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COMPARISON OF THE EFFECT OF SALAMEXTRACT *(Syzygium polyanthum (Wight) Walp)* ADMINISTRATION 200 mg AND 300 mg ON APOLIPOPROTEIN-B LEVELS IN DISLIPIDEMIC PATIENTS

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Abstract

Background: Dyslipidemia is a risk factor for cardiovascular disease. Meanwhile hyper-Apolipoprotein-B is a major and independent risk factor for cardiovascular disease. Bay leaf extract is reported to be effective in reducing cholesterol and triglyceride levels, and is expected to reduce Apolipoprotein-B, but the therapeutic dose is not known with certainty. This study aims to compare the effectiveness of bay leaf extract at a dose of 200 mg and 300 mg against Apolipoprotein-B levels in dyslipidemic patients.

Methods: This research is an experimental study conducted on 30 people with dyslipidemia. Group A (n = 15) and group B (n = 15) were randomly selected in a double disguise, each receiving 200 mg and 300 mg bay leaf extract capsules for 30 days. Apolipoprotein-B levels were measured before and after treatment. Data analysis was performed with SPSS where p <0.05 was stated as significant

Results: Apolipoprotein-B levels before drug administration were compared with after treatment. Examination was found to decrease in group A ((109.8 + 13.71 vs 101.47 + 17.54) ng / dL; p value = 0.001) and group B ((122.6 + 21.08 vs 108.6 + 19.06) ng / dL; p value = 0.001), statistically significant both in group A and group B. The decrease in Apolipoprotein-B levels in group II was greater than in group I, but it was not statistically significant ((14 vs 8.33) mg / dL; p value = 0.567).

Conclusion: Giving bay leaf extract (Syzygium polyanthum) 2x200mg and 2x300mg for 30 days decreased Apolipoprotein-B levels. The decrease in Apo-B levels was greater in 2x300mg extract compared to 2x200mg, but statistically the difference was not significant.

Keywords: Apolipoprotein-B, Syzygium polyanthum, and dyslipidemia.

Introduction

Background

Dyslipidemia is a condition characterized by changes in the concentration of one or more lipoproteins in the blood (ie total cholesterol, low density lypoprotein (LDL), high density lypoprotein (HDL) and triglycerides. In Indonesia, the prevalence of hypercholesterolemia is estimated at 16.2% in women and 14% in men.[1] Dyslipedemia is a risk factor for atherosclerosis and cardiovascular disease.Many evidence shows that dyslipidemia is significantly associated with the inflammatory process Inflammation is triggered by the entry of lipoprotein-rich cholesterol into the walls of blood vessels and followed by macrophages forming foamcells.[2] Previous studies conducted found that there was a significant relationship between HDL, LDL, and triglycerides with Apo-B.[3,4]

Management of dyslipidemia by using synthetic drugs has a high risk because of long-term consumption and side effects that cannot be ignored, including myopathy, tremor, vertigo, parastesia, central nervous disorders, anxiety, abdominal pain, constipation and bloating. Therefore, people are starting to use drugs from natural ingredients that are believed to be safer and have relatively few side effects on long-term use.

Empirically, bay leaf boiled water is used by the community for the treatment of cholesterol-related diseases. Bay leaf contains flavonoids that can reduce cholesterol levels and triglyceride levels in the blood, protect arteries from damage and reduce the amount of cholesterol deposited on the endothelial surface of arteries. Research in mice shows that flavonoids can reduce lipid peroxidation through HMG-CoA reductase enzyme inhibitors so that cholesterol synthesis decreases.[5]

Although bay leaves have long been used in the treatment of dyslipidemia, effective doses for achieving therapeutic effects have not been clearly established. Therefore this study aims to compare the effectiveness of 200 mg and 300 mg bay leaf extracts against apolipoprotein-b levels in dyslipidemic patients.

Methods

This research is an experimental study (double blind randomized clinical trial) conducted in patients with dyslipidemia who are over 18 years old in the Internal Medicine polyclinic at Adam Malik General Hospital Medan from September 2017 to February 2018. Subjects who have impaired kidney, liver, comorbid diabetes mellitus and acute coronary syndromes, or currently in pregnancy, were excluded from this study. All research procedures were approved by the research ethics commission.

A total of 30 subjects were included in this study who were divided into two groups. The first group received bay leaf extract (*Syzygium polyanthum*) 200 mg twice daily, and the second group received the same extract at a dose of 300 mg twice daily in capsule form for 30 days. All study subjects did not take antidislipidemia for 2 weeks before the study began and during the intervention.

