Journal of Traditional and Complementary Medicine 9 (2019) 249–256

Contents lists available at ScienceDirect

Journal of Traditional and Complementary Medicine

journal homepage: http://www.elsevier.com/locate/jtcme

Tualang honey ameliorates viral load, CD4 counts and improves quality of life in asymptomatic human immunodeficiency virus infected patients

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ARTICLE INFO

Article history:
Received 2 January 2018
Received in revised form
17 May 2018
Accepted 17 May 2018
Available online 28 September 2018

Keywords:
Honey
Human immunodeficiency virus
Viral load
CD4 count
Quality of life

ABSTRACT

This is the first study to report on the effects of honey in asymptomatic HIV positive subjects in ameliorating CD4 count, viral load (VL) and quality of life (QOL). It is a randomized, controlled, open labelled study, comparing the effects of Tualang honey (TH) administration for six months at three different doses: 20 g (THL), 40 g (THI) or 60 g (THH) daily compared with control (no administered treatment, THC). Only asymptomatic HIV positive subjects (n=95) having CD4 count 250-600 cell/ml, not on antiretrovirals were enrolled. Blood, (together with QOL questionnaires administration) were investigated at baseline, three and six months (CD4 cell count) while VL was determined only at baseline and six months. Significant reductions in CD4 counts in THL and THC groups (p= 0.003 for both) were seen with no significant reductions in the CD4 counts in THI and THH groups (p=0.447 and 0.053 respectively). There was improvement in VL in THC and THI (130% and 32% respectively) and reductions in THL and THH (26% and 8% respectively). Within and between group analyses for VL indicated significant differences between THL and THH compared to THC. In addition, significant improvement in QOL of groups which received TH was noted. TH has the potential to improve the QOL (physical and psychological) and CD4 counts. There was a trend of lower VL in asymptomatic HIV subjects following TH administration thus supporting the possible role of TH in boosting the immune system by improving CD4 counts, causing VL reductions in HIV positive subjects.
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1. Introduction

Human Immunodeficiency Virus (HIV) infection is reported to be among the top ten leading cause of death in the productive population in the world.[1] Based on the UNAIDS Fact Sheet 2017, there were 30.8–42.9 million people living with HIV (PLHIV) in 2016, affecting women (52%) and children (6%) with approximately 1.8 million people becoming newly infected with HIV yearly. In Malaysia, the situation is also similar with an estimated 108,519 PLHIV cases reported and 3330 new HIV cases detected by the end of 2015. Generally, PLHIV is predominant among Malaysian males (89%) but over time, the pattern is progressively shifted towards increasing infection rates in females with declining male to female ratio [from 9.6 (in 2000) to 5.5 (in 2015)].[2]

HIV infection is a chronic disease whose progression to acquired immune deficiency syndrome (AIDS) varies depending on the patient's state of immunity.[3] The introduction of highly active antiretroviral therapy (HAART) in 1996 which reduces morbidity and mortality, prolongs lives and improves quality of life (QOL) of

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Peer review under responsibility of The Center for Food and Biomolecules, National Taiwan University.

https://doi.org/10.1016/j.jtcme.2018.05.003
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infected patients, has dramatically changed the development of HIV-related disease. Nevertheless, to date, there is still no cure for HIV and AIDS, both of which require life-long adherence since treatment does not completely restore immune system integrity. Currently, the use of HAART is reported to increase the survival rate of PLHIV while its use is associated with reduced AIDS-defining opportunistic infections as well as mortality which are directly related to immune suppression.

In Malaysia, only selected PLHIV are administered with HAART. Based on the Malaysian Guideline for HIV, many factors should be considered before commencing patients on HAART including 1) having CD4 counts <350 cells/mm, 2) patients' willingness to start and adhere strictly to the treatment as well as during follow-up, 3) available antiretroviral options, 4) underlying medical diseases including cardiovascular diseases and diabetes mellitus, 5) the risk of primary resistance and 6) individual factors which may hinder adherence such as irregular working hours and lack of social support.[4] The selection is done to ensure that patients on HAART are compliant to the medications and to avoid the risk of developing HIV resistant strains. Due to these reasons, only 28% of HIV patients was reported to be on HAART in Malaysia in 2015.[2]

