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Original Article

The Effect of Preconcenption Moringa Leaf Extract Supplementation on Cotinine Serum Levels in Pregnant Women Exposed to Tobacco Smoke

Haerani Harun[1,*], Anwar Daud[2], Ridwan Amiruddin[3], M Sabir[4], Veni Hadju[5], Anwar Mallongi[2], Rahma[1], Miranti[4], Tamrin Talebe[6], M. Faris[1]

ABSTRACT

Background: *Moringa oleifera* is known for its nutrition content, antioxidant and medical benefit. Tobacco smoke contains various toxic substance and can affect the pregnancy. To reduce the tobacco smoke effect on pregnancy outcome good nutrition is needed. **Objective**: This study aims to assess the effect of Moringa leaf extract on serum cotinine levels in pregnant women exposed to second-hand tobacco smoke. **Method**: This is an observational study with a prospective cohort study design the study population was pregnant women which were divided by 2 groups, first group received IFA supplements only (n = 30) and the second group receive IFA and Moringa leaf extract supplements (n = 26). The tobacco smoke exposure data collected with questionnaire, and cotinine serum by blood sample. The tobacco smoke exposure and cotinine serum levels were compered between the two groups. **Results:** The tobacco smoke exposures at home were higher in MO+IFA group pregnant women then the IFA group pregnant women (p<0,05). The cotinine serum levels in both groups were found not significantly different (p=0,535). These results indicate that pregnant woman with high exposure of tobacco smoke who MO receive have similar cotinine serum levels with the pregnant woman with lower exposure of tobacco smoke. Conclusion: Moringa leaf extract supplementation to pregnant women with high tobacco smoke exposure has serum cotinine levels similar to pregnant women with lower exposure to tobacco smoke.

Key words: Tobacco smoke, Cotinine, Preconception, *Moringa oleifera*.

Haerani Harun[1,*], Anwar Daud[2], Ridwan Amiruddin[3], M Sabir[4], Veni Hadju[5], Anwar Mallongi[2], Rahma[1], Miranti[4], Tamrin Talebe[6], M. Faris[1]

[1]*Student of Doctoral Program, Faculty of Public Health, Hasanuddin University, Makassar, INDONESIA.*

[2]*Professor, Department of Enviromental Health, Public Health Faculty Hasanuddin University, INDONESIA.*

[3]*Professor, Department of Epidemiology, Faculty of Public Health, Hasanuddin University, Makassar, INDONESIA.*

[4]*Associate Professor, Department of Microbiology,Medical faculty Tadulako University, INDONESIA.*

[5]*Professor, Department of Nutritional Sciences, Faculty of Public Health, Hasanuddin University, Makassar, INDONESIA.*

[6]*Associate professor, Ushuluddin Faculty, Datokarama State Islamic University, INDONESIA.*

Correspondence

Haerani Harun

Student of Doctoral Program, Faculty of Public Health, Hasanuddin University, Makassar, INDONESIA.

E-mail: haeraniharun.unhas@gmail.com

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INTRODUCTION

Moringa oleifera leaves were reported to have a rich content of β-carotene, protein, vitamin C, calcium, potassium, and antioxidants. Moringa plants were also found to contain more anti-inflammatory substances, flavonoids, omega 3 and omega 6 fatty acids and other nutrients compared to other foods. For many years, *Moringa oleifera* has been used for medicinal, nutritional and cosmetic purposes by various traditional communities around the world and has been confirmed by science. Besides being known as a source of nutrition because of its rich nutritional content, *Moringa oleifera* also have other benefits such as anti-fibrotic, anti-inflammatory, antibiotic, anti-hyperglycemia, anti-oxidant and anti-cancer.[1,2]

Tobacco smoke contain various harmful substances including nicotine, cadmium carbonmoxide, asbestos, arsenic, benzene and radon gas.[3,4] Nicotine is the main component of cigarettes, and studies have shown the adverse effects of nicotine on pregnancy in both active and passive smoking mothers.[5,6] Nicotine and carbon monoxide can cause various adverse effect to the fetus, dirupt the placenta and finally effect the fetal circulation.[3,7-9]

