THE EFFECT OF CURCUMIN SUPPLEMENTATION ON LIPID PROFILES IN HEMODIALYSIS PATIENTS

Maryam Haji Nezhad,
MSD, department of nursing Ghaem hospital, Mashhad, Iran
Akram Khoshki,
[*]associate professor,department of nutrition and biochemistry, school of medicine, Sabzevar university of medical science, Sabzevar, Iran
Mostafa Rad,
[*]Corresponding author: kooshki.nutr@gmail.com
Assistant professor, department nursing, school of nursing, Sabzevar university of medical science, Sabzevar, Iran

Abstract. The aim of this study was to determine the effect of curcumin on systemic inflammation and serum lipid profiles in hemodialysis patients. The aim of this study was to determine the effect of curcumin on systemic inflammation and serum lipid profiles in hemodialysis patients. Then, an experimental group received 80 mg of curcumin for 2 months and the control group received placebo. Before and after intervention, after 12 hours of fasting blood cc5, blood samples were taken from patients for triglyceride, cholesterol, HDL-C and LDL-C parameters. Data were then entered into SPSS 16 software and analyzed by Kolmogorov-Smirnov, Chi-square, Fisher test and T-test. According to the results of the analyzes, the results of the assumptions under study indicated that the supplementation of curcumin reduced serum LDL-C concentrations ($P < 0.05$) and increased serum HDL-C ($P = 0.003$) in hemodialysis patients. Serum cholesterol and serum triglyceride in patients without hemodialysis are equal to ($P > 0.05$). The results of this study showed that curcumin supplement can be effective in preventing heart disease and can be used as a complementary therapy.

Keywords: Curcumin, Systemic inflammation, Hemodialysis, Serum lipid profile.

Introduction. Chronic Kidney Disease (CKD) is a disease that is caused by the progressive and irreversible degeneration of the number and function of the nephrons by various factors (1, 2). Chronic renal failure is prevalent in 10-13% of the population, of which only a small segment of the renal end-stage renal disease (ESRD) is progressing and requiring dialysis or transplantation (2, 3). One of the alternative therapies in the final stage of renal disease is hemodialysis (4). The number of patients who underwent hemodialysis is rapidly increasing (5). There are over 11,000 patients undergo hemodialysis in Iran, with an annual increase of about 8%. The mortality rate in dialysis patients is 3.5 to 4 times to the whole general population, with 40% to 50% related to cardiovascular disease, so that cardiovascular mortality rates in hemodialysis patients are 5 to 20 times of the whole general estimated population (4). Also, in the coming years, a significant increase in renal failure, followed by kidney failure requires dialysis, is expected to be due to a significant increase in the prevalence of obesity, diabetes type 2, and increased life expectancy (6). In patients with chronic renal failure, the prevalence of cardiovascular events and cardiovascular mortality is significantly higher in comparison with the general population and in proportion to age parameter (7). The risk of cardiovascular disease and its mortality in early stages of renal failure is well-known, and cardiovascular complications are the leading cause of mortality in patients with end stage renal disease (ESRD) (8).

In hemodialysis patients, the high concentration of inflammatory and hyperlipidemic factors are among the most important risk factors for cardiovascular disease. Various studies have shown that inflammation is found in 30-50% and hyperlipidemia in 50-70% of these patients (11-9). One of the main causes of cardiovascular disease in dialysis patients is lipid abnormalities including hypertriglyceridemia, hypercholesterolemia and low HDL-C concentrations (16-12). The role of chronic inflammation in the pathogenesis of atherosclerotic vascular arteries and cardiovascular disease, mortality and long-term complications has been proven (17,18), and in cases of hemodialysis, a high incidence of inflammation has been reported (21,24). CRP is an acute phase protein produced in the liver (19) and is the most important component of the inflammatory syndrome (20); Because it rapidly increases in response to inflammation and, unlike other acute phase proteins that have other functions, only goes up in inflammatory conditions; Therefore, there is no ambiguity in its interpretation (21).

Existing evidence suggests that CRP plasma may directly affect the progression of atherosclerosis (22,25). It has recently been shown that increased serum CRP levels are associated with an increased risk of infarction and angina and sudden coronary heart disease (28). According to studies, the level of CRP was high in hemodialysis patients and before the onset of dialysis, with a prevalence of 30-50% (20,20,5). Various studies have suggested that CRP is one of the strongest predictors of mortality from cardiovascular disease and overall mortality in dialysis patients (20, 29, 33).

