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ORIGINAL ARTICLE

Effect of Omega-3 Supplementation on Lipid Profile and Inflammatory Markers in Children with Chronic Kidney Disease

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ABSTRACT

Background: Patients with cardiovascular disease, lupus nephritis, idiopathic immunoglobulin A nephropathy, and renal failure may benefit from omega-3 fatty acids via changing the shape and function of cell membranes and the synthesis of lipid mediators such eicosanoids. This study aimed to evaluate the role of omega-3 fatty acids supplementation in minimizing and prevention of cardiovascular disorders in children with chronic kidney disease.

Methods: This clinical trial investigation, which was carried out in the pediatric nephrology section of the pediatric department at Zagazig University, involved twenty pediatric patients with chronic kidney disease (CKD) undergoing hemodialysis. All patients received 1000mg of omega-3 polyunsaturated fatty acids (ω-3PUFAs) daily for three months. Before and after the trial, blood samples were taken from the patients to evaluate hemoglobin, ferritin, triglycerides, total cholesterol, LDL cholesterol, and C-reactive protein.

Results: 20 patients, 11 males and 9 females, mean age was 13.9 ± 2.1 years (11–18 years). There was a significant decrease in CRP levels (median from 6.2 to 1.3, $p<0.001$), total cholesterol decreased by a median of 16.9%, triglycerides by 20.4%, and LDL cholesterol by 15.3%, while HDL cholesterol increased by 10.76% ($p<0.001$) and was clinically meaningful. 100% of patients showed improvements in total cholesterol and triglycerides, while 90% showed improvements in LDL cholesterol. A significant improvement in CHD risk classification, with the proportion of patients in the lowest risk category (class 1) increasing from 20% to 65% after supplementation.

Conclusions: Omega-3 supplementation could be a valuable therapeutic intervention in pediatric CKD patients, offering benefits across multiple parameters, including inflammation, lipid profile, and cardiovascular risk.

Keywords: Omega-3; hemodialysis; inflammation; lipid.

INTRODUCTION

The prevalence of chronic kidney disease (CKD), a public health concern, is rising globally. Chronic kidney disease (CKD) patients have a high frequency of cardiovascular disease (CVD), which is associated with chronic inflammation, dyslipidemia, malnourishment, atherosclerosis, and vascular calcification [1]. Supplementing with omega-3 polyunsaturated fatty acids (ω-3 PUFA) has been linked to a decreased risk of cardiovascular disease. The coronary heart disease mortality rate was reduced among Eskimo people who ate a diet high in ω-3

PUFAs. According to further research, consuming ω-3 PUFAs is linked to a lower risk of CVD [2].

The capacity of ω-3 PUFAs to prevent platelet activation/adhesion, regulate inflammation, and lower thrombosis accounts for their cardioprotective impact [3].

In individuals with hypertriglyceridemia, a condition associated with cardiovascular disease, ω-3 PUFAs mainly reduce triglyceride levels [4].

Furthermore, in a rat model and human investigations, ω-3 PUFAs decreased oxidative stress and may have inhibited vascular calcification [5].

Since CVD is highly prevalent in CKD patients, ω-3 PUFAs, which offer a number of benefits in CVD, may help reduce CVD in these people [6].

This study aimed to study the role of omega-3 fatty acid supplementation in minimizing and preventing cardiovascular disorders in children with chronic kidney disease.

METHODS

This study was a clinical trial study in the pediatric nephrology unit, pediatrics department, Zagazig University Children's Hospital, during a period of 4 months from December 2018 to March 2019. This study included 20 pediatric patients with chronic kidney disease (CKD) on hemodialysis. After our Local Ethics Committee had approved the protocol (IRB# 5016-3-12-2018), the parents or guardians of research participants provided written informed consent. The World Medical Association's code of ethics for human research, known as the Helsinki Declaration, was followed throughout the entire study procedure.

The inclusion criteria comprised individuals under the age of eighteen who had end-stage renal illness and had started hemodialysis as children. Children with CKD who were receiving hemodialysis on a regular basis at least three times per week and who had been receiving hemodialysis for longer than three months were also included. Exclusion criteria comprised patients with primary (non-uremic) cardiovascular disease, metabolic disorders (e.g., primary hyperparathyroidism), patients receiving regular hemodialysis for less than three months, patients receiving chronic peritoneal dialysis, and those with a history of acute inflammatory conditions.