HIV infection increases oxidative stress which can result in further oxidative damage.[5] The extent of the damage is influenced by both the amount of oxidative stress and the host defense mechanisms both of which may be affected by the intake of dietary and non-dietary antioxidants and the levels of antioxidant enzymes. The activity of the latter may in turn be dependent on the intake of nutrients required for enzyme activity. In addition, low plasma selenium concentration during HIV infection is associated with low glutathione peroxidase activity.[6] Significantly higher oxidative stress and lower concentrations of major plasma antioxidants such as ascorbic acid (vitamin C), alpha tocopherol (vitamin E), beta-carotene (pro-vitamin A) and selenium have also been reported in patients compared to seronegative patients.[7] Low levels of antioxidant may hasten disease progression due to impaired defenses.[8] Therefore, in order to boost the defense system, many studies have been conducted on supplementation of PLHIV with micronutrients including the use of selenium, β-carotene[9] as well as vitamins A[10,11] and E.[11]

Additionally, due to gastrointestinal malabsorption, increased metabolic demand, body redistribution, weight loss and muscle wasting, PLHIV are reported to be more prone to suffering from multi-nutrient deficiencies especially that of micronutrients.[12] Therefore, some HIV patients have been reported to be deficient in important micronutrients including thiamine, selenium, zinc and vitamins A, B3, B6, B12, C, D and E.[7,13] Moreover, oxidative stress has been linked to a weakened antioxidant defense system[7] thus contributing to a decreased immunity, increased production of reactive oxygen species (ROS) as well as a higher risk of disease progression as well as mortality in PLHIV, indicating the need for the use of micronutrients.

PLHIV are also at higher risk of developing non-AIDS conditions such as accelerated aging,[14] higher mortality, cardiovascular[15] and other inflammatory-related diseases[16] despite having low VL and high CD4 count[17] since low levels of residual viral replication contribute to residual immune activation and inflammation. Honey may be a good supplement for HIV patients. It contains at least 181 substances which include vitamins, minerals, trace elements, proteins, enzymes, amino acids and carbohydrates.[18,19] Honey also contains phenolic and flavonoids compounds[19,20] which are important antioxidants that can alleviate chronic inflammation and stimulate immune cells.[21] In addition, honey has antibacterial[22] and anticancer properties.[23] Interestingly, the oligosaccharides present in honey has been reported to be rich in bifidobacteria and lactobacilli both of which can act as prebiotics to alleviate diarrhoea.[24] Honey also shortens the duration of bacterial gastroenteritis attributed to its antibacterial properties.[19] Besides being rich in nutrients and antioxidants, honey provides energy where one tablespoon of honey can supply 64 calories of energy.[18] In addition, honey has anti-inflammatory properties[25] which can help quench the inflammatory effects of residual immune activation and inflammation. It is thus postulated that honey is an ideal supplement for HIV patients who are at risk of malnutrition, infection and cancers.

Due to its strong antioxidant, anti-inflammatory effects and the ability to boost the immune system, it is hypothesized that honey can improve the immunity of HIV patients, their CD4 counts hence reducing VL in HIV-positive subjects. To our knowledge, the effects of honey on immunocompromised patients especially in HIV positive subjects have not been investigated. Among the different types of honey present in Malaysia, Tualang honey has been reported to have a high antioxidant properties[26] which may help to improve the QOL of HIV patients. Thus, the objective of this study was to investigate the effects of Tualang honey on CD4 counts, the VL and the QOL in HIV positive subjects with a special focus on patients who were not given anti-retroviral (treatment naïve) since these group of individuals are also prone to opportunistic and other inflammatory reactions.

2. Materials and methods

2.1. Study subjects

The study was approved by the Ethical Committee of Universiti Sains Malaysia (USMKK/PPP/JEPeM [198.3 (1)]) which complies with the Declaration of Helsinki. Subjects were inmates from Pengkalan Chepa Kota Bharu, Kelantan, Malaysia diagnosed to be HIV positive with CD4 counts between 250 and 600 cells/ml and were not on HAART. Written informed consents were signed prior to enrollment. The enrolled subjects were mostly the unfortunate ones who do not meet the criteria for HAART due to their poor social support and difficulty to adhere to treatment and follow up.

2.2. Tualang honey

Tualang honey (AgroMas, Malaysia) was supplied by the Federal Agriculture Marketing Authority (FAMA) of Malaysia. Honey was collected by an authorized honey collector and was transported to the laboratory at room temperature (30 °C). It was evaporated to achieve a 20% water content before being gamma irradiated at 20 Gy to ensure its sterility. It was individually packed in 20 g sachet each to help standardize the amount administered to all subjects.