On the other hand, due to the high serum lipid profile, these Statins are used to treat their hyperlipidemia. Studies have shown that Statins have preventive effects in hemodialysis patients, but these drugs have side effects such as headache, constipation, abdominal pain and memory impairment (34). Several studies have also

been undertaken over the past years to find treatment methods that can reduce the concentration of inflammatory and hyperlipidemic factors in hemodialysis patients, but no valid therapeutic approach has been developed (35, 36). Medicinal herbs in traditional medicine are widely used in the treatment of various diseases. Today, the use of dietary supplements for the treatment of diseases has a special importance. One of these dietary supplements is curcumin, which is an active ingredient in turmeric and has significant antioxidant properties (37). Turmeric is a herbaceous plant whose rhizome is widely used to color and taste the food. Rhizome extraction is called Curcuminoid and includes curcumin, detoxifrequinine and dimetixine curcumin base (38).

Curcumin today is the most important combination of turmeric, with the highest therapeutic effects (30). Curcumin is a cheap and non-toxic antioxidant found in food spices, and is obtained from a dried rhizome of a permanent plant called the Curcuma Longa. Curcumin is the most important active ingredient in Curcumin Langaga, which has a significant antioxidant effect (39, 40). Recent extensive researches on turmeric plant indicate that this plant has many pharmacological effects. Antioxidant, anti-inflammatory, and lipid lowering and high blood glucose levels have been proven in vitro and animal models (19, 41). Since curcumin prevents the formation of free oxygen radicals, its antioxidant effects may be effective in reducing the progression and complications of inflammation and hyperlipidemia (29, 31).

Evidences suggest that curcumin has inhibitory effects on the proliferation of inflammatory cells, invasion of these cells, and angiogenesis with different mechanisms (42). Curcumin is a safe and non-toxic substance that shows its anti-inflammatory effect by reducing the proliferation of inflammatory factors, cytokinases, protein kinases, and enzymes that all cause inflammation (42). It also reduces free radicals, inhibits lipid peroxidation, and increases the activity of superoxide dismutase (43). Various studies have also shown that curcumin inhibits the activity of synthetic fatty acid (FAS) and enhances the β-oxidation of fatty acids. Consequently, it can lead to an effective reduction in fat stores. By this mechanism, curcumin can regulate lipid metabolism (29). In a study by Murillon, a supplement containing curcumin and glucose in placebo in patients with chronic renal failure indicated that this supplement was safe and tolerant and could improve the level of inflammatory cytokines (44). In the Jin Yang Hu study, 0.2 mg/ml metronol curcumin in the diet of obese mice for 9 weeks resulted in weight loss and improved lipid profiles (32). In a study conducted on 24 Wistar Albino Rats, Boycleau et al. found that curcumin was decreased by serum levels of urea, creatinine, and malondialdehyde, as well as a significant increase in serum supra oxide dismutase, catalase and glutathione reductase. Their study results confirmed the adequacy of curcumin prevention in the nephropathy test model (45). In another study by Jacob et al. Entitled "Curcumin reduces the immune-dependent glomerulonephritis", it was observed that curcumin expresses mRNA, inflammatory protein, MCP-1, and beta-copy vector, matrix pertussis, fibronectin, reduces laminin and collagen. Their research clearly demonstrated that curcumin can reduce glomerulonephritis and improve kidney function (46). Studies have shown that curcumin can have protective effects on inflammatory disorders and increase the antioxidant defense in inhibiting lipid oxidation in a viable environment, so it can also be expected that the effects in the human body. Due to various effects such as anti-inflammatory effects of curcumin, no complications have ever been reported.

Considering that most patients undergo hemodialysis, eventually die from hemodialysis complications and mostly cardiovascular complications, according to the role of inflammatory and hyperlipidemic factors in the development of cardiovascular diseases in hemodialysis patients and lack of research on complementary effects Curcumin on serum lipid profiles and inflammation in hemodialysis patients. A limited number of studies on the effects of curcumin on this subject in other patients and considering that nurses, as part of the medical staff, should take steps to help patients recover. With determination to the impact of that step therefore, the author aimed to investigate the effect of supplemental curcumin supplementation on serum lipid profile and systemic inflammation in hemodialysis patients, in order to improve the quality of life and survival rates and reduce the hospitalization costs of these patients. Therefore, the purpose of this study was to investigate the effect of supplemental curcumin supplementation on serum lipid profile in hemodialysis patients.

