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ANTI-INFLAMMATORY POTENTIAL OF BIOTICS AND OMEGA-3 SUPPLEMENTS IN CHRONIC KIDNEY DISEASE: A REVIEW

POTENCIAL ANTI-INFLAMATÓRIO DE SUPLEMENTAÇÃO COM BIÓTICOS E ÓMEGA-3 NA DOENÇA RENAL CRÓNICA: REVISÃO DA LITERATURA

A.R.
ARTIGO DE REVISÃO

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ABSTRACT

INTRODUCTION: Chronic Kidney Disease is a progressive inflammatory condition affecting millions worldwide, contributing to high morbidity and mortality rates. Inflammation plays a critical role in worsening Chronic Kidney Disease outcomes, prompting interest in potential interventions. Omega-3 fatty acids and biotics have emerged as promising adjunct therapies due to their anti-inflammatory properties.

OBJECTIVES: This review critically evaluates the available evidence on the effects of omega-3 fatty acids and biotic supplements in Chronic Kidney Disease management, with a focus on inflammatory biomarkers and clinical outcomes.

METHODOLOGY: A comprehensive keyword search was conducted in major electronic databases to identify relevant studies. A total of 10 articles met the inclusion criteria and were qualitatively synthesized.

RESULTS: Several challenges were noted, including small sample sizes, heterogeneous populations, varied follow-up durations, and differences in supplement types and dosages. The findings suggest that biotic supplements can positively influence gut microbiota composition, reducing the production of uremic toxins and inflammatory markers. Similarly, omega-3 fatty acids, particularly eicosapentaenoic acid and docosahexaenoic acid, demonstrate benefits for inflammatory and cardiovascular profiles in Chronic Kidney Disease patients.

CONCLUSIONS: While omega-3 fatty acids and biotics demonstrate potential as adjunct therapies for Chronic Kidney Disease, further research is needed to determine optimal supplement types and dosages. Large-scale, well-designed studies assessing clinically meaningful outcomes rather than surrogate markers remain essential.

KEYWORDS

Chronic kidney disease, Docosahexaenoic acid, Eicosapentaenoic acid, Fatty acids, Fish oil, Food supplements, Gut microbiome, Inflammation, Metabolic syndrome, Prebiotics, Probiotics

RESUMO

INTRODUÇÃO: A Doença Renal Crónica é uma condição progressiva associada a um estado inflamatório crónico que afeta milhões de pessoas em todo o mundo, contribuindo significativamente para a morbilidade e mortalidade. A inflamação desempenha um papel central na progressão da Doença Renal Crónica, despertando interesse em estratégias terapêuticas complementares. Os ácidos gordos ómega-3 e os bióticos têm emergido como potenciais terapêuticas adjuvantes devido às suas propriedades anti-inflamatórias.

OBJETIVO: Avaliar criticamente a evidência disponível sobre os efeitos da suplementação com ácidos gordos ómega-3 e bióticos na gestão da Doença Renal Crónica, com enfoque nos biomarcadores inflamatórios e nos desfechos clínicos.

METODOLOGIA: Foi realizada uma pesquisa sistemática por palavras-chave nas principais bases de dados eletrónicas para identificar estudos relevantes. Um total de 10 artigos cumpriu os critérios de inclusão e foi incluído numa síntese qualitativa.

RESULTADOS: Foram identificadas várias limitações nos estudos analisados, incluindo reduzida dimensão amostral, heterogeneidade das populações estudadas, diferentes períodos de seguimento e variabilidade nos tipos e doses dos suplementos utilizados. Os resultados sugerem que os suplementos bióticos podem influenciar favoravelmente a composição da microbiota intestinal, reduzindo a produção de toxinas urémicas e marcadores inflamatórios. De forma semelhante, os ácidos gordos ómega-3, particularmente o ácido eicosapentaenoico e o ácido docosahexaenoico, demonstraram benefícios nos perfis inflamatório e cardiovascular dos doentes com Doença Renal Crónica.