Every patient had their chronic kidney disease history thoroughly taken, including the onset, course, duration, progression, medications, and any potential complications; they were also examined for the presence of either localized or generalized edema; they were asked to look for signs of inflammation, such as fever, lethargy, and pain; and they were asked to check for signs of cardiovascular disorders, such as chest pain, chest tightness, shortness of breath, tingling, and numbness.

All patients were treated daily with a 1000mg **ω-3 PUFAs** pill that contains 120 mg of docosahexaenoic acid (DHA) and 180 mg of eicosapentaenoic acid (EPA) for a minimum of three months.

Before the study began and three months later, blood samples were obtained from each patient to measure the following parameters: lipid profile, high-sensitivity C-reactive protein (hs-CRP), complete blood count, urea, serum creatinine, serum albumin, iron, serum ferritin, and total calcium, sodium, potassium, and phosphorous.

Statistical analysis:

The collected data was tabulated, and to analyze the gathered data, SPSS version 24 software was used (SPSS Inc., Chicago, ILL Company). Percentages and figures were used to display categorical data. To assess categorical variables, the chi-square test (X^2) was employed. The range, median, and mean ± standard deviation was used to

express the quantitative data. The normally distributed variables of two independent groups were evaluated using the student "t" test. To evaluate the association between non-parametric variables, use the Wx Wilcoxon test. The p-value was considered significant at $p < 0.05$.

RESULTS

Twenty hemodialysis patients, ages ranging from 11 to 18 years, with a mean of 13.9 years, were involved in this study. Fifty-five percent of them were male. The median length of the hemodialysis period was 3 years, with a range of 0.5 to 10 years (table 1).

Nephrolithiasis accounted for 20% of the causes of renal impairment, followed by obstructive uropathy (20%), unexplained renal failure (20%), neurogenic bladder (15%), and nephrotic syndrome (10%) (table 2).

Following omega-3 administration, there is a statistically significant rise in calcium and hemoglobin levels. Following omega-3 treatment, blood urea, creatinine, phosphorus, sodium, potassium, ferritin, and CRP all show statistically significant decreases. Albumin, WBCs, platelet count, and serum iron all exhibit non-significant changes, as seen in Table 3.

The average percentage of total cholesterol decreased by 16.9%, triglycerides decreased by 20.4%, LDL and VLDL cholesterol decreased by 15.3% and 20.5%, respectively, and HDL increased by 10.76%. All patients experienced a reduction in total cholesterol and triglycerides, 90% of patients showed a reduction in LDL cholesterol, 90% of patients saw an increase in HDL cholesterol, and 80% saw a reduction in VLDL cholesterol, with a statistically significant difference in distribution (table 4).

Table 5 demonstrated that the risk of CHD has changed statistically considerably, with only four individuals having risk class 1 before supplementation and that number rising to 65% after. CHD decreased in 16 patients (80%).

Table 1: Distribution of patients according to baseline data.

	N=20	**%**
Gender		
Female	9	45%
Male	11	55%
	Mean ± SD	**Range**
Age (year)	13.9 ± 2.1	11–18
Weight (kg)	35.8 ± 9.02	18–60
	Median (IQR)	**Range**
Duration of hemodialysis (year)	3(1 – 8)	0.5–10

IQR interquartile range

Table 2: Distribution of patients according to cause of renal impairment.

	N=20	%
Cause		
Nephrolithiasis	4	20%
Obstructive uropathy	4	20%
Unexplained renal failure	4	20%
Neurogenic bladder	3	15%
Nephrotic syndrome	2	10%
Lupus nephritis	1	5%
Polycystic kidney disease	1	5%
Focal segmental glomerulonephritis	1	5%

Table 3: Hematological and biochemical profile of studied patients before and after Omega-3 supplementation

