

Fatty Acids and Renal Disease

Ariana-Bianca Velciov, Georgeta-Sofia Popescu*

Banat's University of Agricultural Sciences and Veterinary Medicine "Regele Mihai I al Romaniei" from Timisoara, 300645, Calea Aradului 119, Timis, Romania

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Abstract

Fatty acids are essential for energetic, metabolic, and structural activities in the body. In the management of renal disease, nutrition has a central role. The declinations of renal function are influenced by dietary intake of calories, phosphorus, sodium, potassium, protein, or acid load in most of the clinically observable abnormalities. More, the renal system is susceptible to self-perpetuating injury, an inherent property of kidney and the extent of this injury may be modified by adjustments in dietary intake of phosphorus and polyunsaturated fatty acids. Furthermore, continued researches are important for clarification of controversies concerning the impact of dietary n-3 fatty acids in all types of renal diseases.

Keywords: fatty acid, urinary stone, urolithiasis, renal disease, risk factors

1. Introduction

Lipids (fats) constitute of numerous chemical compounds, including monoglycerides, diglycerides, triglycerides, phosphatides, cerebrosides, sterols, terpenes, fatty alcohols, and fatty acids. Instead, fatty acids constitute the main component of phospholipids, triglycerides, diglycerides, monoglycerides, and sterol esters. Fatty acid are carboxylic acids frequently with a long unbranched aliphatic chain, which can be either saturated (no double bond), or unsaturated, monounsaturated (one double bond), or polyunsaturated (two or more double bonds), and are essential for energetic, metabolic, and structural activities. Elements, which constituted of fatty acid, are carbon, hydrogen, and oxygen that are arranged as a linear carbon chain skeleton of variable length with a carboxyl group at one end. Coherent nomenclature for fatty acid is necessary, that are recognize of food scientists, nutritionists, biochemists, chemists, and biomedical scientists alike. For fatty acids, there are a number of nomenclature systems, and some researchers

continue to name fatty acids traditionally on the basis of the names of the botanical or zoological species from which they are isolated [1,2,3,4]. Thus naming system provides no answer for the structure of fatty acids. Today fatty acids are in a continually research. It is known that in period of years '80, trans-fatty acids were considerate without effects on clinical behaviour and nutritional aspect of population [1,3,5]. The research studies started at beginning of '90 years have been showing noisome clinical effects on human body [5]. Fatty acids are contained in most diets in the form of triacylglycerol (esters with glycerol). Fat converted from dietary carbohydrate are stored as triacylglycerol in adipose tissue. Afterwards the fatty acids from this fat are released to provide energy for various aerobic tissues [4,6,7]. They are structural and metabolic precursors of essential substances in the body. Instance, phospholipids are essential components of all cell membranes and of plasma lipoproteins, and the essential fatty acids are precursors of prostaglandins and related regulators [1,2,4,7]. When there are defects of fatty acid metabolism then it loom

diseases. For example, defects in the mitochondrial acyl-CoA-dehydrogenases prevent normal fatty acid oxidation [4,8,9,10]. Fatty acids must, first be activated in order to participate in any metabolic process. They are activated by being joined in thioester linkage (Acyl-SCoA) to the -SH group of coenzyme A. The thioester bond is a high-energy bond. Omega ω -3 and ω -6 fatty acids classes are required for the synthesis of prostaglandins and other physiological regulators [7,10]. Our systems cannot introduce double bonds into those positions. Therefore, these fatty acids must come from dietary sources.