2.3. Study design

This is a randomized, controlled, open-labeled study on the effects of Tualang honey administered at three different doses for six months (Fig. 1). Inclusion criteria was PLHIV who were treatment naïve with CD4 counts 250–600 cell/ml. Exclusion criteria include AIDS defining illness,[27] concurrent chronic diseases such as diabetes mellitus, tuberculosis, chronic renal failure and chronic liver diseases. Demographic data and baseline investigations of CD4 count, VL and assessment of QOL were taken upon recruitment. Using a block randomization method, the subjects were randomly divided into four groups. Group THL was administered with honey 20 g daily (low dose), Group THI received 20 g of honey two times daily (40 g/day, intermediate dose), Group THH received 20 g of honey three times daily (40 g/day, high dose) while Group THC did not receive any treatment and served as a control (an acceptable

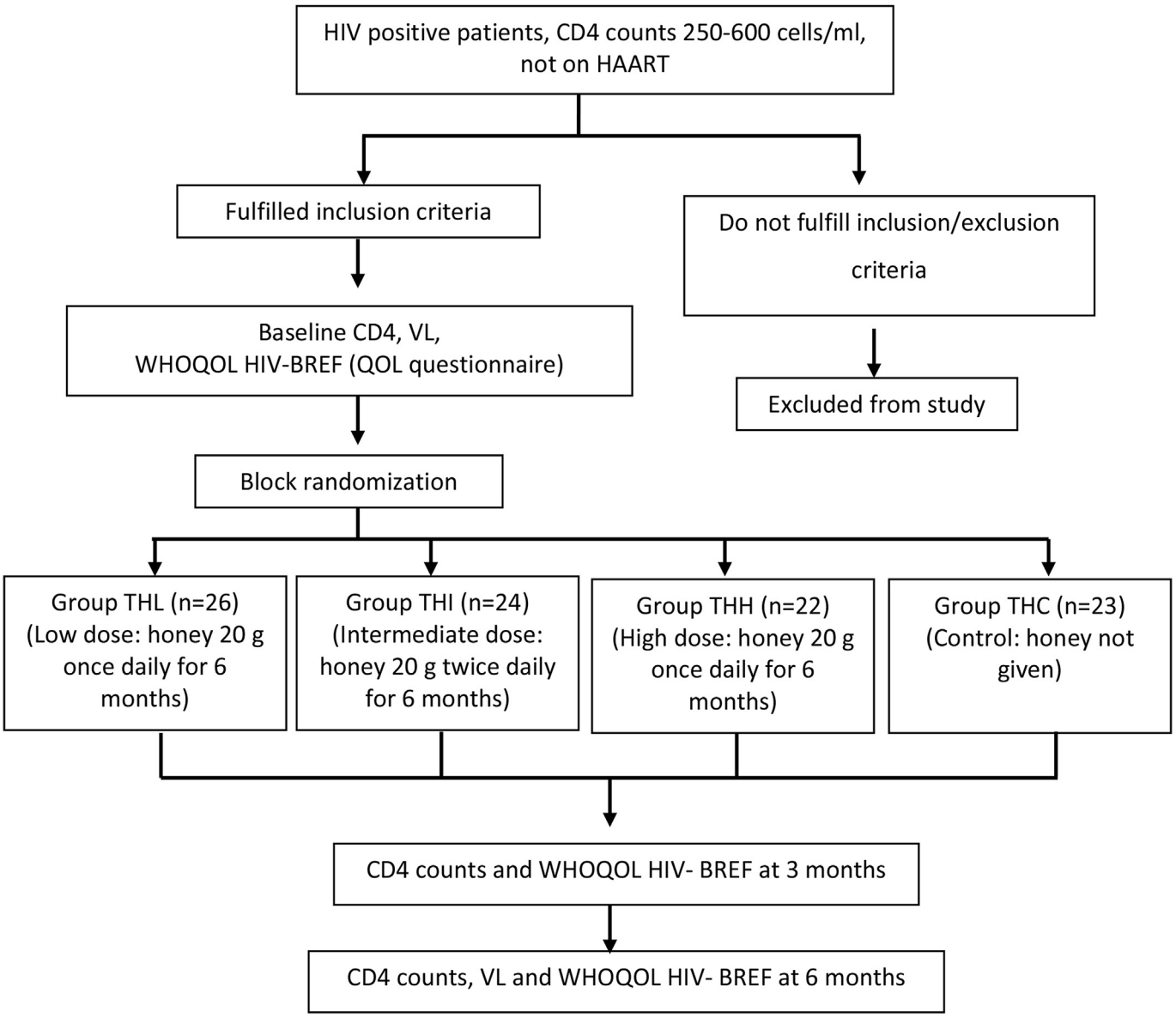

Fig. 1. Study design.

standard approach in the current management of HIV patient). To ensure compliance, honey was consumed with a glass of plain water under supervision of the prison guard, an hour before their main meals. All subjects (treatment and control groups) received similar food as their main meals since they were all inmates of the same prison which can help reduce inter-subject variability. The subjects were followed up after three and six months for the determination of CD4 levels and assessment of QOL. In addition, VL was determined at six months.