	Before supplementation	**After supplementation**	**t**	**p**
	Mean ± SD	**Mean ± SD**		
Hemoglobin (g/l)	9.35 ± 0.99	10.43 ± 0.79	-7.056	<0.001**
WBCs (10^3/mm³)	6.87 ± 1.85	6.72 ± 1.64	0.356	0.719
Platelet count (10^3/mm^3)	254.55 ± 57.83	279.55 ± 64.44	-1.704	0.105
Albumin (g/dl)	4.39 ± 0.63	4.27 ± 0.3	0.81	0.428
Urea (mg/dl)	55.15 ± 13.65	42.99 ± 7.48	4.61	<0.001**
Creatinine (mg/dl)	8.82 ± 2.65	7.55 ± 2.1	5.61	<0.001**
Calcium (mg/dl)	8.81 ± 0.74	9.63 ± 0.59	-6.302	<0.001**
Phosphorus	6.5 ± 1.71	5.48 ± 1.53	3.017	0.007*
Sodium (mg/dl)	137.6 ± 4.22	135.6 ± 2.21	2.338	0.03*
Potassium	5.83 ± 0.74	5.02 ± 0.68	7.228	<0.001**
	Median (IQR)	**Median (IQR)**	**Wx**	**p**
Serum iron	73 (49.3–102.8)	82 (56.1–91.5)	-1.401	0.161
Ferritin	565.8(94.5 – 852.8)	508.5(146.8 – 678)	-2.091	0.037*
CRP	6.2(2.3 – 8.1)	1.3(0.8 – 4.2)	-3.883	<0.001**

t paired sample ttest, Wilcoxon signed rank test *p<0.05 is statistically significant **p≤0.001 is statistically highly significant

IQR: interquartile range.

Table 4: Distribution of studied patients according to percent change in lipid profile after omega-3 supplementation.

	Percent change	Frequency [n=20(%)]			p
	Median (IQR)	Decrease	No change	Increase	
Total cholesterol	-16.9 (-22.2, -7.9%)	20 (100%)	0 (0%)	0 (0%)	-
HDL cholesterol	10.76 (5.95, 15.74%)	2 (10%)	0 (0%)	18 (90%)	<0.001**
LDL cholesterol	-15.3 (-35.4, -4.4%)	18 (90%)	2 (10%)	0 (0%)	<0.001*
VLDL-cholesterol	-20.5 (-35.2, -10%)	16 (80%)	0 (0%)	4 (20%)	0.012*
Triglycerides	-20.4 (-28.2, -13.5%)	20 (100%)	0 (0%)	0 (0%)	-

IQR interquartile range p for one sample test *****p<0.05 is statistically significant **p≤0.001 is statistically highly significant

Table 5: CHD risk of studied patients before and after omega-3 supplementation.

	Before supplementation	After supplementation	Wx	p
	Mean ± SD	Mean ± SD		
CHD risk **1** **2** **3** **4**	 4 (20%) 9 (45%) 6 (30%) 1 (5%)	 13 (65%) 6 (30%) 1 (5%) 0 (0%)	-4	<0.001**
Risk Decrease No change		 16 (80%) 4 (20%)		

The Wilcoxon signed rank test **p≤0.001 is statistically highly significant
CHD: Chronic heart disease

DISCUSSION

Dyslipidemia, Changes in lipid metabolism in patients with end-stage renal disease (ESRD) are known to be a risk factor for cardiovascular diseases (CVDs). Cardiovascular disease is a leading source of morbidity and death in death in end-stage renal disease (ESRD) patients undergoing chronic hemodialysis [7].

Patients in our study were slightly more likely to be males (55%), with an average age of 13.9 ± 2.1 years. Despite the limited sample size, these demographics are similar to those of a number of other pediatric CKD investigations.

This agreed with Momeni et al. [8] they sought to evaluate how acute hemodialysis affected spirometry metrics. According to them, the male to female ratio in our study was (11: 9). This could be because males are more likely than women to have chronic kidney disease (CKD) or because females are less likely to seek treatment because it is too expensive for

them due to societal, cultural, and financial constraints.

In addition, Shaik et al. [9] discovered that 178 cases (71.2%) were male. 62% of patients were male, according to Sharma et al. [10]. According to Lim et al. [11], 44% of CKD patients were male.

In agreement, Elshafie et al. [12] Their goal was to assess how high-dose omega-3 affected the lipid profile of kids with end-stage renal disease (ESRD) undergoing continuous hemodialysis. The mean age of 26 ESRD children receiving chronic hemodialysis was 13.4 ± 2.5 years, with ages ranging from 8 to 17.

While this disagrees with Kumar et al. [13] who discovered 235 (55.72%) slightly more female study participants.

