



JETROMI

Journal of Endocrinology, Tropical Medicine, and Infectious Disease



The Relationship Between Lipoprotein (A) And Lipid Profile In Patients Treated With Bay Leaf Extract [Syzygium Polyanthum (Wight) Walp] In Patients Dyslipidemia

Catur Priawari¹, Santi Syafri²

¹Resident Department of Internal Medicine, Faculty of Medicine, University of North Sumatra

²Endocrinology and Diabetes Division, Department of Internal Medicine, Faculty of Medicine, University of North Sumatra

Abstract. Background: Increased Lp(a) accelerates atherosclerosis using cholesterol deposits in tunica. The purpose of the study was to assess the relationship of decreased Lp(a) with lipid profile in patients with dyslipidemia given bay leaf extract [syzygium polyanthum (Wight) Walp] treatment. **Method:** Thirty subjects were divided into 2 groups: group I received salam leaf extract therapy 2 x 200 mg and group II received salam leaf extract therapy 2 x 300 mg per day capsules for 30 days randomly selected and double blind. Examination of Lp(a), total cholesterol, LDL-C, HDL-C and TG before and after research. The manufacture of bay leaf extract is done by maseration, the extraction process using ethanol 70%, then the extract is inserted in the capsule. **Result:** In groups I and II there were significant differences in variable Lp(a) and lipid profiles after treatment except HDL-C. There is a significant correlation between Lp(a) and LDL at salam leaf extract therapy doses of 2x200 mg per day. **Conclusion:** Decrease in Lp(a) is significantly correlated with decreased LDL-C. Salam leaf extract therapy can predict decreased cardiovascular risk in patients with dyslipidemia.

Keyword: Lp(a), lipid Profile, Dyslipidemia., Syzygium Polyanthum (Wight) Walp

Abstrak. Latar belakang: Peningkatan Lp(a) mempercepat aterosklerosis dengan cara deposit kolesterol pada tunika. Tujuan dari penelitian untuk menilai hubungan penurunan Lp(a) dengan profil lipid pada pasien dislipidemia yang diberikan pengobatan ekstrak daun salam [syzygium polyanthum (Wight) Walp]. **Metode:** Tiga puluh subjek penelitian dibagi atas 2: kelompok I menerima terapi ekstrak daun salam 2 x 200 mg dan kelompok II menerima terapi kapsul ekstrak daun salam 2 x 300 mg perhari selama 30 hari yang dipilih secara acak tersamar ganda,. Dilakukan pemeriksaan Lp(a), kolesterol total, kolesterol LDL, kolesterol HDL dan TG sebelum dan sesudah penelitian. Pembuatan ekstrak daun salam dilakukan dengan cara maserasi, dan proses ekstraksi menggunakan ethanol 70%, selanjutnya ekstrak dimasukkan dalam kapsul. **Hasil:** Pada kelompok I dan II terdapat perbedaan yang signifikan variable Lp(a) dan profil lipid sesudah pengobatan kecuali HDL. Terdapat korelasi yang signifikan antara Lp(a) dengan LDL pada dosis 2x200 mg perhari kapsul ekstrak daun salam. **Kesimpulan:** Penurunan Lp(a) berkorelasi signifikan dengan

*Corresponding author at: Resident Department of Internal Medicine, Faculty of Medicine, University of North Sumatra

E-mail address: prianwaricatur@gmail.com

penurunan kolesterol LDL. Pengobatan kapsul ekstrak daun salam dapat memprediksi penurunan risiko kardiovaskular pada pasien dyslipidemia.

Kata Kunci: *Lp(a), Profil Lipid, Dyslipidemia., Syzygium Polyanthum (Wight) Walp*

Received 14 October 2020 | Revised 23 November 2020 | Accepted 30 November 2020

1 Introduction

Increased levels of Lp(a) have the potential to increase the risk of cardiovascular disease through prothrombotic/ anti-fibrinolytic effects because Lp(a) has a homologous structural with plasminogens and plasmin but has no fibrinolytic activity. Increased Lp(a) accelerates atherosclerosis by means of cholesterol deposits in tunica.[1] To raise awareness of Lp(a), an expert panel from the National Cholesterol Education Program Adult Treatment Panel, the European Atherosclerosis Society, and the National Lipid Association made efforts to advise clinicians on screening and modulating increased Lp(a). [3]

Lp(a) particles consist of apolipoprotein (a), glycoproteins, encoded by the LPA gene and bound to apolipoprotein B of LDL. [2] CAD risk is associated with Lp(a) molar concentration and apo(a) size, and both are independent risk factors for CAD.

