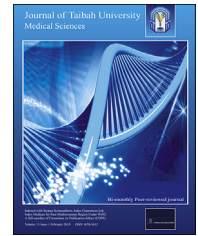Taibah University

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Original Article

The effect of Tualang honey on the quality of life of patients with chronic obstructive pulmonary disease: A randomized controlled trial

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الملخص

أهداف البحث: يعد مرض الانسداد الرئوي المزمن مرضا متعذر العكس، واستخدام العسل كمكمل في العلاج لا يزال قيد البحث. تهدف هذه الدراسة إلى تقييم فعالية نظام ٦-أشهر من مكملات العسل في تحسين جودة الحياة لدى مرضى الانسداد الرئوي المزمن.

طرق البحث: أجريت دراسة عشوائية محكمة على ٣٤ مريضا يعانون من مرض الانسداد الرئوي المزمن. تم تقسيم المشاركين إلى مجموعتين؛ العسل (عدد= ٢٢) ورعاية نموذجية (عدد=١٢). تم استخدام استبانة سانت جورج التنفسية لتقييم جودة الحياة. وحللت مجموع نقاط جودة الحياة باستخدام مقياس انوفا المتكرر.

النتائج: لم يكن هناك فرق ذو دلالة إحصائية بين مجموعة العسل والرعاية النموذجية للمتغيرات الاجتماعية والديموغرافية وجودة الحياة. وأظهر التحليل في الوقت المناسب خطا أساسيا ذا دلالة إحصائية واختلافات ما بعد ٢و٤ و ٦-أشهر لمجموع نقاط جودة الحياة في مجموعة العسل. من ناحية أخرى، تم الكشف عن فرق هامشي فقط بين الخط الأساسي وما بعد شهرين في مجموعة الرعاية النموذجية. المقارنة بين مجموع النقاط لجودة الحياة بين المجموعتين على أساس الوقت (بين وفي غضون) فضل مجموعة العسل. أظهرت مجموعة العسل معدل أقل بكثير لمجموع نقاط جودة الحياة بالمقارنة بمجموعة الرعاية النموذجية في ٤ أشهر و ٦ أشهر.

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الاستنتاجات: أظهرت مكملات العسل عند مرضى الانسداد الرئوي المزمن تغيرات متوسطة وطويلة الأجل أفضل في إجمالي جودة الحياة.

الكلمات المفتاحية: مرض الانسداد الرئوي المزمن؛ العسل؛ عسل توالانغ؛ جودة الحياة؛ دراسة عشوائية محكمة

Abstract

Objectives: This study aimed to assess the efficacy of a 6-months regime of honey supplementation in improving the quality of life (QoL) of patients with chronic obstructive pulmonary disease (COPD).

Methods: A single blind randomized controlled trial on 34 patients with COPD was conducted. The participants were divided into two groups, including honey (n = 22) and standard care (n = 12). St. George's Respiratory Questionnaire (SGRQ) was used to assess the QoL. The QoL total score was analysed using repeated measure ANOVA.

Result: There were no significant differences between the honey and standard care groups for socio-demographic and QoL variables. The within-time analysis showed statistically significant differences between baseline and post 2, 4 and 6-months in the total QoL score in the honey group. Otherwise, only marginally significant difference was detected between baseline and post 2-months in the standard care group. A comparison of total QoL score between the two groups, based on time (between

and within), favoured the honey group. The honey group demonstrated a significantly lower mean total QoL score compared with the standard group at 4-months (28.89; 95% CI: 21.19, 36.59 vs 42.38; 95% CI: 31.95, 52.81) and 6 months (22.91; 95% CI: 14.94, 30.87 vs 41.95; 95% CI: 31.17, 52.73).

Conclusion: Supplementation of honey in patients with COPD results in better intermediate and long-term changes in the overall QoL.

Keywords: Chronic obstructive pulmonary disease; Honey; Quality of life; Randomized controlled trial; Tualang honey

Introduction

Chronic obstructive pulmonary disease (COPD) is a common public health illness with a high prevalence, morbidity and mortality.[1] It is the third leading cause of death in the world,[2] and the death rate from COPD is increasing rapidly, especially among the elderly.[3] COPD is characterized by a progressive, partially reversible airflow obstruction and lung hyperinflation with significant extra pulmonary manifestation that leads to a comorbid condition.[4] The airway limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases. Patients with COPD usually present with a chronic cough and copious sputum production for many years.

