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Role of omega 3 polyunsaturated fatty acid in chronic renal diseases

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Role of omega 3 polyunsaturated fatty acid in chronic renal diseases

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Abstract:

Chronic renal disease (CKD) is a significant global health concern, characterized by a steady deterioration in kidney function and associated complications such as cardiovascular disease, inflammation, and metabolic abnormalities. Omega-3 polyunsaturated fatty acids (PUFAs), namely eicosatetraenoic acid (EPA) and docosahexaenoic acid (DHA), have garnered considerable attention for their potential therapeutic advantages in the treatment of chronic kidney disease (CKD). This review aims to provide a succinct summary of the current knowledge on the impact of omega-3 polyunsaturated fatty acids (PUFAs) on several aspects of chronic kidney disease (CKD) progression and associated consequences. Omega-3 polyunsaturated fatty acids (PUFAs) has several physiological benefits, including the reduction of inflammation, prevention of oxidative damage, inhibition of fibrosis, and dilation of blood vessels. These qualities may provide protective benefits for the kidneys in individuals with chronic kidney disease (CKD). Clinical study has shown that supplementing with Omega-3 may have the ability to reduce renal inflammation, decrease proteinuria, preserve renal function, and mitigate cardiovascular risk in individuals with chronic kidney disease (CKD). Omega-3 polyunsaturated fatty acids (PUFAs) directly affect many processes that contribute to the development of chronic kidney disease (CKD), including inflammation, oxidative stress, endothelial dysfunction, and lipid metabolism. However, there is still ambiguity about the optimal dosage, duration, and composition of omega-3 supplementation for the treatment of chronic kidney disease (CKD), necessitating more investigation. Moreover, it is essential to tailor the medication for each CKD patient due to potential drug interactions and variations in individual responses to omega-3 therapy.

.**Keywords : atherosclerosis, chronic renal diseases, , inflammation, omega 3 , inflammation.**

1- Introduction

Omega-3 fatty acids (FAs) are vital bioactive compounds necessary for the body's growth and development. Although there was a delay in acknowledging their significance, the emergence of these entities has given biomedical research a new direction. The researchers' interest was reignited by two significant achievements in the 1970s about the association between omega-3 fatty acids and cardiovascular and ocular function (Spector and Kim 2019).

In the past, scientists have focused their research on investigating three distinct classifications of omega-3 fatty acids. Some examples of fatty acids include docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), and docosapentaenoic acid. (DPA)(Dyall 2015).

DHA is abundantly found in the brain system. Therefore, it has the ability to effectively address several neurodegenerative conditions, including Alzheimer's disease (AD), dementia, and depression. DHA outperforms EPA in terms of its antibacterial efficacy.(Desbois and Lawlor 2013) and (Mil-Homens, Bernardes and Fialho 2012),

Long-chain Omega-3 fatty acids, namely docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), are polyunsaturated fatty acids mostly derived from fish.

(Wall, Ross et al. 2010, Khandouzi, Shidfar et al. 2015).

Omega-3 fatty acids (FAs) are often used in the management and prevention of several illnesses and their related complications. Omega-3 fatty acids has antioxidant properties that may protect the cardiovascular system from the detrimental effects of oxidative stress and thrombotic issues.

(Agah, Shidfar et al. 2015)

Patients with chronic kidney diseases (CKD) who get dialysis or nephropathy therapy have a higher likelihood of developing coronary heart disease, myocardial infarction, and atherosclerosis (Reiss, Miyawaki et al. 2018, Potier, Roussel et al. 2020). Cardiometabolic variables such as hypertension, dyslipidemia, hyperglycemia, and obesity are important factors that increase the chance of developing health problems in the general population.

(Liu, Tse et al. 2019).

The health and insurance systems worldwide are profoundly affected by cardiometabolic risk factors. These risk factors pose a significant threat to those with pre-existing illnesses such as CKD. Elevated levels of low-density lipoprotein (LDL) cause the buildup of leftover lipoproteins and oxidized LDL (ox-LDL), which leads to the formation of atherosclerosis.

(Vallejo-Vaz, Robertson et al. 2017)

Individuals receiving hemodialysis treatment have a higher vulnerability to metabolic changes, which may result in an increased lipid profile and the onset of undesired diseases that need to be prevented. However, the lipid profile, specifically the levels of total cholesterol (TC), are considered as nutritional indicators. These indicators have shown a strong correlation with cardiometabolic risks in individuals suffering from chronic renal disease. (CKD).(Wilson and Mitsnefes 2009).

2- Literature review

Individuals with chronic kidney disease (CKD) or those at an elevated risk of developing CKD should make dietary modifications to preserve renal function. It is recommended to incorporate non-saturated fats in your diet, including monounsaturated and polyunsaturated lipids like omega-3 fatty acids, while also limiting your salt and protein intake. The reference "Kalantar-Zadeh and Fouque2017"ismentioned. Omega-3 and omega-6 polyunsaturated fatty acids (PUFAs) are considered essential fatty acids since they are not endogenously synthesized by the body. Recent studies suggest that omega-3 polyunsaturated fatty acids (PUFAs) may have beneficial benefits in preserving kidney function in patients with different types of chronic renal diseases (CRD).The reference is from the publication by Fassett, Gobe, and colleagues in 2010. Furthermore, omega-3 polyunsaturated fatty acids (PUFAs) has several physiological benefits, including lipid modification, blood pressure reduction, prevention of blood clot formation, inflammation reduction, and cardiovascular protection. Moreover, a recent comprehensive study conducted by 19 research organizations has shown a strong correlation between higher levels of omega-3 polyunsaturated fatty acids derived from seafood and a reduced likelihood of developing chronic kidney disease (CKD) as well as a slower decline in kidney function. (Ong, Marklund et al.,2023).

