

Original Article

## Honey with Coffee: A new finding in the treatment of Persistent Postinfectious Cough

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### Abstract

#### Introduction:

Persistent postinfectious cough (PPC) is a cough that persists longer than 3 weeks or perhaps for many months after a common cold or an upper respiratory tract infection (URTI). PPC has poor response to routine treatment modalities, so it can be a vexing problem for the patient and the physician alike. Our hypothesis was that honey and/or coffee have some beneficial effects in the treatment of PPC. The aim of this study was to evaluate the therapeutic effects of coffee and/or honey in the treatment of patients with PPC.

#### Materials and Methods:

This was a double blind randomized clinical trial, conducted on adult patients during a 6-year period from 2003 to 2009. Included in this study were 84 adult participants that had experienced PPC longer than 3 weeks. All of them had the history of several referrals to different physicians and despite treatment, their cough had persisted. Patients with other causes of chronic cough, or systemic disease or with abnormal routine laboratory tests were excluded. All the included 84 participants were distributed into three groups. For all the participants, a jam-like paste was prepared. Each 600 grams of the product consisted of "70 grams original instant coffee" in the first regimen, "500 grams of honey" in the second regimen and "70 grams of instant coffee plus 500 grams of honey" in the third regimen. These participants were told to dissolve 25 grams of the prescribed product in about 200<sup>CC</sup> of warm water (under 60° C), and drink this solution every 8 hours for one week. All the participants were evaluated before and at the end of the first week of their treatment, to measure the frequency of their cough. In addition they were under observation for the first month.

#### Results:

Comparing the effectiveness of all three treatment regimens, this study found "honey with coffee" as the most effective treatment modality for PPC ( $P < 0.001$ ).

#### Conclusions:

Combination of honey and coffee can successfully treat the PPC at a short time. Thus, it is recommended for the treatment of PPC.

**Keywords:** Coffee, Honey, Postinfectious cough, Upper respiratory tract infection

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### **Introduction**

Cough is a reflex action of the respiratory tract with a protective nature and defense mechanism by an explosive expiration to clear secretions and foreign materials from the airways (1,2). Generally, cough reflex is triggered by mechanical or chemical stimulation of sensory nerve receptors which are mainly present in the pharynx, larynx, trachea and bronchi (3). Cough can also be a warning sign of disease, and needs to be diagnosed accurately (1). Despite extensive diagnostic evaluation guidelines and numerous treatments; chronic and uncontrollable cough, in a number of cases, still remains as a nuisance (4,5). It is a common problem often resulting in referral to secondary care (5,6).

Common causes of chronic cough are: Lung and tracheal diseases, pharyngitis, upper airway cough syndrome (UACS) due to upper respiratory tract infections (URTI) and allergic rhinitis (3,7,8). Other causes are gastro-esophageal reflux disease, exposure to environmental pollution or cigarette smoke, respiratory tract foreign bodies, psychogenic cough and persistent postinfectious cough (PPC). But UACS has been the most common cause of chronic cough in publications of the United States (1,6,9).

PPC is a cough that persists longer than three weeks after a common cold or other viral respiratory tract infections (7,10). It is reported as 11–25% of the chronic cough (1). This cough that is expected to last only one or two weeks persists for longer than three weeks or perhaps for many months (11).

Patients frequently complain of a persistent tickling or irritating sensation in the throat, which often leads to paroxysms of coughing (1). Because of its morbidity and difficulties, such patients are frequently referred to cough clinics and investigated for other causes of cough (1). It can be a troublesome problem for the patient and the physician alike (4,5).

Specific infectious etiology of PPC is rarely confirmed (12). Respiratory viruses, particularly respiratory syncytial virus (RSV), adenoviruses parainfluenza, influenza and etc, have all been implicated (7,10). The pathogenesis of the PPC is probably long-lasting and widespread pharyngeal mucosal inflammation and desquamation of the epithelial cells with nerve endings damage, that leads to hyperactivity of the cough reflex (1,9,12). This can make it more sensitive to local irritants and can lead to a vicious cycle and more damage to mucosa (1,13).