COPD has no cure and is an irreversible disease.[5] The patients not only suffer physically and mentally, they also have a poor quality of life. A study by E.A. Regan et al. noted that the quality of life (QoL) in her COPD patients worsened in a five year time period and was associated with increased dyspnea and a reduced walking distance.[6] An impaired quality of life was significantly linked to increased medical costs for COPD patients.[7] Thus, a positive perception of health and preserving the quality of life should be the goal in caring for these patients apart from the usual clinical treatment.[8]

There are minimal published clinical studies evaluating at the effects of Tualang honey on COPD patients. Based on animal studies, honey has antimicrobial properties and significantly reduces macrophage recruitment in the airway following inflammatory response due to cigarette smoke inhalation.[9] It is hypothesized that honey might have a beneficial effect on COPD patients by improving airway relief, symptoms, nutritional status and, subsequently, quality of life.

Therefore, this study aimed to assess the efficacy of Tualang honey in COPD patients in terms of nutritional status, pulmonary function and quality of life. In addition, a further assessment on the safety of honey provides additional scientific information on the usefulness of honey, specifically in COPD patients.

Materials and Methods

Study population

Outpatients from two chest clinics, namely, the Hospital Universiti Sains Malaysia and the Hospital Raja Perempuan Zainab II, Kelantan, Malaysia, with follow ups between December 2010 and December 2011 were enrolled. The patients were required to fulfil the COPD diagnostic criteria as defined by the America Thoracic Society, such as history of exposure to risk factors with present of symptoms, such as chronic cough, sputum production or dyspnoea.

Spirometry was done with post-bronchodilator forced expiratory volume in one second, with a forced vital capacity (FEV1/FVC) ratio of <0.7. The diagnosis should be confirmed by spirometry. A post-bronchodilator FEV1/FVC ratio of less than 0.7 confirms the presence of an airflow limitation that is not fully reversible and is currently widely accepted as a diagnostic of COPD.[4] The other inclusion criteria included age within 40–80 years, a smoking history of at least 20 pack-years and a history of exposure to risk factors for the disease with symptoms of chronic cough, sputum production or dyspnoea. Patients with a history of asthma or atopy, left ventricular failure, and clinical evidence of pneumonia and who received at least one month oral steroids were excluded from the study.

The sample for recruitment was 30 for intervention and 30 for the controls with an 80% power and an alpha error of 0.05 and after considering a 10% loss to follow up. The calculation was based on the variable QoL score reported by Abolhassan et al., with a standard deviation of 16.14 and a clinically meaningful difference of 10 score.[5] The ratio of the intervention to control was set at 1:1.

Operational definition

The intervention group consisted of COPD outpatients who consumed Tualang honey as a supplementary therapy apart from their usual COPD treatment. Meanwhile, the control group was comprised of COPD outpatients who received the usual COPD standard care treatment. The standard care for the present COPD patients included medications, such as seretide/simbicort, salbutamol and tiotropium bromide (Spiriva) and advise for a healthy lifestyle.

The efficacy of honey refers to the therapeutic effect of Tualang honey on the COAD patients' QoL, pulmonary function and nutritional status. The safety of honey refers to deteriorating clinical investigations in the COPD patients who received Tualang honey. The clinical safety parameters included blood pressure, renal function, liver function and blood glucose.

Method of data collection

The COPD patients who came to the chest clinic for a follow up and met the inclusion criteria and not the exclusion criteria were sequentially assigned to either the intervention or control group based on a prepared randomized coding in opaque, sealed envelopes. The simple randomization was

performed using a computer generated randomization, with an open-labelled treatment. The investigator was blinded to the treatment allocation. All the participants who provided informed consent and completed the St. George's Respiratory Questionnaire (SGRQ) were measured for body mass index (BMI), assessed for pulmonary function and blood pressure, and their blood was withdrawn as baseline data. The blood was sent to the laboratory for blood glucose, renal and liver function analyses.

The intervention group was given Tualang honey in sachet form and was advised to consume the honey in the morning before breakfast daily. They were reminded to bring all honey sachets (with/without any remaining honey) with them at each trial visit. The sachets were later counted by the investigator for compliance monitoring. A same number of controls was recruited, and they continued with their usual treatment alone, and no placebo was given.

The participants were put up on two monthly appointments and were assessed during their 2, 4 and 6 months follow up visit. The re-assessment includes the QoL score using SGRQ, pulmonary function, BMI, blood pressure, blood glucose, renal function and liver function were tested (Figure 1). Patients who were unable to tolerate honey or those who withdrew or defaulted in more than one follow up were removed from the study.

Research tool

Patients in the honey group received Tualang honey at 20 mg/sacket/day for 6 months in addition to the standard treatment. The supply of honey was obtained from the Federal Agricultural and Marketing Authority (FAMA), which is a government body under the Ministry of Agriculture and Agro-Based Industry (MOA), Malaysia.