Kidney damage often leads to inflammation and tubulointerstitial fibrosis. Consequently, drugs that influence inflammation, such as omega-3 PUFAs, have been assessed. Various empirical studies using a range of models have shown the beneficial effects of omega-3 polyunsaturated fatty acids (PUFAs).(An, Kim et al., 2009) The publication of Yamamoto, Takabatake et al. in 2021.

2.1- Atomic configuration

Understanding the structural features of omega-3 fatty acids is essential for appreciating several biological phenomena, such as their bioavailability, distribution in different tissues, and pharmacological effects. Omega-3 fatty acids are categorized as polyunsaturated fatty acids (PUFAs) because of their distinctive structural characteristics. Furthermore, these fatty acids have comparable characteristics in their chemical composition, therefore justifying their categorization as omega-3. Each of these fatty acids has many double bonds, with the last bond in the structure located at the third carbon atom at the end of the carbon chain. The structures shown in Figure 1 demonstrate that these fatty acids contain several double bonds and are organized in a distinct way.

No discernible pattern was seen in the positioning of the first double bond inside the molecule. However, the double bonds were consistently found at every third carbon atom throughout the whole chain. Fatty acids, because of their many double bonds, exhibit a substantial level of unsaturation, rendering them susceptible to oxidation.(Leng, Kinnun et al. 2018).

The presence of a fish-like smell or taste in the unsaturated fatty acids is a result of their oxidation. This information is crucial for developing a dosage form for omega-3 fatty acids, guaranteeing the quality of the goods, and choosing suitable excipients. The chemicals produced during the process of oxidation are now under investigation. There is a dispute on the potential dangers of oxidative compounds. Oxidation of omega-3 fatty acids results in the production of many distinct chemical compounds, such as acid peroxide, alcohol, and aldehyde. Examples of these compounds are (E, E)-2,4 decadienal, 2-butanol, propane-2-one, (E, E)-2,4-heptadienal, and 4-hydroxy-2-hexenal. Research has shown that oxidized lipids do not have harmful effects on the body since the body's inherent antioxidant and detoxification activities quickly neutralize their influence. Nevertheless, several investigations have shown that oxidized fatty acids include deleterious substances, such as acrolein, that have an adverse impact on one's well-being. These compounds may cause diseases including hypercholesterolemia, atherosclerosis, and even cancer.The citation for this work is Ben Hammouda, Zribi et al. 2017. An interesting finding is that the molecular composition of omega-3 fatty acids, namely EPA, has resemblance to that of arachidonic acid (AA) (Fig. 2). Eicosapentaenoic acid (EPA) may effectively outcompete arachidonic acid (AA) for the enzymes involved in several physiological processes, since it is the primary omega-6 fatty acid in the body. Furthermore, the existence of omega-3 fatty acids (FAs) might possibly alter the quantity of arachidonic acid (AA) in the phospholipids of the cell membrane. The anti-inflammatory impact of these particular fatty acids is associated with it, as will be further upon later. (Shahidi and Ambigaipalan 2018).

The body has Omega-3 fatty acids in four distinct chemical states. The molecules may be classified as free fatty acids (FFA), ethyl esters (EE), phospholipids (PL), or triacylglycerols (TAG). The two most recently examined structural forms are PL and TAG. Phospholipids are composed of a glycerol molecule that links two fatty acids, with the third carbon atom being bonded to a phosphoric acid ester group. Phosphatidylethanolamine, phosphatidylserine, phosphatidylcholine, and phosphatidylinositol may be synthesized by combining the phosphate ester with ethanolamine, serine, choline, or inositol, respectively. These substances demonstrate physiological effects throughout the body. The ω-3 fatty acids in TAG (triacylglycerol) are joined together by a glycosidic bond, forming a structure consisting of three molecules of the fatty acids. These molecules mostly reside inside the cellular membrane of tissues due to their association with phospholipids. The citation "Zhang 2015" refers to a source published in 2015. The EPA acts as a dependable measure of the fundamental quantity of omega-3 fatty acids present in the body, which might possibly vary depending on blood lipoprotein levels. The remaining two are situated inside the inner membrane and are influenced by the process of erythrocyte turnover (Gareri 2022). Omega-3 fatty acid supplements may be acquired in either acylglycerol or ester form. The bioavailability of these fatty acids is affected by their chemical composition. Several studies indicate that triacylglycerols have higher bioavailability compared to other forms, since they may be digested and transformed into monoacylglycerol, which can then passively diffuse during absorption. On the other hand, certain protein mediators facilitate the transportation of various types of omega-3 fatty acids. Research indicates that the sn-2 position is more advantageous for enhancing bioavailability in the esterification of these fatty acids, since it employs a distinct transport route inside the body. This advantage is not seen in the sn-1 and sn-3 locations. The majority of fish oils include ω-3 fatty acids at the sn-2 position. Therefore, terrestrial sources have a higher level of bioavailability than marine sources. By covalently bonding the fatty acid (FA) to the phospholipid at the sn-1 position, it provides protection against oxidative stress, namely hydroperoxide. Several studies indicate that the phospholipid form has the greatest level of bioavailability compared to other forms. (Ahmmed, Ahmmed et al. 2020).

