Virgin Coconut Oil (VCO) as Adjunct Therapy for Nicotine Dependence in Smokers

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Abstract

The number of smokers is high, with increasing number of young smokers. Current pharmacological measures to treat nicotine dependence is overshadowed by severe side effects and the emergence of dependence on the replacing agents in the case of replacement therapy. The present work aimed to seek alternative treatment mode to help quit smoking. Forty smokers, with various intensity of nicotine dependence, were enrolled in this open label study. They were required to take 15 ml VCO twice daily for 14 days. Evaluations were made before the experiments started and upon its completion, consisting of Fagerstrom Test for Nicotine Dependence (FTND) and quality of life (QoL) determination. Results showed that consumption of VCO resulted in significant improvement of FTND (3.43±1.93 to 2.90±1.86, p<0.05) as well as EQ-VAS (86.00±14.55 to 91.85±11.89, p<0.01) scores. This study implies that VCO is beneficial to smokers who wish to reduce dependence on and finally quit smoking.

Introduction and Objectives

One of the programs being campaigned by the World Health Organization (WHO) as well as Indonesian government, through the ministry of health, is reduction of active smokers. In Indonesia alone death tied to smoking-related diseases has reached 225,700 yearly [1]. Tobacco smoking is still claimed to be the biggest single preventable cause of death according to WHO Report on the Global Tobacco Epidemic in 2019 [2].

Tobacco smoking can cause dependence due nicotine content in tobacco, as an addictive substance. To get the effect, a smoker may need an escalating nicotine intake, and when the consumption ceases withdrawal symptoms appear. Relapse to dependence cause by nicotine lasts longer than that induced by other psychoactive agents. Several methods have been applied as therapeutic means for the treatment of dependence due to nicotine
and to suppress its relapse, one of which is by administering nicotine in a tapered-off manner. Unfortunately, substances used to treat nicotine dependence also have detrimental side effects [3]. In addition, new problems often emerge in the form of dependence on the replacing agents, in the case of replacement therapy. It is, therefore, essential to develop alternatives for dealing with dependence on addictive substances, which are safe and effective.

The manifestations of dependence have been related to the brain dopaminergic system, which is the major component of the brain reward system, important for assessing environmental stimuli. During the past three decades, different brain systems have also been tied to the reward substrate. Earlier results have indicated the role of the arachidonic acid cascade (an important component of inflammatory reaction) in the mechanism of development as well as expression of drug dependence, including tetrahydrocannabinol (THC), the psychoactive ingredient of marihuana [4] and methamphetamine [5]. Thus, the cyclooxygenase inhibitor diclofenac has been demonstrated to suppress the expression of THC withdrawal syndrome and relapse to methamphetamine dependence in rodent models.

Virgin coconut oil (VCO) is purified natural oil obtained without heat treatment or addition of chemicals. VCO has therapeutic potentials, one of which is for the treatment of inflammation [6]. Since VCO shares the pharmacological profile of diclofenac, in earlier work we have investigated the effect of VCO on nicotine dependence in a rat model. Using conditioned place preference approach, found that VCO significantly decreased preference score as an indication of dependence, both during development and relapse [7].

Our later unpublished study showed the effect of VCO on withdrawal symptoms in patients undergoing methadone maintenance therapy. VCO showed the potential to reduce the symptoms as demonstrated by the decrease in values of subjective opioid withdrawal symptoms (SOWS) as well as objective opioid withdrawal symptoms (OOWS). The most important among the SOWS reduced was the desire to use the drug, while those belonging to OOWS included hand shaking, sweating, and piloerection.

Based on the above-mentioned consideration, the proposed study aims to:

1. Investigate the effect of VCO administration for 14 days in smokers.
2. Provide basic information to initiate the development of VCO-based product as an alternative therapy for the treatment of drug dependence.

Methods

Study Design

We assigned subjects to an open-label trial, investigating the effect of VCO on smokers using a standard instrument for assessing the intensity of physical addiction to nicotine, the Fagerstrom Test for Nicotine Dependence (FTND). The quality of life (QoL) of subjects was also observed. The scores of FTND and QoL were measured before and after the completion of the trial. The study was conducted between August 2020 and May 2021. The Study was approved by the Institutional Review Board of Hasan Sadikin General Hospital Bandung, Indonesia (123/UN6.KEP/EC/2021).