Both early and long-term dialysis patients were well-represented in our study, with a median hemodialysis duration of 3 years, ranging from 0.5 to 10 years.

In accordance, Shailendra Mane et al. [14] We sought to investigate how hemodialysis affected end-stage renal disease patients' lung function. They found that 91 (44.39%) of the 205 individuals had been receiving hemodialysis for the previous one to three years, and 81 (39.51%) had been receiving hemodialysis for the preceding six to twelve months.

In harmony, Sharma et al. [10] revealed that only 10% of patients had been receiving hemodialysis for less than six months, while 45 (90%) had been receiving it for six months to three years.

According to our research, 20% of cases were caused by nephrolithiasis, obstructive uropathy, and unexplained renal failure. Neurogenic bladder (15%) and nephrotic syndrome (10%) were next.

This was consistent with Elshafie et al. [12], who reported that obstructive uropathy was the most common cause of renal failure in 10 patients (38.4%), whereas unknown etiology was the second most common cause in eight patients (30.7%).

Moreover, Omar et al. [15] they sought to assess how high-dose Omega 3 affected inflammatory markers and lipid profiles in children with ESRD who had chronic HD. They found that among the 49 patients in the study, obstructive uropathy was the most common cause of renal failure in 19 of them (38.7%), followed by unclear etiology in 16 of them (32.6%).

Following omega-3 treatment, our study showed notable improvements in a number of important indices. Better control of anemia was indicated by a significant improvement in hemoglobin levels ($p < 0.001$). Platelet counts rose without achieving statistical significance ($p = 0.105$), while albumin levels and white blood cell (WBC) counts did not change significantly ($p = 0.428$ and 0.719, respectively). Urea, creatinine, phosphorus, and potassium all showed significant decreases (all $p < 0.05$), indicating better inflammation control and renal function. While sodium levels dropped little but significantly ($p = 0.03$), calcium levels rose significantly ($p < 0.001$). Serum iron levels did not vary significantly ($p = 0.161$), but serum ferritin did ($p = 0.037$). These findings show that omega-3 fatty acids have renoprotective effects, although further study is needed to completely comprehend the process.

This partially agrees with Elshafie et al. [12] who stated that the 26 chronic hemodialysis children who took part in our interventional prospective study did not experience any significant changes in blood pressure, albumin, parathyroid hormone level, hemoglobin, platelets, total iron-binding capacity, serum iron, transferrin saturation, serum ferritin, and dialysis efficiency (Kt/V and urea reduction ratio), phosphorus (PO4), calcium (Ca), potassium (K), sodium (Na), or total iron-binding

capacity after receiving high-dose omega-3 (2000 mg/day) for three months.

Contrary results have been reported by Khosroshahi et al. [16] in their RCT, which involved 100 hemodialysis patients divided into two groups one receiving omega-3 (oral capsule: 3 g/day) for two months, and the other receiving a placebo they found no significant differences in hemoglobin, platelet count, serum levels of calcium, sodium, potassium, phosphorus, total iron-binding capacity, and iron between the two groups.

The considerable drop in CRP levels (median from 6.2 to 1.3, $p<0.001$) in our study is particularly noteworthy because it suggests less inflammation. This result is consistent with several studies conducted in both adult and pediatric CKD populations and supports the anti-inflammatory qualities of omega-3 fatty acids.

Tayyebi-Khosroshahi et al. [17] agreed with the results of the current study, which showed that inflammatory markers (CRP) decreased in chronic HD patients who took 3 g of Omega 3 daily for three months. Furthermore, chronic HD patients' high-sensitivity CRP was improved by administering 1800 mg of omega-3 fatty acids daily for four months, according to Dashti et al. [18].

In harmony, Omar et al. [15] demonstrated that a significant decrease in CRP levels ($P <0.001$) occurred after three months of high-dose Omega 3 supplementation for the individuals under study.

Wu et al. [19] also suggested that supplementing with omega-3 FAs may help dialysis patients' inflammatory factors.

This disagrees with Elshafie et al. [12] they revealed that patients receiving omega-3 treatment had a modest decrease in their hs-CRP level; the lack of a substantial decrease in hs-CRP in their study might be due to the fact that higher dosages of omega 3 are required for the anti-inflammatory effect to be effective.