CD4 count was determined by using an immunofluorescence method (BD Multi-test IMK Kit CA, USA). The determination of VL was done using a COBAS®Amplicor HIV-1 Test (Roche Laboratories, CA, USA). The tests were performed in an ISO 15189 accredited laboratory.

QOL was assessed using validated questionnaires which were adapted from WHOQOL HIV-BREF for the local population.[27] The questionnaire assessed six different domains; domain 1: physical wellbeing, domain 2: psychological, domain 3: level of independence, domain 4: social relationship, domain 5: environment and domain 6: spirituality/religion/personal beliefs.

2.4. Sample size calculation

Sample size was calculated using a G*Power software version 3.0.10 (Universitat Kiel, Germany). Based on the software (ANOVA: repeated measures, within-between interaction), the ideal sample size was determined as 76 (where α was 0.05, power 0.9 and effect size 0.20 with four groups and three repetitions conducted). Assuming a dropout rate of 20%, the calculated targeted sample size was 91.

2.5. Statistical analysis

Data entry and statistical analysis were performed using a statistical software package SPSS for Windows version 22.0 (IBM Corporation, USA). One-way ANOVA and Pearson Chi Squared tests were used to compare the means of each group for numerical and categorical data respectively. Factorial analysis of variance for

repeated measurements (repeated measure ANOVA) was applied to investigate the differences in log VL and CD4 counts between the four groups. A two-sided p-value of less than 0.05 is considered as statistically significant. There were no p-values for repeated measures ANOVA between group analyses, with regards to time. If the mean of the group is outside the confidence interval range of the compared group, then the difference is considered as statistically significant.

3. Results

Ninety-five HIV-infected subjects were recruited where the majority (72.6%) were previous intravenous drug users. Most subjects were males (85.3%) and were unmarried (74.7%) (Table 1). There was no significant difference in terms of the baseline data for age, weight, CD4 counts and log VL among the honey-treated groups as compared to the control indicating that the subjects were homogenous. This was as expected since block randomization was performed to ensure that the bias in subject selection is minimized.

All groups had decreased CD4 absolute counts over the investigated period (Table 2). However, the reduction in the count was significant only in groups THC (control group) and THL (low dose group). Nevertheless, there was no significant difference in mean CD4 count between all groups when repeated measures ANOVA between group analysis were performed [F-stat (df) = 0.245,[3] p-value = 0.864].

There was an increase in VL in groups THC and THI (by 130% and 31% respectively) but reductions in groups THL and THH (by 25% and 8% respectively) (Table 3). There were trends of VL increment in control group and reduction in treatment group (Fig. 2). However, the within group analysis were not statistically significant. When between group analysis was conducted, significant differences between groups THL and THH as compared to group THC were seen at six months of treatment (Table 4).

As for the QOL, there were significant difference in the scores for group THC (control group) in domains 1 (physical; p = 0.045) and 2 (psychological; p = 0.033) based on time (Table 4). There was a significant difference in the mean score of domains 1 and 2 between the treatment groups and the control group at three and six months (Table 5). Fig. 3 illustrates the reductions of the means score for domains 1 and 2 where the control group had significant reductions in the mean score as compared to the groups treated with honey which showed improvement in the QOL score.

4. Discussion

To our knowledge, this is the first study to investigate on the effect of Tualang honey administration on CD4 count and QOL of HIV-positive subjects. The natural history of HIV infection in untreated patients is decreased in CD4 cell counts and an increased VL where in the later stages, patients are more prone to opportunistic infections. This phenomenon usually occurs within several years once CD4 count is less than 200 cells/mm3.[28] Nevertheless, the production of new CD4 cells to counter the dead HIV-induced lymphocyte cells requires time.

Our study indicated that there were reductions in the CD4 counts of all the treatment groups and the control specifically groups A (low dose honey) and D (control), showed significant reductions in CD4 counts. On the contrary, the reduction in CD4 counts were not significant in subjects treated with intermediate and high doses of honey (groups B and C respectively). As discussed earlier, even the CD4 counts of patients on antiretroviral therapies with good VL suppression may not return to normalcy. In fact, there were reports showing reduction of CD4 or failure of CD4 levels to return to normalcy even among patients with good VL suppression following treatment with antiretroviral therapies.[29] This phenomenon may be due to persistent HIV infections which shorten the life span of CD4 T-cells,[30] causing functional dysregulation.[31] Another plausible explanation for the poor CD4 cell recovery especially in subjects receiving intermediate and high doses of honey is apoptosis[32,33] secondary to chronic activation of uninfected cells responding to HIV leading to activation-induced cell death.[34] In addition, reduction in CD4 has been reported to be lower among naïve CD4 cell productions,[34] subsequently leading to reduced production of CD4 cells.

