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# Is honey, as adjunctive therapy, effective in alleviating nasal allergy symptoms?

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# A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements for

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies Philadelphia College of Osteopathic Medicine Philadelphia, Pennsylvania

December 14, 2018

# ABSTRACT

OBJECTIVE: The objective of this selective EBM review is to determine whether honey used as adjunctive therapy is effective in alleviating nasal allergy symptoms.

STUDY DESIGN: This is a systematic review of three randomized controlled trials published between 2010-2013, all in the English language.

DATA SOURCES: Three randomized controlled trials, which studied the effects of honey used as adjunctive therapy for the relief of nasal allergy symptoms, these were obtained using PubMed.

OUTCOMES MEASURED: The outcome of each study was a patient reported decrease in the number of days and the severity of nasal allergy symptoms including: sneezing, itching, nasal blockage, and rhinorrhea. These outcomes were measured via daily diary entries, questionnaires regarding symptom severity and need for medication, Sino-Nasal Outcome Test (SNOT-22) questionnaire, and a 7-point visual analog symptom severity scale.

RESULTS: All three RCTs determined that nasal allergy symptoms were decreased a statistically significant amount, as defined by a p-value <0.05, with the addition of honey in subject's daily medication regimen. This was compared to control, which consisted of patients taking only their normal daily medication and no honey products or a visually and taste matched placebo.

CONCLUSIONS: The results of this systematic review have demonstrated that honey is effective in alleviating nasal allergy symptoms in numerous mediums including nasal spray as well as oral intake when produced in the geographic area in which the patient population resides. Whilst positive and promising results were obtained from these studies, additional research with larger patient populations, standardized honey product, and increased time frame of study is required to ascertain how beneficial honey truly is and if these benefits last.

KEY WORDS: honey, allergic rhinitis

#### INTRODUCTION:

The number of people worldwide who suffer from allergies is steadily increasing; whether it be from air pollution, improved hygiene, or increased indoor allergen exposure, the exact cause for this escalation remains unknown.<sup>1</sup> Allergic rhinitis, also identified as "allergic rhinosinusitis" or "AR," is an extremely common disorder affecting upwards of 40 million people in the U.S.<sup>2</sup> It is reported that AR is the cause of, "at least 2.5 percent of all clinician visits, 2 million lost school days, 6 million lost work days, and 28 million restricted work days per year." <sup>3</sup> Currently, AR affects 10-30% of children and adults in the U.S., making it inevitable that healthcare providers will encounter this disease.<sup>3</sup>

AR is attributable to a host of triggers including: pollen, mold, animal dander, and dust mites. When allergy sufferers encounter an allergen, the immune system produces antibodies, immunoglobulin E (IgE), to the allergen.<sup>4</sup> IgE antibodies bind with mast cells, plasma cells and eosinophils, which within minutes produce symptoms such as sneezing and itching.<sup>2</sup> Hours later, the late phase of reaction occurs producing nasal congestion and malaise.<sup>2</sup> AR comprises numerous symptoms including: sneezing, itching, nasal congestion, and rhinorrhea. As the nasal mucosa and the sinuses are adjoining, patients with sinusitis also concomitantly experience nasal symptoms.<sup>3</sup> AR may affect sufferers in a seasonal pattern or for many, is a constant year-round struggle. For something as trivial in many people's minds as "seasonal allergies," the cost to manage this disease has become astronomical. In February 2011, it was reported that approximately \$3.4 billion were spent on allergic rhinitis with almost half due to the cost of prescriptions and over the counter medications.<sup>5</sup> Furthermore, research has shown sufferers of AR have an average number of prescriptions double that of non-sufferers.<sup>3</sup> With this being said, cost effective alternative methods have become a necessity.