Diet affects kidney function, but it is still under investigation whether lipids and their metabolic products affect the development of kidney disease is still under investigation [4,7,11]. Eicosanoids (ECs) are precursors of the various polyunsaturated fatty acids (PUFAs), and they affect blood flow and blood pressure in the kidney, platelet aggregation, and inflammation [1,3,4,7,11]. In a variety of renal pathophysiological states, EC metabolism appears altered. There is an enhancement of EC in various renal diseases. Enhanced of synthesis of ECs may delay further deterioration of kidney function, and the administration of such ECs often retards the development of or improves the disease. However, on the other hand, there are other ECs, which can contribute at improvement in renal function that occurs when inhibitors of these particular compounds are administered. Because the types of ECs produced are dependent on the quantity and composition of the dietary fatty acids, the dietary PUFA intake may modulate some renal diseases [11,13]. It has been demonstrated on the experimental animals a reduction in the progression of renal injury when it was administrated fatty acid precursors of ECs. In this way how ECs seem to promote renal injury, while others appear to protect the diseased kidney from further damage, the dietary significance of these observations are not yet clear. Thus, effects of noneicosanoid-mediated concerning fatty acids that may be beneficial or harmful to renal function include changes in blood rheological properties, membrane composition and function, and serum lipid concentrations. Studies suggested that kidney failure patients taking omega-3 fatty acids are

likely to live longer than patients who do not take them. This has led to the supplementation of most renal diets with fish oils. The full import of fatty acid supplementation is still being worked out.

2. Basic renal function

In the internal environment the kidneys are considerate the guardians. The primary function of the kidneys is given of maintenance of the composition and volume of the extracellular fluid (and indirectly the composition of the intracellular fluid). The kidneys primarily regulated body balances of water and of many of the electrolytes of the extracellular fluid such as sodium, potassium, chloride, and inorganic acids (i.e., the intake and/or metabolic production of such substances must equal their excretion and/or metabolic consumption). Other important role of the kidneys are the excreting of waste products such as urea, uric acid, and creatinine and the elimination from the body of many foreign chemicals such as drugs, pesticides, food additives, and their metabolites. The kidneys have also significant functions as the regulation of arterial blood pressure through their role in regulating sodium balance and blood volume, their participation in the renin-angiotensin system, and their production of various vasoactive substances such as ECs; the regulation of erythrocyte production by the bone marrow via the renal hormone erythropoietin; the hydroxylation of vitamin D to its active form; and gluconeogenesis during starvation [14].

3. Eicosanoids and leukotrienes

The eicosanoids (ECs) and leukotrienes (LTs) are categories of bioactive lipids synthesized from 20-carbon polyunsaturated essential fatty acids. Enzymes involved in their metabolism are present in the tissues of the kidneys, especially the renal medulla [3,4,12,13,14]. The ECs and LTs mostly have functions of autocrine and paracrine mediators. There are specific receptors for all ECs and LTs, allowing for pharmacological blockade of specific compounds. ECs mediate local symptoms of inflammation, control of blood flow through vasoconstriction or vasodilatation, blood coagulation, fever, and pain.

Arachidonic acid (AA; 20:4n-6) is the most plentiful fatty acid precursor which is synthesized from the essential dietary fatty acid linoleic acid (LA; 18:2n-

6). In this way, the membrane concentrations of AA are influenced by dietary levels of LA (the first step in EC synthesis is the release of the 20-carbon fatty acid from membrane phospholipids by phospholipase A2 or from diacylglycerol by phospholipase C). The cyclooxygenase (COX) acts on AA to form the endoperoxide prostaglandin H2 (PGH2), which is then converted to the stable metabolites PGE2 (a potent vasodilator), PGF2 (which may be a weak vasoconstrictor), PGD2 (a vasodilator), and the unstable metabolites thromboxane A2 (TXA2; a potent vasoconstrictor and stimulator of platelet aggregation) and PGI2 (prostacyclin; a potent vasodilator and platelet inhibitor). The major ECs produced by the kidneys appear to be PGE2 and PGI2, with smaller amounts of PGF2, TXA2, and PGD2, and the production of these ECs may be significantly increased in some renal disorders [15,16]. Different segments of the nephron, renal vasculature, and renal interstitium may synthesize different amounts and types of ECs.

4. Urolithiasis and fatty acids

Nephrolithiasis (urinary calculi) have affected of people for millennia. Urolithiasis is a result of metabolic and urodynamic disturbance in the metastable medium of the renal excretion of various organic and inorganic compounds. In addition, renal calculi disease is a common, troublesome, and costly medical problem. Calcium stone (especially calcium oxalate) urolithiasis/nephrolithiasis are a commonly disease with a higher incidence [17,18]. It is necessary continued research to clarify controversies concerning the impact of dietary calcium, oxalate, n-3 fatty acids, and phytate in calcium stone formation. Further, it should explore the long-term effects of dietary interventions in stone formers.