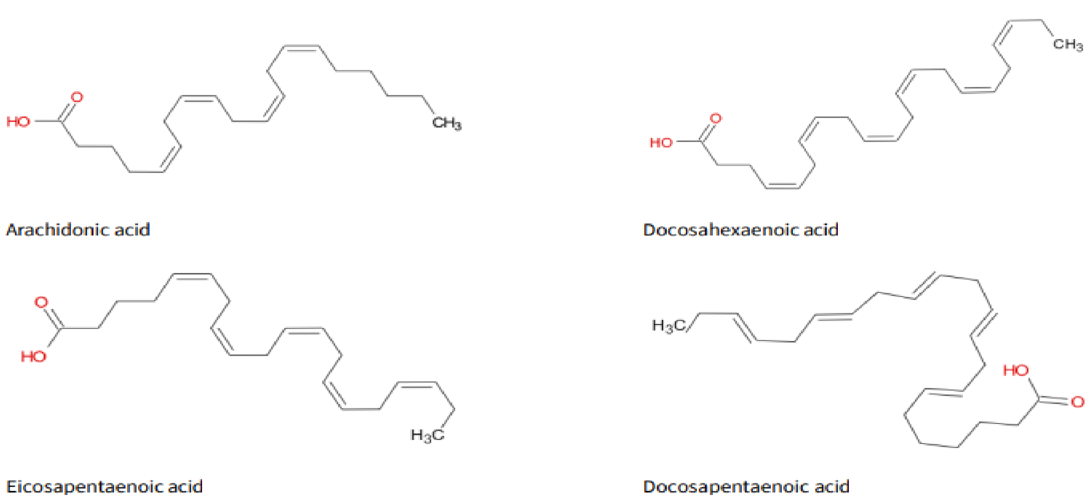

Figure 1 displays the fatty acids omega-3 as well as omega-6

2.2- The potential therapeutic efficacy of Omega-3 polyunsaturated fatty acids (PUFAs) in the treatment of chronic kidney disease (CKD)

Omega-3 polyunsaturated fatty acids (PUFAs), obtained from fish oil and other dietary sources, play a vital role in human physiology. The citation "Scorletti and Byrne 2013" is referenced. Human physiology includes three specific forms of omega-3 polyunsaturated fatty acids (PUFAs): α-linolenic acid, derived from plant oils, and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), often found in marine oils. The possible therapeutic benefits of omega-3 polyunsaturated fatty acids (PUFAs) in some renal diseases have been a topic of conjecture. Various studies have shown that including omega-3 PUFAs into one's diet does not result in a decreased likelihood of death from any cause (Rizos and Elisaf 2017). Previous studies have shown that omega-3 polyunsaturated fatty acids (PUFAs) might potentially decelerate the advancement of renal disorders in both human patients and animal subjects. (Donadio, 1993). The proposed mechanism by which omega-3 PUFAs exert their effects on renal diseases may include the competitive inhibition of EPA and DHA in respect to arachidonic acid (AA). This inhibition leads to a decrease in the manufacture of prostaglandins and leukotrienes, which are less effective. As a consequence, inflammation in the glomerulus and interstitium is reduced, and there is also a decrease in platelet aggregation and vasoconstriction. These variables might potentially contribute to the slowing down of kidney damage. The study conducted by Donadio and Grande in 2002 revealed that Omega-3 polyunsaturated fatty acids (PUFAs), namely EPA and DHA, have the potential to decrease levels of inflammatory indicators such as C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α).(Li, Huang, and colleagues, 2014) Thus, these compounds possess anti-inflammatory properties in renal illnesses, enhancing their severity and slowing down their course, as shown by many authors.(Fassett, Gobe, et al., 2010). Omega-3 polyunsaturated fatty acids (PUFAs), namely eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have been proposed as a secure and efficient treatment for lowering triglyceride (TG) levels. The recommended daily consumption is 4 grams, with a minimum of 3 grams consisting of a combination of EPA and DHA. These polyunsaturated fatty acids (PUFAs) may be used as a monotherapy or in combination with other medications that lower lipid levels.The citation is derived from the research article entitled "Skulas-Ray, Wilson et al. 2019". Furthermore, their capacity to mitigate glomerulosclerosis via anti-inflammatory mechanisms may slow down the progression of chronic kidney disease (CKD) to end-stage kidney disease (ESKD).Figure 1

