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ORIGINAL ARTICLE

THERAPEUTIC EFFECT OF *HIJAMAH* (CUPPING THERAPY) ON LIPID PROFILES AND APOLIPOPROTEIN IN HYPERCHOLESTEROLEMIC PATIENTS

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ABSTRACT

Hijamah or cupping therapy has a therapeutic effect on cholesterol. However, there is still a lack of studies that investigate the potential effect of cupping in managing apolipoprotein B as a proatherogenic agent and apolipoprotein A-1 as an anti-proatherogenic agent. This study aims to explore the effect of cupping therapy on lipid profiles and apolipoproteins in hypercholesterolemic patients. A pre-post experimental design without controls were used. Consecutive sampling was applied to 40 dyslipidemia respondents. The lipid profiles and plasma apolipoproteins A-I (ApoA-I) and apolipoproteins B (ApoB) were measured after the respondents fasted for 12 hours before cupping therapy and 24 hours after cupping therapy. The Wilcoxon sign-rank test was used for the data analysis. The following results were found: average lipid profile (mg/dL) and apolipoprotein (µg/mL) pre vs post cupping: Total Cholesterol (Pre-test vs Post-test) 328 vs 283 (P-value 0.003); TG 238 vs 204 (P- value 0.007); HDL 78.5 vs 85 (P- value 0.000); LDL 195 vs 158 (P- value 0.001); ApoA-1 0.07 vs 0.67 (P-value 0.000); ApoB 2.04 vs 1.82 (P-value 1.000); ApoB/ApoA-1 ratio 30.22 vs 2.93 (P- value 0.000); cholesterol/HDL ratio 4.06 vs 3.08 (P- value 0.332); TG/HDL ratio 3.01 vs 2.83 (P- value 0.104); LDL/ApoB ratio 90.75 vs 83.82 (P- value 0.0837). In conclusion**,** cupping therapy reduces total cholesterol, TG, LDL, and apoB/ApoA-1 ratio and increases HDL significantly in dyslipidemic patients.

Keywords: Apolipoproteins; cupping therapy; hypercholesterolemia; hijamah; nursing

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INTRODUCTION

Atherogenic dyslipidemia occurs when there are elevated levels of triglycerides (TG) and small-dense Low-density Lipoprotein (LDL) in the body. They both play a critical role in atherosclerotic or Cardio Vascular Disease (CVD) (Manjunath et al., 2013). Atherosclerosis is a chronic condition where arteries harden through the build-up of plaques (Bergheanu et al., 2017). Patients with hypercholesterolemia are at risk of atherosclerosis due to their poor awareness of the risks associated with the condition, poor adherence and persistence to prescribed treatment, and consequently low rates of reaching lipid management targets (Wake et al., 2019).

An example of traditional lipid-lowering therapy is cupping therapy. Cupping is a minor excretory surgery that has been medically and scientifically proven to be able to clean the blood and interstitial space from Causative Pathological Substance (CPS). Pathological substances that form CPS consist of total cholesterol, LDL, TG, and Apolipoprotein-B. Additionally, the mechanism of cupping in reducing cholesterol has been described by *Taibah* theory (Al-Bedah et al., 2019).

Taibah theory explains that wet cupping therapy has similar excretory functions to the kidney through its skin capillary filtration and size-dependent excretion resulting from negative suction pressure and scarification. Moreover, while the kidney is only able to excrete hydrophilic materials, cupping therapy can excrete hydrophilic and hydrophobic

substances, such as lipoproteins (cholesterol). The process of wet cupping therapy consists of cupping, puncturing/scarification (about 0.1 millimeters in depth), and then second cupping at the same location.

Wet cupping therapy reduces LDL cholesterol and has the potential to prevent atherosclerosis. The apolipoprotein ratio (Apo-B/ApoA-I) represents the balance between Apo-B atherogenic and Apo-AI antiatherogenic particles. This ratio is a marker of cardiovascular risk as patients with an Apo-B/Apo-AI percentage ratio above 0.9 are at risk of CVD. This ratio is characterized by high TG levels and Atherogenic Index of Plasma (AIP), LDL/apoB ratio, and low Apo-B levels (Kaneva, Potolitsyna, & Bojko, 2015).

Nurses are eligible to deliver cupping therapy to their patients under Nursing Law No.38-Year 2014. However, the mechanism of how cupping can lower the lipid profile and apo-lipoprotein is not yet understood. Therefore, this study aims to review biomedical aspects, identify a causal relationship, and modify the theory of the intervention-outcome paradigm.