There are numerous accepted methods used to treat the myriad of symptoms comprising allergic rhinitis. First and foremost, allergen avoidance is encouraged.<sup>6</sup> However, since it is near impossible to avoid pollen, fungus, mold, or dust in the air, other options must be employed to combat the immune system's exaggerated response. For suffers with mild or episodic symptoms, oral second-generation antihistamines including cetirizine, loratadine, fexofenadine are effective.<sup>6</sup> Gold standard treatment for persistent or moderate to severe AR is glucocorticoid nasal sprays including: mometasone furoate, fluticasone furoate, and triamcinolone acetonide.<sup>6</sup> In addition to an oral second-generation antihistamine or a glucocorticoid nasal spray, patients can augment their treatment by adding: antihistamine nasal sprays such as olopatadine or azelastine, a mast cell stabilizer such as Cromolyn sodium, an anti-leukotriene such as Montelukast, or combination products consisting of an oral antihistamine plus a decongestant.<sup>6</sup> More expensive and time consuming yet, is allergen immunotherapy. As many of the abovementioned products are now over the counter, patients have the ability to self-medicate, and this comes with risks. Many of these products can be sedating, especially if a patient chooses a firstgeneration antihistamine for example, diphenhydramine. Due to their anti-cholinergic properties these medications can cause urinary retention, altered mental status or confusion, blurred vision, dizziness, and other adverse drug reactions.<sup>6</sup>

The usual methods of treatment discussed for nasal allergy symptoms while effective, have potentially adverse side effects or undesirable dosing schedules, which limit their use in certain patients; in addition, maximum relief is often never achieved. This leaves patients to continue to battle daily with their symptoms and search for other options. One of these suggested options, a natural and safe alternative, is honey. Honey has been recognized as an antioxidant, antibacterial, antiviral, anti-inflammatory, and immunomodulating substance.<sup>7</sup> The proposed use of honey is supported by its immunomodulation and anti-inflammatory properties. In animal studies, honey has been proven to reduce circulating IgE levels, suppress histamine release, prevent the production of TNF- $\alpha$  and COX-2, and reduce the creation of nitric oxide.<sup>7.8</sup> With the rising costs of healthcare and the wide availability of natural alternatives, it is proposed that honey be considered as a cost-effective alternative adjunctive method to patient's normal daily medication regimen in relieving nasal allergy symptoms. In this systematic review, the effectiveness of honey in decreasing nasal allergy symptoms will be evaluated through three randomized controlled trials.

#### OBJECTIVE

The objective of this selective EBM review is to determine whether or not honey, as adjunctive therapy, is effective in alleviating nasal allergy symptoms.

#### METHODS

The population studied in this systematic review was obtained from three randomized controlled trials which included patients suffering from physician diagnosed nasal allergy symptoms. Oral consumption of honey or inhalation of honey solution in addition to the patient's traditional allergy medication regimen were the interventions reviewed. In Asha'ari et al. patients, minimum of 18 years of age, were treated with a second generation antihistamine (Loratidine 10mg) for 4 weeks.<sup>8</sup> Loratidine was then discontinued for the remaining 4 weeks of the study and was replaced with honey or placebo. The case group was given Tualang honey, raw and unprocessed, and the control a honey flavored corn syrup as placebo to be ingested at 1g per kg of body weight.<sup>8</sup> Thamboo et al. had subjects, 19 years of age and up with a diagnosis of allergic fungal rhinosinusitis who had failed standardized treatment methods, spray 2mL of a 50/50 mixture of honey and saline into one nostril nightly with a mucosal atomization device.

The other nostril, which received no honey spray, was utilized as the control; this solution was in addition to their usual daily medication regimen for 30 days.<sup>9</sup> Saarinen et al. compared two types of honey: a locally collected, unpasteurized and unfiltered organic honey ("regular honey" or "RH") against the very same honey enriched with bee-collected pollen from Birch trees, deemed "Birch pollen honey" ("BPH") versus control, which consisted of patients on their regular allergy medication.<sup>10</sup> Patients were instructed to ingest the honey daily starting in November at <1g and increasing the dose at 3 week intervals to a maximum of 8g until the end of March.<sup>10</sup> Reduction in nasal allergy symptoms was the result assessed in each study.

The key words employed in the author's search for sources via PubMed included "honey," and "allergic rhinitis." Articles utilized in this systematic review were selected from published peer- reviewed journals in the English language. Articles were chosen if they included outcomes which were patient oriented (POEMs) and if they related to the author's clinical question. Articles selected fit the inclusion criteria of: randomized controlled trials published after 2010 with no other systematic review, meta-analysis, or articles published in the Cochrane database regarding the same clinical question. Exclusion criteria consisted of any patient with a known hypersensitivity to bees or honey. Noted statistics include p-value, mean change from baseline, and standard deviation.