The SGRQ is a standardized questionnaire for measuring the quality of life in patients with airway diseases.[10] It consists of 16 questionnaires with 76 items and is divided into two sections. Section 1 (Question 1–8) is about the symptoms over the last one year, such as cough, sputum, shortness of breath, wheezing, exacerbation of COPD and duration and severity of the COPD attack. Section 2 (Questions 9–16) is about the daily physical activity and psychosocial dysfunction. Each item was accorded a weight determined by the degree of distress according to each symptom or state described. The total score and the score for each of the individual items of the SGRQ was calculated using the formulae given by the producer. The overall score ranged from 0 (no effect on quality of life) to a maximum score of 100 (maximum perceived distress). Therefore, a better QoL is reflected by a lower SGRQ score, and a higher SGRQ score indicates a poor QoL. The questionnaire is a self-
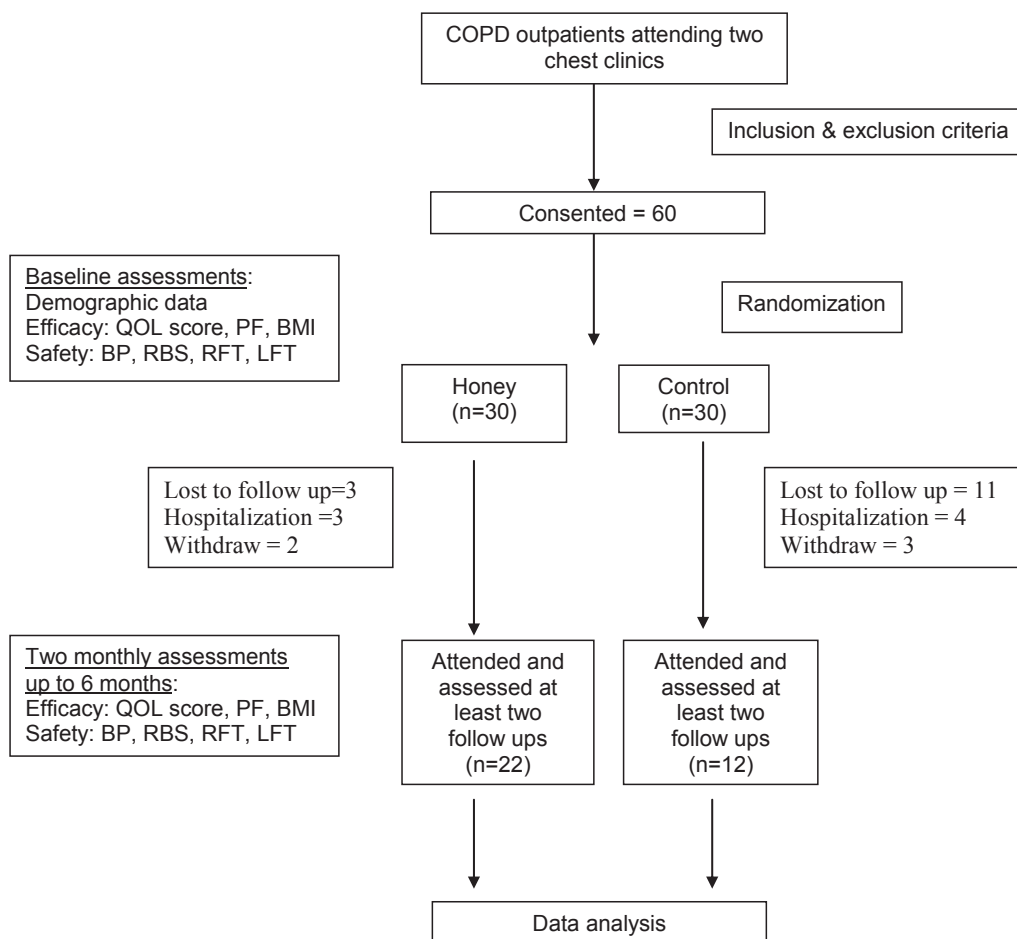

Figure 1: Flow chart of study.

administered questionnaire and requires approximately 15—20 min to complete. The St. George's Respiratory Questionnaire is validated in many different languages.[11] In this study, The St. George's Respiratory Questionnaire (SGRQ), Malay version, was applied to measure the QoL of the participants. Written permission was obtained in order to use this questionnaire in this study.

