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Efforts in Hypercholesterolemia Treatment Using Turmeric (Curcuminoid) Extract Phytotherapy on Obese Patients: Preclinical Study

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Abstract

Hypercholesterolemia is an escalation in total cholesterol levels in the blood which can cause various cardiovascular diseases, hypertension, and stroke. Obesity is one of the risk factors of hypercholesterolemia. Turmeric extract (a curcuminoid) therapy including phytotherapy can be used to overcome hypercholesterolemia. This research aims to identify hypercholesterolemia with turmeric extract for obesity patients. The method used in this research was quasi-experimental with one group pretest and posttest design. The sampling technique used in this research was purposive sampling. The research subjects consisted of 18 respondents who met the criteria of hypercholesterolemia (total cholesterol> 200 mg/dl) or with obesity who had a body mass index (BMI)> 25 kg / m^2) and they were not taking cholesterol-lowering drugs. Subjects were given turmeric extract with a dose of 1 gram/day for 28 days. Before and after the intervention, total cholesterol levels of respondents were examined. Data analysis was done by using t-paired test. The results showed that the average total cholesterol level before the patient was given turmeric extract therapy was 234.44 mg/dl and 202.06 mg/dl after the treatment. There was a significant decrease in the average cholesterol level after they were given turmeric extract therapy with p-value 0.0001 (α <0.05). The results showed that there was a significant decrease in cholesterol levels, although it was still included in the category of borderline high cholesterol levels. Researchers suggest that respondents continue their turmeric extract therapy with a low cholesterol diet until their total cholesterol levels achieve the normal state.

Keywords: Hypercholesterolemia, obesity, turmeric extract.

Introduction

Hypercholesterolemia is an escalation in total cholesterol levels in the blood. Hypercholesterolemia occurs due to a disturbance of fat metabolism which can cause a rise in blood fat levels. Blood fat levels increase possibly from a deficiency of lipoprotein enzymes, lipase, or abnormal receptor of low-density lipoprotein (LDL). It can also be caused by genetic abnormalities which results in a dramatic increase in cholesterol production in the liver or a decrease in the ability of the liver to cleanse cholesterol in the blood (Jeong, 2005). Hypercholesterolemia is a major cause of atherosclerosis associated with coronary heart disease (CHD), cerebrovascular ischemia and peripheral vascular disease (Goodman, 2007). Coronary heart disease (CHD) or cardiovascular disease is currently one of the primary and first causes of death in developed and developing countries including Indonesia. In Indonesia, there were around 36 million people or about 18% of the population of Indonesia who suffer from the fat disorder, of that number 80% of patients died suddenly with a heart attack (Jempormase, 2016).

A risk factor for hypercholesterolemia is in people with obesity. Obesity can be determined by calculating the body mass index (BMI) by weight in kilograms divided by the square of the body height in meters. If the BMI is > 25 kg/m2, it is categorized as obesity. Results of research in Ghana show that out of 207 men > 18 years old living in peri-urban communities there were 24.6% of subjects in overweight conditions with BMI > 25 kg/m2 (Frederick, 2016). Also, people with obesity will be more at risk for various diseases such as atherosclerosis, obstructive sleep apnea, cardiovascular disease, and hypertension. Firmansyah's research reinforces the findings, which suggests that obese people are 8.499 times more at risk of developing hypertension than people who are not obese. A person with obesity will have more body fat and the risk of causing fat deposits in the blood vessels (Firmansyah, 2017).

Fat deposits in the lining of the blood vessels (cholesterol plaque) make the blood vessels drain and the blood flow to be less smooth. Cholesterol plaque on the blood vessel wall is fragile and easily break, leaving a "wound" on the walls of blood vessels that can activate blood clot formation. Due to narrowing and hardening of the cholesterol plaque, this blood clot can quickly and completely block the blood vessels.

