The Effects of Nano-curcumin Supplementation on Serum Level of hs-CRP, Adhesion Molecules, and Lipid Profiles in Hemodialysis Patients, A Randomized Controlled Clinical Trial

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Introduction. Hemodialysis (HD) patients are considered as a high-risk population for cardiovascular disease, within which morbidity and mortality have been determined to be associated with dyslipidemia, pro-inflammatory cytokines, increased levels of C-reactive protein (CRP), and adhesion molecules (ICAM-1, VCAM-1). Different markers have been investigated to detect inflammation in hemodialysis patients, as well as the prognostic values of these markers.
Methods. The present study aimed to investigate the effect of nano-curcumin (120 mg) over 12 weeks on hs-CRP levels, adhesion molecules (ICAM-1, VCAM-1), and serum lipid profiles on hemodialysis patients in a randomized controlled clinical trial.
Results. The results revealed that the mean serum hs-CRP level in the nano-curcumin group exhibited a decrease by the end of the study, when compared to mean serum hs-CRP level in the placebo group. However, this intra-group trend was not found to be statistically significant ($P > .05$). Nevertheless, a significant difference was determined between the values in the group receiving nano-curcumin, in comparison with the placebo group, at the end of the study ($P < .001$). Based on the attained results, mean serum levels of VCAM-1 in the nano-curcumin group were significantly reduced at the end of the study, compared with the placebo group ($P < .001$). Furthermore, the intra-group changes comparison showed significant reductions in serum levels of ICAM-1 in patients treated with nano-curcumin at the end of the study ($P < .05$). Additionally, though decreases in mean triglycerides, total cholesterol, LDL-C were noted, there were no statistically significant intra-group differences ($P > .05$). Moreover, intra-group changes comparison of HDL-C levels and fasting blood sugar did not show any significant changes.
Conclusion. The current study indicates that nano-curcumin may show beneficial effects in lowering inflammation and hs-CRP levels, as well as adhesion molecules (ICAM-1, VCAM-1), in hemodialysis patients. However, the evidence is still insufficient.

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INTRODUCTION

Chronic kidney disease (CKD) is defined as progressive and irreversible failure in renal function which leads to complete kidney failure. End-stage renal disease (ESRD) is the most prominent expression of kidney disease, in which the need for

renal replacement therapy, dialysis (hemodialysis and peritoneal dialysis), or kidney transplantation becomes necessary.[1]

Inflammation is a common complication in patients with CKD, especially hemodialysis (HD) patients, and studies have shown that 30 to 60% of these patients have inflammation.[2, 3] The presence of inflammation in HD patients can contribute to the development of cardiovascular disease, malnutrition, resistance to erythropoietin, anemia, bone disease, susceptibility to infection, cancer, and reduced residual renal function.[4, 5] There is a special pattern of inflammatory markers in HD patients, including C-reactive protein (CRP) and pro-inflammatory cytokines (e.g., IL-1β, IL-6, IL-6 and tumor necrosis factor-α (TNF- α).[6, 7]

Intracellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) are known as two inflammatory factors, which increase their secretion levels under inflammatory conditions. Furthermore, it has been shown that ICAM-1 and VCAM-1 are considered as endothelial activation indicators in ESRD patients on HD.[8, 9]

Finding a safe and effective anti-inflammatory agent is a real challenge in modern medicine. Curcumin (an active component of turmeric) is highly pleiotropic molecule with multiple molecular targets and therapeutic effects.[10]

Several studies have been carried out on the biological effects of curcumin, which have shown antioxidant, anti-inflammatory, anti-proliferative, and pro-apoptosis effects, thus having great therapeutic potential in the treatment of diseases.[11, 12] Studies have shown that nano-curcumin has a higher bioavailability, solubility, and delivery than curcumin in the body.[13-15]

Since curcumin – in addition to its beneficial effects on reducing inflammation and improving vascular function – has antioxidant effects, it can therefore be used as a targeted drug for the treatment of dialysis patients.[16-18]

The present evidence emphasizes the role of inflammatory indices, especially vascular inflammatory parameters, in the development of cardiovascular diseases in HD patients. Therefore, the present study was designed to evaluate nano-curcumin supplementation on certain inflammatory factors and serum levels of lipid profiles among patients attending a HD program.