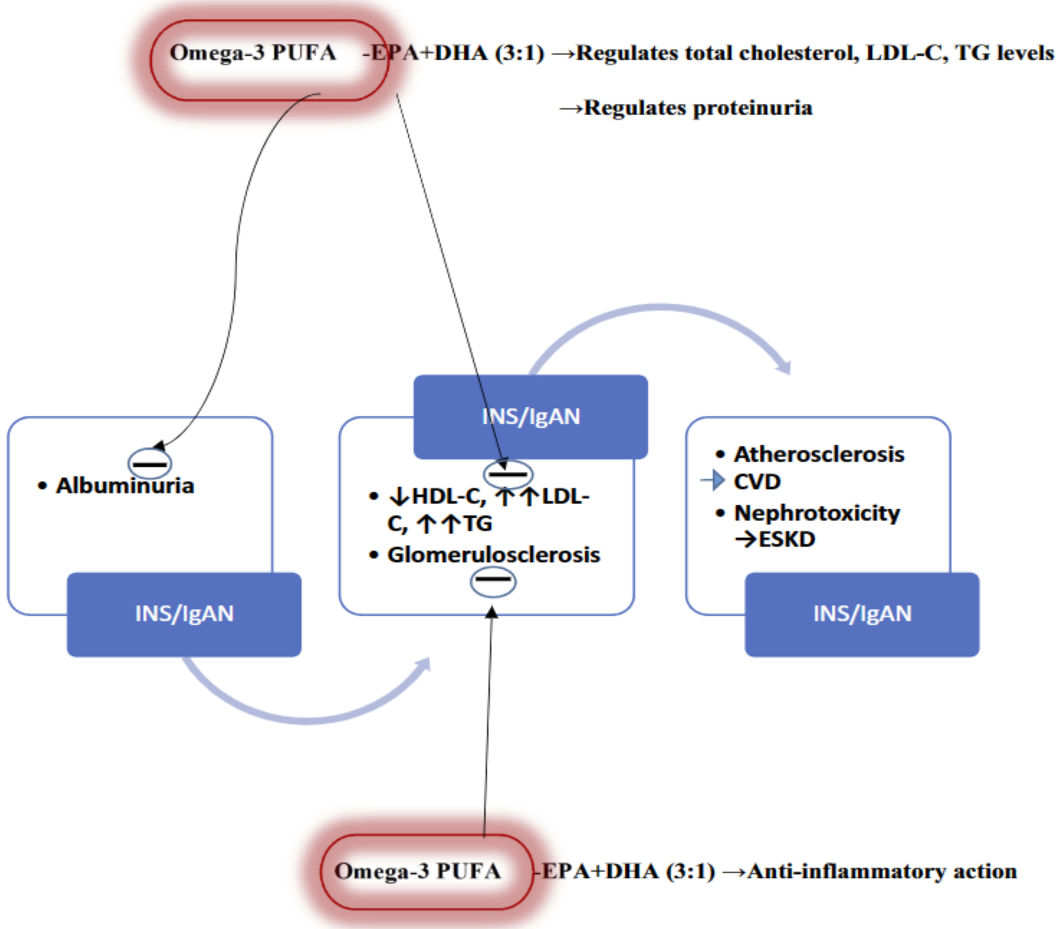

Figure 1 illustrates potential therapeutic targets for omega-3 polyunsaturated fatty acids in idiopathic renal disease and IgA nephropathy.

2.3- Clinical investigations have shown conclusive evidence that Omega-3 PUFAs are effective in treating IgAN.

As far back as thirty years ago, clinical trials were undertaken to investigate the effects of omega-3 polyunsaturated fatty acids (PUFAs) on patients with IgA nephropathy (IgAN). Hamazaki et al. conducted a randomized controlled study (RCT) to evaluate twenty individuals diagnosed with IgAN. A cohort of 10 participants were administered omega-3 polyunsaturated fatty acids (PUFAs) in a specific proportion of 1.6 grams of eicosapentaenoic acid (EPA) and 1 gram of docosahexaenoic acid (DHA). Meanwhile, a distinct group of 10 people served as the control group and did not get any fish-oil supplements. The patients were monitored for a duration of one year. The clinical examination showed improved renal function in these individuals.

The reference is from Hamazaki, Tateno, and Shishido in 1984. In a trial conducted by Alexopoulos et al., a "very low dose" of PUFAs (0.85 gram EPA and 0.57 gram DHA) was given to fourteen individuals with severe IgAN. Fourteen more patients, who were used as a control group, were given symptomatic therapy. During a span of four years, a group of 58 people was closely monitored. The main criteria used were a ≥50% increase in serum creatinine or a ≥50% decrease in glomerular filtration rate (GFR) at the conclusion of the trial. There were significant statistical disparities seen between the patients who got PUFA therapy and those who did not, including the rise of ≥50% in serum creatinine levels and the reduction of ≥50% in GFR levels. Therefore, a little amount of polyunsaturated fatty acids (PUFA) has been shown to effectively slow down the decline of kidney function in individuals with a high risk of IgA nephropathy (IgAN), particularly those with advanced renal illness.
..(Alexopoulos, Stangou et al. 2004).

2.4- Systematic reviews and meta-analyses have examined clinical studies that study the impact of omega-3 polyunsaturated fatty acids on individuals with IgA nephropathy (IgAN) and idiopathic nephrotic syndrome (INS).

