Complementary Therapies in Medicine 41 (2018) 154–160

Contents lists available at ScienceDirect

Complementary Therapies in Medicine

journal homepage: www.elsevier.com/locate/ctim

Long-term effects of honey on cardiovascular parameters and anthropometric measurements of postmenopausal women

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ARTICLE INFO

Keywords:
Tualang honey
Honey cocktail
Post-menopausal women
Cardiovascular parameters
Anthropometric measurements

ABSTRACT

Objective: To investigate the long-term effects of Tualang Honey versus Honey Cocktail (mixture of honey, bee bread, and royal jelly) on cardiovascular markers and anthropometric measurements of postmenopausal women.
Methods: We conducted a randomised, double blinded, two-armed parallel study comparing 20 g/day of Tualang Honey versus 20 g/day Honey Cocktail among postmenopausal women aged 45–65 years. The cardiovascular parameters and anthropometrics measurements were assessed at baseline, 6 months, and 12 months of the intervention.
Results: 100 subjects were successfully randomised into the groups. There was a significant decrease in the diastolic blood pressure from 77.92 mmHg at baseline to 73.45 mmHg at 12 months (F-statistic = 2.55, p-value = 0.047) in the Tualang Honey group compared to Honey Cocktail. There was also a significant decrease in the fasting blood sugar from 6.11 mmol/L at baseline to 5.71 mmol/L at 12 months (F-statistic = 4.03, p-value = 0.021) in the Tualang Honey group compared to the Honey Cocktail group. The body mass index remained unchanged at 27 kg/m2 (F-statistic = 1.60, p-value = 0.010) throughout 12 months of the intervention in the Honey Cocktail group.
Conclusion: Subjects who received Honey Cocktail showed remarkable effects on body mass index. However, Tualang Honey supplementation showed superior effect in lowering diastolic blood pressure and fasting blood sugar compared to Honey Cocktail. Further studies are required to ascertain the underlying mechanism(s) of Tualang Honey and Honey Cocktail on each observed parameter.

1. Introduction

Cardiovascular disease is one of the long-term complications of menopause with the highest morbidity and mortality rates.[1,2] Hormone replacement therapy (HRT) has been widely prescribed for the management of menopausal symptoms. However, owing to the concerns over its side effects, safety, efficacy, and long-term complications, many postmenopausal women turn to alternative treatment.[3] One of the alternative management modalities for menopausal symptoms and complications is the use of honey and bee hive products.[4,5]

Honey polyphenols have been demonstrated to ameliorate cardiovascular disease through various mechanisms such as improving endothelial function, improving coronary vasodilatation, inhibiting platelet aggregation, reducing inflammatory responses, reducing low density lipoprotein (LDL) oxidation, providing antioxidant protection and decreasing oxidative stress.[6] In our pilot study, systolic blood pressure (SBP) was significantly lower in postmenopausal women who consumed Tualang honey (TH) than in those who received HRT.[7] The antioxidants in honey were found to reduce body weight and ameliorate abnormalities of lipid profiles in rats and diabetic human subjects.[8,9] In another study, a general trend of improvement in the lipid profiles was seen in obese subjects that were supplemented with honey.[10] Furthermore, a clinical study showed that natural honey reduced the fasting blood glucose in obese participants by 4.2%.[11]

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https://doi.org/10.1016/j.ctim.2018.08.015
Received 9 April 2018; Received in revised form 24 July 2018; Accepted 31 August 2018
Available online 05 September 2018

Other bee hive products such as bee bread and royal jelly contain higher amounts of minerals, vitamins, free fatty acids, proteins and essential amino acids than honey.[12] In rats, preexposure to bee honey and royal jelly provided near complete protection in terms of serum biochemical changes, renal histopathology and immunohistochemistry of fibrogenic biomarkers against subchronic cisplatin toxicity.[13] A 3-months treatment protocol using Melbrosia, a combination of flower pollen, perga (fermented flower pollen), and royal jelly, significantly reduced the levels of total cholesterol (TC) and low-density lipoprotein (LDL) and significantly increased the level of high-density lipoprotein (HDL) in postmenopausal women.[14] Furthermore, a combination of royal jelly and bee pollen has been scientifically proven to reduce the prevalence of cardiovascular risk factors in an oophorectomised rat model.[15]

The use of products derived from honey and other bee products for medicinal purposes is known as apitherapy.[16] In apitherapy, it is common to combine two or more bee hive products in treating various kinds of diseases to achieve their maximum desired effects.[17] Hence, we hypothesised that supplementation with a combination of bee hive products known as Honey Cocktail (HC), may provide additional medicinal values than using Tualang honey alone. Therefore, this study aims to evaluate whether HC is more beneficial than TH alone for improving the cardiovascular parameters and anthropometric measurements in postmenopausal women.