The pulmonary function or the airway limitation assessment, which consists of the forced expiratory volume in one second (FEV1), the force vital capacity (FVC), the FEV1/FVC and the forced mid expiratory flow rate (FEF25—75%), was measured by spirometry. First, patients were instructed by trained nurses to relax either in a standing or sitting position. A nose clip was put on the patient's nose. Then, the patient was ordered to put the mouthpiece inside their mouth and close her or his lips tightly around the mouthpiece. After that, the patient was asked to take a deep breath and blow through the mouthpiece into the spirometer. The patients were asked to blow the air as hard and fast as they could and then to continue to blow for 6 s. If the patient coughed, stopped blowing or was not strong enough, then the procedure was repeated.

The SECA weighing scale and ruler were used to measure the participants' body weight and height. The patients' weight was measured in light clothing without shoes. The blood pressure was measured manually using a mercury sphygmomanometer and was taken twice, and the average blood pressure was calculated. Approximately 3 ml of non-fasting venous blood was withdrawn during every visit. The investigations included blood glucose and, renal and liver function tests.

Statistical analysis

The data entry statistical analysis was performed using IBM SPSS 20.0. Missing data in at least one follow up were replaced by the most recent observation (the last observation was carried forward). The demographic and baseline clinical data were analysed for the descriptive statistics and the mean comparison between the intervention and control group. The group comparison at baseline was performed using a Mann—Whitney test and Fisher's exact test. A repeated measure ANOVA was performed to determine the between, within and between within group differences of the health outcomes between the honey and control groups at baseline, 2, 4 and 6-months. A Friedman test was applied for the within group analysis only if the assumption for the repeated measure ANOVA was violated.

Ethics

The trial was approved by the Human Research Ethic Committee, Universiti Sains Malaysia, and the Medical Research Ethics Committee, Ministry of Health Malaysia, in 2010. This clinical trial was conducted according to the Declaration of Helsinki.

Results

Sixty participants met the criteria and were consented and randomized. Eight participants from the honey group withdrew from the intervention arm due to intolerable hot flushes that they claimed due to the honey, a long hospitalization after enrolment, and not showing up during the follow-up. In addition, 18 participants withdrew from the control group due to a long hospitalization after enrolment, not showing up during the follow-up with the main reason being that they went to their children's house during a school holiday or on holidays. A total of 22 participants in the honey group and 12 participants in the control group attended at least two subsequent follow ups were included in the analysis.

The participants were all male, with a median age of 68 years; the majority had quit smoking (82.4%), were unemployed (76.4%) and low income. There were no significant differences in the demographics, clinical profiles and QoL scores between the honey and standard care group at baseline (Table 1).

A comparison of the total QoL, symptoms, activity and impacts domains score between the two groups based on time (between and within) favoured the honey group. The honey group demonstrated a significantly lower mean total QoL score compared with the standard group at 4 months (28.89; 95%CI: 21.19, 36.59 vs 42.38; 95%CI: 31.95, 52.81) and 6 months (22.91; 95%CI: 14.94, 30.87 vs 41.95; 95%CI: 31.17, 52.73) (Table 2).

Similarly, a significantly lower mean activity score was observed compared with the standard group at 4 months (43.28; 95%CI: 32.85, 53.70 vs 62.52; 95%CI: 48.41, 76.64) and 6 months (34.01; 95%CI: 24.25, 43.77 vs 62.30; 95%CI: 49.09, 75.51) (Table 2). The impacts score was reduced in the honey group at 4 months (21.71 (95%CI: 14.24, 29.18) vs 34.88 (95%CI: 24.76, 44.99)) and 6 months (16.87 (95%CI: 8.96, 24.79) vs 32.72 (95%CI: 22.00, 43.44)) (Table 2).

There were statistically significant differences in the FEV1 and FVC for both groups by time. Both groups demonstrated a slight increase in the FEV1 ($p = 0.013$, honey and $p = 0.031$, standard care) and a reduced FVC ($p = 0.009$, honey and $p < 0.001$, standard care) from 2 to 6 months (Table 3). Otherwise, no statistically significant BMI differences by time was found. The honey group demonstrated a steady increase in BMI from the two to six month follow up compared to the control.

The within time analysis revealed a statistically significant reduction in blood pressure by time in the honey group only. The systolic blood pressure reduced from 125.0 mmHg at baseline to 120.0 mmHg and 113.5 mmHg at 4 and 6 months, respectively ($p = 0.001$). The diastolic pressure also reduced from 80 mmHg at baseline to 70 mmHg at 6 months ($p = 0.001$). However, both groups demonstrated a statistically significant slight reduction in sodium levels by time. The sodium level reduced from 140.0 mmol/L at baseline to 137.0 at 6 months in the honey group (p < 0.001) and control (p = 0.023) (Table 4). Otherwise, no differences by time were found for random blood sugar and other parameters of renal and liver function.