Although there is a theoretical foundation supporting the therapeutic advantages of omega-3 polyunsaturated fatty acids (PUFAs) in IgA nephropathy (IgAN) and idiopathic nephrotic syndrome (INS), the existing research, including both anecdotal evidence and published studies, presents contradictory results regarding their efficacy in treating these conditions. The current investigation highlights the contentious nature of their proposition in certain forms of chronic renal disease, as seen in Table 1. This study included of four systematic reviews and two non-randomized trials that examined the therapeutic efficacy of omega-3 PUFA supplementation in lowering proteinuria in individuals diagnosed with IgAN or idiopathic steroid-resistant nephrotic syndrome (SRNS). In 2014, a clinical practice recommendation, backed by research, recommended the use of omega-3 PUFAs as a potential means to enhance kidney outcomes in persons with IgAN. Although there is less scientific evidence to back their assertion, they may still be regarded as a viable therapeutic choice (Yuzawa, Yamamoto et al. 2016).
The meta-analysis conducted by Chou et al examined five randomized-controlled trials (RCTs) with a total of 233 participants. The researchers assessed the effectiveness of omega-3 polyunsaturated fatty acids (PUFAs) in treating IgA nephropathy by examining the correlation between the dosage of omega-3 PUFAs and their impact on kidney function and proteinuria. The

notable results indicated that the glomerular filtration rate (GFR) was not impacted, although there was a considerable decrease in proteinuria, regardless of the dosage. The researchers determined that omega-3 polyunsaturated fatty acids (PUFAs) had no effect on the maintenance of renal function in IgA nephropathy, despite the reduction in proteinuria..(Chou, Chiou et al. 2012).

Table 1 presents a concise overview of the results obtained from published systematic reviews and meta-analyses on the therapeutic advantages of Omega-3 Polyunsaturated Fatty Acids in treating IgA Nephropathy and Idiopathic Nephrotic Syndrome.

Authors (Year), Country	Types and Numbers of Included Primary Studies	Population Characteristics and Sample Size	Intervention	Outcome Parameters	Major Findings
Chou et al[67] (2012), Taiwan	RCT (n = 5)	Patients with IgA nephropathy,† n = 233	Omega-3 PUFA treatment	-Renal function (GFR) -Proteinuria	-No effect on renal function -Significant reduction in proteinuria
Reid et al[68] (2011), Australia, the US, Italy, and Sweden	RCT (n = 56‡ & n = 7‡‡)	Adult and pediatric patients with biopsy-proven IgA nephropathy, n = 2838	Non-immunosuppressive therapy including fish oil	-Progression or improvement in renal disease -All-cause mortality	-Anti-hypertensive drugs (ACEIs/ARBs) reduced proteinuria (a surrogate outcome) -All-cause mortality unaffected
Miller et al[69] (2009), Spain, US	RCT (n = 4) & non-RCT (n = 1)	Adult patients of any age with IgA nephropathy, n = 626§	Omega-3 PUFA supplementation	-Renal function (GFR) -Renal damage (urine protein excretion)	-Reduction in urine protein excretion but no improvement in GFR
Colquitt et al[70] (2007), UK	SR (n = 2)* RCT (n = 11)**	Children (n = 5) with idiopathic SRNS (FSGS, MPGN)- all either malnourished or stunted	Omega-3 PUFA supplementation (tuna fish oil)	-Renal function (urine protein, creatinine clearance, serum creatinine) -Lipid profile (triglycerides, total cholesterol, HDL, LDL)	- No statistically significant improvements in proteinuria, creatinine clearance, serum creatinine or lipid profile compared with placebo

Furthermore, Reid and his colleagues conducted a comprehensive analysis of 56 randomized controlled trials (RCTs) that investigated the efficacy of non-immunosuppressive treatment for IgA nephropathy. Out of these randomized controlled studies (RCTs), 7 specifically examined the use of fish oils. The number corresponds to the evaluated outcome parameters, which include the progression or improvement of renal disease, assessed by proteinuria as an alternative outcome, as well as mortality from any cause. Antihypertensive medications, namely ACE inhibitors and ARBs, effectively decreased proteinuria. However, these medications had no impact on the overall death rate. (Reid, Cawthon, and colleagues, 2011) Furthermore, Miller et al performed a comprehensive meta-analysis that included a total of 17 research. However, only five of these studies specifically focused on individuals with IgAN, consisting of four randomized controlled trials and one non-randomized controlled study. The researchers evaluated renal function, namely glomerular filtration rate, and renal damage, specifically urine protein excretion, as the last measurements after the administration of omega-3 polyunsaturated fatty acid (PUFA) supplementation. The urinary excretion of protein decreased, but there was no corresponding rise in the glomerular filtration rate (GFR) Period.(Miller III, Juraschek et al. 2009).

Colquitt et al did a meta-analytical inquiry, evaluating a total of two systematic reviews and eleven randomized controlled trials (RCTs).The numerical value is 70. Among the randomized controlled trials (RCTs), only one study specifically investigated the efficacy of tuna fish oil in children diagnosed with idiopathic steroid-resistant nephrotic syndrome (SRNS), which encompasses focal segmental glomerulosclerosis (FSGS) and membranoproliferative glomerulonephritis (MPGN). The study investigated the efficacy of omega-3 PUFA supplementation by evaluating the renal function of the patients, which included analyzing protein levels in urine, the rate of creatinine clearance, and the concentration of creatinine in the blood. Furthermore, the study also assessed the lipid profile of the participants, including assessments of triglyceride levels, total cholesterol, HDL (high-density lipoprotein), and LDL (low-density lipoprotein). Surprisingly, there were no noticeable improvements in proteinuria, creatinine clearance, serum creatinine, and lipid profile when compared to the administration of a placebo. The source cited is Colquitt, Kirby et al. (2007).