2. Materials and methods

2.1. Study design

This was a randomised, double-blind, two-armed parallel comparative study of TH versus HC amongst postmenopausal women. The inclusion criterion was postmenopausal women aged between 45 and 65 years either surgically or naturally in menopause for more than 5 years. The exclusion criterion was being on HRT treatment within 3 months prior to randomisation. Women who had taken any form of natural health products or dietary supplements within 3 months before the study and during the study period; who had significant abnormal laboratory results; who had been diagnosed with clinically relevant cardiovascular problems or renal, gastrointestinal, hepatic, or other major systemic disease that would influence the interpretation of the results; who had major uncontrolled psychiatric disorders; and those who showed abnormal findings on pelvic ultrasound examination were excluded.

2.2. Investigational product

The orally administered TH and HC were taken from a single batch of honey supplied by Federal Agricultural Marketing Authorities (FAMA), Malaysia. After evaporation and sterilisation, the honey was packed in 20-g sachets by a good manufacturing practice-certified laboratory at the School of Pharmaceutical Sciences, Universiti Sains Malaysia. The content in the TH sachet was 100% honey whereas the HC sachet contained 95% honey, 4% bee bread, and 1% royal jelly. The percentages of the constituents of HC were suggested by a certified apitherapist. The subjects were advised to take TH or HC directly from the sachet once every morning for 12 months.

The choice of the dose used in the study was based on an animal study involving ovariectomised rats.[18] The lowest dose shown to increase the testosterone level was 0.2 g kg^{-1} day^{-1} in the animal model. After taking the average human weight as 60 kg, the dose calculated for humans was 12 g (0.2 g/kg × 60 kg [average human weight] = 12 g). Twenty grams was considered the medium dose,[19] and this dose was chosen to study the effect of honey in human beings.

2.3. Sample size calculation

Sample size was calculated for all objectives of this study and the largest generated sample size was taken as sample size for this study. The calculations were performed using power and sample size calculation software for comparing two means between two groups.[20] The largest sample size was generated from total cholesterol. With a standard deviation of 1.0 and detectable difference of 0.7,[21] power of 90%, and the level of significance of 0.05, the calculated minimum required sample size was 44 for each group. However, after considering drop-out rate of 10%, the sample size calculated for each group was 50.

2.4. Study intervention

Women were recruited from the Outpatient Clinics Hospital Universiti Sains Malaysia. They were given an appointment to visit the Clinical Trial Unit (CTU), HUSM for a pre-study visit and screening procedures. Written informed consent was obtained during their screening visit.

Demographic data, medical history, physical examination, and pelvic ultrasound were performed at the screening visit. At this time, cardiovascular parameters and anthropometric measurements were taken as the baseline measurements. Eligible participants were scheduled for a second visit where they were randomised into either the TH or HC group. Randomisation procedure was describe in Section 2.5.

The women were followed up at 3-month intervals for 12 months (Month 3, Month 6, Month 9, and Month 12). At every visit, the subjects were interviewed and examined by the clinicians and researchers involved in the trial. Any adverse event (AE) and concomitant medications were recorded. The subject's compliance was calculated using the number of sachets taken. Cardiovascular parameters and anthropometric measurements were repeated at Month 6 and Month 12.

2.5. Randomisation

The randomisation sequence was generated using Microsoft Excel 2010 with 1:1 allocation using random block sizes of 4 by an independent doctor with no clinical involvement in this study. TH and HC were packed in identical sachets. The sachets were then prepacked in a transparent plastic container (30 sachets per container). The containers were consecutively numbered according to the randomisation sequence. The randomisation sequence was concealed from the researchers in sequentially numbered, opaque, sealed envelopes. The envelopes were given to the eligible subjects during the second visit. Once the envelopes were opened, the subjects received honey in the corresponding prepacked container. All researchers and subjects were kept blinded to the allocation arm.

2.6. Outcome parameters and measurement tools

2.6.1. Cardiovascular parameters

2.6.1.1. Systolic and diastolic blood pressure. Systolic and diastolic blood pressure (SBP and DBP) were measured using an automatic blood pressure monitor TM-2540R.[22] The subjects were asked to be rested and seated properly with their arms supported at the heart level and their feet on the floor prior to the blood pressure measurement. They were also advised to avoid caffeine, exercise, and smoking at least 30 min prior to measurement. After 30 min of rest, the blood pressure recording was taken twice from the right arm of the patients.

2.6.1.2. Serum lipid level. About 3 mL of venous blood was collected in a plain bottle and sent to a certified biochemistry laboratory on the same day for serum total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) measurement.