MATERIALS AND METHODS

Trial Design and Ethical Aspects

The current study was a parallel, randomized, double blind, controlled clinical trial, which included patients with CKD undergoing HD at the dialysis center of Taleghani Hospital of Urmia, Iran, from December 2017 to October 2018. This study was approved by the Ethics Committee of the Science and Research Branch, Islamic Azad University, Tehran, Iran (Ethical code: IR.IAU.SRB.REC.1395.25).

In addition, the present study was registered in the Iranian Registry of Clinical Trials (IRCT ID: IRCT20180328039154N1). This article describes work on a part of the project examining the effects of nano-curcumin on HD patients. In this study, informed consent forms were collected from all patients before initiating the study, with the information remaining completely confidential. Patients had the right to cease participation at any stage.

Sample Size

The minimum sample size was calculated as being 26 for each group – at a power of 80% and an alpha of 0.01 for a 2-arm parallel study, in order to reveal a difference of 2.1 mg/L in serum CRP level using 2-tailed test. A pooled standard deviation of 2.5 ng/mL was considered in the study, and obtained from the study of Panahi *et al*.[19]

Participants

60 eligible HD patients were selected from the HD units at Taleghani Hospitals in Urmia, Iran.

Inclusion criteria included: aged 18 to 80, attending a HD program 3 times a week for 4 hours, initiation of dialysis at least 6 months before the study, hemodialysis with polysulfone. Exclusion criteria included: Receiving antioxidant vitamins C and E, omega-3 fatty acids, fish oil and L-carnitine at least one month before the study; thyroid disorders, liver disease, active infection; patients with chronic infectious diseases and/or chronic inflammatory diseases; receiving steroidal and non-steroidal anti-inflammatory drugs; patients who had undergone surgery and/or been hospitalized within the last one month. Other exclusion reasons included planned renal transplantation during the study period, sensitivity to turmeric supplementation, and unwillingness to cooperate. It is worth noting

that the HD program, procedure and type of filters (high flux polysulfone) were not altered for any of the participants.

Intervention, Randomization, and Blinding

The patients were randomly allocated to either a nano-curcumin group or placebo group by randomization procedure after stratification based on diabetes mellitus, sex and body mass index (BMI). For randomization, a block randomization method was used.

Considering the sample size (60) and the existence of two groups, the size of the blocks was considered as 6 and possible balanced combinations with 3 C (Curcumine) and 3 P (Placebo) subjects were calculated (CCCPPP, CCPPCC,CPCPCP,..). A specific code was given, and from all these codes, according to the sample size, 10 blocks were randomly selected to determine the assignment of all patients into groups. The block randomization was performed by a trained dietician.

Patients in the intervention group received 120 mg of nano-curcumin supplement each day as 3 nano-curcumin soft gel capsules (Exir Nano Sina, Tehran, Iran), dosed at breakfast, lunch and dinner, for 12 weeks. The placebo group, however, received 3 placebo soft gel capsules containing paraffin which were similar to the package of soft gel capsules in the intervention group in terms of color, figure, and size. These were also synthetized by Exir Nano Sina Company Tehran, Iran.

In order to maximize the absorption of supplementation, patients were asked to take supplements with food and meals. Patients were advised to take their medication after the end of HD to prevent the drug from being removed by dialysis (on HD days). In addition, patients were asked to not change their usual diet and physical activity during the study, and to refrain from taking other supplements and medications, except for those prescribed by a physician. The blinding procedure was conducted by a trained dietician, and all other parties (subjects and researchers) in the study were kept unaware of the grouping.

At the final appointment, patients were asked to bring their unused capsules. Consumption of less than 90% of supplements by the end of the 12th week was considered as unwillingness to participate in the study.

Anthropometric Measurements

Body weight, height, BMI were determined at the beginning and the end of the study. Patients were weighed after dialysis to determine the patient's dry weight.

BMI was calculated based on the relevant formula by dividing the weight (kg) by the square of height in meters (kg/m^2).