CONCLUSÕES: Os ácidos gordos ómega-3 e os bióticos apresentam potencial como terapêuticas adjuvantes na Doença Renal Crónica. Contudo, são necessários mais estudos para definir os tipos e doses ideais de suplementação. Permanecem essenciais estudos de grande dimensão e metodologicamente robustos que avaliem desfechos clínicos relevantes, em vez de apenas marcadores substitutos.

PALAVRAS-CHAVE

Doença renal crónica, Ácido docosahexaenoico, Ácido eicosapentaenoico, Ácidos gordos, Óleo de peixe, Suplementos alimentares, Microbiota intestinal, Inflamação, Síndrome metabólica, Prebióticos, Probióticos

INTRODUCTION

The Kidney Disease: Improving Global Outcomes characterizes chronic kidney disease as abnormalities in kidney structure or function persisting for more than three months, with implications for health (1). Chronic Kidney Disease (CKD) represents a progressive disorder impacting millions globally, exhibiting an age-standardized worldwide prevalence of around 9.5% (2), and is linked to elevated morbidity and mortality. Furthermore, it is recognized as a chronic inflammatory state, evidenced by heightened inflammatory markers in affected patients (3). Inflammation constitutes a pivotal element in CKD pathophysiology (4). Although inflammation serves as a fundamental protective response to injury or noxious agents, protracted inflammation can inflict tissue damage and provoke fibrosis (5). The kidneys are instrumental in modulating the immune system through the clearance of cytokines and proinflammatory mediators from the bloodstream. Nevertheless, their substantial blood perfusion—accounting for 25% of cardiac output—and the presence of inflammatory agents within renal tubules render them highly susceptible to inflammatory injury (6).

Disruptions in inflammatory signaling pathways, frequently initiated by factors such as diabetes, repeated insults, or suboptimal resolution of acute kidney injury, impair physiological repair processes and exacerbate progressive renal deterioration (7). Moreover, CKD-associated inflammation is a primary instigator of cardiovascular disease, the predominant cause of mortality in this cohort. This enduring inflammatory state is perpetuated by the buildup of uremic toxins, oxidative stress, and aberrant lipid metabolism, positioning inflammation as an active promoter of disease advancement rather than a mere byproduct (8, 9).

Advancing CKD also profoundly influences nutritional status. According to the National Kidney Foundation, shifts in nutrient demands heighten susceptibility to metabolic and nutritional derangements, underscoring the value of tailored nutritional strategies (10).

Within this framework, dietary supplementation has surged in popularity over recent years (11, 12). Among these, omega-3 fatty acids and biotics, including probiotics, prebiotics, and synbiotics, have emerged as promising adjunctive options owing to their anti-inflammatory attributes. Probiotics denote live microorganisms that impart health benefits upon sufficient intake; prebiotics comprise nondigestible substrates that preferentially foster beneficial microbial growth; synbiotics integrate both to optimize microbial viability and functionality (13). Such interventions can reshape gut microbiota profiles, thereby modulating immune functions and attenuating systemic inflammation (14, 15). Likewise, omega-3 fatty acids—such as eicosapentaenoic acid, docosahexaenoic acid, and alpha-linolenic acid—are acknowledged for their anti-inflammatory and cardioprotective properties (16, 17).

While numerous systematic reviews and meta-analyses have assessed probiotics and omega-3 fatty acids in CKD (18, 19) these predominantly examine individual modalities and prioritize quantifiable endpoints. An integrated overview concurrently evaluating both interventions, emphasizing their anti-inflammatory pathways and synergistic potential, remains scarce.

Therefore, this review aims to provide a critical and integrative synthesis of the current evidence on biotics and omega-3 supplementation in CKD, with particular emphasis on their anti-inflammatory effects and underlying mechanisms.

METHODOLOGY

This narrative review aimed to summarize the available evidence on the anti-inflammatory potential of biotics and omega-3 supplements in CKD.