PPC is stimulated by cigarette smoke, chemical fumes, aerosol sprays, dust, perfumes, drinking, eating crumbly dry food, taking a deep breath, laughing, talking over the phone for more than a few minutes, changes in ambient temperature and breathing cold air (1).

Successful treatment of the PPC depends on making an accurate diagnosis and giving the specific therapy. Currently available treatments for PPC are: bronchodilators and anti-inflammatory medications, particularly inhaled or systemic corticosteroids (7,10). narcotics, centrally acting antitussive agents such as codeine and dextromethorphan (10-12), nedocromil sodium and cromoglycate (7,10,12), inhaled ipratropium bromide and antihistamines (7,10).

Despite all these treatments, this chronic cough is usually intractable and has no remarkable response to routine drugs. So, it is worth to find a better treatment for PPC. Based on our previous knowledge and personal experience, our hypothesis was that honey and/or coffee may have some beneficial effects in the treatment of PPC.

In the Review of Literature, to find some information, we searched about Honey and Coffee. To the best of our knowledge, we did not find any report that has noted such a therapeutic combination for PPC, but it was found that:

A- "Honey has been regarded as a health giving substance since ancient times and

its medical use is recorded from around 3000 B.C. onward. Honey has been used, also in modern times for maintenance of health and in several diseases (14). World Health Organization (WHO) has cited honey as a potential treatment for cough, URTI and cold symptoms (15). Also it suggests that honey demulcents may soothe the throat (15). It can be effective and recommended to provide some relief from cold symptoms and cough (15-17). It is a natural substance, cheap, popular and safe (15). In addition, honey has antioxidant efficacies and increases cytokine release, which may cause its antimicrobial effects (15). Honey is an ancient remedy which has been re-discovered for the treatment of wounds with induction of tissue repair and stimulation of wound healing (15,18). These effects may have been associated with its hyper osmolarity and with its anti-inflammatory and antioxidant properties (15, 16)."

B- "Caffeine is found in coffee, tea, cola drinks and cocoa (19). Methylxanthines (such as theophylline and caffeine) are bronchodilator drugs which are believed to stimulate breathing efforts and have been used to prevent apnea (19, 20). Also caffeine is hypoalgesic, and it has anti-inflammatory effects (19, 20). It is the world's most commonly consumed psychoactive substance that stimulates the CNS. Caffeine improves vigilance and psychomotor performance, and increases levels of self-reported alertness and decreases levels of self-reported fatigue and sleepiness."

Considering all above, the aim of this study was to scientifically evaluate the therapeutic effects of coffee, honey and their combination, in treatment of patients with PPC.

### **Materials and Methods**

This was a double blind randomized clinical trial of participants presenting with PPC. It was performed during a 6-year period at the Baqiyatallah University

Hospital, Tehran, Iran from 2003 to 2009. Our study was conducted on included 84 adult patients which only 74 of them kept track until the end of this study (42 men and 32 women).

*Ethical Considerations:* "The participants were all volunteers and they were fully informed about the aim of the study, the prescribed regimens which consist of natural safe edible substances, moreover the follow up sessions and their own duty as participants. Also they were told about the benefits of this research, the potential complications such as dyspepsia and insomnia, and how to face them. They were reassured that the data and their files are kept confidential. Then, an informed consent was taken from them before they were enrolled in the study. The project design of this prospective study was approved by the Ethics Committee of the Baqiyatallah University of Medical Sciences."

In our cough clinic, all the patients were assessed and registered after their check list was completed. It was about personal data including age, sex, weight, education, occupation, duration of their illness and presence or absence of systemic disease. All the participants underwent a comprehensive history, physical examination of respiratory system and complete examination of ear, nose and throat. They were thoroughly examined for every abnormality and also underlying causes of cough. Also routine laboratory tests and chest X-Ray were taken. Other evaluations were carried out as necessary. For example Spirometry, Computed Tomography (CT scan) of paranasal sinuses, and High-Resolution Computed Tomography (HRCT) of thorax.