Study	Type	#	Age	Inclusion Criteria	Exclusion	W/D	Interventions
	• •	Pts	(years)		Criteria		
Asha'ari, 2013	RCT	Pts 40	(years) 20-50	Patients 18 years + with a diagnosis of allergic rhinitis using clinical history and positive skin prick test. Must be willing to consume a	Criteria Known hypersensitivity to honey, history of asthma, diabetes, or other chronic illness, history of allergy desensitization for the past 5 years, or pregnancy.	Not reported	1g/kg of Tualang honey daily in separate doses for four weeks in addition to 10mg of Loratadine.
Thamboo, 2011	RCT	38	19+	considerable amount of honey. Patients who had undergone bilatoral	Patients allergic to pollen, honey, or boos	4	2mL nasal spray of
Section	DOT		8.70	bilateral functional endoscopic sinus surgery with a definitive diagnosis of allergic fungal rhinosinusitis who failed budesonide irrigations for $\leq 12$ weeks and have tried a course of systemic antifungals and steroids.	or bees.		50/50 honey- saline solution using a mucosal atomization device in selected nostril once a day (at night) for 30 days in addition to regular nasal regimen.
Saarinen, 2010	RCT	61	8-79	Patients with physician diagnosed pollen allergy suffering from nasal, conjunctival, and other allergy symptoms.	No mentioned exclusion criteria.	11	Each patient consumed honey on a daily basis starting with <1g in November and increasing intake to 1 tsp (about 8g) until the end of March.

Table 1: Demographics and Characteristics of Included Studies

#### OUTCOMES MEASURED:

In this review three RCTs were employed, two single blind and one double blind, with the measured outcomes being POEMs. The POEMs measured in this review were improvement (reduction) of allergic nasal symptoms including: sneezing, nasal obstruction, rhinorrhea, hyposmia, and nasal itching as well as decreased need for usual medication. This was ascertained using diary entries including daily symptom severity, questionnaires regarding symptoms and need for medication, Sino-Nasal Outcome Test (SNOT-22) questionnaire, and a 7-point visual analog scale to evaluate symptom severity score. All data was continuous and was statistically measured by means of the patient's self-reported decrease in nasal allergy symptoms or decreased need for daily medication displayed as mean change from baseline and p-values assessed against the control group for comparison.

#### **RESULTS**:

To determine if the effect of honey on nasal allergy symptoms was advantageous the three articles being evaluated in this systemic review claimed a statistically significant outcome was obtained if the consequential p-value was <0.05. The data statistically analyzed from all three studies was continuous, therefore a mean change in baseline was reported. In Asha'ari et al. no significant differences were reported between the experimental and control groups in terms of the mean total symptom score (i.e. the severity of symptoms) at the onset of the study as well as no significant differences between the groups according to demographics. Forty patients were utilized and were split evenly between control and experimental arms of the study.<sup>8</sup> Reported time intervals were from weeks 0-4, weeks 4-8, and weeks 0-8.<sup>8</sup> Those patients in the experimental group reported statistically significant decreases in their nasal allergy symptoms from weeks 0-4, 4-8, and 0-8 as demonstrated in tables 2, 3, 4 and 5.<sup>8</sup> In contrast, the control

arm (placebo) also noted a statistically significant decrease in nasal allergy symptoms from

weeks 0-4; however, from weeks 4-8 there was no longer any noteworthy reduction reported.<sup>8</sup> In

this study, we focus on weeks 4-8, which highlights singularly the use of honey versus placebo.

<u>- unit 21 million sour symptom score comparison between experimental and control</u>							
Week	Difference in total symptom	P- value: Difference in total		P- value:			
	score: Experimental	Experimental	symptom score: Control	Control			
0-4	3.05 (4.76)	0.010	2.10 (4.15)	0.036			
4-8	2.30 (3.28)	0.005	1.03 (3.54)	0.209			
0-8	5.35 (4.98)	0.000	3.13 (4.10)	0.003			

Table 2: Mean total symptom score comparison between experimental arm and control <sup>8</sup>

Table	3:	Change	in mean	from	baseline s	symptom	severity	score from	weeks 0-4 <sup>8</sup>	3