Our research showed that taking omega-3 supplements significantly improved the lipid profile. HDL cholesterol rose by 10.76%, triglycerides by 20.4%, LDL cholesterol by 15.3%, and total cholesterol by a median of 16.9%. These alterations were clinically substantial and statistically significant ($p<0.001$). Notably, 90% of patients had decreases in LDL cholesterol and 100% of patients had improvements in total cholesterol and triglycerides. These high response rates imply that omega-3 supplements may be especially beneficial for children with chronic kidney disease.

Elshafie et al. conducted three-month interventional prospective research to supplement 26 adolescents with end-stage renal disease (ESRD) receiving chronic hemodialysis [12]. A high-dose of omega-3 (2000 mg/day) including 360 mg of eicosapentaenoic acid and 240 mg of docosahexaenoic acid was found to increase HDL levels while significantly ($P < 0.001$) lowering serum TG, TC, and LDL levels.

According to El-Shinnawy et al. [20], in their prospective case-control study, which included 80 chronic hemodialysis patients (range: 40–60 years) chosen from the El-Maadi Liver and Kidney Transplantation Hospital in Egypt, omega-3 significantly decreased serum TG, TC, and LDL levels while raising HDL levels. For six months, the experimental group was given four omega-3 capsules daily, each containing 1000 mg of omega-3.

This is also consistent with the findings of Omar et al. [15], who reported that three months of high-dose omega 3 supplementation led to a highly statistically significant increase in HDL ($P <0.001$) and a drop in TC, TG, and LDL levels in the research participants.

This also slightly agrees with Fazelian et al. [7] they showed that supplementing with omega-3 FAs dramatically lowers TC and TG. They did, however, demonstrate that consuming omega-3 FAs had no discernible impact on HDL or LDL.

There are a number of possible explanations for how consumption of omega-3 FAs affects TC levels. By inhibiting endogenous cholesterol production, omega-3 FAs have been demonstrated to lower cholesterol levels [21]. In the manufacture of cholesterol, 3-Hydroxy-3-Methyl-Glutaryl-Coenzyme A reductase (HMG-CoA reductase), a restricted rate enzyme, has actually been shown to have much lower mRNA expression levels when omega-3 FAs are consumed [22]. It has recently been demonstrated that microRNA regulation also controls the metabolism of cholesterol. MicroRNAs (miRNAs), which are small non-coding RNAs, are essential for posttranscriptional gene regulation [23]. Numerous studies have shown that omega-3 fatty acids modulate many miRNAs to control cholesterol metabolism. Thus, omega-3 supplementation may have an impact on cholesterol through the control of miRNAs.

The difference in the impact of omega-3 on lipid profile between their research and ours could be explained by the use of a modest dose of omega-3 (1g/day) in those investigations.

Following supplementation, the percentage of patients in the lowest risk category (class 1) rose from 20% to 65%, indicating a significant improvement in CHD risk classification. Given the high cardiovascular mortality rate among CKD patients, even in pediatric populations, this study is especially significant. The risk reduction seems to be unaffected by age, gender, or length of hemodialysis, indicating that the intervention may be widely applicable.

It is unclear if omega-3 FA consumption lowers the risk of death or ESKD in participants with chronic kidney disease, although Saglimbene et al. [24] showed that it may lower cardiovascular mortality in hemodialysis patients, which is consistent with our findings.

Fazelian et al. [7] shown how consuming omega-3 FAs can help patients with chronic kidney disease by improving their cardiometabolic markers.

The percentage changes in lipid profile did not significantly correlate with age, gender, or length of hemodialysis, according to our study. This implies that the advantages of taking omega-3 supplements might apply to all patient groupings. Additionally, there was no discernible link between changes in lipid profiles and concurrent drugs, suggesting that omega-3 supplementation may be beneficial independent of other therapies.

Limitation:

There was a tiny sample size, to generalize the findings, the study must be conducted in a multicenter with a larger sample.

Conclusion:

This study concluded that omega-3 supplementation may be a useful therapeutic strategy for children with chronic kidney disease (CKD), providing advantages in a number of areas, such as cardiovascular risk, lipid profile, and inflammation. To validate these results and determine the best dosage schedules, larger, multicenter studies with longer follow-up times would be helpful.

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