In patients with chronic cough, there is a positive relationship between cough frequency and cough reflex sensitivity (21). Additionally, in PPC, the frequency of cough is equal to severity of cough. Considering these two facts, from now on, "frequency of cough" represents "severity of cough" in this article. Thus, all the

participants were evaluated for frequency of their cough before and after the treatment. Their cough frequency, according to them, was degreed as: Zero (0), low (1<sup>+</sup>), moderate (2<sup>+</sup>), and severe (3<sup>+</sup>), (22).

Patients with PPC for more than three weeks of duration were included in this study. But, the ones with systemic disease and/or abnormal routine laboratory tests were excluded. As a matter of fact, a high majority of the patients have more than a single cause at the same time for chronic cough (7, 23- 26). Therefore, in this study we excluded every patient with other causes of cough, or we first treated that other condition. Participants' ages ranged from 21 to 65 years and the peak age was the third decade (29.7% of patients). Their weight ranged from 50 to 90 kgs. Moreover, most of them were highly educated (Table 1).

For this study, we prepared three types of medical jam-like pastes, (A, B, and C products):

1- Each 600 grams of the "A" product (first regimen), consisted 70 grams of original instant coffee (caffeinated coffee), given to every member of the first group (n=16).

2- Each 600 grams of the "B" product (second regimen), consisted 500 grams of honey, given to every member of the second group (n=14).

3- Each 600 grams of the "C" product (third regimen), consisted 70 grams of original instant coffee, and 500 grams of honey, given to every member of the third group (n=54).

It's necessary to mention that all the three products were similar in packaging, color, shape, viscosity and the taste (by adding enough edible brown color, coffee essence, and liquid glucose). Materials of each product were gently mixed and homogenized. The natural honey which was used in this study was obtained from the mountain region in the west of Iran. The mentioned samples were produced by our pharmacist with the proportion of 1, 1, 4.

They were encoded confidentially and distributed randomly between patients. This difference of proportion was intended to show the importance of the third regimen. It should be considered that the first and second groups can play the role of control groups for the third one. These participants were told to dissolve 25 grams of the prescribed jam-like paste in about 200 <sup>CC</sup> of warm water (under 60<sup>oC</sup>), then drink this solution. They were asked to repeat it every 8 hours for one week.

**Table 1:** Characteristics of participants in the three treatment groups: Count and "Percentage within Treatment group"

Factors	Treatment group 1	Treatment group 2	Treatment group 3
	Coffee (n=14)	Honey (n=12)	honey with coffee" (n=48)
<b>Age:</b>			
21-30 y	4(28.5)	5(41.3)	13(27)
31-40 y	3(21.4)	4(33.3)	11(22.8)
41-50 y	2(14.2)	2(16.6)	13(27)
51-60 y	4(28.5)	1(8.3)	10(20.8)
61-56 y	1(7.14)	0	1(2)
<b>Sex:</b>			
Male:	9 (64.2)	6 (50)	27 (56.1)
Female	5 (35.7)	6 (50)	21 (43.6)
<b>Level of schooling:</b>			
Primary& Diploma	5 (35.7)	5 (41.6)	13 (27)
Technical & higher education	9 (64.2)	7 (58.3)	35 (72.8)
<b>Occupation:</b>			
House worker:	4 (28.5)	3 (25)	12 (25)
Student & employer:	7 (50)	7 (58.3)	26 (54)
Physician:	2 (14.2)	2 (16.6)	10 (20.8)

They were evaluated before and at the end of the first week of their treatment, and the check list for the measurement of

the frequency of their cough was completed. The participants were under observation for the first month even if the cough was cured. Study investigators who checked patients' signs and symptoms were unaware about the prescribed regimen. The process of this research is illustrated in the attached flow diagram.

All the analyses were carried out using SPSS version 15.0 software. Continuous variables were presented as mean and standard deviation. Categorical variables were presented as absolute and relative frequencies. One-way ANOVA, Chi-square test and Wilcoxon Signed Rank test were used for comparison groups. All reported P-values were based on two-sided hypotheses.