Several studies have shown that the moringa plant provides benefits against the bad effects of smoking. Moringa tea can reduce nicotine-related oxidative stress and prevent damage to the frontal brain cortex in experimental animals.[10] Moringa plants can reduce the extent of inflammation in smokers, by preventing the cytokines interleukin-8 (IL-8), tumor necrosis factor (TNF) and IL-6 which play a role in mediating inflammation and tissue damage.[11,12] Moringa leaf extract also helps protect against DNA damage in pregnant women exposed to tobacco smoke.[13] Supplementation of Moringa leaves during pregnancy helps protect the offspring from malnutrition and stunting.[14,15] Moringa leaves also can improve Hb levels, pregnant women's weight and baby's weight.[16,17]

The benefits of moringa plants for smokers and pregnant women have been widely studied, but their benefits for pregnant women exposed to tobacco smoke are limited. Measurement of exposure to cigarette smoke can be done with a questionnaire and examination of serum cotinine levels, derivatives of nicotine in metabolism.[18] This study aims to assess the effect of Moringa leaf extract (MO) on serum cotinine levels in pregnant women exposed to second-hand smoke from environment tobacco smoke (ETS).

METHOD

This study is a prospective cohort study, conducted in North Polombangkerng District, Takalar Regency, South Sulawesi. The subjects were intervaned with *Moringa oleifera* leaf extract (MO) with the controls receiving iron folic acid (IFA) tablet supplements. MO and IFA were given since the preconception in 200 young women age of less than 30 years who were planning to pregnant. supplements of MO + IFA were given to 100 women and IFA supplements only were given to 100 women.

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Table 1: Karakteristik ibu hamil dan keluarga.

Subject characteristics	Group		Total n=56
	IFA n=30	MO + IFA n=26	
	n (%)	n (%)	n (%)
Age			
< 20 years	5 (16,67)	4 (15.38)	9 (16,07)
1-30 years	25 (83,33)	22 (84,51)	47 (83,92)
Mother's occupation			
Working	9(30)	9 (34,61)	18 (32,14))
Not Working	21(70)	17 (65,38)	38 (67,86)
Father's occupation			
Entrepreneur	12 (40)	11 (42,30)	23 (41,07)
Farmer	10 (33,33)	4 (15,38)	14 (25)
Agency employee	6 (20)	10 (38,46)	16 (28,57)
Not working	2(6,67)	1 (3,84)	3 (5,35)
Mother's education			
6-9 years	1 (3,33)	1 (3,84)	2 (3,57)
10-12 years	20 (66,67)	19 (73,07)	39 (69,64)
>12 years	9 (30)	6 (23,07)	15 (26,78)
Father's education			
<6 years	1 (3,33)	1 (3,84)	1 (1,78)
6-9 years	4 (13,33)	4 (15,38)	7 (12,5)
10-12 years	18 (60)	16 (61,53)	38 (67,85)
>12 years	7 (23,33)	5 (19,23)	10 (17,85)
Family income			
<1 million	15 (50)	12 (46,15)	27 (48,21)
1-2 million	9 (30)	11 (42,30)	20 (35,71)
>2 million	6 (20)	3 (11,53)	9 (16,07)

Table 2: Analysis of tobacco smoke exposure risk in pregnant women in the IFA group and the MO + IFA group.