Research Methodology. Sampling was done in a basic random sampling. According to the statistics consultant, according to similar studies, the mean and standard deviation of triglyceride in the curcumin experimental group was 141.74 ± 52.02, respectively, and in the placebo group, respectively, was 197.59 ± 96.96, 95% confidence a sample of 80% of the sample size was determined by the formula below 32.

$$= \frac{2\left(\frac{}{2} + \frac{}{}\right)^{2}}{(\ _1 - \ _2)^2}$$

$$= \frac{2(1.96 + 0.84)^2 \times 6243.26}{(141.74 - 197.05)^2} = 32$$

$$^2 = \frac{(\ _1 - 1)\ ^2_1 + (\ _2 - 1)\ ^2_2}{(\ _1 + \ _2 - 2)} = 6243.26$$

The instruments used in this study were demographic questionnaire, laboratory information, interview and observation questionnaire. serum lipid profiles and other blood parameters were measured with Pars test

kits, which are valid and stable. After approval of the research project by the research council of the Faculty of Nursing and obtaining permission from the relevant authorities, with sampling ethical considerations and explaining the purpose and manner of conducting the research to the officials of Montasiari Hospital in Mashhad, sampling was done.

In this study, adult hemodialysis patients referred to Montsarieh Hospital in Mashhad, who had been at least 6 months old since their onset of dialysis and who had inclusion criteria, were invited to participate in this study. The subject of the study, the research objectives, and the non-hazardous complement of curcumin, they were explained to them. If they wished to cooperate with patients, they received written informed consent and were asked to fast at the next dial-up center for 14-12 hours. At the start of the study, all patients took 5 ml of venous blood (for serum lipid profiles). Before dialysis were taken at hemodialysis apparatus and after dialysis, the height and weight of patients were measured. A randomized trial was conducted in a group of patients receiving curcumin supplementation or placebo group. The sampling was done randomly. Then, a randomized block method was used for random allocation of individuals in Sina curcumin capsules and the placebo capsule group. Sampling in this research by random allocation method in the form of inverting blocks is such that at first, as if a sample of the output of software R was prepared for this purpose and used for obtaining samples.

Then, considering that there are two therapies available, each block contains 4 different letters (ABCD), it is decided which two letters will be allocated to the cure by accident. Then the author choses the number of blocks in a crash. All patients eligible for inclusion criteria were assigned to one of the following two categories: the letters A and B are the "Curcumin group", the letters C and D of the placebo group.

In this study, patients received 8 mg of curcumin (Sina Curcumin on the market) once a day (80 mg after breakfast) or placebo. To duplicate this study, at the time of the study, a collection of cancers containing complementary curcumin or placebo was coded by a person other than the researcher B and A to exclude the knowledge of the researcher from the complementary type received by each group. Blood samples were also given to the individual in the laboratory, and he did not know which patient was in which group (case or placebo). Also, all patients were asked to make no changes in their diet and physical activity during the study period and to inform any researchers of any changes in their medicines. At the end of the study, again, after 5-12 hours of fasting, patients were taken 5 ml of blood before being connected to the hemodialysis apparatus. After completion of dialysis, the height and weight of the patients were measured. Patients tracked patients in order to control their use of supplements, preventing the loss of specimens, almost every 7 days through visits to patients in the hemodialysis department, and patients who did not consume more than 15% of their supplements (9 tablets) were excluded from the study. This item was evaluated by giving patients a daily tablet intake table and ticking them after eating each pill. In this study, blood samples were taken from patients at the beginning of the study and at the end of the eighth week in a 5-cavity tube. They were not added to this anticoagulant tube and centrifuged for 10 minutes at a rate of 2,000 rpm to separate them. Then the isolated serum was kept at freezing temperature of 20 ° C until biochemical tests were performed. Also, in this study, serum HDL lipoproteins were isolated using Pars Tests by means of phosphotangestric acid and magnesium chloride separators. Then the cholesterol concentration in HDL (or HDL-C), total cholesterol and serum triglyceride was measured by enzymatic methods using Selectra 2 Autoanalyser and using Pars Tests. In this study, serum triglyceride concentration in patients with hemodialysis was less than 400 mg/dL. Therefore, determination of LDL-C concentration using the formula LDL-C = TC-HDL-C (TG / 5), which is known as Friedwald (97) took place. Blood serum albumin concentration was measured by Kerzol Green bromine method by using Selector 2 Autoanalyser and using pars test kits. The rate of change in the level of triglyceride, total cholesterol, HDL-C and serum albumin was 2.9, 4.2, 5 and 3.6%, respectively. Urea and creatinine were measured using Pars test kit at a wavelength of 340 nm at 37°C while the photometer with Blanc was set to zero. After completion of the data collection, the forms are encoded and entered into the computer. After ensuring that the data is entered correctly, data analysis is analyzed by SPSS 16 software and Wilkasson, Chi-square, T and Kolmogorov-Smirnov tests. The Kolmogorov-Smirnov test was used to measure the normality of the data. T-test was used for weight, blood urea nitrogen, creatinine, cholesterol and LDL-C, and Wilcason test for albumin, fasting blood glucose, triglyceride, HDL- C were used and chi-square test was used for gender variable.