### Results

In this clinical trial the mean and (standard deviation) of age, weight and duration of their illness were according to appearance: 39.9 (12.6) (years), 74.9 (10.9) (kgs), and 3.1 (3.4) (months). The distribution of mentioned base line data are shown in the table number 1. Also, the frequency of cough before and after the treatment was degreed as: 2.97 (0.16) and 0.82 (0.81). In all three groups, the difference between variables including age, sex, duration of disease and frequency of cough before the treatment, according to statistics were not significant ( $P>0.05$ ), (Table 2).

Chi-square test showed the distribution of variables including sex, education and occupation were the same in these three groups ( $P>0.05$ ). The cough frequency was similar in all three groups before the treatment ( $P>0.05$ ).

According to Wilcoxon Signed Rank test, the frequency of cough before and after each treatment proved to be significant ( $P<0.05$ ). Therefore, all the three regimens were effective in treating the condition. Analysis of variances showed that the difference between the means of "frequency of cough before and after the

treatment" with three regimens were significant ( $P<0.001$ ).

In addition, Post Hoc Tests (Tukey) showed that the change of "cough frequency before and after the treatment" in the first and second groups were not significant whilst the mean of "change of cough before and after the treatment" in the third group was lower and the mean differences was statistically significant ( $P<0.001$ ).

**Table 2:** Mean (STD) differences between treatments and some explanatory variables

Variables	Treatment group 1	Treatment group 2	Treatment group 3	P-value
	<b>coffee (n=14)</b>	<b>honey (n=12)</b>	<b>honey with coffee (n=48)</b>	
<b>Age: years (std)</b>	41.9 (14.8)	36.8 (10.2)	40.1 (12.6)	>0.05 (NS)*
<b>Weight: Kgs (std)</b>	74.6 (11.3)	78.4 (8.8)	74.1 (11.4)	>0.05 (NS) *
<b>Duration of illness: months (std)</b>	3.3 (1.4)	2.3 (1.5)	3.3 (4.1)	>0.05 (NS) *
<b>Frequency of cough:</b>				
<b>a- before the treatment: degree (std)</b>	3.0 (0.0)	3.0 (0.0)	3.0 (0.2)	>0.05 (NS)*
<b>b- after the treatment: degree (std)</b>	1.8 (0.4)	1.4(0.5)	0.4(0.6)	<0.001 (S)**
* NS= Not Significant ** S = Significant				

### Discussion

PPC is usually intractable and has no effective response to routine treatments. Considering the great number of people around the world suffering from PPC, every reasonable and safe remedy is worth to be thoroughly investigated. Our hypothesis was that the honey and/or coffee have therapeutic effect on PPC.

Generally, it seems that the effect of honey in treatment of PPC is about that sweet substances naturally cause reflex salivation and may also cause the secretion of airway mucus which can improve mucociliary clearance in the airway, and lead to a demulcent effect in the pharynx, thereby they reduce cough (24). Moreover, honey by its properties such as hyper osmolarity, as an anti-inflammatory substance, can expedite repairing and healing of the pharyngeal mucosal irritation (14).

This study demonstrated that the "combination of honey with coffee" (the "C" product) was the most effective treatment modality for PPC. It concedes that the efficacy can be due to the synergistic effect of these two substances. Despite the fact that the exact mechanism of action of the combination of honey and coffee is almost unveiled and is not yet fully explained; this combination can bring about notable improvements in mucosal tissue healing by repairing the "nerve ending damage" due to "mucosal irritability" and "mucosal desquamation". These can provide possible explanation for the role of "combined coffee and honey",

in the successful treatment of PPC. However applying our innovate therapy, we could treat PPC and also eliminate "unpleasant consequences" of the illness for the patients and the physicians (1, 27). The advantages of this new treatment modality are: (a) It is more effective especially in a short time. (b) It has natural edible substances which makes it safe and agreeable. (c) It is cost effective and easily available.