A reverse research strategy was used as this therapy has been used as a clinical treatment for thousands of years. Although cupping has been reported as a therapy against cholesterol, there is no explanation yet for its potential reduction in apolipoprotein B and the lipid profiles of LDL. Therefore, researchers need to understand the theoretical basis underlying this therapy as a disease treatment technique (Al-Bedah et al., 2019). Controversial opinions state that cupping therapy only has a placebo effect. The placebo theory is still believed until a valid mechanism is determined. It is hoped that this research will open the doors to scientific theories and evidence-based scientific explanations that will help with the application of safe and effective cupping therapy (Fikri et al., 2017).

According to the *Standard Intervensi Keperawatan Indonesia (SIKI)* or the Indonesian Nursing Intervention Standards, cupping therapy is included as a nurse intervention (PPNI, 2018). Thus, the results of this study can be added to support this evidence-based practice in the nursing field so that nurses may offer cupping therapy to their hypercholesterolemic patients in the clinic. The finding may also contribute to the development of complementary nursing therapies as cupping is regarded as a traditional method rather than conventional therapy.

METHOD

Study Design

This study implemented a pre-post experimental design with one intervention group and no control group. All respondents with a history of hypercholesterolemia were assigned to the intervention group.

Sample

The subjects of our study were 40 respondents with dyslipidemia. All participants were considered free from serious and chronic illnesses at the time of recruitment. Consecutive sampling was used and the participants were recruited from the university's clinic (Assabil Holy holistic, a *Hijamah* clinic) and the nearby community (UIN staff who live close to the Faculty of Health Science, UIN Syarif Hidayatullah Jakarta). The inclusion criteria were any patient who has a history of hypercholesterolemia as diagnosed by doctors and those who have elevated total cholesterol levels (above 200 mg/dL) detected by peripheral blood sampling before recruitment. The exclusion criteria were anyone who suffered from acute and chronic illnesses and who regularly consumed prescribed medicines. Each subject gave their informed consent to participate in this study.

Instrument

Blood samples were taken from the respondents' antecubital veins into vacutainers (containing EDTA) before and after the wet cupping technique was performed. The respondents were asked to fast 12 hours before blood sampling, and after that, they were asked to break their fast while the therapist prepared for the intervention. The second round of blood samples was taken 24 hours after the intervention (Widada & Anggraini, 2020). The blood samples collected were stored in a cool box before being delivered to the laboratory. The samples were then centrifuged, and the plasma was placed into Eppendorf microcentrifuge tubes and stored at −40◦C until analysis.

Intervention

Wet-cupping therapy (*hijamah*) was performed according to the Indonesian Cupping Association's (PBI) standard procedure. A lancet device was used for the scarification and 7 *hijamah* acupoints were used (also called *sunna* points as these points were suggested by the Prophet Muhammad SAW). These 7 points are called *al-akhda'ain, al-kaahil, al-katifain,* and al-waarik (Assabil holy holistic, 2018). The intervention was performed by certified therapists from the Assabil Holy Holistic Education Center, who is also the founder of the Indonesian Cupping Association (PBI).

Data collection

Data was collected between September to October 2019 by the nursing staff in our university clinic. The respondents' informed consent was obtained before the study.

Data analysis

The measurement of lipid and proatherogenic profiles; cholesterol, triacylglycerol, LDL, and plasma HDL concentrations were conducted using enzymatic methods with commercially available kits (Diasys). The measurement of plasma ApoB and ApoA-I concentrations was done using the ELISA technique (Abcam).

Next, each parameter was measured for all samples in duplicate. The absorbance readings and levels were calculated with the help of standard solutions. The calculations were also conducted through the Cholesterol/HDL ratio; ApoB/ApoA1, LDL/ApoB, and Atherogenic Index of plasma AIP (TG/HDL). Statistical analysis was performed using SPSS version 21. The difference between the groups before and after the cupping intervention was analyzed using the Wilcoxon sign rank test due to the data's abnormal distribution (non-parametric test). Values of P <0.05 were accepted as statistically significant.

Ethical consideration

This study was approved by the ethics committee of the Faculty of Health Sciences at the State Islamic University Syarif Hidayatullah Jakarta (ethic number Un.01/F10/KP.01. 1/KE.SP/09.00.017/2019).