Symptom	<b>Experimental Mean</b>	P- value	Control Mean	P- value
	difference (SD)		difference (SD)	
Nasal itchiness	0.45 (0.95)	0.046	0.45 (1.19)	0.107
Sneezing	0.48 (0.88)	0.031	0.23 (0.84)	0.244
Nasal blockage	0.42 (0.95)	0.043	0.19 (0.44)	0.121
Rhinorrhea	0.38 (0.44)	0.063	0.56 (0.78)	0.052

### Table 4: Change in mean from baseline symptom severity score from weeks 4-8<sup>8</sup>

Symptom	Experimental Mean difference (SD)	P- value	Control Mean difference (SD)	P-value
Nasal itchiness	0.30 (0.47)	0.010	0.10 (0.64)	0.494
Sneezing	0.32 (0.89)	0.047	0.18 (0.54)	0.124
Nasal blockage	0.39 (0.78)	0.04	0.39 (0.87)	0.087
Rhinorrhea	0.25 (0.49)	0.112	0.14 (0.38)	0.135

#### Table 5: Change in mean from baseline symptom severity score from weeks 0-8<sup>8</sup>

Symptom	Experimental Mean difference (SD)	P- value	Control Mean difference (SD)	P-value
Nasal itchiness	0.75 (0.97)	0.03	0.55 (0.94)	0.17
Sneezing	0.80 (1.32)	0.025	0.41 (0.74)	0.045
Nasal blockage	0.81 (1.11)	0.021	0.58 (1.01)	0.115
Rhinorrhea	0.63 (0.72)	0.044	0.70 (0.72)	0.77

Thamboo et al. utilized honey as a nasal spray for patients with nasal allergy symptoms due to allergic fungal rhinosinusitis. Subjective nasal allergy symptoms were recorded via the Sino-Nasal Outcome Test (SNOT-22) pre and post study (4 weeks in length).<sup>9</sup> Out of the 38 subjects involved in this study, 20 completed both the pre and post SNOT-22 questionnaire. A significant improvement in nasal allergy symptoms was expressed by sixteen out of the twenty

patients in this study, as evidenced by a p-value of 0.0220.<sup>9</sup> In this trial, four patients claimed "burning sensation" in their sinuses however, this did not alter their compliance with the study, and one patient claimed the honey solution induced nausea and subsequently discontinued participation in the study.<sup>9</sup>

Saarinen et al. divided subjects into 3 groups: control receiving no honey products, those receiving birch pollen honey (BPH), and those receiving regular honey (RH).<sup>10</sup> Here, we focus on the BPH group. Patients were given diaries in which daily recordings of: sneezing, runny, itchy, or blocked nose were documented. Patients were additionally responsible for a questionnaire which rated daily symptoms and need for medication. Of the original 61 subjects in this study, 11 dropped out.<sup>10</sup> Subjects in the BPH group demonstrated increased days symptom free, decreased days with nasal symptoms, and decreased need for nasal medication compared to control. In regard to symptomatic days, the BPH group had the most significant change, p-value < 0.01.<sup>10</sup> Those patients in the BPH group also showed a statistically significant decrease in the need for nasal antihistamines p-value < 0.001 when compared to control.<sup>10</sup> See Table 6 for results.

Table 6: Number of days with allergy symptoms and use of nasal antihistamine medication<sup>10</sup>

# of days	BPH	RH	Control	P-value
Symptom free	32.1 <u>+</u> 14.2	26.6 <u>+</u> 16.5	14.1 <u>+</u> 12.6	0.004
Nasal symptoms	23.0 <u>+</u> 12.9	29.8 <u>+</u> 20.5	44.2 <u>+</u> 12.3	0.001
Use of nasal spray	8.0 <u>+</u> 13.5	13.4 <u>+</u> 23.4	19.5 <u>+</u> 22.0	0.247

In addition, "better general health" and a reduction in number of colds and stomach upset was reported by 35% of those who used the birch pollen honey and 38% in the regular honey group.<sup>10</sup>

#### DISCUSSION:

Honey is a reasonably safe adjunctive method to augment the treatment of nasal allergy symptoms. In the three articles discussed, minimal side effects were mentioned including: mild itching of mouth or skin, dislike for taste, burning sensation in the sinuses, and nausea.<sup>8,9,10</sup> However, it should be noted that those who suffer from allergy to bees or honey should not incorporate this therapy into their daily routine due to the risk of anaphylaxis.<sup>10</sup> Patients are also advised to never administer honey products to children less than one year in age due to the risk of botulism. If patients choose to utilize honey as adjunctive therapy they unfortunately would have to pay for it out of pocket, potentially limiting access to this method of care. However, depending on where the honey is purchased, it is relatively low in cost when compared to the price of standard allergy medications. The studies discussed in this systematic review establish the potential worth as well as the effectiveness of utilizing honey as an adjunctive therapy in reducing nasal allergy symptoms, there are limitations to each.

