reaction in these subjects. Several animal studies have indicated the immunosuppressive activity of honey. For example, in mice, ovalbumin-specific IgE antibody responses elicited

Table 2. Mean total symptoms score between case and control group at the start (week 0), week 4 and week 8 of the study.

Week	Group	Total symptoms score Mean (SD)	*t* test for equality of means (Equal variances assumed)	df	*P* value
Week 0	Case	17.2 (3.64)	t=0.74	38	.464
	Control	16.3 (4.45)			
Week 4	Case	14.2 (4.85)	t=0.00	38	1.00
	Control	14.2 (4.87)			
Week 8	Case	11.9 (5.66)	t=0.8	38	.428
	Control	13.1 (4.28)			

df: degree of freedom, SD: standard deviation

Table 3. Comparison of the mean total symptom score between week 0 & week 4, week 4 & week 8, and week 0 & week 8 within the case and the control group.

Week	Case			Control		
	Differences of the total symptoms score between the weeks. Mean(SD)	*t* test (df 19)	*P* value	Differences of the total symptoms score between the weeks. Mean(SD)	*t* test (df 19)	*P* value
0-4	3.05 (4.76)	t=2.86	.010	2.10 (4.15)	t=2.26	.036
4-8	2.30 (3.28)	t=3.14	.005	1.03 (3.54)	t=1.30	.209
0-8	5.35 (4.98)	t=4.81	.000	3.13 (4.10)	t=3.41	.003

df: degree of freedom, SD: standard deviation

Table 4. Comparisons of the improvement of the mean symptoms score of the 4 cardinal symptoms of allergic rhinitis (nasal itchiness, sneezing, rhinorrhea & nasal blockage) in the case and the control group.

Symptoms	Week	Case			Control		
		Mean different of symptom score (SD)	*t* test, df 19	*P* value	Mean different of symptom score (SD)	*t* test, df 19	*P* value
Nasal itchiness							
	0-4	0.45(0.95)	t=2.13	.046	0.45(1.19)	t=1.69	.107
	4-8	0.30(0.47)	t=2.85	.010	0.10(0.64)	t=0.70	.494
	0-8	0.75(0.97)	t=3.47	.003	0.55(0.94)	t=2.60	.017
Sneezing							
	0-4	0.48(0.88)	t=2.33	.031	0.23(0.84)	t=1.20	.244
	4-8	0.32(0.89)	t=2.13	.047	0.18(0.54)	t=1.61	.124
	0-8	0.80(1.32)	t=2.43	.025	0.41(0.74)	t=2.15	.045
Nasal blockage							
	0-4	0.42(0.95)	t=2.17	.043	0.19(0.44)	t=1.62	.121
	4-8	0.39(0.78)	t=2.20	.04	0.39(0.87)	t=1.80	.087
	0-8	0.81(1.11)	t=2.52	.021	0.58(1.01)	t=1.65	.115
Rhinorrhea							
	0-4	0.38(0.44)	t=1.97	.063	0.56(0.78)	t=2.07	.052
	4-8	0.25(0.49)	t=1.67	.112	0.14(0.38)	t=1.56	.135
	0-8	0.63(0.72)	t=2.16	.044	0.70(0.72)	t=1.87	.077

SD:standard deviation, df:degree of freedom

against different allergens were found to be completely suppressed by different sources of commercial honey.[18] Other animal studies showed the anti-allergic mechanism of honey involves the inhibition of IgE-mediated mast cell activation both in vivo and in vitro.[19,20] In another study, royal jelly, a principal food of the queen bee, suppressed antigen-specific IgE production and histamine release from mast cells, restored macrophage function, and improved Th1/Th2 cell responses, resulting in the suppression of allergic reactions in mice.[21] Although evidence from human studies is still lacking, a study involving patients with allergic fungal rhinosinusitis provided evidence that the patients gained symptomatic benefits from topical application (spray) of manuka honey into the nose.[22] The authors found that the patients with a better response had higher IgE

levels in their blood, pointing to the potential suppression of an IgE-mediated hypersensitivity reaction.