Discussion

This trial was carried out on 34 patients with COPD from two hospitals, and a majority of them were men, Malay and elderly. COPD is basically a male disease due to the high

Table 1: Demographics and baseline clinical characteristics of the participants.

Baseline characteristics	Median (IQR)		P value
	Honey (n = 22)	Control (n = 12)	
Demographic			
Age (year)	67 (11.0)	69 (15.0)	0.312[b]
Ethnic			
Malay	21 (65.6)[a]	11 (34.4)[a]	1.000[c]
Non-Malay	1 (50.0)[a]	1 (50.0)[a]	
Occupation			
Employed	6 (75.0)[a]	2 (25.0)[a]	0.681[c]
Unemployed	16 (61.5)[a]	10 (38.5)[a]	
Income (RM)	475 (685)	500 (613)	0.942[b]
Smoking status			
Current smoker	2 (33.3)[a]	4 (66.7)[a]	0.154[c]
Ex-smoker	20 (71.4)[a]	8 (28.6)[a]	
No. of cigarettes (unit)	20 (15)	7.50 (22)	0.228[b]
Quit smoking duration (year)	10 (17)	5.5 (157)	0.365[b]
Physical profile			
BMI (kg/m2)	23.001 (6.2)	22.683 (5.2)	0.914[b]
SBP (mmHg)	125 (22)	130 (20)	0.474[b]
DBP (mmHg)	80 (10)	80 (10)	0.230[b]
Lung function			
FEV1(I)	1.23 (1.04)	1.25 (1.05)	0.759[b]
FVC(I)	2.26 (1.08)	2.17 (1.02)	0.540[b]
FEV1/FVC	59.15 (19.1)	57.15 (24.9)	0.397[b]
FEF 25−75%	0.70 (0.69)	0.54 (0.3)	0.601[b]
Renal function			
Sodium (mmol/L)	140.0 (2)	140.0 (2)	0.514[b]
Potassium (mmol/L)	4.5 (0.9)	4.3 (1.4)	0.773[b]
Urea (mmol/L)	5.4 (2.3)	5.6 (1.7)	0.857[b]
Creatinine (mmol/L)	103.0 (18)	106.5 (16)	0.576[b]
Calcium (mmol/L)	2.3 (0.14)	2.3 (0.15)	0.678[b]
Liver function			
AST (IU/L)	21.5 (6)	20.5 (16)	0.942[b]
ALP (IU/L)	97.5 (15)	91.0 (35)	0.576[b]
ALT (IU/L)	22.0 (6)	21.0 (27)	0.690[b]
Blood glucose profile			
RBS (mmol/l)	4.8 (0.9)	5.0 (1.7)	0.564[b]
Quality Of Life			
Symptom (score)	46.0 (36.41)	50.1 (21.60)	0.732[b]
Activity (score)	70.4 (40.17)	70.5 (29.00)	0.900[b]
Impact (score)	33.3 (31.89)	38.9 (11.74)	0.900[b]
Total SGRQ (score)	45.4 (33.96)	49.0 (22.60)	0.845[b]

Abbreviations: BMI body mass index; SBP systolic blood pressure; DBP diastolic blood pressure; FEV1 Forced expiratory volume in one second, FVC Forced vital capacity; FEF 25−75% = forced midexpiratory flow rate; AST aspartate aminotransferase; ALP alkaline phosphatase; ALT alanine transaminase; RBS random blood sugar

[a] n (%).
[b] Mann−Whitney test.
[c] Fishers-Exact.

prevalence of smoking in this gender, and males are more exposed to more occupational exposures compared to females.[12,13] The present trial showed that the used of 'Tualang' honey significantly improved the patients' quality of life. We found that honey helped patients to indulge better in their daily living activities with positive psychological and social impacts. Generally, 1 tablespoon

of honey provides 64 calories of energy to the muscle and body. Honey has a complex composition, including 17.1% water, 82.4% carbohydrates and 0.5% proteins, amino acids, vitamins and minerals.[14] Tualang honey was recently reported by Sarfarz and Norhayati to have higher levels of antioxidant activity compared to other local Malaysian honey varieties (such as Gelam, pineapple honey) and other commercially available honey. The antioxidant elements include phenolic acids, flavonoid, amino acids and proteins compounds.[15] Therefore, the reduction of the oxidative stress status among COPD patients after honey supplementation could be partly attributed to the antioxidant properties of honey.