Blood Sampling Procedure

At the beginning and the end of the study, 5 ml of venous blood was taken from the patients after 12 - 14 hours fasting in gelatinous tubes (Clot Activator), before individuals were connected to the HD apparatus at midweek.

Blood samples were placed in the laboratory for 30 minutes in order to create a clot. After complete blood clotting, they were centrifuged immediately for 20 minutes at 1080 g (3000 rpm), then serum samples were collected and immediately stored in a freezer at -80 °C until use.

Measuring the Serum Level of Hs-CRP, VCAM and ICAM

To measure the serum level of hs-CRP, an immunoturbidimetry kit (Pars Azmoon kits; Tehran-Iran) was used. The serum level of sVCAM-1 and sICAM-1 was detected using a human ELISA kit (Diaclone SAS Biotech Co., Ltd, France).

Measurement of Biochemical Variables

Total cholesterol, triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and fasting blood sugar (FBS) were measured by using various colorimetry methods with commercial kits (Pars Azemoon, Tehran, Iran).

Calculate Kt/V

The adequacy of dialysis, based on the Kt/V index, was shown for each subject at the beginning and end of the 12th week by applying the Kt/V software, based upon the patient medical records – including the concentration of blood urea nitrogen before dialysis, post-dialysis blood urea nitrogen, dialysis session length, post-dialysis weight, and ultrafiltration volume.

Statistical Analysis

SPSS version 21 (IBM Corp. Armok, NY, USA)

was used for statistical analysis. Normal distribution of data was assessed using the Kolmogorov-Smirnov test.

All variables between groups before and after the study were analyzed by t-test, paired t-test, Wilcoxon Signed Ranks test, Mann-Whitney test, Multivariate linear regression analysis, and the Chi-square test using SPSS version 21 (IBM Corp. Armok, NY, USA).

RESULTS

Of the 60 HD patients qualified for this clinical trial, 3 patients were excluded in the nano-curcumin supplement group because of an allergic reaction to curcumin, surgery, and personal reasons. 3 patients in the placebo group were also excluded because of hospitalization, change of dialysis center, and death (Figure 1).

Mid-term follow-up (every two weeks) and follow-up at the end of the study showed that none of the patients in either study group reported any specific adverse effects, and both supplements and placebo capsules seemed to be readily acceptable.

Demographic and Clinical Findings of Patients

The baseline characteristics of the patients, including age, sex, BMI, dialysis duration (months), the distribution of the cause of renal failure, albumin level and vascular access type did not differ significantly between the two groups. There was no significant difference in dialysis adequacy between the two groups at baseline and the end of week 8 (Table 1).

Medication Use

In Table 2, medication used during the study was given in accordance with the prescribing physician and based on the patient report. Using Chi-square