From previous research, it concluded there was no clear evidence that statin treatment can lower levels of Lp(a). [5] Administration of bay leaf extract (*Syzygium polyanthum*) for 30 days at doses of 2x200 mg and 2x300 mg can significantly decrease the level of Lp(a) (25.52 + 31.36 vs 22.66 + 31.12 ng/dL, $p = 0.001$ and 27.81 + 33.79 vs 25.65 + 33.23) ng/d, $p = 0.013$, respectively). [6]

The purpose of the study was to assess the relationship of decreased Lp(a) with lipid profile in patients with dislipidemia given the treatment of bay leaf extract.

2 Methods

Dyslipidemia is determined as an increase or decrease in low-density lipoprotein (LDL) cholesterol, or a decrease in high-density lipoprotein cholesterol (HDL) as an important risk factor against coronary heart disease (CHD) and stroke.[7] The subject research is divided into 2: group I received bay leaf extract therapy 2 x 200 mg and group II received extract therapy 2 x 300 mg daily for 30 days randomly selected and double blind, monitored eating compliance and consumption of bay leaf extract capsules. Examination of Lp(a), total cholesterol, LDL-C, HDL-C and TG before and after research. The manufacture of bay leaf extract is done by means of maceration, the extraction process using ethanol 70%, then the extract is included in the capsule. [8] Method of measuring Lp(a) using monoclonal anti-apo(a) antibodies and commercial kits measure Lp(a) using radial immunodiffusion assay. [9]

Data were analyzed using the SPSS-21 application. Independent T Test or Man Whitney U analytical statistical analysis is used to test the differences in numerical variables between group I and group II. The Dependent T or Wilcoxon test to test differences in numerical variables in each research group before and after was given a superman correlation treatment and test. Differences are considered statistically meaningful when the value of $p < 0.05$.

3 Results

In table 1. there is no significant difference except total cholesterol and Lp(a) between groups 1 and group II.

Table 1 Basic research data

Variable	Group I (n = 15) mean±SD	Group II (n = 15) mean±SD	p
Gender: W/M	15 / 0	14/ 1	
Age (year)	50.40 ± 5.22	50.07 ± 4.73	0.818
WC (cm)	88,33 ± 7,18	92,36 ± 8,54	0.207
BMI (kg/m ²)	27.54 ± 3.22	27.40 ± 0.97	0.836
FBG (mg/dL)	94,20 ± 15,03	91,47 ± 85,00	0.604
TC (mg/dL)	229,13 ± 14,99	271,73 ± 52,17	0.005*
LDL-C (mg/dL)	155,00 ± 22,55	175,73 ± 35,40	0.066
HDL-C (mg/dL)	51,13 ± 7,73	49,33 ± 8,53	0.550
TG (mg/dL)	149,93 ± 70,56	202,80 ± 114,57	0.139
Lp(a) (mg/dL)	25,52 ± 31,36	27,81 ± 33,79	0.013*

Note: D: day; WC: waist circumference; BMI: body mass index; FBG: fasting blood sugar; TC: total cholesterol; LDL-C: low density lipoprotein; HDL-C: high density lipoprotein; TG: triglyceride; Lp(a): lipoprotein (a); * $p < 0.05$

In table 2. There is a significant difference between variable lipid profiles and Lp(a) after treatment of bay leaf extract except HDL-C.