Reduced COPD symptoms might be another reason for the significant increase in quality of life among the participants in the honey group. The COPD patients are at higher risk for having recurrent acute and chronic, upper and lower respiratory tract infections, which are very clearly linked with increasing the exacerbations of COPD and hospitalization.[16] The exact molecular and pathologic mechanism of how Tualang honey improves the QoL in COPD remains largely unexplored. However, honey has a broad-spectrum antimicrobial action against various gram-positive and gram-negative bacteria.[17] It is well-known that honey displays substantial effects with regards to anti-viral, anti-microbial, antioxidant and anti-inflammatory properties, which might help in repairing the lungs cells.[18−20] Alleviation of the severity of inflammation prevents of the progression of COPD, which in turn improves their symptoms and disability.

Honey was also demonstrated to significantly suppress the expression of inflammatory mediators, such as pro-inflammatory cytokines, e.g., TNF-α, anti-inflammatory cytokines, e.g., IL-8, as well as to reduce inflammatory cells. These inflammatory mediators and cells are elevated in COPD patients as a result of cigarette smoke or genetic abnormalities.[21] Thus, taking honey might reduce hypersecretion, infection, airway mucous cell metaplasia, and emphysematous lesions.

In this study, a regular consumption of honey for a period of six months might help to reduce the acute and chronic part of respiratory infections, which subsequently might reduce the symptoms of coughing and difficulty in breathing. At the same time, the antioxidant property might protect the lung cells from the damaging effect of free radicals (environmental irritants and smoking). The potent anti-inflammatory effect that honey has will further counter both acute and chronic inflammatory processes that occur in COPD patients to sooth the condition and make it less susceptible for upcoming infections. Additionally, a gradual decline in the symptom score was clearly observed in the honey group, even though the result did not reach a significant level. Additionally, the use of honey substantially achieves a reduced exacerbation, an increased mobility and a better performance activity in daily living, which, in the end, contributed to significant increase in the quality of life among the participants in the honey group.

The effectiveness of honey in treating cough among healthy people and children has been reported in many studies, which might further support our findings since no data are available among COPD patients.[22] Furthermore, a recent study by Zeynab Zare et al. on the effect of honey

Table 2: Comparison of the total QoL, symptoms, activity and impacts score between the Honey and standard treatments based on time.

SGRQ and domain	Time	Adjusted mean score (95% CI)		F statistics (df)	p- value[a]
		Honey (n = 22)	Standard (n = 12)		
Total QoL	Baseline	48.19 (40.98, 55.40)	47.87 (38.11, 57.64)	5.942 (3)	0.001
	Month 2	32.71 (26.28, 39.15)	40.72 (32.01, 49.44)		
	Month 4	28.89 (21.19, 36.59)	42.38 (31.95, 52.81)		
	Month 6	22.91 (14.94, 30.87)	41.95 (31.17, 52.73)		
Symptom domain	Baseline	46.91 (37.01, 56.81)	49.16 (35.75, 62.56)	0.509 (3)	0.677
	Month 2	27.77 (16.85, 38.69)	32.57 (17.78, 47.36)		
	Month 4	25.59 (16.58, 34.60)	29.61 (17.41, 41.81)		
	Month 6	21.94 (12.48, 31.40)	34.30 (21.49, 47.11)		
Activity domain	Baseline	67.87 (57.50, 78.24)	66.97 (52.93, 81.01)	5.968 (3)	0.001
	Month 2	48.76 (39.28, 58.24)	58.40 (45.56, 71.23)		
	Month 4	43.28 (32.85, 53.70)	62.52 (48.41, 76.64)		
	Month 6	34.01 (24.25, 43.77)	62.30 (49.09, 75.51)		
Impact domain	Baseline	37.36 (30.14, 44.58)	36.57 (26.79, 46.34)	5.690 (3)	0.001
	Month 2	25.09 (18.91, 31.28)	33.19 (24.81, 41.56)		
	Month 4	21.71 (14.24, 29.18)	34.88 (24.76, 44.99)		
	Month 6	16.87 (8.96, 24.79)	32.72 (22.00, 43.44)		

Assumptions of normality, homogeneity of variances and compound symmetry were checked and fulfilled.
[a] Repeated Measure ANOVA

on relieving cough in elderly patients diagnosed with chronic obstructive pulmonary disease noted that the severity of the coughs significantly declined by 63.2% in 89.5% of the honey cases with routine treatment compared with the group receiving only routine treatment.[23] Furthermore, a study by Eccles also suggests the possibility that the sweetness of the substance stimulates salivation and mucus production, which leads to a demulcent effect and reduces the cough. He also suggests that the interaction between opioid-responsive sensory fibres and the gustatory nerve helps produce an antitussive effect via the central nervous system.[24] Thus, probably, all of these help to improve the quality of life for patients with COPD rather than if they used medications, such as cough syrup, which has multiple side effects in the elderly.