Study Subjects

The criteria of inclusion for the potential trial subjects were healthy male and female of ≥18 years of age, smokers of all dependence level (very low, low, medium, and high). Subjects were not eligible for the study if
they had underlying diseases, and pregnant as well as breast feeding female subjects were excluded. All subjects provided informed consent to participate in this investigation, which was approved by the Institutional Review Board of Hasan Sadikin General Hospital Bandung, Indonesia. Subjects were compensated for their participation in the trial upon completion of the study.

**Study Interventions**

The test substance was virgin coconut oil (produced by PT Tamba Sanjiwani, Indonesia, Reg. No. MD 207922001142, Batch No. A200626IV, CoA No. 09231/DBBPAM, ED. 20230626). Subjects received 15 ml of VCO twice daily for 14 days. Before the intervention, each subject was checked for their vital status, followed by assessment on nicotine dependence intensity, based on FTND criteria, and measurement of QoL. The evaluations were repeated upon completion of treatment. Compliance with the protocol was assessed by a weekly phone call with all subjects, during which evaluation of adverse events was also carried out.

**Study Outcome**

The primary outcome was dependence score according to FTND criteria, as secondary outcome we recorded EuroQol-visual analogue scales (EQ-VAS). All of the outcomes were measured at baseline and after the completion of intervention period.

**Sample Size and Statistical Analysis**

Calculation of sample size was based on anticipated decrease in FTND scale from 4 to 3, alpha value of 0.05, and power set at 90%. With this setting we came up with a minimum number of samples of 24. Experimental data are represented as means ± standard deviation (SD). Within group differences over time were analyzed using paired t-tests for all parameters measured. Statistical significance was defined at p <0.05.

**Results and Discussion**

**Study Population**

A total of 40 subjects were eligible for the study. Upon obtaining subjects informed consent, they immediately received VCO, 15 ml twice daily for 14 days. All subjects completed the protocol. Demographic data of the 40 is presented in Table 1.
**Table 1. Demographic Data of Subjects Who Completed the Study**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>40</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>34.25 ± 12.37</td>
</tr>
<tr>
<td>Male (%)</td>
<td>87.5</td>
</tr>
<tr>
<td>Female (%)</td>
<td>12.5</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21.38 ± 4.45</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>122.05 ± 10.95</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>81.83 ± 10.22</td>
</tr>
<tr>
<td>Heart rate</td>
<td>78.00 ± 9.95</td>
</tr>
<tr>
<td>Respiration rate</td>
<td>17.65 ± 3.49</td>
</tr>
<tr>
<td>FTND score</td>
<td>3.43 ± 1.93</td>
</tr>
<tr>
<td>Intensity of nicotine dependence (n)</td>
<td></td>
</tr>
<tr>
<td>Very low</td>
<td>18</td>
</tr>
<tr>
<td>Low</td>
<td>8</td>
</tr>
<tr>
<td>Medium</td>
<td>8</td>
</tr>
<tr>
<td>High</td>
<td>6</td>
</tr>
</tbody>
</table>

Observation of vital signs in subjects completing the study did not show significant changes from baseline values. In an open-label pilot study, VCO has been shown to have good safety profile at the dose level used in the present study [8].

**Changes in FTND Score**

As presented in Figure 1, the average of FTND score at the end of intervention was significantly lower compared to that of the initial value (2.90 ± 0.29 vs 3.43 ± 0.30, p<0.05). The data demonstrated that administration of VCO improved nicotine dependence intensity. Upon further analysis based on intensity of nicotine dependence (Figure 2) it was found that subjects belonging to high dependence intensity were the most improved compared to other groups, with a decrease in score of 1.17. FTND contains six items that evaluate the quantity of cigarette consumption, the compulsion to use, and dependence. Itemized observation revealed that the change in quantity of cigarette consumed was the significant contributor, as shown in Figure 3. Scoring for this aspect of FTND is based on the number of daily cigarettes consumed, as follow: 0=10 or less, 1=11-20, 2=21-30, 3=30 or more [9]. The data showed that VCO intervention in the subjects lead to reduction of almost two cigarettes each day. When subgroup analysis was made according to dependence intensity, it was found that the change in subjects with high nicotine dependence was the highest (Figure 4).
Figure 1 Effect of administration of VCO on FTND score. VCO was administered 15 ml twice daily for 14 days. FTND score was measured before VCO treatment and after the intervention period was complete. Data represents averages ± SD of 40 subjects. *p<0.05 vs pretreatment, paired t-test.

Figure 2 Effect of administration of VCO on FTND score in different intensity of nicotine dependence. VCO was administered 15 ml twice daily for 14 days. FTND score was measured before VCO treatment and after the intervention period was complete. Data represents average ± SD of 6-18 subjects. Grey and black bars indicate pretreatment and posttreatment data, respectively.