A structured literature search was conducted in PubMed, Scopus, and Web of Science for studies published up to October 2024, using keywords such as “chronic kidney disease”, “inflammation”, “probiotics”, “prebiotics”, “symbiotics”, “omega-3 fatty acids”, and “supplements”.

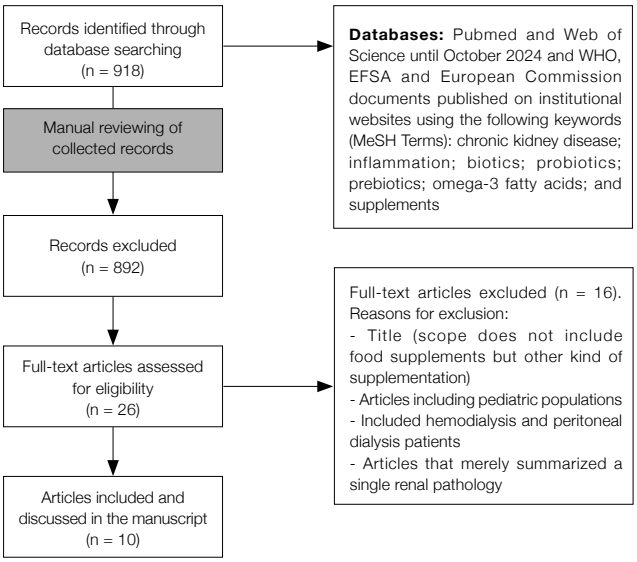
Studies were screened based on relevance to the topic, focusing on clinical outcomes, inflammatory biomarkers, and mechanisms of action. Articles involving pediatric populations, dialysis patients (hemodialysis or peritoneal dialysis), or studies addressing a single renal pathology without broader applicability were excluded.

From the identified literature, 10 studies were selected for detailed qualitative analysis, prioritizing randomized controlled trials and studies with higher methodological relevance. The study selection process is summarized in Figure 1.

A qualitative synthesis was performed to summarize the findings, focusing on the impact of biotics and omega-3 supplements on inflammatory markers and clinical outcomes in CKD.

Figure 1

Flowchart of study selection process for the narrative review



WHO: World Health Organization
EFSA : European Food Safety Authority

RESULTS

The pathophysiology of CKD is highly complex, with its clinical progression influenced by a wide range of underlying causes (20). Inflammation contributes significantly to CKD progression by promoting fibrosis, vascular calcification, and endothelial dysfunction, which are also key drivers of cardiovascular disease (21). Additionally, inflammation has been associated with increased susceptibility to infections, immune system dysfunction, and insulin resistance, all of which worsen the prognosis for CKD patients (22).

Several pathways involved in the inflammatory response have been identified. Interleukin-6 is one of the most extensively studied cytokines in kidney disease, recognized for its proinflammatory effects. A key mechanism linking IL-6 to CKD progression is its role in promoting atherosclerosis. Similarly, interleukin-18 induces inflammatory mediators, although it appears to have a more specific role in renal pathophysiology (20).

These mechanisms underscore the intricate relationship between inflammation and CKD progression, highlighting the potential for anti--inflammatory therapies to improve patient outcomes. This section

presents the results of the review, categorized into two groups: biotics and omega-3 supplements. Each of these categories has emerged as a promising intervention in managing inflammation associated with CKD. The results of the most relevant selected studies are presented in each category.

Probiotic Supplements

Numerous studies have examined biotic supplements as a natural therapeutic option due to their various health-enhancing properties. Although biotics include probiotics, prebiotics, and synbiotics, the studies included in this review primarily investigated probiotic supplementation. Researchers have been particularly interested in how these supplements affect the pathophysiological inflammatory mechanisms involved in the progression of CKD. Findings concerning the five studies selected are summarized below in Table 1.

Wager *et al.* performed a cross-sectional study to investigate the effects of probiotics and yogurt on inflammation. Notably, yogurt is considered a probiotic, containing two characteristic bacterial strains: *Lactobacillus delbrueckii subsp. bulgaricus* and *Streptococcus salivarius subsp. thermophilus*. The study included 888 patients with stage 3–5 CKD and available data on serum C-reactive protein (CRP) levels. The median CRP levels were significantly lower in participants consuming regular yogurt or probiotics than in those who did not. This association remained significant even after adjusting for other known major determinants of inflammation (23).