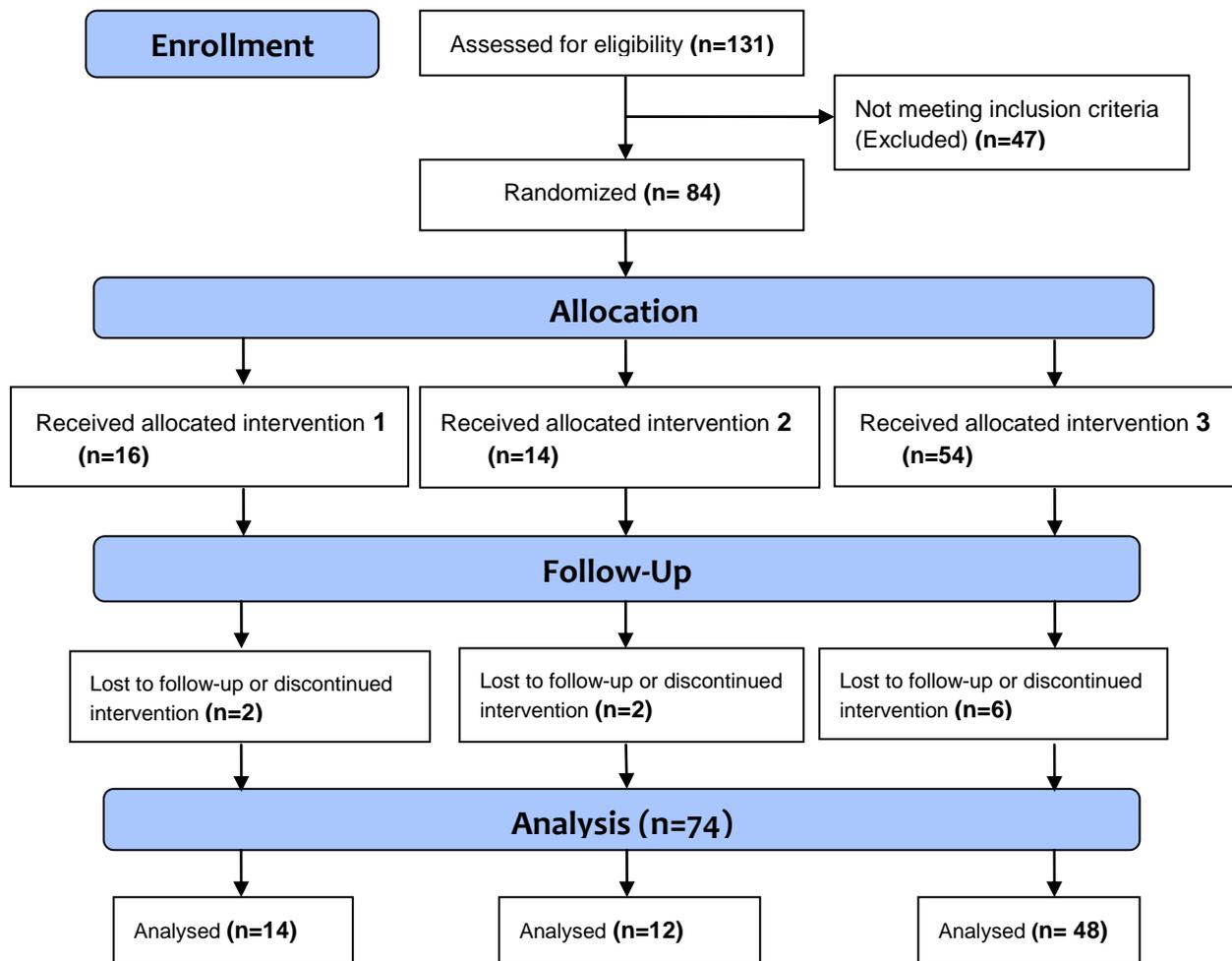
### ***Conclusion***

PPC can be successfully treated by "combination of honey and coffee" at a short time. We therefore recommend the use of this effective treatment modality for PPC patients. It is suggested that further studies should be carried out in different clinical settings.

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## Flow Diagram



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