This narrowing and hardening, if it is severe enough, will cause inadequate blood supply to the heart muscle, causing pain or chest pain referred to as angina. If it continues, it will cause the death of heart muscle tissue called myocardial infarction, and its spread causes heart failure. According to the National Cholesterol Education Program the Adult Panel Treatment III (NCEP APT III), the total normal cholesterol levels are < 200 mg/dl; cholesterol levels > 200 mg/dl are considered high and cholesterol levels > 240 mg/dl very high.

Hypercholesterolemia can cause various diseases and treatment efforts are needed so that cholesterol levels can be in the normal range. The use of cholesterol-lowering drugs that are widely used such as lovastatin, simvastatin can reduce cholesterol levels but the use of drugs that are not good enough if it is very often for the body and it also can cause side effects.

WHO recommends the use of traditional medicines including herbs in the maintenance of public health, prevention, and treatment of diseases, especially for chronic and degenerative diseases as well as cancer. The use of traditional medicine, in general, is considered safer than the use of modern medicine. It is because traditional medicine has relatively fewer side effects. Treatment or prevention using herbs, parts of plants or preparations made from plants is known as phytotherapy. The Food and Drug Supervisory Agency (BPOM) has stipulated nine superior medicinal plants that have been studied or tested clinically. Nine medicinal plants are sambiloto, guava, Dutch teak, java chilli, ginger, red ginger, mengkudu, salam and turmeric.

Turmeric (also turmeric in English) or curcuma (Dutch) is a type of root that contains curcuminoid consisting curcuminoid compounds and their derivatives. Curcuminoid is a combination of polyphenolics and other

active substances contained in turmeric roots (Mirzabeigi, 2015).

Turmeric is an agricultural commodity produced abundantly by the people in the area of West Java. Yielded from rhizomes or tuber roots, it has many uses in the community, such as a cooking ingredient. In the field of health, turmeric is widely used to make herbal medicine. One of the well-known, long, and hereditary uses in the community is asem kunyit made from turmeric juice added with brown and tamarind sugar, believed to be useful for smooth skin, dysmenorrhea, blood glucose levels and body fat for obese people. So far, the use of turmeric is for traditional herbal medicine. The development in health research shows that turmeric has proven to be useful as an antioxidant, anti-inflammatory, antibacterial, antiviral, tumor prevention, and cardioprotective agent with the role of anti-angiogenesis in various organs including adipose tissue (Zhao, 2017). Adipose tissue is fat deposits under the skin layer which is a source of energy, insulation and padding for organs. If it is excessive, it will cause various disorders in the body with the formation of cholesterol plaque deposits in the blood vessels that can lead to ischemia, coronary heart disease, and stroke. This increase in cholesterol or hypercholesterolemia is found mostly in people with excess body weight and obesity.

Using turmeric to reduce blood cholesterol levels has been proven through experimental animal, preclinical, and human testings (clinical testing). A reference for preclinical research on animals related to obesity is a study by Shao (2012). It discussed curcumin therapy for the prevention of fat increase, insulin resistance, and obesity through the decomposition of liver fat and adipocyte inflammation. The study observed mice for 28 weeks with 16 weeks of high-fat diet and 28 weeks of curcumin extract. The results showed decreased insulin and leptin resistance, weakening of cytokine inflammation, and increased burning of fatty acids. The results of the study concluded that mice with a high-fat diet and curcumin extract consumption reduced the expression of lipogenic genes in the liver and inflammatory response in adipose tissue. Additionally, curcuminoid therapy has been applied in clinical trials for healthy people (such as DiSilvestro, 2012), where 19 adult respondents aged between 40 and 60 received low doses of 80 mg curcuminoid extract/ day for four weeks. Their blood and salivary samples showed a significant decrease in plasma triglyceride levels, decreased salivary amylase levels accompanied by an increase in anti-free radical activity (DiSilvestro, 2012). The same type of respondents also took part in Lao's study which focused on the administration of curcuminoid extract with therapeutic doses from 500-12,000 mg per day. Only 7 out of 24 respondents (30%) showed a minimum effect of toxicity, while most of the respondents were able to tolerate it, there was no presence of curcumin in the blood serum of respondents who consumed doses of 500; 1,000; 2,000; 4,000; and 8,000 mg; and only two respondents perscribed with 10,000 and 12,000 mg had low levels of curcumin in blood serum (Lao, 2006). Based on the description, a hypothesis can be formulated showing that the treatment of turmeric extract can be used as an anti-hypercholesterolemic therapy. Besides being a therapy using natural ingredients, turmeric can be well-tolerated by the body and useful for the treatment of hypercholesterolemia. However, the development of such research in the country is currently still at their clinical stage, especially in hypercholesterolemic patients.