Our study on honey cannot be compared with that of an antiretroviral therapy since the mode of actions are different and honey is given merely as a supplement, not for treatment. With its good antioxidant and anti-inflammatory activities, honey consumption is expected to boost the immunity which can help the body combat infections naturally and are not intended for killing of the HIV virus. The insignificant reduction in CD4 seen in groups which received both intermediate and high doses of honey suggests that the HIV subjects might have benefited from honey administration since the decreased in CD4 counts seen was lower than that

Table 1
Baseline characteristics of the subjects.

Characteristics	Groups				Total	F statistics *(df)*	p-value
	THL (n = 26) (low dose)	THI (n = 24) (intermediate)	THH (n = 22) (high dose)	THC (n = 23) (control)	freq (%)		
Mean age (SD)	33.42 (7.65)	32.96 (4.86)	36.50 (7.78)	36.35 (7.29)		1.698 (3,91)	0.173[a]
Weight (kg) (SD)	56.35 (7.80)	58.75 (8.25)	54.89 (6.83)	58.28 (7.14)		1.287 (3,91)	0.284[a]
Mean BMI (SD)	21.47 (2.62)	22.22 (3.05)	20.80 (2.40)	22.71 (2.55)		2.159 (3,91)	0.099[a]
Mean CD4 (SD)	410.41 (104.16)	412.89 (99.84)	414.67 (99.55)	421.28 (82.33)		0.055 (3,91)	0.983[a]
Mean VL (SD)	74512.14 (149219.59)	61280.85 (91513.23)	64330.82 (57153.31)	79934.44 (95014.57)		0.159 (3,91)	0.924[a]
Sex							
Male	22 (27.2)	20 (24.7)	19 (23.5)	20 (24.7)	81 (85.3)		0.985#
Female	4 (28.6)	4 (28.6)	3 (21.4)	3 (21.4)	14 (14.7)		
Marital status							
Married	6 (23.1)	5 (20.8)	5 (22.7)	5 (21.7)	21 (22.1)		0.979#
Single	19 (73.1)	19 (79.2)	16 (72.7)	17 (73.9)	71 (74.7)		
Divorced or widow	1 (3.8)	0 (0.0)	1 (4.5)	1 (4.3)	3 (3.2)		
Transmission							
Sexual intercourse	5 (19.2)	10 (41.7)	6 (27.3)	3 (21.7)	24 (25.3)		0.422#
Needle sharing	20 (76.9)	14 (58.3)	16 (72.7)	19 (82.6)	69 (72.6)		
Unknown	1 (3.8)	0 (0.0)	0 (0.0)	1 (4.3)	2 (2.2)		

[a] A one-way ANOVA was applied to compare the means of each group.# A Pearson Chi Square test was applied to compare the means of each group. Normality and homogeneity of variances assumptions are met for both statistics. SD: Standard deviation, Freq: frequency, BMI: body mass index.

Table 2
Comparison of CD4 absolute count within each treatment group based on time (n = 95).

Comparison	Treatment group							
	THL		THI		THH		THC	
	MD (95% CI)	p-value	MD (95% CI)	p-value	MD (95% CI)	p-value	MD (95% CI)	p-value
Week 1–2	−38.41 (−73.57, −3.25)	0.029*	−1.54 (−66.14, 63.06)	>0.95	−14.11 (−66.77, 38.55)	>0.95	−9.98 (−67.18, 47.23)	>0.95
Week 2–3	−28.66 (−75.81, 18.49)	0.394	−34.23 (−85.13, 16.68)	0.288	−48.85 (−98.48, 10.78)	0.147	−55.64 (−94.04, −17.25)	0.003*
Week 1–3	−67.07 (−113.05, −21.08)	0.003*	−35.76 (−97.61, 26.09)	0.447	−57.96 (−116.75, 0.83)	0.054	−65.62 (−110.94, −20.30)	0.003*

A repeated measure ANOVA within group analysis was applied followed by pairwise comparison within 95% confidence interval adjustment by Bonferroni correction. MD = mean difference. * significant difference.

Table 3
Descriptive statistics of viral load at baseline, 6 months and the percentage difference.

Group	Time	Mean (cp/ml)	SD	^Percentage difference (%)
THL (Low dose) (n = 26)	Baseline 6 months	74512.14 55352.64	149219.59 84792.96	−25.7
THI (Intermediate dose) (n = 24)	Baseline 6 months	61280.85 80557.92	91513.23 171606.66	31.5
THH (high dose) (n = 22)	Baseline 6 months	64330.82 59009.32	57153.31 61103.25	−8.3
THC (control) (n = 23)	Baseline 6 months	79934.44 183973.85	95014.57 506879.91	**130.2**

^Percentage difference was calculated using the formula $\left(\frac{6\boldsymbol{months} - \boldsymbol{baseline}}{\boldsymbol{baseline}}\right)$ x 100%. Group D showed marked increment of VL (130%) with smaller increment seen in group B. However, groups A and C showed some reductions in VL.