Result and Discussion. Comparison of serum triglyceride maen, cholesterol, LDL-c, HDL-c, serum levels showed no statistically significant difference between the two placebo groups and the intervention group at the beginning of the study. Also, there was no significant difference between the two placebo groups and the intervention group before the intervention (factors such as age, gender, height, etc.) before intervention.

The first hypothesis was that the addition of curcumin reduced the concentration of triglycerides, cholesterol, LDL-C and increased serum HDL-C in hemodialysis patients. According to this study, serum LDL-C was decreased and serum HDL-C increased, but the concentration of triglycerides and cholesterol decreased but did not materialize. The results of the present study, according to the results of the study by Ledeb et al., showed that there is a significant difference between the serum LDL-c and HDL and levels between the placebo and intervention groups after the intervention. But other results obtained in this study with the results It is contradictory from the study of Adab et al. Adab and his colleagues conducted a study titled "The effect of turmeric consumption on anthropometric indices, glycemic status and lipid profile in type 2 hyperlipidemic

patients with type 2 diabetes mellitus" at the Endocrine Research Center of Firoozgar, Tehran University of Medical Sciences (90). The results of their study indicated that after 8 weeks of intervention, there was a significant decrease in serum triglyceride and LDL-c in the turmeric group, BMI, BMI. Also, at the end of the study, there was a significant difference in LDL-c, serum triglyceride concentration between the two groups. Total cholesterol, serum HDL-c and apolipoprotein A-1 were also significantly different between the two groups at the end of the study. There were no significant differences in other variables such as glycemic status and body weight at the end of the study. Turmeric powder intake increased the lipid profile of type II diabetic patients but did not have a significant effect on glycemic status (90). Perhaps one of the reasons for not significantly altering the serum triglyceride and cholesterol status is the use of pure turmeric powder instead of curcumin and dosage. It also seems that if the present study continued longer, the variation of the parameters is also meaningful. Because in the present study, for example, triglyceride, before and after intervention, some changes have occurred, but this change has not been meaningful, it may be meaningful if continued for a longer time. In addition, the type of patients may have an effect on that the triglyceride changes in this study. So, the author can conclude that the results of the present study are consistent with the results of the study by Palma et al. Curcumin alone cannot have anti-inflammatory and protective effects on all patients with dialysis and can be used as a complementary combination therapy. In the study of Palma et al., Oxidative stress parameters in blood, kidney, and liver of diabetic rats treated with curcumin and insulin were investigated. In conclusion, plant-derived antioxidants can have a combined effect in the treatment of endocrinopathies rather than being treated alone (55). A study by Sklandar et al in 2010 in people with diabetes type 2 mellitus in Indonesia showed ethanolic extract of garlic and turmeric in three different doses, 1.2 g, 1.6 g and 2.4 gram per a day for 12 weeks, the levels of triglyceride, total cholesterol, LDL, fasting glucose, HbA1C and BMI decreased significantly. There was also a significant increase in serum HDL level in 4.2 g compared to two other doses (91). the present study is consistent with above mentioned study in a view of the increase in serum HDL and LDL, but other results in our study contradict the results of this study. The reason for this inconsistency is that in the above mentioned study, patients received combination therapy of garlic and turmeric, while in the present study, patients only received curcumin supplement, and the dosage of curcumin was different in the present study. In a study conducted by Adroos Alvoy et al. In 2008 on patients with acute coronary syndrome, 75 patients received curcumin in three doses of 90 mg / dl (45 mg / dl, 90 mg / dl) 2 months. The findings showed that low dose curcumin reduced total cholesterol, LDL-c and increased C-HDL levels (92).