Method

The study subjects were hypercholesterolemic patients with obesity. The number of samples used a paired numerical formula, and 18 respondents fulfilled the prerequisites. Respondents must also meet the inclusion criteria of obesity by measuring body mass index (BMI) using the calculation of body weight (kg) divided by squared height (meters) to obtain the BMI values > 25 kg/ m^2 or clients with hypercholesterolemia (total cholesterol > 200 mg/dl) based on the measurements of total cholesterol levels via cholesterol check instrument namely the ultra cholesterol meter. Furthermore, the respondent must be registered as a patient in Puskesmas Cimahi Selatan. In this study,

the ethical clearance (120/KEP/STIKES-A-YANI/VIII/2017) was obtained from the Health Research Ethics Committee Stikes Jenderal Achmad Yani Cimahi.

Making the Turmeric Extract, the material for turmeric extracts comes from turmeric tuber roots obtained from traditional markets in the Cimahi City. They are washed, thinly sliced, and dried for a week. Subsequent drying is done using an oven for an hour. Then the dried product is mashed to its powder state with a food processor. The powder is weighed for each sachet so that they contain a gram. Furthermore, dried turmeric powder was extracted using the infusion method. The infusion method of turmeric extract consisted of 1 gram of dried turmeric powder added with 100 ml of mineral water heated at 900C for 15 minutes by using two pans arranged in stages. The powder and 100 ml of mineral water were poured on the top layer while the bottom pan was filled with enough mineral water to avoid overcooking. Below is a picture of how to make turmeric extract:

Figure 1 How to make turmeric extract

After 15 minutes the boiling process was complete, and the extract floated in the top boiling pan to be poured into a glass and consumed after cooling.

Phytotherapy Procedure, turmeric extract is one way to take substances that are in turmeric root. The use of turmeric extract to overcome various disorders or diseases in the body such as hypercholesterolemia and obesity is known as phytotherapy. The therapeutic dose of the turmeric extract is based on evidence-based studies in research articles (Lao, 2006) which is as much as 1 gram/day. The duration of the therapy was 4 weeks (28 days), based on the research DiSilvestro (2012) made. It states that the treatment of turmeric extract for 28 days can reduce plasma triglyceride levels. Respondents were asked to drink turmeric extract every day at 5:00 p.m.

Cholesterol total examination, total blood cholesterol levels were measured by extracting blood from the fingers of the patient using a lancet and read from a strip using the Acon Mission Ultra cholesterol system.

The nature of the research is that of a quasi-experimental with one group pretest and posttest design. The sampling technique used purposive sampling and obtained as many as 18 respondents with hypercholesterolemia patients with obesity. Furthermore, the results of the research data were tested for normality. A skewness test obtained the BMI data as 0 = 0.785 ≤ 2, cholesterol level data before therapy = 0.466 ≤ 2, cholesterol level data after treatment = 1.19 ≤ 2. Thus, it can be concluded that BMI data related to cholesterol levels before and after the treatment were normally distributed and can use the parametric tests. Then the parametric analysis used the dependent t-test. Data collection was conducted in October 2017 at Puskesmas Cimahi Selatan in Cimahi.