Aspect of tobacco smoke exposure	Kelompok		p-value*
	IFA n=30	MO + IFA n=26	
	n(%)	n(%)	
There are smoker family members at home			
• Yes	18(60)	24(92,30)	0,005**
• None	12(40)	2(7,69)	
Number of smokers in the house			
• 0	12(40)	3(11,53)	
• 1	12(40)	12(46,15)	
• 2	5(16,67)	11(42,30)	0,018*
• 3	1(3,33)	0(0)	
Number of tobaccos consumed by smokers at home			
• 0	12(40)	3(11,53)	
• 1-4	7(23,33)	5(19,23)	0,002*
• 5-10	10(33,33)	14(53,84)	
• >10	1(3,33)	4(15,38)	
Amount of time in a day smoking at home			
• Never	12(40)	3(11,53)	
• < 1 hour	9(30)	9(34,61)	0,026
• 1-4 hours	6(20)	10(38,46)	
• >4 hours	3(10)	4(15,38)	
Amount of days in a week smoking at home			
• 0	12(40)	3(11,53)	0,020*
• 1-3 hari	6(20)	5(19,23)	
• 4-7 hari	12(40)	18(69,23)	
There are smokers in work place			
• Yes	2(6,67)	2(7,69)	0,638***
• None	28(93,33)	24(92,30)	
Amount of time in a day coworker smoking at work place			
• Never	28(100)	24(92,30)	
• < 1 hour	1(3,33)	1(3,84)	0,868*
• 1-4 hours	1(3,33)	0(0)	
• >4 hours	0(0)	1(3,85)	
Amount of days in a week coworkers smoking at work place			
• 0	28(93,33)	24(92,30)	0,883*
• 1-3 days	1(3,33)	1(7,69)	
• 4-7 days	1(3,33)	0(0)	

* Mann-Whitney test, **Pearson Chi-Square, ***Fisher's Extract test

Table 3: Comparison of serum cotinine levels between pregnant women in the IFA group and the MO + IFA group.

Variable	Group		p-value*
	IFA n=30	MO + IFA n=26	
	Mean ±SD	Mean ±SD	
Cotinin serum (ng/mL)	55,81±16,83	58,57±16,70	0,535

*Independent T test

In the third trimester, 56 pregnant women met the criteria with 26 receiving MO + IFA supplements and 30 pregnant women receiving IFA supplements only. Tobacco smoke exposure data were collected by a questionnaire, serum cotinine levels were taken in the third trimester by blood sampling. Examination of serum cotinine levels using the ELISA method in the Human Research Center laboratory, Hasanuddin University Hospital. Data on exposure to tobacco smoke and analyzed by compare the tobacco smoke exposure between MO + IFA group and IFA group. Serum cotinine levels were compared between the two groups with independent T test.

RESULTS

Generally, pregnant women in both groups are aged 20-30 years, do not work, have studied for 10-12 years with a family income of more than 1 million rupiah. The data also shows that the husbands of pregnant women in both groups mostly work in the private sector and have studied for 10-12 years. Data of tobacco smoke exposure in pregnant women based on a questionnaire is shown in the following table.

Based on the questionnaire data, it was found that pregnant women in the MO + IFA group had a higher risk of tobacco smoke exposure than the IFA group at home. This can be seen from the presence of smokers at home, the number of smokers at home, the number of tobacco consumed and the frequency of exposure to secondhand smoke at home. The results of the different test analysis of cigarette smoke exposure at home showed a significant difference ($p<0.05$). Exposure to tobacco smoke in the workshop did not show a significant difference in the two groups, apart from the fact that generally the pregnant women did not work, only a few reported exposures to secondhand smoke in the workplace.

Examination of serum cotinine in pregnant women in the two groups did not show a significant difference ($p=0.535$) although serum cotinine levels in pregnant women in the MO + IFA group were higher than in the IFA group.