A double-blind and placebo-controlled trial conducted by Guida *et al.* included 30 patients with stage 3–4 CKD, randomised to receive either a food supplement or a placebo for four weeks. This supplement was administered in 5 g powder sachets. The powder was dissolved in water and ingested three times daily, separate from mealtimes. According to the manufacturer, each sachet contained a blend of lyophilized bacteria, including *Lactobacillus plantarum* (5×10^9 colony-forming units (CFU)), *Lactobacillus casei subsp. rhamnosus* (2×10^9 CFU), *Lactobacillus gasseri* (2×10^9 CFU), *Bifidobacterium infantis* (1×10^9 CFU), *Bifidobacterium longum* (1×10^9 CFU), *Lactobacillus acidophilus* (1×10^9 CFU), *Lactobacillus salivarius* (1×10^9 CFU), *Lactobacillus sporogenes* (1×10^9 CFU), and *Streptococcus thermophilus* (5×10^9 CFU) (24).

These two studies reveal a clear disparity in the composition of the tested supplements and the dosages administered. One of these RCTs specifically examined the effect on p-cresol, a uremic toxin, and reported a significant reduction ($p<0.05$) in the synbiotic group (24, 23).

Another randomised, double-blind, placebo-controlled trial assigned 44 patients to receive either 200 mL/day of soy milk containing *Lactobacillus* plantarum A7 or conventional soy milk for 8 weeks. The probiotic soy milk contained Lactobacillus plantarum A7 at a concentration of 2×10^7 CFU/mL. A total of 40 patients completed the study. Trial *et al.* showed the consumption of the probiotic soy milk resulted in a significant reduction in serum IL-18, an inflammatory marker ($p = 0.002$), and serum sialic acid levels ($p = 0.001$), a biochemical marker associated with cell membrane injury, particularly vascular damage (25).

Alatriste *et al.* assessed the impact of different doses of *Lactobacillus casei Shirota* (LcS) in reducing blood urea levels. A total of 30 patients were included in this RCT, with stage 3–4 CKD; participants were divided into two groups. Group A received a fermented dairy drink in an 80 mL bottle containing 8×10^9 CFU of LcS. In contrast, Group B received two 80 mL bottles, providing a total of 16×10^9 CFU of LcS. A significant reduction in blood urea levels was observed in Group B ($p = 0.003$) (26).

Although these four studies yield compelling evidence supporting the beneficial effects of probiotics on CKD, they are nevertheless constrained by several limitations. The observational design of one study precludes establishing causality for the observed associations. Moreover, it evaluated only a single inflammatory biomarker, with CRP data derived from multiple local laboratories, potentially introducing variability. Details on the dosage and formulation of the probiotic supplements were also lacking. The remaining studies encountered issues such as small sample sizes and short follow-up periods, which may undermine the robustness and generalizability of their results.

The heterogeneity of results reported in the literature is evident. An RCT conducted by de Faria Barros *et al.* involved 22 non-dialysis patients with CKD who had been adhering to a prescribed low-protein diet for

Table 1

Summary of studies evaluating probiotic supplementation in patients with Chronic Kidney Disease