Continued research is warranted to clarify controversies concerning the impact of dietary calcium, oxalate, n-3 fatty acids, and phytate in calcium stone formation. Further randomized controlled studies should explore the long-term effects of dietary interventions in stone formers. Increased levels of arachidonic acid in cell membranes may promote the hypercalciuria and hyperoxaluria that are characteristic of idiopathic calcium nephrolithiasis. The intake of n-3 fatty

acids, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), may decrease the arachidonic acid content of cell membranes and reduce urinary excretion of calcium and oxalate. Greater intake of EPA and DHA (through dietary sources or fish oil supplementation) may reduce the risk for kidney stone formation [19,20].

Hyperoxaluria (HyOx) is an important risk factor for urolithiasis and nephrocalcinosis in children, and can coexist with hypercalciuria. In patients with enteric HyOx, calcium binds to fatty acids instead of oxalate, and this soluble oxalate is better absorbed [21].

Eicosapentaenoic acid (EPA) by reducing urinary calcium might favorably affect urine composition in a way that possibly reduces the risk of calcium stone formation. The low incidence of various degenerative diseases, including urolithiasis, in the Greenland Eskimo (from Japan) has been attributed to their high consumption of oily fish with its high concentration of EPA. In research study of Yasui and coworkers observed that with a westernized diet, the oxygenated products of renal prostaglandin synthesis are metabolites of the n-6 series and these are known to play important roles in several pathophysiological processes involved in calcium stone formation. Buck's group presented a hypothesis that the initiating factor for lithiasis triggers prostaglandin synthesis, and showed that this influenced by EPA treatment [15,22]. In order to specify the effects of EPA on plasma lipids and urinary parameters, Yasui and coworkers [10,22] undertook a clinical study whereby a highly purified preparation was administered (1,800 mg/day) to 88 patients with urinary stones for 3 months (short term) and 18 months (long term). Their results was that hyperlipemia improved the affected individuals and urinary calcium was significantly reduced in the hypercalciuric but not in the normocalciuric group, and then in conclusion, the results suggest that EPA by reducing urinary calcium might favourably affect urine composition in a way that possibly reduces the risk of calcium stone formation [20,22].

In countries that are more highly developed hyperoxaluria seems to be a greater problem. An increasing incidence of calcium oxalate stone disease seems to have accompanied gradual changes in dietary trends [21]. Oxalate absorption, oxaluria, and calcium oxalate stone disease increase as animal

protein and fat intake increases. Increased dietary fat allows for an increase in calcium complexation. Fatty acids can cause a mild form of enteric hyperoxaluria.

One theory to explain a very low incidence of renal stone disease in Greenland Eskimos and coastal Japanese is that n-3 and n-6 polyunsaturated fatty acids affect the activity of cell membrane transporter proteins [22]. The administration of fish oil (n-3) and evening primrose oil (n-6) has been shown to have significant effects in rat models of nephrolithiasis [20]. Nevertheless, it should be noted that many fish oil preparations are high in calcium and vitamin D and this may have an adverse effect. This is an area in need of further research.

5. Obesity and renal disease

Independent of blood pressure and diabetes mellitus, high body mass index (BMI) has been reported to be a strong risk factor for the development of end-stage renal disease in humans. Obesity represent one of the defining criteria of the metabolic syndrome (together with hypertriglyceridemia, low serum LDL level, raised blood pressure, and an elevated fasting blood glucose level), and this syndrome has been shown to be a strong independent risk factor for chronic kidney disease. The mechanisms linking metabolic syndrome to renal disease may include impaired pressure natriuresis, insulin resistance, excess excretory load, endothelial cell dysfunction, chronic inflammation, hyperfiltration, and a prothrombotic status [3,23]. Research studies on the animals showed that obesity in dogs caused by a high-fat diet is associated with glomerular hyper, alteration, thickening of the glomerular membrane, proliferation of mesangial cells, activation of the rennin-angiotensin system, and expansion of Bowman's capsule and obesity is associated with the eventual development of glomerulosclerosis (GS). Also, diet induced obesity in mice has been shown to cause lipid accumulation in the kidneys, GS, and proteinuria, and the effects were mediated by a sterol regulatory element-binding protein (SREBP) pathway (high fat feeding stimulates this pathway) that activates genes involved in fatty acid and cholesterol synthesis [24].