Second, it is possible that the introduction of honey into the body may have induced low-dose oral tolerance to these aeroallergens. Exposure to a constant low dose of the allergen (honey) may have made the body accustomed to its presence (tolerance) and decreased the chance of an overwhelming immune system response such as an anaphylactic reaction when exposed to the same aeroallergen. Saarinen et al showed that the oral desensitization of an aeroallergen resulted in a less severe form of rhinitis and that the use of anti-allergy medications was reduced in such orally desensitized patients compared with a control group.[2] There is evidence that early exposure in life to environmental and food allergens reduces the subsequent risk of allergic diseases by developing tolerance.[23-25] The balance between allergy and tolerance is dependent on regulatory T-cells.[26] In healthy individuals, intact functional allergen-specific regulatory T-cells induce tolerance as a normal immunological response to allergens, but this response is impaired in allergic sufferers.[26]

Thirdly, honey has been reported to have an anti-inflammatory property.[27,28] AR is an inflammatory disease resulting from an allergic cascade, which is characterized by inflammation of the mucosa surface, leading to stasis of mucus secretion, blockages of the airway, and, later on, the sinuses. In our case, the complementary effect of honey on the improvement in the symptom score may be attributable to the direct anti-inflammatory property of honey, rather than the anti-allergy effect. We gave the antihistamine to both groups because it is useful in relieving the allergic symptoms of itchiness, sneezing, and rhinorrhea, but less so in relieving the nasal blockage.[17] The improvement in nasal blockage with honey ingestion was possibly mediated by the reduction in nasal inflammation, thereby opening up the nasal airway. Finally, in addition to the high sugar content, the type of honey used in this study contained, on average, higher amounts of antioxidants, including phenolic acids and flavonoids.[29,30] According to a comprehensive review article of available epidemiological, animal, molecular, and immunological data, there are potentially beneficial associations between combinations of antioxidant supplements and allergic diseases.[31] However, the exact mechanism for the associations remains unclear.

Rajan et al found that subjects who ingested honey did not experience relief from their symptoms in excess of that seen in a placebo group.[1] Our study differed from theirs in terms of the study population, the environment, and the study methodology. We used higher honey dosages and administered standard antihistamine treatment to all the patients in the case and the control groups. Repeated exposure to antigens is a prerequisite for the development of tolerance. In our study, higher dosages of honey may have increased the development of tolerance, possibly via T-cell anergy.[32] Standardizing the treatment in both groups, regardless of the symptoms, should have eliminated the potential biases from over- or under-treating AR with the usual standard medications. The timing of the exposure to the allergen may also have influenced the results of our study. The study by Rajan et al was conducted only during the pollen season. Another similar study of honey ingested constantly during 5 pre-seasonal months showed a different outcome in the improvements of AR symptoms.[2]

We found that the high dose of honey ingestion is beneficial and that it appears to improve the symptoms of AR, at least, for a short duration. Determining the potential long-term effect of honey ingestion is beyond the scope of this study. However, these findings should be considered preliminary, as there are several limitations of this study. Firstly, we used clinical criteria to determine symptoms severity, which can be subjective. Although we limited this potential bias by using a validated scoring instrument and employing an independent assessor to conduct the symptom score, an immunological test would be more objective. Work is currently under way to study the potential relationship between honey ingestion and the amelioration of the symptoms of AR using objective molecular analysis. The honey used in this study was a raw, unprocessed one and not a standardized commercially manufactured honey. Therefore, the results are only applicable to the batches of honey used here. The sample size of this study is relatively small; hence, further evidence in a larger randomized-controlled trial is needed to validate the results.

In conclusion, we found that the ingestion of high dose of honey had a significant complementary effect in improving the overall symptoms in AR patients compared to the placebo. The result indicates that honey could serve as a complementary therapy for AR.

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