STUDY	COUNTRY	DESIGN	n (I/C)	INTERVENTION	DOSAGE	TIME OF INTERVENTION	TARGET → OUTCOME
Wagner *et al.*	France	Cross-sectional	788 (777/11)	**Probiotics / yogurt**	Not specified	5 years	CRP → ↓
Guida *et al.*	Italy	RCT	30 (18/12)	**Multi-strain probiotic:** *Lactobacillus plantarum* (5×10^9 CFU), *Lactobacillus casei subsp. Rhamnosus* (2×10^9 CFU), *Lactobacillus gasseri* (2×10^9 CFU), *Bifidobacterium infantis* (1×10^9 CFU), *Bifidobacterium longum* (1×10^9 CFU), *Lactobacillus acidophilus* (1×10^9 CFU), *Lactobacillus salivarius* (1×10^9 CFU), *Lactobacillus sporogenes* (1×10^9 CFU), and *Streptococcus thermophilus* (5×10^9 CFU)	5 g powder sachets 3×/day	4 weeks	Uremic toxins → ↓ p-cresol
Abbasi *et al.*	Iran	RCT	40 (20/20)	**Probiotic soy milk:** *Lactobacillus plantarum* A7 2×10^7 CFU/mL	200 mL/day	8 weeks	Inflammation → ↓ IL-18; ↓ Sialic Acid
Alatriste *et al.*	Mexico	RCT	30 (dose comparison 15/15)	**Fermented dairy drink:** *Lactobacillus casei shirota* 8×10^9 CFU and 16×10^9 CFU	80 mL/day; 160 mL/day	8 weeks	Blood urea → ↓ (dose-dependent)
de Faria Barros *et al.*	Brazil	RCT	22 (12/10)	**Multi-strain probiotic:** *Streptococcus thermophilus*, *Lactobacillus acidophilus* and *Bifidobacterium longum* (30 billion CFU)	3 capsules/day	3 months	IS, p-CS, IAA, CRP, IL-6 → ↓ IAA; ↓ IL-6

CFU: Colony-forming units
CRP: C-reactive protein
IAA: Indole-3-acetic acid
IL: Interleukin
IS: Indoxyl sulfate
p-CS: p-cresyl sulfate
Notes: n, sample size; I/C, intervention/control; RCT, randomized controlled trial. Sample size is presented accordingly. Arrows indicate direction of effect (↑ increase; ↓ decrease).

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over a year. The treatment group received a supplement containing a combination of three encapsulated probiotic strains of gram-positive bacteria: Streptococcus thermophilus, Lactobacillus acidophilus, and Bifidobacterium longum. Each capsule provided 30 billion CFU, and the dosage was 3 capsules per day for 3 months. Inflammatory markers, including CRP and IL-6, were measured, and plasma levels of uremic toxins—indoxyl sulfate (IS), p-cresyl sulfate (p-CS), and indole-3-acetic acid (IAA)—were quantified. This study presented conflicting findings, as no significant changes were observed in any parameter in either the treatment or placebo groups after the supplementation period. Interestingly, IL-6 plasma levels increased following probiotic supplementation, while IAA levels decreased in the placebo group. None of the other parameters showed significant alterations after the intervention (27). This study was also constrained by a small sample size, making it challenging to draw meaningful comparisons.

Additionally, the heterogeneity of all the populations studied further complicates comparisons between studies.

Omega-3 Fatty Acid Supplements

Fatty acid supplementation, particularly omega-3 polyunsaturated fatty acids (PUFAs), has been studied extensively for its potential benefits on cardiovascular health and renal diseases and its anti-inflammatory and lipid-lowering. As before, the most relevant findings regarding the records discussed here are summarized in Table 2.

Many studies have tried to prove that improving cardiovascular profile ameliorates CKD (28). Ian H. de Boer *et al.* tested the effects of omega-3 fatty acid supplements, which could help slow the progression of CKD. The study included 1312 participants, of whom 289 received 1 g/day of EPA and DHA. The study concluded that there were no differences in the range of eGFR, therefore, there is no support or evidence that supplementation reduces the progression of CKD (29).

In Algeria, a randomized controlled trial was conducted in patients with dyslipidemia, hypertriglyceridemia, and/or hypercholesterolemia, who were allocated into two groups: an intervention group receiving omega-3 supplementation (fish oil capsules) and a control group without active supplementation (28). Although no significant differences were observed in creatinine, urea concentration, and eGFR in the omega-3 supplemented group, there was a 43% reduction in triacylglycerol levels. Additionally, there was a significant decrease in lipid and protein peroxidation (illustrated by thiobarbituric acid-reactive substance values, TBARS) and a significant increase in antioxidant parameters, including superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) activity.