RESULTS

The respondents in this study were individuals who had a history of hypercholesterolemia or elevated total cholesterol before the intervention. The profiles of the respondents in this study are shown in Table 1. Table 2 exhibits the decrease in the levels of cholesterol, triacylglycerol, and LDL, as well as an increase in HDL and ApoA-1 protein levels. ApoB protein

was also found to have decreased after cupping therapy. This causes the ApoB/ApoA-1 ratio to decrease significantly.

Table 1. Respondents' characteristics (N = 40)

Characteristic	n (%)
Gender	
Man	18%
Woman	82%
Age	
Adult	94%
Elderly	6%
IMT	
Normal	82%
Obesity	18%
Cupping therapy experience	
1-3 time	69%
4-6 time	23%
≥7 time	8%

Table 2. Lipid and Apolipoprotein levels in pre-post cupping therapy among hypercholesterolemic patients (N = 40)

Parameter	Pre-cupping Median ± SD (min – max)	Post-cupping Median ± SD (min – max)	*P* value <0.05
Cholesterol (mg/dL)	328 ± 53 (228.9 – 450.3)	283 ± 54 (147.2 – 383.6)	0.003**
Triglyceride (mg/dL)	238.2 ±61.9 (134.8 –368.5)	204 ± 53,8 (151.1 – 359.8)	0.007**
HDL (mg/dL)	78.5 ±10.2 (58.2 – 90.4)	85.2 ± 18 (68.5 – 151.9)	0.000**
LDL (mg/dL)	195 ± 49 129.5 – 323	158.9 ± 48 21.8 – 232.9	0.001**
Apo-A1 protein (ng/mL)	0.07 ± 0.026 (0.027 – 0.118)	0.67 ± 0.242 (0.197 – 1.106)	0.000**
Apo-B protein (ng/mL)	2.04 ± 0.74 (0.82 – 3.55)	1.82 ± 0.71 (0.51 – 3.28)	1.000
Apo-B/Apo-A1 ratio	30.22 ± 1.66 (25.36 – 33.96)	2.93 ± 0.18 (2.59 – 3.35)	0.000**
Cholesterol/HDL ratio	4.06 ± 0.79 (2.49 – 6.34)	3,80 ± 0,66 (2.72 – 5.31)	0.332
AIP (Triglyceride/HDL ratio)	3.01 ± 1.2 (1.48 – 6,2)	2.83 ± 0.83 (1.48 – 5.2)	0.104
LDL/Apo B ratio	90.75 ± 98 (33–477)	83.82 ± 104 (41–481)	0.0837

**Wilcoxon sign-rank test *P* <0.05

DISCUSSION

The increase in Apo-A1 after cupping intervention indicates that proatherogenic cholesterol is reduced through its excretion into the liver and bile salts. The increase of Apo-A1 levels in the plasma will also increase proatherogenic cholesterol levels that will be discharged into bile salts through the liver. HDL synthesis is influenced by Apo-A1, Pre-HDL, and cholesteryl ester transfer protein (CETP). Pre-β-HDL is a form of HDL that induces the release of cholesterol from tissues to form HDL. It has a very important role in the process of cholesterol transport in peripheral tissues (Trajkovska & Topuzovska, 2017).

HDL particles are small and flat newborn particles that contain Apo-A1 and are synthesized in the small intestine and liver. Apo-A1 is a component of HDL that supports the efflux of cholesterol from cells and is important for maintaining cellular cholesterol homeostasis. In addition, receptors are involved in the binding of HDL to cell membrane proteins. The smaller HDL precursors (pre-β-HDL) in tissues take up free cholesterol from cell membranes. Free cholesterol is also esterified by the action of LCAT, which makes it more hydrophobic. The increase in Apo-A1 is very significant in cupping therapy and indicates the protection of blood vessels from lipid oxidation and atherosclerosis formation (Rousset et al., 2009).

The decrease in Apo-B in this study is a good sign because it is proatherogenic. The lower the plasma Apo-B level, the less proatherogenic cholesterol will be in the blood circulation. Apo-B is the main apolipoprotein of chylomicron particles, VLDL, IDL, and LDL in all tissues. Apo-B in LDL particles acts as a ligand for LDL receptors in various cells. LDL particles are easily internalized into the subintimal space where they adhere to the proteoglycan matrix, which would then be oxidized and increases the risk of atherothrombotic events. One Apo-B particle represents one LDL cholesterol. Therefore, the decrease in the amount of Apo-B in this study showed that cupping therapy could reduce the ABC1 protein and result in a 70% reduction in cholesterol, especially in plasma phospholipids, and if continued to be HDL, almost no LDL (McNeish et al., 2000).