In Asha'ari et al. the improvement demonstrated in both the control and experimental groups from week 0-4 can be attributed to the use of Loratidine during this time.<sup>8</sup> However, the data displays patients in the control arm of the study no longer had any improvement of their symptoms in the subsequent weeks (as Loratadine was discontinued in both groups at week 4). This suggests that the use of honey unaided in the experimental group from weeks 4-8 was effective in reducing patient's symptom severity score.<sup>8</sup> The strength of this study was that it utilized honey alone as treatment after week 4, thus any improvement in symptoms is credited to the use of honey. The downfall of this study was the small patient population utilized, 20 subjects in the experimental group and 20 in control.<sup>8</sup>

Thamboo et al. demonstrated that nasal inhalation of a honey-saline mixture did produce a statistically significant improvement in allergic nasal symptoms in those patients who filed a SNOT-22 questionnaire pre and post-study.<sup>9</sup> This study is limited by the fact that patients acted as their own control, therefore the improvement in their symptoms could be attributed to the fact that patients were not truly blinded.<sup>9</sup> In addition, this study was thirty days in length. Most notably, the questionnaire utilized incorporated other allergic symptoms therefore a decrease in the total score could have been due to improvement of symptoms other than nasal. Regardless, inhalation of the honey saline solution did improve symptom severity and this warrants deeper investigation. If this study was expanded to include a larger patient population, the length of the study was increased, and a more accurate way to blind patients was instilled, a more reliable interpretation of the effect of honey on nasal symptom severity could be obtained.

Saarinen et al. established that the use of either regular honey or birch pollen honey resulted in less need for nasal antihistamine spray, fewer days with nasal symptoms, and increased number of symptom free days.<sup>10</sup> All of which had statistically significant results. The strength of this study was that it utilized a "preloading period" in which patients consumed honey in five preseason months, November through March.<sup>10</sup> This study highlights the benefit of augmenting natural raw honey with additional pollen as demonstrated by subjects decreased symptoms and reduced need for nasal antihistamines. The extended length of this study allows one to deduce the potential benefits of honey employed as natural allergen desensitization.<sup>10</sup> Limitations of this study are that both the experimental groups contained more patients than control; BPH group: 25 patients, RH: 19 patients, control: 17 patients.<sup>10</sup> This could have skewed statistics in favor of the experimental groups. This study also employs a relatively small patient population.

The outcomes of these three studies are limited as the type of honey used was not standardized, therefore the results could be said to only apply to that one particular type of honey in that one specific location. Therefore, sufferers of nasal allergy symptoms can find relief in using honey produced in their geographic area of residence. The time period in which honey was administered to patients also affects the outcome of this review. In order to validate the use of honey as adjunctive therapy, a specific time period in which honey is administered would need to be regulated. There were also numerous approaches taken in which patients rated the severity of their symptoms, if a universal method to score symptom severity were utilized, a more conclusive, standardized result could be obtained.

#### CONCLUSION:

The conclusion deduced from these three studies is that honey is a safe and effective adjunctive method of reducing the severity of nasal allergy symptoms in suffers of the same geographic area in which the honey was produced. A statistically significant decrease in symptom severity was achieved in patients who used honey in addition to their routine allergy medication regimen in all three studies. In order to entirely validate the effectiveness and the success of honey in reducing nasal allergy symptoms, more research would need to be completed with a greater patient population. Furthermore, it would be advantageous to perform additional research on the time frame in which patients employ the addition of honey into their daily routine. This could demonstrate if there is increased effectiveness in "preloading" the body prior to allergy season for those who specifically suffer from seasonal allergies. It would also be advantageous to research the potential long-term benefits of honey use, if any exist.

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