Another study in Australia has shown that omega-3 fatty acids significantly benefited BP and HR and reduced serum triglycerides. The fall in BP was independent of effects on renal function (proteinuria and eGFR), which may not be surprising given the magnitude of the BP change and the relatively short intervention (30). The vasodilatory effect of omega-3 fatty acids may promote improved renal function and blood pressure control. Omega-3 was shown to act both directly (by replacing arachidonic acid as an eicosanoid substrate and inhibiting arachidonic acid metabolism) and indirectly (by altering the expression of inflammatory genes through effects on transcription factor activation) (28).

Improving cardiovascular profile reduces oxidation and inflammation, and improves renal function (27). In patients with moderate CKD, we observed that omega-3 fatty acids supplementation may attenuate the increase in IL-18 compared with placebo but had no effects on either IL-12 or hsCRP, suggesting that the immune-modulatory effects of omega-3 fatty acids may be pathway specific as opposed to generalised inhibition of inflammation (31).

Christine Dawczynski *et al.* proved that following daily intake of 3 g n-3LC-PUFA for 10 weeks, n-3LC-PUFA levels increased significantly

Table 2

Summary of studies evaluating omega-3 fatty acid supplementation in patients with Chronic Kidney Disease

STUDY	COUNTRY	DESIGN	n (I/C)	INTERVENTION	DOSAGE	TIME OF INTERVENTION	TARGET → OUTCOME
De Boer *et al.*	USA	RCT	1312 (289/320)	**EPA and DHA**	1 g/day	5 years	eGFR → no effect
Bouzidi *et al.*	Algeria	RCT	40 (20/20)	**Fish oil**	2.1 g/day	90 days	eGFR; Creatinine; Urea; TG; SOD; GSH-Px; TRABS → ↓ TBARS; ↑ SOD; ↑ GSH-Px
Mori *et al.*	Australia	RCT	40 (21/19)*	**Fish Oil** Group 1: Omega-3 Group 2: CoQ Group 3: both Control group: Olive oil	Group 1: 4 g/day Group 2: 200 mg/day Group 3: 4 g/day + 200 mg/day Control: 4 g/day	8 weeks	eGFR; Albuminuria; Proteinuria → no effect ↓ BP
Yong *et al.*	Australia	RCT	40 (21/19)	**Omega-3**	4 g/day	8 weeks	IL-12; IL-18; CRP → ↓ IL-18; ↑ IL-12; unmodified CRP
Dawczynski *et al.*	Germany	RCT	43 (33/10)**	**Enriched yogurt** n-3 PUFA	Group 1: 0.8 g/day Group 2: 3 g/day	10 weeks	RBC; EPA-derived mediators (PGE3, 12-, 15-, 18-HEPE); CV risk factors (HDL, TAG, AA/EPA ratio, n-3 index) → ↓ RBC; ↑ EPA-derived mediators; improve CV risk factors

*This study had 3 intervention groups illustrated here as Group 1, 2 and 3.
**This study had 2 intervention groups illustrated here as Group 1 and 2.
AA/EPA ratio: Arachidonic acid/eicosapentaenoic acid ratio
BP: Blood pressure
CRP: C-reactive protein
DHA: Docosahexaenoic acid
eGFR: Estimated glomerular filtration rate
EPA: Eicosapentaenoic acid
GSH-Px: Glutathione peroxidase
HDL:H igh-density lipoprotein
HEPE: Hydroxyeicosapentaenoic acids
IL: Interleukin
n-3 index: Omega-3 index
PGE3: Prostaglandin E3
RBC: Red blood cells
SOD: Superoxide dismutase
TAG: Triacylglycerols
TBARS: Thiobarbituric acid reactive substances
TG: Triglycerides
Notes: n, sample size; I/C, intervention/control; RCT, randomized controlled trial. Sample size is presented accordingly. Arrows indicate direction of effect (↑ increase; ↓ decrease)