The making of bay leaf extract is carried out by pharmacists at the Faculty of Pharmacy, University of North Sumatra, starting from the supply of bay leaf (*Syzygium polyanthum (Wight) Walp*), processing, determination of water content and levels of water and ethanol soluble extracts, making capsule preparations, filling granular powders into the capsule until determining the weight of the capsule and the time of disintegration. All capsules, both containing 200 mg bay leaf extract and 300 mg have the same final capsule weight, which is 500 mg.

All subjects underwent anthropometric examinations, measurements of waist circumference, blood pressure and blood tests before and after treatment. Blood tests include lipid profile (Apo-B, total cholesterol, triglycerides, LDL cholesterol and HDL), routine blood, kidney function (ureum, creatinine), liver function (SGOT, SGPT) and fasting blood glucose levels through venous blood examination using the technique of enzymatic calorimetric. On the 11th day, 21st, and 31st, all subjects were evaluated to determine the side effects that might occur during the treatment.

Statistical analysis was performed with the using SPSS software, where a p value <0.05 was declared significant.

Results

This research involved 30 subjects who were divided into 15 people in group A (treated with 200 mg bay leaf extract) and 15 people in group B (treated with300 mg bay leaf extract). The baseline characteristics of the research subjects can be seen in table 1.

Table 1 shows that there were no significant differences between the two groups, except in terms of total cholesterol levels. There were no significant differences in demographic, anthropometric and Apo-B characteristics between the two groups.

Table 1. Characteristic of subjects

Baseline characteristic	**Group A 2x200 mg (n = 15)**	**Group B 2x300 mg (n = 15)**	***p***
Gender Female / Male	15 / 0	14/ 1	-

Age (years old)	50.40 ±5.22	50.07 ±4.73	0.81
Waist size(cm)	88,33 ± 7,18	92,36 ± 8,54	0.20
Height (m)	1,56 ±0.04	1,55±0,05	0.93
Weight(kg)	67.00 ±10.65	66.33±5.56	0.78
BMI(kg/m^2)	27.54 ±3.22	27.40±0.97	0.83
SBP (mmHg)	118,33 ± 5,23	118,67 ± 7,19	0.92
DBP (mmHg)	77,33 ± 4,58	76,00 ± 5,07	0.44
TC (mg/dL)	229,13 ± 14,99	271,73 ± 52,17	0.005*
LDL (mg/dL)	155,00 ± 22,55	175,73 ± 35,40	0.06
HDL (mg/dL)	51,13 ± 7,73	49,33 ± 8,53	0.55
TG (mg/dL)	149,93 ± 70,56	202,80 ± 114,57	0.13
ApoB	109,8 ± 13,71	122,6 ± 21,08	0.56
FBG (mg/dL)	94,20 ± 15,03	91,47 ± 85,00	0.60
Ureum (mg/dL)	21.93 ±10.35	25.13±13.75	0.24
Creatinin (mg/dL)	0.61±0.10	0,75 ± 0,28	0.27

BMI=body mass index, SBP=systolic blood pressure, DBP=diastolic blood pressure, TC= total cholesterol, LDL=low density lipoprotein, HDL=high density lipoprotein, TG=triglyceride, ApoB=apolipoprotein B, FBG=fasting blood glucose

Furthermore, bay leaf extract was administered for 30 days in each group, and a statistical analysis was performed with the results attached in table 2:

Table 2. Comparison of ApoB levels and lipid profiles in group A and group B

Variable	**Group A (n = 15)**				**Group B (n = 15)**				**Δ*p***
	Mean ± SD				**Mean ± SD**				
	D_0	**D_{30}**	**Δ**	***p*$_a$**	**D_0**	**D_{30}**	**Δ**	***p*$_b$**	
ApoB	109,9 ± 13,71	101,47 ± 17,54	8,33	0,001*	122,6 ± 21,08	108,6± 19,06	14	0,001*	0,567*
KT (mg/dL)	229,13 ± 14,99	217,53 ± 23,10	11,60	0,012*	271,73 ± 52,17	225,93 ± 30,80	45,80	0,002*	0,785
LDL (mg/dL)	155,00 ± 22,55	145,67 ± 29,37	9,33	0,035*	175,73± 35,40	145,72± 33,10	30,47	0,001*	0,573
HDL (mg/dL)	51,13 ± 7,73	50,07 ± 7,5	1,07	0,318	49,33 ± 8,53	47,73 ± 5,80	1,60	0,344	0,019*
TG (mg/dL)	149,93 ± 70,56	112,13 ± 37,92	37,80	0,009*	202,80 ± 114,57	138,60 ± 49,76	64,2	0,016*	0,050*

SD: Standard Deviation, TC= total cholesterol, LDL: *Low Density Lipoprotein*, HDL: *High Density Lipoprotein*, TG=triglyceride, D_0: day 0 (before treatment), D_{30}: day 30 (after treatment), delta: the difference between the results of the examination before being given the drug is reduced after being given the drug for 30 days