The most important factors that influence urinary excretion and concentration of lithogenic and inhibitory substances are diet and related metabolic disorders. Increasing incidence of urolithiasis in western countries in the last decades due to changes in lifestyle factors raises particular attention to dietary habits and nutritional status of stone formers. A higher risk of urinary stone formation can be associated with larger body size (height, weight, and BMI). Body size is the major determinant of urinary oxalate excretion was indicated on the study in healthy subjects. Therefore, increasing body size might increase the risk of calcium oxalate stone formation. In the development of recurrent urinary stones a risk factor may be overweight or obesity and associated dietary pattern. The mechanisms for this effect are still unclear. The study performed of Siener [25] and co-workers (2004) have been revealed a significant positive relationship between BMI and urinary calcium excretion, one of the main risk factors for calcium oxalate stone formation. The present data demonstrate that overweight and obesity are strongly associated with an elevated risk of stone formation in both genders due to an increased excretion of urinary promoters but not inhibitors of calcium oxalate stone formation. Overweight and obesity are strongly associated with an elevated risk of stone formation in both genders due to an increased urinary excretion of promoters but not inhibitors of calcium oxalate stone formation. Overweight and obese men are more prone stone formation than overweight women. Overweight, obesity related food pattern and non adjusted drinking habits are related to increased risk of calcium oxalate stone formation and other metabolic disorders.

6. Hypertension, fatty acid and renal disease

The primary role in both the development and prevention of hypertension are plaing of the kidneys. Hypertension may result from excess renin-angiotensin activity, sympathetic nervous stimuli, or excess renal vasopressor ECs. A deficiency in renal EC vasodilators is fundamental to essential hypertension (hypertension without apparent cause). Renal ECs are important regulators of sodium excretion and blood volume through their effects on renal vascular resistance, GFR, and renal sodium reabsorption.

ECs regulate the levels of circulating vasoconstrictors (such as angiotensin II) and aldosterone (which acts on the kidneys to increase sodium reabsorption in the distal and collecting tubules), by modulating rennin release. The prevention of hypertensive renal damage may occur as a result of an enhanced incorporation of long-chain n-3 fatty acids in the kidney (such as EPA and docosahexanoic acid [DHA]); n-6 fatty acids exacerbated the development of renal failure in these salt-loaded rats. In such tissues, it appears a reduction in AA when usually is feed fish oil [4]. About how PUFAs modify membrane functions and thus impact renal disease and hypertension deserve further study. The blood pressure are diminishing through the agency of gamma-linolenic acid (GLA), this pressure lowering effect involves increases in the vasodilatory epoxyeicosatrienoic acids (EETs) and decreases in the vasoconstrictive hydroxyeicosatetraenoic acid (20-HETE) [26].

7. Chronic renal failure

There are a large number of renal and extra renal disorders that alter the function of the kidneys. The kidneys have many important functions, all of which are liable to suffer when the kidneys are affected by disease processes. This is especially true when the renal disease is chronic.

Chronic renal failure (CRF) is a syndrome in which there is a progressive and usually irreversible decrease in the GFR (the glomerular filtration rate) even when the disease that caused the renal damage has disappeared or abated. CRF (like ARF) occurs in association with a variety of primary renal diseases (such as inflammation and infection of the kidneys), systemic diseases (diabetes mellitus, hypertension, atherosclerosis, and lupus erythematosus), and nephrotoxins, with the most common histological manifestations of CRF being glomerular damage. Some investigators believe that immunological mechanisms account for the initial damage in many chronic renal diseases; however, the rate of progression may be influenced by a variety of non immunological factors [27]. CRF can be classified into three basic groups (prerenal, renal and postrenal causes).