Table 2 Differences in Anthropometric Variables and Lipid Profile Before and after Research

Variable	Kelompok I (n = 15) Mean \pm SD			Kelompok II (n = 15) Mean \pm SD		
	D ₀	D ₃₀	p _a	D ₀	D ₃₀	p _b
WC (cm)	91,46 \pm 4,43	91,50 \pm 4,37	0,056	93,33 \pm 1,71	93,36 \pm 1,65	0,317
BMI (kg/m ²)	27,54 \pm 3,21	27,53 \pm 3,19	1,000	27,39 \pm 1,71	27,39 \pm 0,95	0,635
FBG (mg/dL)	94,20 \pm 15,03	89,05 \pm 13,24	0,116*	91,46 \pm 18,27	88,06 \pm 16,47	0,880
TC (mg/dL)	229,13 \pm 14,99	217,53 \pm 23,10	0,012*	271,73 \pm 52,17	225,93 \pm 30,80	0,002*
LDL-C (mg/dL)	155,00 \pm 22,55	145,67 \pm 29,37	0,035*	175,73 \pm 35,40	145,72 \pm 33,10	0,001*
HDL-C (mg/dL)	51,13 \pm 7,73	50,07 \pm 7,5	0,318	49,33 \pm 8,53	47,73 \pm 5,80	0,344
TG (mg/dL)	149,93 \pm 70,56	112,13 \pm 37,92	0,009*	202,80 \pm 114,57	138,60 \pm 49,76	0,016*
Lp(a) (mg/dL)	25,52 \pm 31,36	22,66 \pm 31,12	0,001*	27,81 \pm 33,79	25,65 \pm 33,23	0,013*

Note: D: day; WC: waist circumference; BMI: body mass index; FBG: fasting blood sugar; TC: total cholesterol; LDL-C: low density lipoprotein; HDL-C: high density lipoprotein; TG: triglyceride; Lp(a): lipoprotein (a); *p<0.05

In table 3, there is a significant correlation between Lp(a) and LDL-C with a dose of bay leaf extract 400 mg per day (r: 0,561, p: 0.030*).

Table 3 Correlation between Lp (a) with anthropometric variables and lipid profiles

Variabel	Group I		Group II	
	r	p	r	p
WC (cm)	0,360	0,188	0,109	0,699
BMI (mg/dL)	0,025	0,929	-0,209	0,454
FBG (mg/dL)	0,181	0,465	0,725	0,002
TC (mg/dL)	0,490	0,64	- 0,182	0,510
LDL-C (mg/dL)	0,561	0.030*	0.425	0,114
HDL-C (mg/dL)	-0,244	0,381	-0,579	0,019*
TG (mg/dL)	0,079	0,781	0,221	0,428

Note: D: day; WC: waist circumference; BMI: body mass index; FBG: fasting blood sugar; TC: total cholesterol; LDL-C: low density lipoprotein; HDL-C: high density lipoprotein; TG: triglyceride; Lp(a): lipoprotein (a); *p<0.05

4 Discussion

Bay leaves contain tannins, *galokatekin*, flavonoids, *saponins (triterpenoids)*, and essential oils (*sesquiterpen*). In addition, bay leaves also contain several vitamins, including vitamin A, vitamin C, vitamin E, thiamin, riboflavin, niacin, vitamin B6, vitamin B12, and folate. The results of in vitro studies show flavonoids work as inhibition of the enzyme *HMG-CoA reductase* so that cholesterol synthesis decreases. *Saponins* can form complex bonds that are insoluble with cholesterol derived from food, bind to bile acids forming micelles and increase cholesterol binding by fiber so that cholesterol cannot be absorbed by the gut. Tannin inhibits the absorption of fat in the intestine by reacting with mucosal proteins and intestinal epithelial cells .[10]

The results of the study in mice model dyslipidemia showed that infusion of bay leaves with concentrations of 5%, 10%, 20% for 2 weeks significantly lowered TC ($p < 0.05$), and its potency was equivalent to simvastatin. [11] Some studies in families with CVD, there is a positive correlation between Lp(a) and LDL-C, TC, and *Apolipoprotein B*, this suggests there is a link between Lp(a) levels and lipid profiles. Serum Lp(a) does not correlate with ESR ($r: 0.27$, $p: 0.028$), MHAQ ($r = 0.11$, $p: 0.37$). [12] In addition to Lp(a) correlated with LDL-C is also negatively correlated with TG levels in diabetic patients. Therefore, these results suggest that the treatment of diabetic dyslipidemia can indirectly affect the concentration of Lp(a). [13]

In this study, treatment of bay leaf extract of 2x200 mg per day: decrease in Lp(a) was significantly correlated with LDL-C ($r: 0.643$; $p: 0.010$), while treatment of bay leaf extract was 2x300 mg per day, decreased Lp(a) significantly negatively correlated with HDL-C ($r: -0.573$; $p: 0.026$).