Result

The effects of turmeric extract phytotherapy with a gram daily dosage for 28 days on 18 respondents appear in the following tables:

Based on Table 1, a respondent (5.6%)

Table 1 BMI Distribution

BMI Category	f	%
Underweight	1	5.6
Normal	3	16.7
Overweight	8	44.4
Obesity	6	33.3
Total	18	100.0

Table 2 Average Cholesterol Levels Before and After Treatment of Turmeric Extract

Variable	Mean	Median	St. Deviation	Min-Max	p-Value
Before	234.44	228.00	21.217	207–264	0.0001
After	202.06	201.50	35.112	147–285	

belonged to the underweight category, three respondents (16.7%) in the normal weight category, eight respondents (44.4%) in the overweight category (44.4%), and six respondents (33.3%) as the obesity category. Table 2. Average Cholesterol Levels Before and After Treatment of Turmeric Extract

Based on Table 2, the average cholesterol level before the intervention was 234.44 mg/dl with a standard deviation of 21.217. The average cholesterol level after the treatment 202.06 mg/dl with a standard deviation of 35.112. The results of paired t-test yielded the p-value = 0.0001 ($\alpha < 0.05$), leading to the conclusion that there is a significant effect of turmeric extract therapy on the reduction of Cholesterol levels. Research Limitations, this study has its limitations, namely the absence of trials on animals and the subsequent clinical stage research needed to learn more about the benefits of turmeric extract in helping to lower cholesterol levels.

Discussion

Based on the results of the study in Table 1, a respondent (5.6%) belonged to the low weight category, 3 respondents (16.7%) in the ideal/normal weight category, 8 respondents (44.4%) in the overweight category and 6 respondents (33.3%) as the obesity category. Body mass index (BMI) is a measure of nutritional status by calculating the ratio of height and weight. BMI is one of the parameters that can be used in determining the criteria of a person's body proportions because BMI correlates with the total amount of body fat in humans and it can describe a person's weight status (Linta, 2008).

In identifying overweight and obesity in adults, BMI is used since measuring body fat directly is difficult. It is reinforced by the Sandhu, which states that there is a positive relationship between BMI and triglyceride levels in people aged 31–61 years (Sandhu, 2017). Adults, especially over 30 years, are overweight since their organs generally begin to decline in function, the metabolic rate begins to wane, and food accumulation occurs. The condition worsens due to habits that allow high food consumption and the lack of physical activities. Some factors that influence obesity are genetic, damage to the hypothalamus lateral and ventromedial parts that drive appetite; overeating patterns; lack of activity, emotion, socio-cultural, economic and drug environment. As their age increases, people tend to engage in less physical activity and diet will change along with increased financial capacity. These factors cause the body mass without fat to decrease, while the fat tissue will increase so that the value of cholesterol in the blood will also be high. However, fat removal from the blood in each person varies: an individual may be able to consume large amounts of animal fat and never have total cholesterol levels of more than 200 mg/dl, while another individual who undergoes a strict low-fat diet may never have cholesterol levels total below 260 mg/dl. It may be related to genes and the variety of speed of lipoproteins entry to and exit from the bloodstream.

Research conducted by Linta in East Java found a relationship test showing a significant relationship between moderate and positive levels between BMI and abdominal circumference with blood cholesterol levels with p-value = 0.018 ($\alpha < 0.05$). It entails an increase in BMI and abdominal circumference followed by the rise in blood cholesterol levels. BMI and abdominal circumference are predictors of cholesterol levels in the blood. Research by Sitepu (2014) attempted to show the relationship between BM and lipid profile. It involved the prevalence of BMI with a body weight of 4%, a normal weight category of 45%, the preobesity category of 41%, and a 10% obesity category. Twenty-two (55%) male and thirty (56%) female adult patients had excess BMI, but the statistical tests using Spearman obtained p-value > 0.05, showing an insignificant relationship. Other researches indicate differences in results, showing that most of the respondents are in

the normal weight category and only a few respondents fit in the obese category. Also, there is a difference in the relationship test which shows that previous studies did not show a relationship between BMI with a lipid profile. The similarity of the results of earlier studies lies in the fact that they included people belonging to the underweight category. From the discussion, the authors concluded that the increase of BMI is not always congruent with an increase in cholesterol levels. Most of the respondents belonged to the overweight and obesity categories with an increase in cholesterol levels, but there were also respondents who were in the normal weight and underweight categories experiencing an increase in cholesterol levels. However, to facilitate the screening of patients with hypercholesterolemia, BMI and other measurements such as abdominal circumference can be used.