Figure 3 Effect of administration of VCO on the quantity of daily cigarettes consumed. VCO was administered 15 ml twice daily for 14 days. The score of cigarettes consumption was measured before VCO treatment and after the intervention period was complete. Data represents averages ± SD of 40 subjects. **p<0.01 vs pretreatment, paired t-test.
Figure 4 Effect of administration of VCO on the quantity of daily cigarettes consumed in different intensity of nicotine dependence. VCO was administered 15 ml twice daily for 14 days. The score of cigarettes consumption was measured before VCO treatment and after the intervention period was complete. Data represents averages ± SD of 6-18 subjects. Grey and black bars indicate pretreatment and posttreatment data, respectively.

Changes in Quality of Life

The consequence of VCO administration on quality of life of smokers is presented in Figure 5. The data showed that EQ VAS score increased significantly (p<0.05) after 14 days of treatment, with respective values of 86.00 ± 14.55 and 91.85 ± 11.89, before and after the treatment. On the basis of intensity of nicotine dependence, as shown in Figure 6, it was found that subjects with the highest improvement belonged the group with high dependence intensity.

Figure 5 Effect of administration of VCO on quality of life of smokers. VCO was administered 15 ml twice daily for 14 days. The score of EQ VAS was measured before VCO treatment and after the intervention period was complete. Data represents averages ± SD of 40 subjects. **p<0.01 vs pretreatment, paired t-test.
Figure 6 Effect of administration of VCO on quality of life in different intensity of nicotine dependence. VCO was administered 15 ml twice daily for 14 days. The score of cigarettes consumption was measured before VCO treatment and after the intervention period was complete. Data represents averages ± SD of 6-18 subjects. Grey and black bars indicate pretreatment and posttreatment data, respectively.

Early study has demonstrated that VCO has analgesic, antipyretic and anti-inflammatory activities [6]. This range of biological effects are specific to non-steroidal anti-inflammatory drugs, that interfere with the arachidonic acid cascade. Cumulating evidence has shown the involvement of the endogenous metabolic pathway in dependence and relapse of addictive substances. Thus, prostaglandin, an end product of the cyclooxygenase pathway, has been shown to prevent the expression of withdrawal signs in THC-dependent mice. This was corroborated by the withdrawal-inducing activity of diclofenac in mice treated repeatedly with THC [4]. By observing withdrawal expression, it was further found that the signs were demonstrated in cannabinoid-naive mice receiving consecutive diclofenac treatment followed by challenge with a cannabinoid receptor antagonist [10]. In regard to relapse, using methamphetamine self-administering rats, it was found that diclofenac prevented methamphetamine-seeking behavior upon challenging with small dose of the drug or even with drug-related cues (Anggadiredja et al., 2004) [5].

Neuroprotective effect provided by chemical group contained in coconut oil has been postulated to be, at least in part, through anti-inflammatory action [11], which was in line with the study of Intahpuak and collaborators (2011), showing anti-inflammatory activity of VCO. Neurologically, addicts share several conditions found in patients with psychiatric disorder, such as stress and depression [12]. A study in a model of stress and depression demonstrated that VCO could be potential to overcome such psychiatric disorders, affecting not only behavioral parameters but also organic as well as biochemical changes, including normalization of relevant neurotransmitter and hormone levels [13]. Indeed, in the present study we found that the most profound contributing factor for improvement of QoL, based on the five domains of the QoL measuring instrument, was amelioration in the aspect of depression, whose score decreased by 0.20 points (p<0.01).

An important aspect from the results we observed in this study is that improvements of the study’s end-points were majorly contributed to the ameliorating changes in subjects with high intensity of nicotine dependence (FTND and number of cigarette scores reduced by 1.17 and 0.5 points, respectively). Taking this observation into consideration, one might suggest that VCO is potential for heavy smokers.
Reported Adverse Events and Death

The major adverse event was such as upset stomach reported by 27 (67.5%) subjects. In addition, four (10%) subjects reported lightheadedness. All adverse events were manageable and resolved within two to three days. No death occurred during this trial. The safety profile of VCO was found to be consistent with previous results both in preclinical [14] and clinical [15] settings.

Conclusion

In conclusion, this study implies that VCO is beneficial to smokers who wish to reduce dependence on and finally quit smoking. The use might be particularly essential for heavy smokers.

References

3) Hays, J.T., and Ebbert, J.O., Drugs, 70(18): 2357-2372.