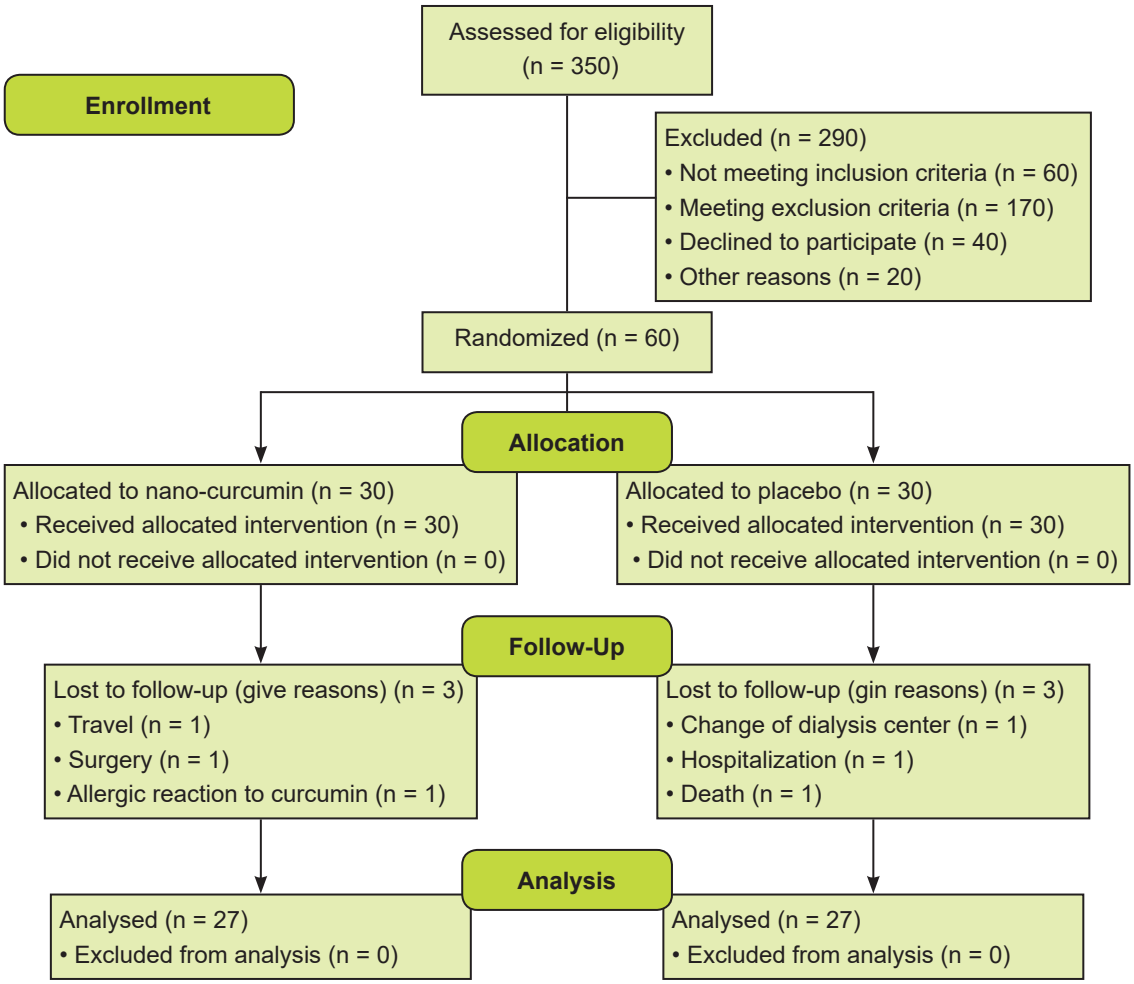

Figure 1. It mentions CONSORT flow diagram of the progress through the phases of the randomized clinical trial of the two groups.

Table 1. Baseline Characteristics of Hemodialysis Patients in 2 Groups

Characteristics	Nano-curcumin Group (n = 27)	Placebo Group (n = 27)	*P*
Age, y	55.33 ± 12.95	59.05 ± 7.68	> .05[a]
Sex			
Male	18 (66.7%)	16 (59.3%)	> .05[b]
Female	9 (33.3%)	11 (40.7%)	
Dialysis Duration, mo	39.76 ± 27.69	36.46 ± 21.44	> .05[a]
Dialysis adequacy (KT/V)			
Before	1.34 ± 0.18	1.31 ± 0.17	> .05[a]
After	1.31 ± 0.15	1.29 ± 0.14	
BMI			
Before	26.10 ± 5.19	27.19 ± 5.19	> .05[a]
After	25.95 ± 4.97	27.11 ± 5.04	
Albumin, g/dL	4.13 ± 0.47	4.26 ± 0.47	> .05[a]
Vascular Access			
Arteriovenous Fistula	21 (77.8 %)	23 (85.2 %)	> .05[b]
Arteriovenous Graft	6 (22.2 %)	4 (14.8 %)	
Causative Factor for Dialysis			
Diabetes	12 (44.4%)	10 (37%)	> .05[b]
Hypertension	7 (25.9%)	12 (44.4%)	
Diabetes and Hypertension	2 (7.4%)	3 (11.1%)	
Glomerulonephritis	3 (7.4%)	2 (7.4 %)	
Urologic Disorders	3 (11.1%)	0 (0 %)	

All values are expressed as means ± SD or numbers.
[a]Mann–Whitney U test
[b]Chi-square