in plasma and red blood cells (RBC) with a concomitant increase in the EPA-derived mediators (PGE3,12-,15-, 18-HEPE) in plasma while cardiovascular risk factors such as HDL were positively influenced. These findings highlight the value of n-3 LC-PUFA-enriched yogurt as a means of improving cardiovascular health. The observed increase of n-3 LC-PUFA in RBC and plasma lipids, resulting from n-3 LC-PUFA enriched yogurt intake, led to a reduction in cardiovascular risk factors and inflammatory mediators, demonstrating that daily consumption of n-3 PUFA enriched yogurt can be an effective way to supplement the daily diet and improve cardiovascular health. The dose-dependent incorporation of EPA and DHA in plasma and lipids after daily intake of 0.8 g or 3 g n-3 LC-PUFA supplemented yogurt resulted in a dose-dependent improvement of the cardiovascular risk factors (32).

DISCUSSION OF THE RESULTS

Unlike prior systematic reviews and meta-analyses, this review adopts a more comprehensive and integrative approach by concurrently examining biotic and omega-3 supplementation in CKD, with particular emphasis on their anti-inflammatory properties. Whereas previous investigations have predominantly assessed these interventions independently and prioritised quantitative outcomes, the current analysis synthesises clinical evidence with mechanistic insights, illuminating potential synergistic pathways and interactions that may elude detection in purely quantitative evaluations.

Biotic Supplements

Under healthy conditions, the gut hosts a diverse microbial community that regulates various physiological functions, including metabolism, nutrition, and immune responses. However, this delicate balance can be disrupted in chronic inflammatory conditions such as CKD, leading to intestinal dysbiosis — a condition characterized by an overgrowth of pathogenic bacteria and a decline in beneficial symbiotic microorganisms (22). This imbalance triggers the production of harmful metabolites such as indoles, phenols, and amines, which can compromise the intestinal barrier and allow the translocation of endotoxins into the systemic circulation, thereby contributing to systemic inflammation (33).

Uremic toxins, including IAA, p-CS, and IS, are known to compromise the epithelial tight junctions of the intestinal wall. This damage increases permeability, leading to endotoxemia and systemic inflammation, further exacerbating kidney dysfunction (34). In turn, these inflammatory processes lead to renal endothelial dysfunction, fibrosis, and tubular damage, creating a vicious cycle of worsening kidney health (22).

Elevated urea levels in CKD may play a significant role in this dysbiotic environment. Urea enters the intestinal lumen, altering the local biochemical environment and promoting the growth of urease- and uricase-producing bacterial families. These bacteria generate increased levels of inflammation-related toxins (22).

Given this interaction between the gut and the kidney, therapeutic strategies to restore microbial balance have gained attention.

The authors reviewed five studies regarding the effects of probiotics, prebiotics, and symbiotics on inflammation in CKD. Although this review aimed to address biotics broadly, the available evidence is predominantly focused on probiotics. Four studies described promising interventions (23, 24, 35, 36). However, high-quality clinical trials are still needed to fully establish these supplements' efficacy in CKD management. The selection of specific strains and their mechanisms of action are crucial for achieving the desired clinical outcomes, and more robust data are required to guide therapeutic use in this population. Various systematic reviews have already highlighted these limitations. The available studies are generally small and have short follow-up periods, exhibiting marked heterogeneity in patient ethnicity, eligibility criteria, disease progression, and the types and dosages of probiotics used.

Omega-3 Fatty Acid Supplements

Patients with CKD face an 8- to 10-fold higher risk of cardiovascular disease and mortality, primarily driven by chronic inflammation, which plays a critical role in the pathogenesis of CKD (31). The inflammatory response in CKD is mediated by cytokines, chemokines, and other pro-inflammatory molecules, which exacerbate oxidative stress and contribute to tissue damage, further increasing cardiovascular risk (37).