The improvement in the lung function test in the honey group is important to discuss. It has been reported that the changes in inflammatory cells during the exacerbation of COPD are the same as those observed during the exacerbation of asthma.[25] A study in rabbits using aerosolized honey showed that the asthma in rabbits was effectively treated and managed, and it proved to be a promising treatment for asthma in humans. Histopathological data showed that aerosolized honey leads to changes of the epithelium, mucosa, and submucosal regions, and it reduces the number of airway inflammatory cells present in the bronchoalveolar lavage fluid and inhibits goblet cell hyperplasia.[26] This shows that honey improves cell changes in asthma and probably also in COPD.

Despite the comprehensive nutritional elements that honey contains, this six-month study was still unable to demonstrate any statistically significant BMI differences by time in the honey group; however, it revealed a steady increase in BMI from the two to six months follow up compared to the control group. The possible reasons for this are either that the dose given was still not adequate or that the length of time was too short for honey to work, especially

in patients with progressive and chronic illnesses such as COPD. Honey, in a normal and healthy man, feeds the muscles and helps with performance and workout efficiency, which helps gain muscle mass.[14]

It has also been postulated that regular honey intake provides a positive effect on blood pressure and heart rate. The significant reduction in blood pressure that we observed in this study is most likely due to the vasodilatation effect that honey possesses.[18] It relaxes the arterial smooth muscle cells and decreases the vascular resistance, which subsequently leads to an upsurge in blood flow. Therefore, it leads to a drop in the arterial blood pressure and, also, heart rate.[27] This finding is compatible with those of Olusola et al. and Erejuwa et al., who reported immediate changes in blood pressure after the administration of 20 ml of honey, which could be seen as early as 15 min in men and had a slight delay in women.[28,29] In the Erejuwa et al. study, honey was administered to streptozotocin-induced diabetic rats with spontaneously hypertension for 3 weeks and resulted in the reduction of systolic blood pressure.[29] Another possibility is that honey also function as an anti-cholesterolaemia, which might enhance the reduction of blood pressure in our participants. Honey has also been reported to have an anti-diabetogenic effect.[30] It triggers insulin sensitivity and insulin secretion and subsequently absorption, which results in vasodilatation.[27] These changes are observed by a significant reduction in blood pressure. However, the reduction in blood glucose levels in the honey group was not significant.

For most people with chronic illnesses, they will also turn to complementary and alternative medicine (CAM) to get at least some relief of their suffering. One study done on patients with moderate to severe COPD noted that 41% of the patients used CAM. Mostly, they chose multivitamins and minerals, as well as garlic as their most commonly used herbal preparations. The reasons for this were that CAM promotes general well-being, counteracts drug side effects,

Table 3: Pulmonary function and body mass index differences from baseline to 2, 4 and 6 months.

Variable	Honey n = 22						Control n = 12					
	Baseline	2 months	4 months	6 months	X^2 (df)	*p*-value[a]	Baseline	2 months	4 months	6 months	X^2 (df)	*p*-value[a]
Pulmonary function												
FEV1 (I)	1.23 (1.04)	1.21 (0.69)	1.24 (0.70)	1.24 (0.61)	10.78 (3)	0.013	1.25 (1.05)	1.00 (0.97)	0.89 (0.99)	0.96 (0.00)	11.67 (3)	0.009
FVC (I)	2.26 (1.08)	2.06 (0.99)	2.10 (1.07)	2.23 (1.03)	8.90 (3)	0.031	2.17 (1.02)	2.11 (1.30)	1.81 (0.86)	2.27 (0.00)	18.88 (3)	<0.001
FEV1/FVC (I)	59.15 (19.1)	59.00 (14.5)	58.80 (15.3)	59.00 (17.3)	4.65 (3)	0.199	57.15 (24.9)	53.20 (22.0)	54.50 (22.2)	51.00 (0.0)	3.02 (3)	0.362
FEF 25−75% (I)	0.70 (0.69)	0.60 (0.34)	0.59 (0.36)	0.58 (0.38)	4.47 (3)	0.215	0.54 (0.30)	0.52 (0.52)	0.43 (0.60)	0.45 (0.00)	4.91 (3)	0.179
Body mass index (BMI)												
BMI (kg/m^2)	23.00 (6.2)	22.45 (6.3)	23.36 (5.7)	24.43 (7.1)	2.32 (3)	0.509	22.68 (5.2)	22.08 (5.0)	21.55 (5.0)	22.28 (0.0)	1.40 (3)	0.705

p < 0.05. Values are the median and interquartile range.

Abbreviations: FEV1 Forced expiratory volume in one second; FVC *Forced vital capacity*; FEF 25−75% Forced Midexpiratory Flow Rate

[a] Within − group differences using a Friedman test

Table 4: Blood pressure, renal function, liver function and blood glucose differences from baseline to 2, 4 and 6 months.