This study is also true in many ways, since the present study curcumin has been shown to lower serum LDL and increase serum HDL. In a study by Musli et al in 2011 on lipid-rich rats, the lipid profiles of rats consuming 80 mg / dl 80 curcumin supplement for 60 days were reduced and serum levels of HDL increased (93). This study, which is similar to the present study, since this curcumin dosage is about 80 mg/dl. Particularly, curcumin, like the present study, has decreased lipid profiles including serum LDL and increased HDL. In a study by Jin Yang Ho et al in 2012 on 32 obese mice, interventional rats receiving 0.25 methanol curcumin for 9 weeks reduced the weight gain and adipose tissue in comparison with The control group was observed. Also, levels of total cholesterol and triglyceride in serum and liver significantly decreased, which did not match the findings with the present study. It seems that if the present study lasted longer then, changes in serum lipid profiles may be significant. Morillon et al., conducted a study by using a supplement consisting of curcumin and glucose in placebo in patients with chronic renal failure. The results of the study showed that chronic mild to moderate renal insufficiency with chronic inflammation and low antioxidant activity is associated. Curcumin and buckwheat are safe and tolerant and improve the levels of inflammatory cytokines, which is not consistent with the results of the present study. However, since the effect of curcumin has been investigated with candy, the effect of curcumin alone cannot be studied (44).

Jacob, in an animal study, showed that curcumin stimulates glomerulonephritis by immune complexes in mice. Curcumin reduced the expression of the mRNA gene of the monocyte inflammatory proteins, reduced the change in the growth factor B and the matrix proteins, fibronectin, laminin and collagen. The results of this study clearly demonstrated that curcumin reduces glomerular corrosion, improves renal function, and therefore has human studies of dialysis, it can be used as a complementary drug in dialysis patients. It should be noted, however, that this study, in addition to being carried out in an animal sample, also has a number limitation. This study is also about glomerulonephritis, mediated by immune complexes, so its results can not be completely generalized to our study (46).In another study by Lee-Nassan et al. About the protective effects of curcumin on inflammatory process in diabetic nephropathy, a study was conducted and exprimented on mice. The results showed that kidney volume was significantly increased in the two diabetic groups compared to the placebo group, and the kidney weight ratio increased to body weight, but this increase was significantly lower in the treatment group with curcumin than in the untreated group. The researchers concluded that curcumin had the potential for diabetic nephropathy treatment by inhibiting the inflammation gene by reversing phosphorylation of tyrosine-cavolin-1 (89). In a study by Wang et al., the anti-inflammatory effects of a monocarbonyl-curcumin A13 analogue were investigated in vitro. A13 enhances elevated plasma levels of NO and TNF-α, IL-6 and significantly inhibits the proliferation of inflammatory gene in the liver and improves lung damage. Also, the A13 substance in the mice`s Cancer Research Institute mice reduces vascular permeability and inhibits pain

response in chemical induction models. In the end, researchers have concluded that, overall, A13 has shown anti-inflammatory activity both in the lab and in the body of living organisms through inhibition of various inflammatory mediators (47). The two above mentioned studies, it has been shown that the protective and anti-inflammatory effects of curcumin on the kidney in contrast-induced nephropathy in diabetic rats, and although all of these studies have been conducted as case-control, these studies have been limited to a limited number of laboratory animals. The results cannot be generalized to human specimens. Other findings from this study showed that the mean concentration of albumin and creatinine did not change in the intervention and control groups at the end of the study. However, the mean concentration of blood urea nitrogen at the end of the study was modest in the intervention and control group. At the end, the results also showed that the mean fasting blood glucose level at the end of the study was reduced in the experimental and control groups. The results of the present study suggest that there is no change in the mean creatinine concentration and an increase in the mean concentration of blood urea nitrogen with the results of the study by Boyuklo and Sadooghi. In a study, Boyooko investigated the protective effects of curcumin in contrast-induced nephropathy. The results of his study showed that curcumin administration before and after administration of contrast significantly reduced the level of urea and creatinine (45). However, in this study, the sample size was less than the present study was performed on male rats in this study. In a study titled Corkumin on pituitary adrenal axis and kidney indices in diabetic rats with alloxan, curcumin was injected intraperitoneally into experimental diabetic groups for 25 days. At the end of the injection period, serum urea, uric acid, creatinine, albumin and adrenocorticotropin, cortisol and aldosterone hormones were measured. The kidney tissue sections were prepared and examined by optical microscopy. Serum urea, uric acid and creatinine levels were significantly reduced in curcumin-treated diabetic groups compared to the diabetic control group, and albumin significantly increased ($p < 0.05$). Treatment of diabetic rats by dose-dependent curcumin improves kidney nephron damage (98).

Result. The results of this study showed that curcumin supplementation can be effective in preventing heart disease, since it reduces serum LDL and increases serum HDL and decreases triglyceride (in a meaningless way), and it can be used as a complementary treatment.

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