5 Conclusion

Decreased Lp(a) is significantly correlated with a decrease in LDL-C with treatment of bay leaf extract. Treatment of bay leaf extract can predict decreased cardiovascular risk in patients with dyslipidemia.

REFERENCES

- [1] Nordestgaard BG, Chapman MJ, Ray K, Borén J, Andreotti F, Watts GF, et al.. Lipoprotein(a) as a cardiovascular risk factor: current status. *European Heart Journal* vol.31, p:2844–53. 2010
- [2] Davidson, MH, Ballantyne CM, Jacobson TA, Bittner VA, Braun LT, Brown, AS. et al.. Clinical utility of inflammatory markers and advanced lipoprotein testing: advice from an expert panel of lipid specialists. *J. Clin. Lipidol.* vol. 5, p: 338–67. 2011
- [3] Schmidt K., Noureen A., Kronenberg F., Utermann G. Structure, function, and genetics of lipoprotein (a). *J Lipid Res* vol. 57, p:1339–59. 2016
- [4] Kral B.G., Kalyani R.R., Yanek L.R., Vaidya D., Fishman E.K., Becker D.M., et al. Relation of plasma lipoprotein(a) to subclinical coronary plaque volumes, three-vessel and left main coronary disease, and severe coronary stenoses in apparently healthy

- African-Americans with a family history of early-onset coronary artery disease. *Am J Cardiol* vol. 118, p:656–61. 2016
- [5] Julius U. Lipoprotein apheresis in the management of severe hypercholesterolemia and of elevation of lipoprotein(a): current perspectives and patient selection. *Medical Devices: Evidence and Research*. Vol.9, p:349–60. 2016
- [6] Prianwari C, Lindarto D, Syafril S. Comparison Bay Leaf (*Syzygium Polyanthum* (Wight) Walp) Ekstrakt With 400 Mg And 600 Mg Dose On Lipoprotein(A) Concentration In Dyslipidemic Patients. *International Journal of Research Science & Management* 6(9): September, 2019
- [7] Fodor G. Primary prevention of CVD: treating dyslipidaemia. *Clin Evid Handbook* p:39-40. Dec 2010
- [8] Depkes RI, Parameter Standar Umum Ekstrak Tumbuhan Obat, Edisi I, Departemen Kesehatan Republik Indonesia, Jakarta. 2000
- [9] Utermann G.. Lipoprotein(a). In: *The Metabolic and Molecular Bases of Inherited Disease*. 8th ed. Scriver CR, Beaud, Sly WS, Valle D (eds). McGraw-Hill. New York. 2001
- [10] Yulinda W, Lindarto D, Syafril S.. Efektifitas Kombinasi Ekstrak Sambiloto (*Andrographis paniculata* (burm.f.) nees) dan Daun Salam (*Syzygium polyanthum* (wight) walp) terhadap Kadar hs-CRP pada Pasien Dyslipidemia. *Majalah Kedokteran Nusantara*. Vol.15, no.31, p.133-7. 2018
- [11] Prahastuti S, Tjahjani S, Hartini E. The effect of bay leaf infusion (*Syzygium polyanthum* (Wight) Walp) to decrease blood total cholesterol level in dyslipidemia model wistar rats. *Jurnal Medika Planta*. Vol.1, no.4, : 27-32. 2011
- [12] Correlation between lipid profile and lipoprotein (a) with inflammatory activity of rheumatoid arthritis. Rezaieyazdi Z, Maghrebi M, Hashemzadeh K, Hatef M, Esmaily M, Khodashahi M. *Rheumatology Research*., Vol. 4, No. 3, July. 2019
- [13] Hernández, C, Chacón, P, García-Pascual L, Simó, R. Differential Influence of LDL Cholesterol and Triglycerides on Lipoprotein(a) Concentrations in Diabetic Patients. *Diabetes Care* 24:350–55, 2001.