Table 2. Medication Used by Patients in the 2 Groups

Characteristics	Nano-curcumin Group (n = 27)	Placebo Group (n = 27)	*P*[a]
Calcium Carbonate	16 (59.3)	10 (37)	> .05
Calcitriol	13 (48.1)	11 (10.7)	> .05
Renagel	9 (33.3)	6 (22.2)	> .05
Apex	26 (96.3)	27 (100)	> .05
Vennofer	15 (55.6)	17 (63)	> .05
Atorvastatin	19 (70.4)	16 (59.35)	> .05
Blood Pressure Reducing Drugs	19 (70.4)	24 (88.9)	> .05
Glycemic Control Drugs	14 (51.9)	13 (48.1)	> .05

Values are in the number (%).
[a]Chi-square

test, there was no significant difference between the two groups in terms of medication use.

Findings of FBS and Lipid Profiles

The mean of FBS, TG, total cholesterol, LDL-C and HDL-C showed no significant difference between the two groups at the beginning and the end of the study (Table 3, $P > .05$). Additionally, the Wilcoxon test showed no significant difference at the end of the study in terms of mean FBS and lipid profile levels in the studied groups ($P > .05$).

Serum Levels of Hs-CRP and Adhesion Molecules

The effects of nano-curcumin supplementation on serum hs-CRP concentrations are presented in Table 4. In the nano-curcumin group, hs-CRP levels significantly decreased compared to the beginning of the study, but there was no significant difference between the two groups by the end of the study ($P < .001$). In the placebo group, serum hs-CRP levels did not change significantly at the end of the 12th week ($P > .05$). In the single-variable analysis, the mean hs-CRP at the end of the study was not significantly different between the two groups ($P > .05$). To control for the effects of confounding factors, regression analysis using the backward method was applied, which demonstrated significance after adjusting for confounders ($P < .05$), indicating the effectiveness of the intervention.

As shown in Figure 2A, the results of the study indicated that mean serum hs-CRP levels decreased by 40.93 (95% CI: - 46.56 to -35.3), which was statistically significant ($P < .001$).

After 12 weeks of intervention, mean serum

Table 3. Serum Level of Lipid Profile and FBS in Hemodialysis Patients in 2 Groups

Characteristics	Nano-curcumin Group (n = 27)	Placebo Group (n = 27)	*P*[a]	*P*[b]
FBS, mg/L				
Before	111.89 ± 39.12	103.26 ± 32.26	> .05	> .05
After	105.41 ± 29.55	99.96 ± 38.79	> .05	
Difference	6.48 ± 15.93	3.30 ± 15.89	> .05	
P[c]	> .05	> .05		
Triglyceride, mg/dL				
Before	133.67 ± 54.02	165.63 ± 87.52	> .05	> .05
After	132.00 ± 43.37	161.26 ± 119.3	> .05	
Difference	1.67 ± 40.68	4.37 ± 23.100	> .05	
P[c]	> .05	> .05		
Total Cholesterol, mg/dL				
Before	141.30 ± 40.72	155.00 ± 50.64	> .05	> .05
After	141.22 ± 32.89	152.56 ± 42.69	> .05	
Difference	0.07 ± 25.2	2.44 ± 26.51	> .05	
P[c]	> .05	> .05		
LDL-C, mg/dL				
Before	82.26 ± 28.02	84.83 ± 36.83	> .05	> .05
After	82.15 ± 21.52	86.26 ± 29.15	> .05	
Difference	0.11 ± 17.85	- 1.43 ± 23.55	> .05	
P[c]	> .05	> .05		
HDL-C, mg/dL				
Before	32.81 ± 7.84	35.41 ± 11.61	> .05	> .05
After	33.81 ± 8.14	34.63 ± 9.73	> .05	
Difference	-1.00 ± 5.82	0.78 ± 6.84	> .05	
P[c]	> .05	> .05		

All values are expressed as means ± SD.
Abbreviations: FBS, fasting blood glucose; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol
[a]Mann–Whitney U test
[b]Multiple Linear Regression, adjusted for confounding factors of age, sex, BMI, duration of dialysis, calcitrole, and atrovastatin consumption
[c]Wilcoxon Signed-rank test