Both n-6 (LA) and n-3 (ALA), essential fatty acids have been part of our diet since the beginning of human life. Eicosanoids derived from n-6 fatty acids have opposing metabolic properties to those derived from n-3 fatty acids. For health it is essential a balanced intake of both n-6 and n-3 fatty acids. In recent studies are suggested an association between polyunsaturated fatty acids (PUFAs) and the development of chronic kidney disease, namely the higher dietary intake of PUFAs, both n-3 and n-6 fatty acids, may be protective against progression to chronic kidney disease [7,11,13]. High PUFA concentrations, both n-3 FA and n-6 FA, may attenuate the age-associated decline in renal function among older community-dwelling women and men. Chronic kidney disease is emerging as a major public health problem among older adults and can result in end-stage renal disease with need for dialysis or transplantation for kidney failure. In chronic kidney disease, the major risk factors are increasing age, hypertension, diabetes, cardiovascular disease, and a family history of the disease. A contribution in glomerular and interstitial injury and progression of renal disease may have abnormalities in lipids and atherogenic lipoprotein metabolism.

Low total plasma PUFA levels were associated with an accelerated decline of kidney function in older adults. Examining the relationship between total plasma PUFA levels and change in creatinine clearance tested this hypothesis over a 3-year follow-up in the older participants a population-based epidemiology study conducted in Tuscany, Italy. In fact, ω -6 and ω -3 fatty acids have anti-inflammatory properties. In increased concentrations PUFAs are found not only in fish oil but also in vegetable oils. High quantities of ω -6 fatty acids are present in sunflower oil, soybean/corn oil, and safflower oil, whereas large quantities of ω -3 fatty acids are present in flax oil and hemp oil [12,28].

Chronic renal failure (CRF) patients have an elevated incidence of cardiovascular disease and increased premature mortality. n-3 polyunsaturated fatty acids (PUFAs) decrease plasma triglyceride levels, reduce blood pressure (BP), and have a cardio protective effect in subjects with normal renal function [12,29,30].

The research of Svensson [29] showed a significant increase in high-density lipoprotein cholesterol levels and a significant decrease in serum triglyceride levels in the group administered n-3 PUFA supplements. There were no changes in total cholesterol or low-density lipoprotein cholesterol levels in any group, and n-3 PUFAs had no effect on 24-hour ambulatory BP. Supplementation with n-3 PUFAs had a favourable effect on lipoprotein profile in patients with CRF [7,13,28,29,30].

Studies suggest that kidney failure patients taking omega 3 fatty acids are likely to live longer than patients who do not take them. This has led to the supplementation of most renal diets with fish oils. The full import of fatty acid supplementation is still being worked out.

In CRF a critical aspects are playing of the nutritional management. As hyperlipidemia is a common fact in patients with renal disease, dietary recommendations to improve the serum lipid profile may serve to prevent associated disorders. In patients with chronic renal disease, a number of investigators have demonstrated an increased incidence of myocardial infarction and coronary artery disease, but some dispute any causal connection between lipid abnormalities seen in renal failure and the atherosclerotic lesions that frequently develop in such patients. Notwithstanding, the GS occurring in some renal disorders is thought to be partly due to elevated lipoproteins. In CRF, plasma triglycerides are increase, HDL cholesterol is usually low, and LDL cholesterol is often elevated.

8. Conclusions

For the future, it is required more researchers study to defining of define the cellular origin of the ECs, to determine the extent to which renal diseases can be ameliorated by modulating EC synthesis or action via the use of specific coenzymatic inhibitors or receptor blockers, and to determine how changes in fatty acid membrane composition affect renal processes. Further work is needed to elucidate fully the relationship and the extent to which renal disease can be changed by altering the serum lipids. The modification in dietary fats could be a relatively easy and practical way to attenuate or prevent some renal diseases. Certainly,

nowadays dietary PUFA modulation seems to be the useful strategies, with increasing clinical application.

Compliance with Ethics Requirements. Authors declare that they respect the journal's ethics requirements. Authors declare that they have no conflict of interest and all procedures involving human/or animal subjects (if exist) respect the specific regulation and standards.

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