2.5 The impact of omega-3 polyunsaturated fatty acid on individuals undergoing hemodialysis.

The majority of research investigating the beneficial impacts of omega-3 fatty acids in individuals with HD mostly focused on assessing indicators of inflammation.(Zabel, Ash et al. 2010). McEwen et al. found that a 4-week consumption of omega-3 PUFAs (640 mg/day) resulted in a decrease in PLT levels in healthy individuals, but not in those with cardiovascular disease (CVD). The authors emphasized the need of delivering elevated dosages of omega-3 PUFAs in order to attain optimal levels of PLT in the plasma. In addition, Li et al. proposed that the inclusion of EPA at a dosage of 6 g/day might potentially decrease platelet adhesion. The citation is derived on a research investigation carried out by McEwen, Morel-Kopp, and their associates in 2013. Recent randomized controlled studies investigating the addition of n-3 PUFA in hemodialysis patients have shown cardioprotective benefits on intermediate outcomes. These effects include improvements in lipid profile, heart rate, and a decrease in systemic inflammation. (He, Li, et al., 2016).

A recent extensive evaluation of randomized controlled trials (RCTs) examined the impact of n-3-PUFA supplementation on outcomes associated with dialysis vascular access. The research revealed that although there were positive impacts on the dilation of significant blood arteries, there was no significant impact on the mortality rate caused by heart-related problems in patients receiving hemodialysis (Viecelli, Irish et al. 2018).

The attenuated progression to end-stage kidney disease (ESKD) in persons who get n-3 PUFA supplementation may be associated with the several beneficial benefits of this compound. These effects include the decrease in blood pressure, anti-inflammatory properties, improvement of endothelial function, and modification of the fluidity and functioning of cell membranes. The reference provided is the paper by Mori and Beilin in 2004.

2.6- The relationship between omega-3 polyunsaturated fatty acids and chronic kidney disorders

Our theory posited that elderly individuals with low levels of plasma polyunsaturated fatty acids (PUFAs) would have a more rapid decline in renal function. To validate this hypothesis, we examined the relationship between the total concentrations of polyunsaturated fatty acids (PUFA) in the blood plasma and the variation in creatinine clearance during a three-year timeframe. This study was conducted on senior persons who were participants in the In CHIANTI study, which is a population-based epidemiological research project conducted in Tuscany, Italy. The study conducted by Lauretani, Semba et al. in 2008.

The results indicate that including higher amounts of polyunsaturated fatty acids (PUFA) into one's diet may act as a preventative strategy against the development of chronic kidney disease. These findings align with previous studies conducted on animals, which have shown that the addition of polyunsaturated fatty acids (PUFA) may hinder the advancement of kidney disease. The citation is derived from the publication by Simopoulos, Leaf, and Salem Jr. in 2000.

2.7-The ideal dietary consumption of omega-3 polyunsaturated fatty acids (PUFAs) for persons suffering from chronic kidney disease (CKD)

The particular daily recommended intake of n-3 PUFA for the general population, including those with specific diseases, has not yet been determined. Significant endeavors are now being made to provide recommendations for the intake of n-3 PUFA in our diet (Harris, Mozaffarian et al. 2009). The US Institute of Medicine of the National Academies now recommends a daily dose of EPA and DHA that is about 10% of the total ALA consumption. According to Trumbo, Schlicker et al. in 2002, this would correspond to a dose range of 110-160 mg per day. This quantity is lower than the recommended limit established by health authorities in the majority of Western countries and by the AHA for patients with confirmed coronary disease. However, it roughly corresponds to the AHA criterion for those who are in excellent physical condition. The referenced paper is Kris-Etherton, Harris, and Appel's work published in 2002. There are two compelling justifications for advocating that patients with severe chronic kidney disease (CKD) should eat larger amounts of food, regardless of the agreed-upon objectives. The potential positive effects of n-3 PUFA are inversely correlated with the initial intake and levels of n-3 PUFA in the diet and in the blood or tissues. The referenced study is Mozaffarian and Rimm's research conducted in 2006.

Initial investigations suggest that individuals with advanced chronic kidney disease (CKD) have relatively low levels of intake and blood concentration of n-3 polyunsaturated fatty acids (PUFA). Furthermore, the level of consumption is quite moderate, considering the many and severe underlying medical conditions, including cardiovascular problems, that are often seen in individuals with advanced chronic kidney disease (CKD) (Harris and Von Schacky 2004).

3- Dialysis

Studies investigating the use of omega-3 supplements in individuals receiving dialysis have shown favorable effects on triglyceride levels, the longevity of dialysis access, and perhaps the alleviation of uremic pruritus and oxidative stress (Lim, Manley et al. 2007). While omega-3 supplementation provides advantages, it is not often recommended or used in individuals who rely on dialysis (Locatelli, Vecchio, and Pozzi 2006).