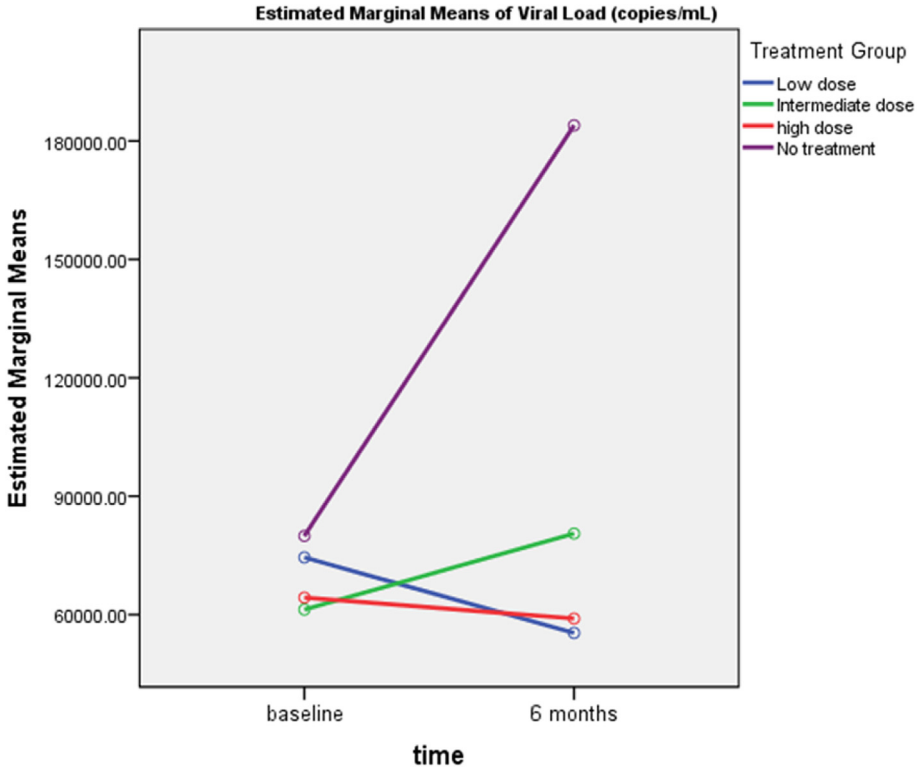

Fig. 2. Trend of VL reduction in the treatment groups with increment seen in both intermediate and control groups.

of the control and low dose groups, as normally shown in the natural progression of HIV infections among untreated patients. The finding suggests that the improvements in CD4 counts in groups which received intermediate and high doses of honey are useful since improvements in CD4 count is one of the important prognostic outcomes for HIV patients.[35] Moreover, honey being a natural product is known to confer its effects relatively slower as compared to modern medicine while the production of CD4 cells in countering dead HIV-induced lymphocyte cells requires time. Although honey has also been reported to increase apoptosis in cancer cells and is protective against apoptosis for normal cells,[36] no studies have been conducted to confirm apoptosis in HIV-infected cells treated with honey so far. In addition, honey was also known to be protective against blood cells damage[37] indicating its utility in actively-proliferating cells.

The VL findings showed 130% increment from baseline (group THC) and 31% (group THI) while reductions were seen in groups THL and THH (by 26% and 8% respectively). However, within group analyses indicated no significant differences between groups THL and THH as compared to Group THC. This result is not surprising

Table 4
Comparison of viral load between the groups based on time.

Time	Treatment group	Adjusted mean viral load (cp/ml)	95% CI
Baseline	THL	74512.14	33339.83, 115684.45
	THI	61280.85	18427.35, 104134.35
	THH	64330.82	19571.80, 109089.84
	THC	79934.441	36159.25, 123709.63
6 months	THL	55352.64*	−49463.22, 160168.50
	THI	80557.92	−28537.89, 189653.73
	THH	59009.33*	−54937.53, 172956.18
	THC	183973.85	72531.63, 295416.07

F-stat (df) = 1.083(3), p-value = 0.301 Repeated measures ANOVA between group analysis with regards to time was applied. Assumptions of normality, homogeneity of variances and compound symmetry were checked and fulfilled. * significant difference compared to control (group D).