Furthermore, this study can prove that wet cupping therapy can significantly reduce the Apo-B/Apo-A1 ratio in hypercholesterolemic patients. The lower the ratio of Apo-B/Apo-A1 in plasma, the less proatherogenic cholesterol in the blood circulation. Apo-B is a protein involved in fat metabolism and is a major constituent of proteins such as VLDL and LDL lipoproteins. Chylomicrons are lipoprotein particles that carry dietary lipids from the digestive tract, through the bloodstream to tissues, and especially to the liver. In the liver, the body repackages these dietary lipids and

combines them with Apo B-1 to form triglyceride-rich VLDL (Rousset et al., 2009).

Cholesterol reduction in cupping therapy can control other stable lipid profiles to normal. A diet high in saturated fat and trans unsaturated fat, or genetic factors can cause high blood cholesterol levels. Excess cholesterol is stored in plaques on the walls of blood vessels. This plaque can narrow blood vessels and consequently result in atherosclerosis, which puts you at risk for heart disease and stroke. In this study, the respondents' cholesterol levels decreased, which can lower LDL and prevent atherosclerosis (Calabrese et al., 2015).

Furthermore, the HIF-1α transcription factor activates macrophages in the skin, which in turn induces proinflammatory genes such as IL-1, IL-4, IL-6, and TNF-α. Interleukin-6 plays a role in stimulating the immune response. For example, after tissue damage due to cupping, the release of IL-6 will stimulate young macrophage cells to mature and perform phagocytosis. The accelerated migration of macrophages can also increase due to IL-6 stimulation. Additionally, IL-6 particles also stimulate monocytes to produce inflammatory cytokines that play a role in local and systemic inflammation, thereby accelerating the proliferation and differentiation of macrophages (Duque & Descoteaux, 2014).

The total cholesterol levels in the body are comprised of HDL, LDL, and TG levels. In the body, cholesterol is found in the form of free cholesterol and esterified cholesterol. Normally, about two-thirds of total plasma cholesterol is present in the form of esters. About 60-70% of cholesterol is transported by LDL and a small portion (15-25%) is transported by HDL (Uydu et al., 2012). The control of blood lipid levels, especially LDL reduction, could be done by drugs through the inhibition of HMG-CoA reductase in the liver. This lowers total cholesterol levels and increases the formation of LDL receptors in liver cells. This increases the number of LDL transport on the surface of hepatocytes from blood vessels to liver cells (Fikri et al., 2017).

This study found a significant decrease in TG. Patients with hypercholesterolemia generally have a high level of cholesterol, TG, and LDL. LDL is a primary atherogenic lipoprotein and is the main therapeutic target for coronary heart disease. In general, TG-rich lipoproteins include HDL and LDL. Approximately 50% of patients with this atherogenic lipoprotein disorder have an increased risk of CVD. Therefore, treatments also aim for a decrease in TG in target hyperlipidemia.

Cholesterol and triglycerides are non-polar or insoluble in water. Lipoproteins are fatty-acid-binding proteins/transport proteins. These complex particles have a central core that contains cholesterol esters and triglycerides surrounded by free cholesterol, phospholipids, and apolipoproteins (Rousset et al., 2009). Cholesterol, free fatty acids, and triglycerides are difficult to remove through cupping therapy because their solubility is small, so they bind to the protein. Its large macromolecule structure also makes it difficult to penetrate the skin barrier and remove it through cupping therapy. When hypercholesterolemia occurs, the Sterol Binding Protein Element (SREBP) in the endoplasmic reticulum is inhibited. In this study, it is suspected that the inhibition of SREBP in cells and inhibition of HMG-CoA reductase activation prevents the mevalonate pathway of intracellular cholesterol synthesis. Blood that comes out through cupping therapy is likely to secrete the transcription factor SREBPs (Benito-Vicente et al., 2018).

HDL has protective properties against heart disease, therefore therapeutic intervention efforts aim to increase HDL concentrations. HDL removes lipids from macrophage phagocytosis to other lipoproteins. It also contains the highest proportion of apolipoproteins compared to other lipoproteins. The major apolipoproteins, ApoA-I and ApoA-II, are secreted into plasma by the liver and intestines. Thus, the presence of both apolipoproteins slows down atherogenesis, protects the body against atherosclerosis, and increases cardioprotective function.