DISCUSSION

Exposure to ETS in pregnant women causes increased levels of CO, nicotine and cotinine in the mother's serum or urine, in fetus and in the amniotic fluid. The ETS effect the pregnant women from the first semester to the third semester. Pregnant women are usually exposed to ETS in various places for different durations. Places that have the potential to become ETS exposure spots is at home, at work and the social place.[19]

Nicotine exposure in pregnant women cause placental vascular vasoconstriction, reduce placental blood flow and reduce trophoblast invasion which disrupt the formation of good placental circulation. Furthermore, placental hypoxia interferes the placental invasion. Placenta previa is a form of placental invasion disorder.[20] Nicotine can lead a significant decrease in the mitotic potential of cytotrophoblast tissue in in vitro tests. This effect is also found in smoker women. This effect may explain the mechanism of impaired placental development during the early phase of pregnancy caused by placental ischemia that lead to fetal death.[8]

Serum cotinine in this study is the result of nicotine metabolism which is the main component in tobacco cigarette. Nicotine exposure in pregnant women can cause placental vasoconstriction which inhibits the formation of good placental circulation. Furthermore, placental hypoxia interferes of placental invasion. Impaired placental circulation lead to impaired fetal development and increasing the risk of low birth weight (LBW). It is still unclear which smoking component effect the reduction in birth weight due to the complexity of the tobacco components. However, it has been confirmed that smoking components affect uterine blood flow and ultimately affect fetal growth.[20]

Based on the tobacco smoke exposure data, it was found that the risk of exposure to secondhand smoke in pregnant women in the MO + IFA group was significantly higher ($p<0.05$) compared to pregnant women in the IFA group. It can be assumed that nicotine levels in pregnant women in the MO + IFA group were expected to be higher and the risk of pregnancy due to smoking is greater in this group. However, the results of examination of serum cotinine levels showed that there was no significant difference in serum cotinine levels in pregnant women in the MO + IFA group (58.57 ± 16.70 ng/mL) and pregnant women in the IFA group (55.81 ± 16.83 ng/ mL), although the mean serum cotinine level of the MO + IFA group was higher than that of the IFA group.

This shows that although the risk of exposure to secondhand smoke in pregnant women in the MO + IFA group was significantly higher, the serum cotinine levels in that group were not much different from the IFA group. This discrepancy can be caused by several things, the first is the possibility of under reported or over reported questionnaire data. Another possible cause is the effect of MO intervention on serum cotinine levels.

Moringa leaves is known as a source of nutrition and are referred to as superfoods and contain antioxidants. Currently, we have not found specific study on the effect of Moringa leaves on serum cotinine levels, but there are studies that examine the effect of antioxidants on nicotine metabolism. The results of the study showed that smokers who consume antioxidant supplements (ascorbic acid) have a significant decrease urinary cotinine level compared to controls who received placebo. Supplementation of the antioxidant ascorbic acid likely suppresses CYP450-dependent nicotine metabolism over time. The effect of the same antioxidant effect may also be found in other sources of antioxidants such as moringa leaves which can suppress nicotine metabolism so that serum cotinine levels in the MO + IFA group are almost the same as in the IFA group, but this requires further study by measuring oxidative stress or other variables relate.[21,22]

Nicotine metabolism is mediated by CYP2A6 in the liver. CYP2A6 expression influences nicotine metabolism in pregnant women and related to nicotine clearance. Increased metabolism and nicotine clearance during pregnancy have an impact on reducing the adverse effects of nicotine and reduced the effect on pregnancy.[18,23] Nicotine and cotinine levels in the body are the result of exposure to tobacco smoke that enters the body, nicotine metabolic rate, nicotine and cotinine clearance and various influencing factors such as nutrition, metabolic, hormonal and immunity. With improved nutrition, it is expected to lower effects of tobacco smoke on pregnant women and the risk of poor pregnancy outcomes.

The limitation of this study is that there was no examination of serum cotinine levels before the intervention so the changes in cotinine levels were not known. More study is needed on the effect of Moringa leaf extract on oxidative stress in pregnant women exposed to ETS and its effect on the placenta and pregnancy outcomes.

CONCLUSION

Moringa leaf extract supplementation to pregnant women with high tobacco smoke exposure has serum cotinin levels similar to pregnant

women with lower exposure to tobacco smoke. Moringa leaf extract help pregnant women exposed tobacco smoke to reduce the effects and improve the pregnancy outcomes.

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