One promising therapeutic approach is the supplementation of omega-3 long-chain PUFAs, primarily sourced from fish oil. These fatty acids are essential for maintaining a healthy diet and have potential therapeutic applications in patients at elevated risk of inflammatory and cardiovascular diseases. Omega-3 PUFAs exert their benefits through several key biological processes, including regulating eicosanoid synthesis, cell membrane integrity, metabolic signaling pathways, and gene expression (37). Studies have shown that CKD patients often have significantly lower blood levels of omega-3 fatty acids than those in the general population, likely due to reduced food intake, chronic inflammation, nutrient malabsorption, and metabolic dysregulation (37).

Despite their potential in treating inflammation-driven conditions, omega-3 supplements are not routinely recommended for CKD patients, possibly due to limited awareness of their therapeutic benefits. However, interest in omega-3 PUFAs has increased recently (37).

The progression of CKD is closely associated with an elevated inflammatory response, which worsens as renal function declines. Markers such as CRP, IL-6, fibrinogen, and other acute-phase proteins—many of which are atherogenic—are consistently elevated in CKD patients (38). A key player in renal inflammation is monocyte chemotactic protein-1 (MCP-1), a member of the C-C chemokine family. MCP-1, produced by tubular epithelial cells and immune cells such as monocytes and macrophages, activates transcription factors such as NF-κB and activator protein-1 (AP-1), promoting IL-6 production. IL-6 is central to immune regulation, and MCP-1 also promotes vascular smooth muscle cell proliferation, contributing to further renal damage (38).

Abnormal fatty acid profiles, particularly a deficiency in essential fatty acids, are commonly observed in CKD patients (39). Omega-3 PUFAs offer several clinical benefits, including cardiovascular protection, immune modulation, and anti-inflammatory effects, with minimal adverse side effects (39). Omega-3 and omega-6 PUFAs are classified as essential fatty acids because the human body cannot synthesize them (40). Growing evidence supports the role of omega-3 PUFAs in lipid regulation, blood pressure reduction, antithrombotic activity, and anti-inflammatory effects, all contributing to cardiovascular protection (40).

Since inflammation and tubulointerstitial fibrosis are common final pathways in kidney damage, therapies targeting inflammation—such as omega-3 PUFAs—are increasingly being investigated (40). In CKD, the heightened risk of cardiovascular death may be driven by inflammation, oxidative stress, and altered mineral metabolism, leading to vascular calcification (18). Omega-3 PUFAs, derived from fatty fish and fish oil, have beneficially affected oxidative stress and inflammation in this population (18). Additionally, omega-3 PUFAs may help improve endothelial dysfunction in CKD patients through their antioxidant and anti-inflammatory properties (41).

These five studies aimed to evaluate the influence of omega-3 supplementation on kidney disease. While omega-3 supplements

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did not directly improve renal function, they positively impacted the cardiovascular profile, which is closely linked to kidney health, particularly in the prerenal phase. Omega-3 supplements have been shown to help reduce blood pressure, lower heart rate, and improve lipid profiles, thereby decreasing the risk of metabolic syndrome. This, in turn, reduces inflammation associated with the syndrome, addressing one of the key factors in kidney disease progression.

Although the studies showed no direct benefit to renal function, they demonstrated improvements in cardiovascular health, indicating that omega-3 supplements may influence kidney health indirectly through their effects on the vascular system. However, these studies had limitations, such as small sample sizes, most involved only a few patients (except for one study with 300 participants). As a result, the conclusions and statistical significance of the findings may be limited.

CONCLUSIONS

Biotics and omega-3 supplements may be a promising adjuvant therapy for CKD. While some supplements may benefit renal disease management, their use should be personalized and guided by healthcare professionals. Further research is needed to establish clear recommendations regarding the types and dosages of safe and effective supplements for individuals with renal disease. Regular monitoring and assessment of kidney function are crucial to ensure the safe use of any supplement in this population.

CONFLICTS OF INTEREST

None of the authors reported a conflict of interest.

AUTHORS' CONTRIBUTIONS

BPF and AM: Contributed equally to the study design, literature search, selection and analysis of the literature, and manuscript drafting. MJC and HR: Critically reviewed the scientific content of the manuscript and approved the final version for publication.

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