Furthermore, the results of the study in Table 2 found the average cholesterol level before therapy of turmeric extract was 234.44 mg/dl, while the average cholesterol level after turmeric extract intake was 202.06 mg/dl. Hypercholesterolemia occurs when total cholesterol exceeds 200 mg/dl. It has been proven to be a risk factor for atherosclerosis which can lead to acute coronary syndrome, stroke and hypertension.

Turmeric has a beneficial ingredient for the body such as yellow curcumin (curcuminoid), essential oils, as well as high minerals such as potassium, calcium, iron and magnesium. Curcumin in turmeric is an antioxidant because turmeric does not contain cholesterol and is rich in fiber; it will control low-density lipoprotein (LDL) in the blood. As an antioxidant, turmeric is widely used to increase appetite, improve digestive function, reduce blood fat (cholesterol) and help inhibit blood clotting (Bagschy, 2012). Curcumin can protect the body from several types of degenerative diseases by preventing the occurrence of fat peroxidation. The hydroxyl group in the chemical structure of curcumin can inhibit peroxidation activity and it is also known that its function as an antioxidant plays a significant role against hyperlipidemia activity (Suryantoro, 2007).

In this study, each respondent received 1 gram of turmeric extract taken every day for 28 days. The result of paired t-test shows p-value = 0.0001 ($\alpha < 0.05$) which leads to the conclusion that there is a significant effect of turmeric extract on the decrease of cholesterol levels. It is because turmeric rhizome extract can inhibit the increase in blood serum cholesterol levels because it inhibits the reabsorption of exogenous cholesterol and increases the enzyme Hmg-CoA so that fat synthesis can take place (Muchtadi, 2003). It proves the potency of curcumin in inhibiting the Hmg CoA enzyme and cholesterol formation from free fatty acids. Furthermore, the results of this study indicate that there is a mean decrease in cholesterol levels even though the average decline has not yet reached the normal cholesterol category. It may be due to the absence of rules for limiting fat consumption in respondents. Thus the formation of fat from external factors can trigger an increase in cholesterol, triglyceride and LDL levels so that curcumin acting as an inhibitor of the Hmg-CoA reductase enzyme is not optimal. The intake of foods containing fat levels is closely related to the educational background of respondents. The influence of education is closely associated with the mindset in determining attitudes and actions, including applying a high-fat diet that requires a good knowledge of the right types and portions of fat for patients with hypercholesterolemia.

The research that supports the results of this study was conducted by Hasanah in Surabaya who examined the effect of turmeric rhizome extract intake at 500 mg taken twice daily for seven days to reduce total cholesterol, LDL, and increase HDL levels on ten dyslipidemia patients. The results showed a significant decrease in their total cholesterol, LDL levels and increase in HDL levels with a p-value < 0.005 (Hasanah, 2016). The results of previous studies are consistent with this research where the administration of turmeric extract can reduce total cholesterol levels.

The results of this study prove that turmeric extract can be used in anti-hypercholesterolemic therapy. It is well known that hypercholesterolemia is a risk factor for various diseases, such as hypertension, atherosclerosis and stroke. Turmeric therapy can be used as a promotive and preventive action in the nursing profession to prevent

and control various kinds of diseases that potentially caused by hypercholesterolemia. Turmeric therapy can also be applied as one of the nonpharmacological interventions to improve nursing care services.

This study has its limitations, namely the absence of trials on animals and the subsequent clinical stage research needed to learn more about the benefits of turmeric extract in helping to lower cholesterol levels.

Conclusion

Based on the results and the discussion of the study, it can be concluded that the increase in BMI is not always followed by the rise in cholesterol levels even though the results of the study indicate that excess body weight and obesity have a higher risk of developing hypercholesterolemia. Furthermore, it can be concluded that phytotherapy of turmeric extract can significantly reduce total cholesterol levels in hypercholesterolemic patients or with obesity.

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