Statistical analysis showed that there was a significant decrease in ApoB levels of dyslipidemic patients who were the subjects of the study, both in group A and in group B. The mean ApoB levels of subjects in group A (obtaining 2x200 mg bay leaf extract) dropped significantly from 109.8 ± 13, 71mg / L to 101.47 ± 17.54mg / L ($p < 0.05$). There was also a significant decrease in ApoB levels in group B (obtaining 2x300 mg bay leaf extract) from 122.6 ± 21.08 mg / L to 108.6 ± 19.06 mg / L ($p < 0.05$). The decrease in cholesterol levels in subjects who received 2x300 mg bay leaf extract was greater than those who received 2x200 mg bay leaf extract, but this difference was not statistically significant ($p = 0.56$)

In addition to ApoB, bay leaf extract was also proven to be able to reduce total cholesterol, LDL, and triglyceride levels, both at doses of 2x200 mg and 2x300 mg. Although the decrease in the levels of the three variables was greater in the group that received 2x300 mg bay leaf extract, statistical analysis showed that the difference was not significant ($p > 0.05$). The only parameter that did not experience significant changes after giving bay leaf extract for 30 days was serum HDL levels, both in group A and in group B.

In general, it can be concluded that bay leaf extract can significantly reduce Apo-B, LDL, total cholesterol and HDL levels, and there is no significant difference in effectiveness between 200mg and 300mg doses.

Discussion

Dyslipidemia has been widely recognized as a risk factor for atherosclerosis and cardiovascular disease. Meanwhile, atherosclerosis itself is a disease of blood vessels due to chronic inflammation and is the single most important contributor to cardiovascular-related morbidity and mortality[6.]

Bay leaf has long been trusted by the community as a traditional medicine for dyslipidemia. Previous studies showed that bay leaves contained various active substances. which can reduce cholesterol and triglyceride levels, including flavonoids that can reduce cholesterol levels by inhibiting the enzyme HMG-Co A reductase which plays an important role in cholesterol biosynthesis so that the synthesis of apoB 100 decreases and LDL receptor expression on the surface of hepatocytes increases. Blood LDL cholesterol will be uptake by hepatocytes to be metabolized resulting in blood LDL cholesterol levels also decreased[5,7.]

Bay leaf also contains saponins that can increase bile acid excretion thereby increasing the conversion of cholesterol to bile acids and can inhibit the absorption of cholesterol from food in the intestine by forming complex bonds that do not dissolve. Another active ingredient of bay leaf is tannin which is able to react with mucosal proteins and intestinal epithelial cells thereby inhibiting fat absorption.[5,7]

Giving salam leaf extract to white male Wistar hyperlipidemia strain rats with stratified doses obtained from fresh bay leaves by 0.18 grams, 0.36 grams and 0.72 grams every day for 15 days, can reduce the serum triglyceride levels of these mice, by the greatest reduction in dosing is 0.72 gram[7]

The results of this study indicate that there are significant differences in total cholesterol, LDL cholesterol, and triglyceride levels with $p < 0.05$ before and after treatment with different doses. Evidently there was a significant decrease in total cholesterol, LDL cholesterol and triglyceride levels in both groups for 30 days (11.6 mg / dL, p 0.012 and 45.8 mg / dL, p 0.002) (9.33 mg / dL , $p < 0.035$ and 30.47 mg / dL, $p < 0.001$) (37.8 mg / dL, p 0.009 and 64.2 mg / dL, $p < 0.016$).

This is in line with Siregar's study of 20 people with hypercholesterolemia using a non-comparative clinical trial method, who found that the combination of bitter extract and bay leaf with a dose of 3 x 1 capsule daily for 14 days significantly reduced cholesterol levels (p value < 0.05) without significant side effects. Decrease in cholesterol levels on the 7th day by 20.03% and 14th day 35.5% .[8]

The weakness of this study is that there is no uniform diet and physical activity on the research subjects so that it can cause bias in the results of the study. The treatment time of 30 days was also considered too short to detect long-term side effects that might arise due to the administration of bay leaf extract (*Syzygium polyanthum*). Given the statistically insignificant difference in decreasing Apo-B levels between treatment groups A and B, further research needs to be done using higher drug dosages, monitoring diet compliance, and longer duration of treatment to obtain better results.

Conclusion

Both 200 mg and 300 mg bay leaf extract capsules have been shown to be effective in reducing Apolipoprotein-B levels in dyslipidemic patients. The decrease in Apo-B levels was greater in 2x300 mg extract than 2x200 mg, but it was not statistically significant.

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