Table 4. Serum Level of hs-CRP, ICAM, and VCAM in Hemodialysis Patients in 2 Groups

Characteristics	Nano-curcumin Group (n = 27)	Placebo Group (n = 27)	*P*[a]	*P*[b,d]
hs-CRP, mg/L				
Before	12.95 ± 8.57	11.5 ± 7.75	> .05	< .05[d]
After	6.9 ± 3.58	11.1 ± 7.17	> .05	
Difference	6.05 ± 5.37	0.39 ± 1	< .001	
P[c]	< .001	> .05		
ICAM-1, ng/L				
Before	877.89 ± 246.54	844.80 ± 220.46	> .05	< .05
After	719.59 ± 211.11	838.79 ± 223.91	< .05	
Difference	158.30 ± 78.11	6.01 ± 74.83	< .001	
P[c]	< .001	> .05		
VCAM-1, ng/L				
Before	1159.84 ± 119.28	1172.99 ± 79.24	> .05	< .05
After	1092.39 ± 98.70	1146.74 ± 78.05	< .05	
Difference	67.45 ± 78.11	29.68 ± 79.14	< .05	
P[c]	< .001	> .05		

All values are expressed as means ± SD.
Abbreviations: hs-CRP, high-sensitivity C-reactive protein; ICAM-1, Intercellular adhesion molecule-1; VCAM-1, Vascular cell adhesion protein-1
[a]Mann–Whitney U test
[b]Multiple Linear Regression, adjusted for confounding factors of age, sex, BMI, duration of dialysis, calcitrole, consumption
[c]Wilcoxon signed-rank test
[d]Multiple Linear Regression, adjusted for confounding factors of age, sex, BMI, duration of dialysis, calcitrole, albumin, consumption

VCAM-1 levels were significantly different between the two groups ($P < .05$, Table 4, Figure 2B).

After controlling for the effect of confounders with a linear regression test, only the group variable remained significant ($P < .05$), showing the effectiveness of the intervention. As shown in Figure 2B, the mean serum level of VCAM-1 was reduced by 5.3% (95% CI: -8.06 to -2.99), as compared to baseline values, which was statistically significant ($P < .05$).

Furthermore, the between-group means of serum ICAM-1 level after 12 weeks were significantly different ($P < .05$, Table 4, Figure 2C). The mean serum level of ICAM-1 in the nano-curcumin group decreased at the end of the study, exhibiting significantly lower levels ($P < .001$). After controlling for the effect of confounders with the multivariate linear regression test, only the group variable was found to be significant ($P < .05$), indicating the effectiveness of the intervention.

As shown in Figure 2C, mean serum ICAM-1 levels showed a decreased trend to 17.56% (95%CI: -21.30 to -13.81), which was statistically significant ($P < .001$).

DISCUSSION

Ample evidence suggests that that metabolic factors and dialysis clearance inflammation are involved in the morbidity and mortality of HD patients, where morbidity has been found to be linked to an increased level of CRP, pro-inflammatory cytokines (e.g. IL-2 or IL-6), and adhesion molecules (ICAM, VCAM).[20, 21]

Studies have shown that serum CRP levels have been found to annually increase over 3 years of follow-up among HD patients.[22] Based on the current evidence, the biological inter-individual and intra-individual variability of CRP has been revealed to be higher in dialysis patients, as compared to healthy populations. However, there are only a few studies that have reported the long-term CRP consequences, none of which has examined hs-CRP in dialysis patients.[5, 23, 24]

CRP is considered to be a potentially valuable marker for predicting inflammation in patients suffering from chronic renal failure. Serum levels of hs-CRP have demonstrated increased trends in patients suffering from chronic renal failure.[25, 26]

In the present study, the mean serum hs-CRP level in the nano-curcumin group was lower at