Table 5
Comparison of adjusted mean score for domains 1 (physical) and 2 (psychological) between honey treatment groups and control based on time.

Time	Treatment group	Mean Score	95% CI
Domain 1			
Baseline	THL (low dose)	12.31	11.55, 13.07
	THI (intermediate dose)	12.63	11.83, 13.42
	THH (high dose)	12.64	11.81, 13.46
	THC (control)	11.83	11.02, 13.64
3 months	THL (low dose)	**12.50***	11.59, 13.41
	THI (intermediate dose)	**12.21***	11.26, 13.15
	THH (high dose)	**12.00***	11.01, 12.99
	THC (control)	10.17	9.21, 11.14
6 months	THL (low dose)	**12.08***	10.58, 13.56
	THI (intermediate dose)	**12.00***	10.44, 13.56
	THH (high dose)	**11.23***	9.60, 12.86
	THC (control)	9.22	7.63, 10.81
Domain 2			
Baseline	THL (low dose)	13.51	12.71, 14.31
	THI (intermediate dose)	13.43	12.60, 14.27
	THH (high dose)	13.64	12.77, 14.51
	THC (control)	12.84	11.98, 13.69
3 months	THL (low dose)	**13.97***	12.89, 15.04
	THI (intermediate dose)	**13.98***	12.85, 15.09
	THH (high dose)	**13.35***	12.18, 14.51
	THC (control)	11.48	10.33, 12.62
6 months	THL (low dose)	**13.75***	12.11, 15.39
	THI (intermediate dose)	**14.07***	12.36, 15.77
	THH (high dose)	**12.73***	10.95, 14.51
	THC (control)	9.77	8.03, 11.52

Repeated measures ANOVA between group analyses with regards to time was applied. Assumptions of normality, homogeneity of variances and compound symmetry were checked and fulfilled. *significant difference compared to control (group D).

since honey is known for its antibacterial[22] and antifungal properties.[38] However, to our knowledge there were no previous reports on the inhibitory effects of honey on HIV and our report is the first to demonstrate this effect.

Tualang honey contains phenolic compounds including caffeic acid[39] and flavonoids such as quercetin which are strong antioxidants that are also reported to have anti-HIV 1 activity.[39] Tualang honey is also reported to contain another potent antioxidant named pinobanksin.[39] The presence of the various types of antioxidants may contribute to the reduction in VL in the treated group and increment of VL in the control group. Methylglyoxal in honey is also reported to confer some anti-HIV activities since it has been reported to interfere with the assembly of new HIV virions and maturation of the virions in the later stages of HIV infection.[40] High amounts of methylglyoxal has also been reported to be present in Manuka[41] and Iranian honeys[40] although its presence was not reported in Tualang honey previously.

Besides honey, other bee products have also been reported to be useful against HIV infection. An example is propolis, a substance collected by the honey bees which is reported to confer some anti-HIV-1 activity in CD4 lymphocytes and microglial cell cultures.[42] Although the products were not investigated in our study, honey may also contain propolis, royal jelly, bee venom and pollen during the cultivation process, all of which are important substances that have anti-HIV effects. In addition, mellitin, another important substance present in the bee venom has been reported to suppress HIV-1 gene expression.[43] These are some of the plausible mechanism of actions for honey's anti-HIV activity.

In terms of QOL, significant improvements in physical and psychological scores for all subjects who received honey treatment were seen as compared to control at three and six months following treatment. Honey contains some important carbohydrates including fructose and glucose which can supply some energies to the individuals thus improving the subjects' physical wellbeing as confirmed by the enhanced physical scores seen among the groups administered with honey. In addition, honey also contains tryptophan and phenylalanine[44] which is a precursor for serotonin[45] and dopamine[46] respectively. Neurotransmitters produced in the body can affect mood and social behavior, appetite and digestion, sleep, memory as well as sexual desire and function.[47]

We investigated HIV subjects with CD4 counts between 250 and 600 cells/ml because these individuals already have a decreased immunity, are more prone to having infections and malnutrition but have not yet received antiretroviral treatment. It is plausible that honey supplementation may help the subjects achieve a better QOL as also shown by Rosediani et al. (2017) and delay disease progression to AIDS.[48] Honey is also known to have anti-inflammatory activities[49] which may reduce the risk of inflammation-related diseases in HIV patients including cardiovascular problems.[50] HIV, being a chronic disease, may result in chronic diarrhoea and a poorer appetite, both of which may also contribute to malnutrition. In addition, honey is a natural product which contains not only carbohydrates, but also other important nutrients, minerals, vitamins, trace elements and proteins. Overall, the antibacterial, anticancer, antioxidant, antidiarrhoeal and nutritional properties of honey may boost the nutritional status and physical wellbeing of HIV patients all of which may help them better combat opportunistic infections, improve nutritional status and quality of lives.