Cells in extrahepatic tissues also transport cholesterol from the periphery to the liver for biliary secretion and excretion of cholesterol through feces, even though it is only 5% of body lipid (Mika et al., 2020) This mechanism is quite effective compared to cupping therapy. However, it is difficult for HDL to cross the skin barrier through cupping therapy. The increase in HDL due to increased Apo-A1 was seen in this study.

TG synthesis is the liver's attempt to store and export fatty acids. The main pathway for TG synthesis is the Glycerol-3-P pathway, which accounts for more than 90% of total TG synthesis. Conversely, TG levels could decrease through the inhibition of long-chain acyl-CoA esterification to G3P and inhibition of microsomal Glycerol-3-P acyltransferase enzyme. Molecular lysophosphatidic acid is not produced in this reaction and the resulting compound is acylated, so no phosphatidic acid is formed by acylglycerol-3-phosphate acyltransferases in the ER membrane. PA is also not formed, thereby causing cytidine diphosphate diacylglycerol to not be formed due to decreased TG synthesis.

The decrease in TG can also be thought to be caused by a decrease in the expression of lipogenic enzymes in the cupping tissue, such as the group of enzymes involved in the synthesis of oleic acid, the main component of triglycerides. The decrease in TG occurs due to the rapid release of blood through cupping as this reduces the components needed for the synthesis of TG. In addition, increased lipolysis is associated with increased carnitine activity via beta-oxidation metabolism. As less TG is formed, fatty acids accumulate, thereby causing carnitine palmitoyl transferase to be involved in the transport of FA into the mitochondria for degradation (Mika et al., 2020).

The decrease in LDL can also be caused by several factors such as a decrease in TG synthesis, cholesterol ester transfer protein activity, and liver lipase activity. The mechanism of wet cupping therapy is to inhibit cholesterol synthesis and TG also effectively inhibits LDL synthesis. Therefore, anything that has predicted TG levels through cupping therapy can increase HDL cholesterol levels and decrease LDL particles. Cupping therapy is effective in reducing cholesterol, TG, and LDL to prevent the risk of CVD events. This type of therapy also reduces the ratio of AIP (TG/HDL) with a smaller molecular size. This ratio can be used to identify patients with an atherogenic lipid profile and may be relevant for assessing CVD risk (Boizel et al., 2000).

The Apo-B/Apo-A1 ratio reflects the balance of proatherogenic and antiatherogenic particles. A higher Apo-B/Apo-A1 ratio was associated with a higher risk of all-cause and CVD-related mortality. A higher Apo-B/Apo-A1 ratio is an important parameter for predicting the risk of cardiovascular events and causes of death. This overexpression of ApoA-I causes atherosclerotic regression. High LDL levels and high Apo-B/Apo-A1 ratios are also associated with coronary arteriosclerosis. Whereas LDL levels were independently

associated with aortic valve calcification but not coronary artery calcification in the familial hypercholesterolemic population (Ljungberg et al., 2017).

Next, the Apo-B/Apo-A1 ratio in this study showed a significant decrease. Apolipoproteins are small molecules and are easily soluble in water. Therefore, it could be easily removed through cupping therapy, as evidenced by the significant reduction ratio by being 10 times lower compared to before cupping.

Cupping is effective in reducing the risk of death from CVD regardless of the respondent's normal BMI (Table 1). This study showed a positive effect of cupping therapy in hypercholesterolemic patients by reducing total cholesterol, triacyl glycerides, LDL, and increasing HDL.

As a limitation, this study did not control other factors that may interfere with the results, such as age, gender, food consumption, regular physical exercise, smoking habits, and prescribed medications (a few respondents had a history of using statin medications). The factors that may interfere with the results such as diet and exercise were not controlled in this study. The respondents at the time of the study were also not undergoing lipid therapy or taking prescribed medication.

CONCLUSION AND RECOMMENDATION

This study used cupping therapy techniques to reduce lipid levels in the blood. This intervention was implemented on hypercholesterolemic patients before and after cupping. Blood samples were taken to test for their lipid profiles and apolipoproteins. The results showed that cupping therapy could reduce cholesterol, triacylglycerol, LDL, the ratio of Apo-B/Apo-A1 levels, and increase HDL levels. This shows that cupping therapy may have the potential to reduce the incidence of vascular disorders due to the blockage of blood vessels by lipids.

Hijamah or cupping therapy may become a nurse-independent intervention for the management of hypercholesterolemia in adult patients.

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