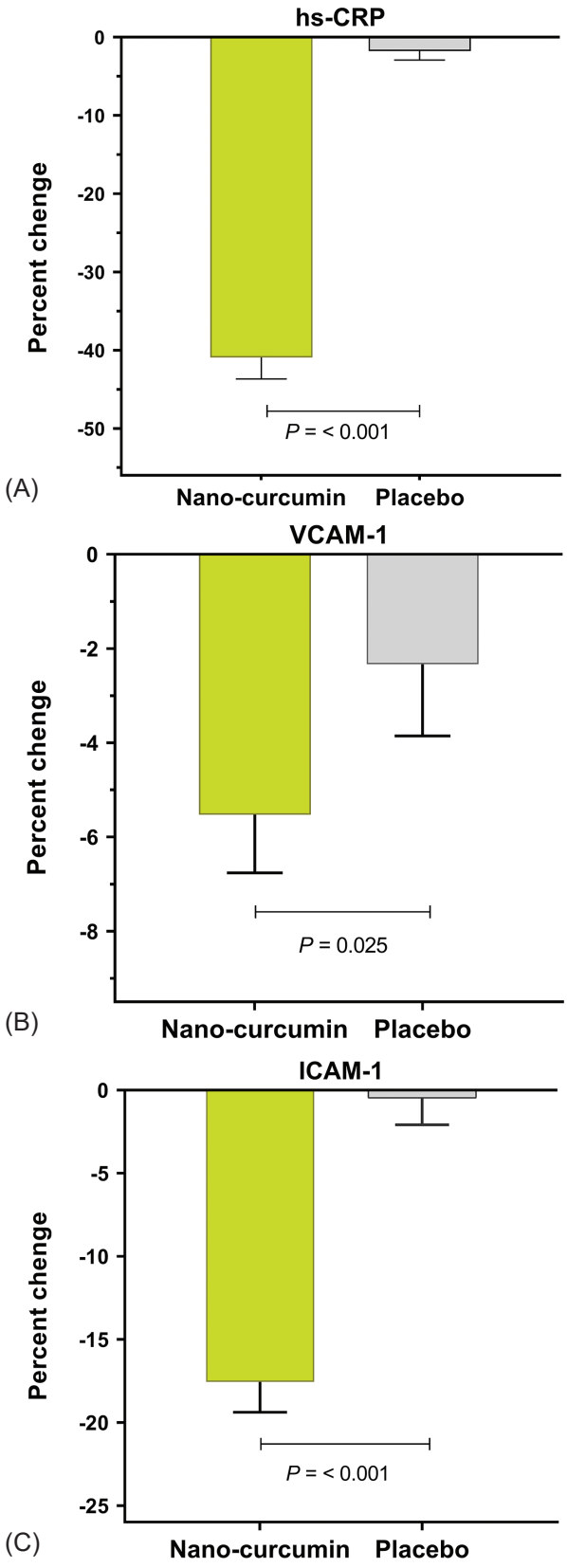

Figure 2. It shows the percentage reduction of hs-CRP (A), VCAM-1 (B), and ICAM-1 (C) after 12 weeks of intervention in hemodialysis patients in the two groups.

the end of the study as compared to the mean serum hs-CRP level in the placebo group, but this difference was not found to be statistically significant. However, a significant difference was observed between the values in the group receiving nano-curcumin at the end of the study, as compared to the placebo group. To control for the effects of confounding factors, regression analysis using the backward method was applied, taking into account variables such as age, sex, BMI, length, duration of dialysis and the use of calcitriol. This demonstrated a significant difference in hs-CRP levels after adjusting for confounders, indicating the positive effect of the intervention in terms of reducing inflammation.

The current findings are consisted with results of Samadian *et al.*, 2017, which indicated hs-CRP levels were significantly decreased in the turmeric group. However, they observed there were no significant differences between the values in the turmeric and placebo groups at the end of the study, demonstrating the effectiveness of turmeric for reducing inflammation.[27] A study suggested that curcumin supplementation was linked to improvements in hs-CRP values[28], which is in consistent with our results. A pilot study revealed that the use of curcumin has been attributed to decreased clinical symptoms of inflammatory bowel disease and CRP levels.[29]

An increasing body of evidence suggests that curcuminoids supplementation may be capable of decreasing circulating levels of CRP, depending on the bioavailability of curcumin preparations (in order to address curcumin's poor bioavailability) and the duration of treatment.[30] Further studies require in-depth understanding of curcuminoids' effects and mechanisms underlying the regulation of the inflammatory process in order confirm the effect of curcuminoids on CRP levels and other inflammatory factors. Our study revealed that the mean serum level of VCAM-1 in the nano-curcumin group had significantly decreased at the end of the study, as compared to placebo group. Additionally, the findings exhibited significantly lower levels of ICAM-1 in the patients under treatment of nano-curcumin at the end of the study, as compared to placebo group.