To our knowledge, this is the first extensive study to investigate on honey treatment in a group of HIV patients. Heidari et al. 2012[51] reported a 1% increment in CD4 and CD8 cell counts in a single patient administered with 80 g of honey daily for 30 days. Al-Waili et al. reported that honey administered at 80 g daily for 21 days to a 40 year old patient with a long history of AIDS showed decreased prostaglandin level, elevated nitric oxide production and improved lymphocytes, platelet count, serum protein, albumin and copper levels.[52]

Our study has some limitations. A longer duration of honey administration (up to one year) should be conducted to perceive a

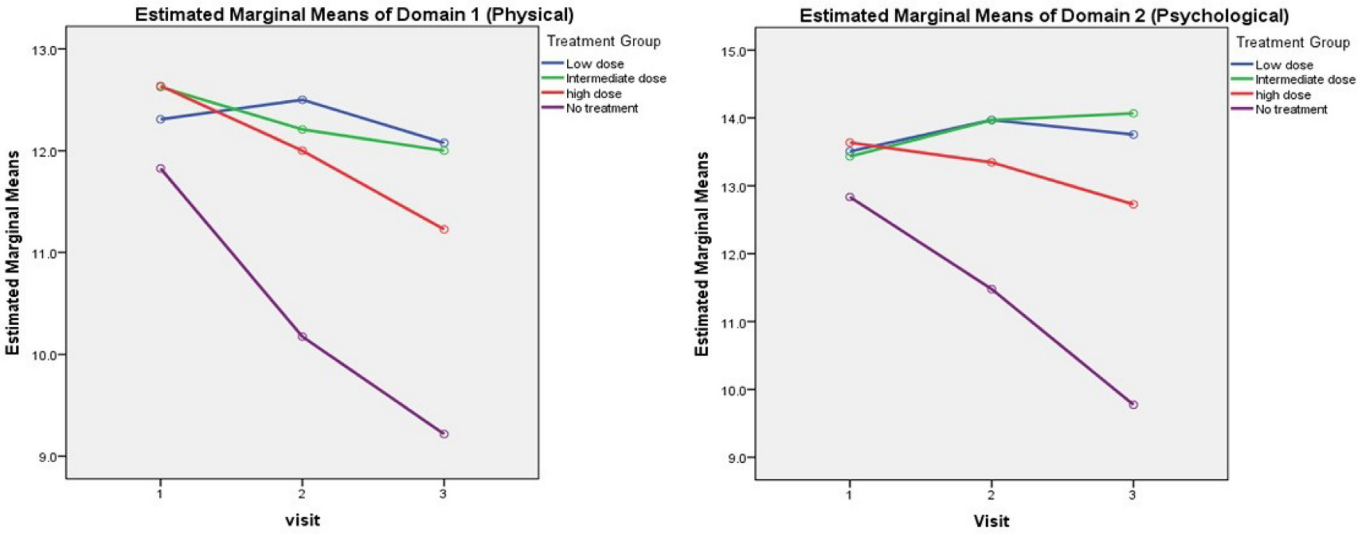

Fig. 3. The Profile Plot of Adjusted Means of Domain 1 (Physical) and Domain 2 (Psychological) at baseline (visit 1), 3 months (visit 2) and 6 months (visit 3).

more positive trend. In our study, the subjects were administered with a maximum dose of 20 g of honey thrice daily based on an in-house study conducted previously. In addition, dose of honey may be increased to 80 g daily to achieve a more significant finding. Further studies are required to elucidate the molecular mechanisms of action of Tualang honey in asymptomatic HIV subjects which may address some of these issues.

5. Conclusion

Honey, especially at 40 g and 60 g daily doses, has the potential to improve QOL (both physical and psychological) and CD4 counts in asymptomatic HIV subjects not on HAART. There was a trend of lower VL following Tualang honey administration in asymptomatic HIV subjects thus supporting the possible role of honey in boosting the immune system by improving the CD4 counts and reducing VL in HIV positive subjects.

Acknowledgement

We would like to thank Universiti Sains Malaysia for providing a Research University Grant (1001/PPSP/8120209). We are also grateful to the staff of Prison Centre in Pengkalan Chepa, Kelantan, Malaysia for their full cooperation during our study. We would like to thank Dr Siti Azrin and Assoc. Prof Dr Kamarul Imran Musa (USM) for their invaluable help in statistical analyses as well as Mr Jamaruddin Mat Asan (USM) for his assistance in conducting the CD4 counts in this study. Finally, we would like to thank Dr Aida Maziha for her assistance in content clarity.

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