Achieving the best possible performance of an arteriovenous hemodialysis access is a significant clinical difficulty. Research has been conducted on the ability of fish oil to improve the patency of hemodialysis access due to its antithrombotic, antiproliferative, and anti-aggregatory platelet properties. A controlled trial was conducted with 24 hemodialysis patients who were randomly assigned to receive either a daily dose of 2.7 g of fish oil or a placebo. The results showed that the group receiving fish oil had a graft patency rate that was 60% higher after one year. The following study conducted by Bowden, Wilson et al. in 2007 did not provide evidence to support this extraordinary discovery. Currently, there are at least two ongoing randomized studies examining whether fish oil may substantially prolong the longevity of dialysis vascular access (Irish, Dogra et al. 2009).

3.1 - Mortality

There is evidence suggesting that there is a negative relationship between the intake of n-3 PUFA and the levels of these fatty acids in tissues, as well as the mortality rate, in patients undergoing continuous dialysis. A study done by Kutner et al. (Kutner, Clow et al. 2002) found that among 216 dialysis patients, those who consumed fish had a mortality rate that was about 50% lower over a span of 3 years.

A recent study done on a sample of typical hemodialysis patients discovered a notable and inverse relationship between the levels of erythrocyte n-3 PUFA (polyunsaturated fatty acids) and mortality. It is crucial to acknowledge that the research was conducted with a limited number of participants. The reference originates from an academic work written by Friedman, Saha, and Watkins in 2008. Nevertheless, both studies failed to eliminate the possibility that the consumption of fish (resulting in elevated levels of n-3 PUFA in the bloodstream) merely served as an indicator of other variables that could potentially contribute to reduced mortality rates, such as a superior socioeconomic status or a more nourishing overall diet. The reference is attributed to Cohen, Garg et al. in 2008.

3.2- Clinical applications in advanced chronic kidney disease (CKD): Elevated triglyceride level

Hypertriglyceridemia has been shown as a confirmed marker for coronary heart disease (Sarwar, Danesh et al. 2007).

N-3 PUFA, sometimes referred to as omega-3 polyunsaturated fatty acids, decrease blood triglyceride levels via many processes. The referenced source is Davidson's publication from 2006. They are well recognized as an effective treatment for severe hypertriglyceridemia in the general population. Chronic kidney disease (CKD) is linked to a changed lipid profile characterized by increased triglyceride levels and decreased high-density lipoprotein (HDL) levels. The referenced source is Prichard (2003).

Randomized clinical studies have shown that n-3 PUFA may successfully lower triglyceride levels in persons with advanced CKD (serum creatinine 1.7–4.5 mg/dl) and end-stage renal disease (ESRD), even when administered at low to moderate dosages (1.0 to 2.5 g daily). (Saifullah, Watkins et al. 2007) Hypertension is a prevalent occurrence that may be seen at any stage of renal disease. An analysis of 90 randomized studies conducted on individuals with hypertension and no other accompanying medical conditions revealed that consistent consumption of substantial quantities of fish oil results in a reduction in both systolic and diastolic blood pressures by 2.1 and 1.6 mmHg, respectively.

The citation is derived from the research done by Geleijnse, Giltay, et al. in 2002. This tendency is particularly evident in older persons and those with hypertension. The effects on individuals afflicted with Chronic Kidney Disease (CKD) are not well described. A study done on a cohort of 64 individuals with moderate-to-advanced chronic kidney disease (CKD) revealed that the administration of a daily dose of 2.4 grams of fish oil over a period of 8 weeks did not result in a decrease in blood pressure compared to the control group. (Svensson, Christensen et al. 2004) However, a recent study randomly assigned 85 patients with advanced chronic kidney disease (CKD), who had an average estimated glomerular filtration rate of 36 ml/minute/1.73 m2, to either consume 4 grams of n-3 polyunsaturated fatty acids (PUFA) daily or not. The results showed that those who consumed the PUFA experienced a decrease of 3.3 mmHg and 2.9 mmHg in their 24-hour ambulatory systolic and diastolic blood pressures, respectively. While the definitive effect of n-3 PUFA on blood pressure in CKD patients remains uncertain, it is probable that administering large doses of n-3 PUFA (particularly, a minimum of 3 grams per day) has a little, but noticeable, lowering influence on blood pressure.(Mori, Burke et al. 2009)

3.3- The correlation between lipids and vascular calcification in chronic kidney disease (CKD)

Dyslipidemia is a crucial factor in the calcification of the inner layer of arteries. Cholesterol and lipid buildup are closely linked to the development of plaque and calcification, making them significant risk factors for atherosclerosis. Research examining the effects of HMG-CoA reductase inhibitors has shown substantial effectiveness in lowering cholesterol levels and decreasing the risk of cardiovascular disease. However, these investigations did not consistently show a decrease in VC. (Xu, Smith, and colleagues, 2022) The KDOQI recommendations for nutrition in CKD emphasize the significance of selecting appropriate foods and propose that recommending a Mediterranean diet may enhance lipid profiles in patients with CKD stages 1-5 who are not undergoing dialysis and have dyslipidemia or not. Consuming a higher quantity of fruits, legumes, and vegetables might lead to a reduction in body weight and blood pressure in patients with CKD stages 1-4.(Ikizler, Burrowes et al., 2020).