Another study demonstrated that the levels of CRP, VCAM-1, and ICAM-1, cholesterol, and LDL-C were significantly decreased in rats fed a high-sucrose, high-fat diet.[31] In many *in vitro* and *in vivo* studies in both animals and humans, the anti-inflammatory effect of curcumin has been demonstrated. In this regard, Kim *et al.* concluded that curcumin was capable of inhibiting TNF-α-induced mRNA expression of ICAM-1 and VCAM-1 in a dose-dependent manner in human endometriotic stromal cells.[32] Moreover, another study by Belcaro *et al.* (2010) observed the remarkable long-term efficacy of Meriva® supplementation as a curcumin-phosphatidylcholine complex for improving both the clinical and biochemical endpoints in osteoarthritis patients, where curcumin was capable of providing a significant improvement in the clinical symptoms of the disease for 8 months, and reducing the levels of VCAM-1.[33] Another study revealed that di- (2-ethylhexyl) phthalate (DEHP) has been attributed to an increased level of ICAM-1 and IL-8, which were inhibited by curcuma longa Linn via the ERK and p38 MAPK signaling pathways in human umbilical-vein endothelial cells.[34] Another study indicated that curcumin was capable of suppressing VCAM-1 expression levels in human intestinal microvascular endothelial cells via inhibiting Akt, p38 MAPK, and NF-κB.[35] An increasing body of evidence suggests that curcumin may serve a novel therapeutic approach for targeting endothelial activation in inflammatory disease.

The present results show that mean TG, total cholesterol, LDL-C and FBS levels did not show significant differences between the nano-curcumin and placebo groups. Conflicting findings have been published for the effects of curcumin supplementation on serum lipid profiles. Many studies have indicated the hypolipidemic properties of curcumin in high-risk populations.[28, 36-41]

A randomized controlled trial indicated that curcuminoids supplementation has been attributed to a decreased serum level of atherogenic lipids (nonHDL-C and Lp (a)) in type 2 diabetes mellitus (T2D). This study suggested that curcuminoids can be considered as a tool for decreasing the risk of cardiovascular events in dyslipidemic individuals suffering T2D.[39]

Low doses of curcumin (80 mg/d) have been demonstrated as being capable of reducing plasma TG in healthy middle-aged individuals, and high doses of 1000 mg/d were able to decrease the plasma levels of TG in obese patients, whereas they were not capable of affecting serum levels of

total cholesterol, LDL-C and HDL-C.[42, 43]

The effects of curcuminoids on serum lipid profiles are still controversial, therefore further evidence from randomized controlled is needed for clarification of this issues. These controversial observations could be due to many reasons, for example: type of study, population (RCT, healthy subjects, short trials without evaluating all profiles), as well as different doses of curcuminoids, etc.[28]

The common dosages of curcumin for different purposes (i.e., type of disease) are likely to vary, in order to address its poor systemic bioavailability, poor absorption, metabolism, and bio-distribution. Nano-curcumin was prepared as nanomicelles in order to improve its bioavailability, and thus may be used effectively. Daily doses of 1200 mg-2 g have been applied without any serious side effects and curcumin doses up to 12 g have been reported to be tolerated.[28, 44]

CONCLUSION

The present study suggests that nano-curcumin can be capable of decreasing inflammation and mean hs-CRP levels, as well as adhesion molecules (ICAM-1, VCAM-1) in HD patients.

Further confirmation of the efficacy and safety of nano-curcumin supplementation is required through randomized clinical trials with larger sample sizes, and long-term follow-up in HD patients.

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CONFLICT OF INTEREST

None declared.

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