Variable	Honey n = 22						Control n = 12					
	Baseline	2 months	4 months	6 months	X^2 (df)	*p*-value[a]	Baseline	2 months	4 months	6 months	X^2 (df)	*p*-value[a]
Blood pressure												
SBP(mmHg)	125.00 (22)	120.00 (13)	120.00 (21)	113.50 (23)	15.49 (3)	0.001	130.00 (20)	130.00 (35)	125.00 (25)	130.00 (0)	3.45 (3)	0.327
DBP(mmHg)	80.00 (10)	80.00 (16)	80.00 (10)	70.00 (10)	16.13 (3)	0.001	80.00 (10)	80.00 (20)	80.00 (10)	80.00 (0)	1.70 (3)	0.637
Renal function (mmol/L)												
Sodium	140.00 (2)	139.00 (2)	−	137.00 (4)	15.74 (2)	<0.001	140.00 (2)	140.00 (2)	−	137.00 (4)	7.51 (2)	0.023
Potassium	4.45 (0.9)	4.35 (0.7)	−	4.50 (0.7)	1.87 (2)	0.392	4.25 (1.4)	4.20 (1.0)	−	4.25 (0.8)	2.13 (2)	0.344
Urea	5.35 (2.3)	5.00 (1.3)	−	5.40 (1.3)	3.68 (2)	0.159	5.55 (1.7)	5.40 (2.0)	−	5.40 (2.5)	3.83 (2)	0.826
Creatinine	103.00 (18)	105.00 (17)	−	108.00 (17)	0.53 (2)	0.767	106.50 (16)	110.50 (18)	−	105.00 (16)	1.11 (2)	0.574
Calcium	2.30 (0.14)	2.78 (0.11)	−	2.25 (0.13)	1.56 (2)	0.457	2.28 (0.15)	2.28 (0.08)	−	2.23 (0.16)	2.09 (2)	0.352
Liver function (IU/L)												
AST	21.50 (6)	23.00 (7)	−	23.00 (4)	3.61 (2)	0.164	20.50 (16)	22.00 (9)	−	21.00 (9)	1.23 (2)	0.541
ALP	97.50 (15)	94.50 (16)	−	96.00 (18)	6.18 (2)	0.046	91.00 (35)	99.00 (34)	−	91.00 (23)	2.91 (2)	0.233
ALT	22.00 (6)	23.50 (10)	−	20.50 (8)	1.92 (2)	0.382	21.00 (27)	23.00 (21)	−	22.00 (23)	0.70 (2)	0.706
Blood glucose (mmol/L)												
RBS	4.80 (0.9)	4.70 (0.9)	−	4.45 (1.1)	5.71 (2)	0.058	4.95 (1.7)	5.10 (2.3)	−	5.40 (2.1)	1.17 (2)	0.558

p < 0.05. Values are the median and interquartile range.

Abbreviations: SBP Systolic blood pressure; DBP diastolic blood pressure; AST aspartate aminotransferase; ALP alkaline phosphatase; ALT alanine transaminase; RBS random blood sugar

[a] Within − group differences using a Friedman test

compensates for dietary deficiencies and ameliorates their disease. With the positive findings highlighted here, we suggest that COPD patients should also be put on a honey supplement, since it is proven to play a role, as an add-on therapy for their disease.[31]

Honey contributes to the significant improvement in the quality of life in patients with COPD by enhancing their activity and improving their chest condition. It is considered safe because it did not clinically and significantly affect pulmonary function, blood sugar and other parameters of renal and liver function. On the other hand, its positive effect in reducing blood pressure in patients with COPD necessitates further investigation. In this study, there was a high dropout rate, especially in the control group, and this probably due to the severe symptoms that occur among the participants, which often requires hospitalization for a long duration. In addition, many of them were unable to come for the study follow-up because they were dependent to other people to bring them to the hospital. Finally, in this study, a majority of the patients were of the Malay population; therefore, it does not represent the other races.

Conclusion

Supplementation of honey in patients with COPD results in better intermediate and long term changes in the overall QoL. Larger scale and comprehensive studies are required to confirm the role of honey in the management of COPD.

Authors' contribution

RM conceived and designed the study, conducted research and corrected the final draft of the article. ND conducted the research, wrote initial and final draft of the article. AAA organized, analyzed and interpreted data. SA conducted research and collected data. MZMJ conducted research and collected data. All authors have critically reviewed and approved the final draft and responsible for the content and similarity index of the manuscript.

Conflict of interest

The authors have no conflict of interest to declare.

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