Omega-3 polyunsaturated fatty acids (PUFAs), namely eicosapentaenoic acid and docosahexaenoic acid, are lipids that serve several vital roles in biological processes. Endo and Arita (2016) have shown the ability to reduce inflammation and the production of atherosclerotic plaques in arteries, perhaps leading to a reduction in mortality associated with cardiovascular disease. Omega-3 polyunsaturated fatty acids (PUFAs) are suggested as a therapeutic treatment for high levels of triglycerides in individuals with a diagnosis of chronic kidney disease (CKD). Omega-3 fatty acids may be derived from fish oil, some microorganisms such as bacteria and marine microalgae, as well as plant sources including flaxseeds, chia, and walnuts. Figure 1. The current KDOQI recommendations in nutrition do not often endorse PUFA supplementation as a means to decrease mortality and cardiovascular disease. However, they do recognize that it may enhance lipid profile. (Saini, Prasad, et al 2021)

Figure 1 depicts the correlation between food consumption and the occurrence of vascular calcification (VC) in people suffering from chronic kidney disease (CKD). The green arrows symbolize the protective effects of dietary components on Vitamin C (VC), while the red arrows indicate a beneficial impact on the development of VC.

Multiple studies have examined the impact of polyunsaturated fatty acids (PUFAs) on chronic kidney disease (CKD). Studies have shown that polyunsaturated fatty acids (PUFAs) may enhance the membrane potential and adenosine triphosphate (ATP) levels in mitochondria, hence providing a protective effect on the kidneys and arteries. A recent research has shown that maslinic acid has the ability to attenuate renal interstitial fibrosis, hence potentially acting as a prophylactic intervention against the advancement of chronic kidney disease (CKD) and its associated consequences (Sun, Byon et al. 2021). 1 Randomized controlled studies have shown that the addition of omega-3 PUFA supplements greatly alleviates the symptoms of uremic pruritus, a condition linked to CKD-MBD. The reference for this study is Panahi, Dashti-Khavidaki et al. (2016).

Figure 1 illustrates the harmful impact of monounsaturated fatty acids on health. In contrast to the beneficial qualities of PUFAs, Son et al. found that individuals undergoing hemodialysis who had arterial medial calcification of the foot had a notably elevated level of monounsaturated fatty acids in their erythrocyte membranes compared to those without calcifications (Son, Lee et al., 2012). The ketogenic diet, characterized by a restricted consumption of carbs and a significant consumption of fats, has lately garnered significant attention. The research done by O'Neill and Raggi in 2020 has shown the efficacy of this strategy in managing type 2 diabetes mellitus and retarding the progression of renal cysts. The 2019 paper authored by Carriazo, Perez-Gomez, and colleagues. Hence, individuals suffering from diabetic kidney disease and autosomal-dominant polycystic kidney disease might experience advantages by following this diet, such as slowing down the advancement of the illness and ultimately reducing the frequency of difficulties. The publication may be referenced as Torres, Kruger et al. (2019).

Implementing this may lead to increased levels of cholesterol, thus, it is crucial to closely monitor and provide medicine for dyslipidemia. Altering one's diet may enhance and sustain the presence of ketone bodies in the bloodstream, namely β-hydroxybutyrate (β-HB), which is one of the most prevalent ketone bodies in the human circulatory system (Han, Ramprasath, & Zou, 2020). Lan et al. discovered that β-hydroxybutyrate (BHB), a ketone body generated during the ketogenic diet, efficiently inhibits vascular calcification (VC) in chronic kidney disease (CKD) by reducing the activity of HDAC9 (Lan, Chen et al. 2022).

Intermittent fasting, a technique that involves restricting calorie intake, has several benefits for various health conditions including atherosclerosis, cardiovascular disease, and obesity. This has been shown in both preclinical studies and clinical trials (De Cabo and Mattson 2019). However, more investigation is required in future studies to fully understand the impact of vascular calcification (VC) on this issue.

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4- Conclusion

The involvement of omega-3 polyunsaturated fatty acids (PUFAs) in chronic renal diseases is complex and important. Although further study is required to completely understand how they work, current data indicates a variety of beneficial outcomes. Omega-3 polyunsaturated fatty acids (PUFAs) provide anti-inflammatory qualities that might potentially reduce the chronic inflammatory condition often linked to renal failure. Furthermore, they have the potential to mitigate oxidative stress, hence potentially decelerating the advancement of renal disease. Furthermore, omega-3 polyunsaturated fatty acids (PUFAs) have been linked to improvements in lipid profiles and cardiovascular health, making them important considerations in the treatment of renal failure patients who are at a greater risk of developing cardiovascular problems. Moreover, new research suggests that omega-3 polyunsaturated fatty acids (PUFAs) may have a safeguarding effect on the kidneys by modulating several pathways associated with renal injury and fibrosis. It is crucial to recognize that while omega-3 PUFAs show promise in treating renal failure, they should be included into a comprehensive treatment regimen that encompasses dietary modifications, medication delivery, and lifestyle adaptations. Furthermore, it is crucial to consider the distinct characteristics and simultaneous medical problems of individual patients when determining the ideal dosage and duration of omega-3 PUFA supplementation.

In conclusion, omega-3 polyunsaturated fatty acids (PUFAs) have promise as a supplementary treatment for renal failure. These benefits are present because to their possession of anti-inflammatory, antioxidant, and Reno protecting properties. However, more research, including in-depth clinical trials, is required to establish the optimal dose regimens and get a more thorough comprehension of their precise mechanisms of action in this specific context.

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