Effect of Omega-3 And SCFA in Human Hypertension and Cardiovascular Health

Yuxuan Zhang *

Shanghai Weiyu High School, Shanghai, 200000, China

* Corresponding author: zhangyx.wy0209@ldy.edu.rs

Abstract. Hypertension is an urgent and increasingly prevalent issue in global public health. Its regulation through diet has become a crucial focus. Dietary Omega-3 and SCFA have demonstrated multiple health benefits, including the blood pressure management. This article delves into their effects and mechanism on hypertension in humans. Epidemiological and clinical studies provide empirical support for the assertion that the intake of PUFA is correlated with reduced cardiovascular mortality. This reduction is achieved through various mechanisms, such as control of cellular metabolic pathways, alteration of gene transcription patterns, and favorable effects on control of blood pressure and lipid. Furthermore, this article also analyzed the effects of SCFA on hypertension. The utilization of dietary fiber by intestinal flora resulting in the synthesis of several SCFAs which subsequently influence hypertension. Additionally, a correlation exists between hypertension and gut microbiota composition, with significant variations observed in the gut microbiota composition among spontaneously hypertensive groups.

Keywords: Hypertension, omega-3 fatty acids, SCFAs.

1. Introduction

Hypertension bears significant implications for global public health, being strongly correlated with cardiovascular and cerebrovascular diseases [1, 2]. Due to demographic changes towards an ageing population and lifestyle-related risk factors, the prevalence of hypertension has increased [1]. Additionally, hypertension is often associated with overweight individuals and influenced by factors like heightened sympathetic activity, insulin resistance, and hyperinsulinemia [3]. Notably, changes in dietary patterns can impact blood pressure levels even before weight gain ensues. Increased caloric intake leads to elevated plasma catecholamines, a consequence of heightened sympathetic nervous system activity, followed by higher blood insulin levels and the advancement of insulin resistance. The surge in insulin levels is primarily attributed to increased sympathetic activity [1]. Fatty acids, especially omega-3 fatty acids (ω-3) and short-chain fatty acids (SCFAs), have emerged as pivotal subjects of study in the field of hypertension regulation, garnering significant attention in research endeavors, because they are often found in diets related to hypertension prevention and treatment.

Ω-3, a subclass of polyunsaturated fatty acids, are distinguished by a diene structure, indicated by at the third position from the omega terminal of the fatty acid chain, there is a carbon-carbon double bond. Alongside ω-6, they constitute a crucial group of lipids. These "essential fatty acids" must be acquired through eating habit or supplements, as the body cannot produce them independently. Ω-3 play diverse roles in physiological activities, including regulating inflammatory responses and maintaining cell membrane integrity [4]. Unlike essential fatty acids, the body can synthesize various other types of fatty acids, including saturated and monounsaturated ones [5].

SCFAs constitute a specific group of fatty acids characterized by their linear structure. The primary SCFAs found in the gastrointestinal system are acetate, propionate, and butyrate, collectively constituting approximately 95% of the total SCFA population [6]. The molar ratio of SCFAs in the cecum and colon is roughly 60:20:20. SCFAs are produced through microbial fermentation, facilitated by the presence of complex polysaccharides that undergo incomplete degradation in the human gastrointestinal tract. This process yields various metabolites, influenced by factors like carbohydrate substrates, their breakdown degree, and the specific bacterial strains present in the gastrointestinal tract [7].

Given the escalating significance of hypertension in recent years, providing a concise overview of its impacts is crucial. This article aims to analyze the effects of both ω-3 and SCFAs on hypertension in humans.

2. Hypertension and ω-3

A correlation exists between ω-3 and hypertension, ultimately influencing blood pressure within the human body. Research findings revealed a notable alteration in fatty acid composition, particularly a decrease in DHA concentration compared to a meticulously matched control group [8]. A thorough examination of clinical trials is used to back up this assertion, which was found to have a dose-response relationship showing that DHA had a stronger link with blood pressure than EPA. Ingestion of DHA has been found to lead to a reduction in blood pressure in hyperlipidemic adults, in comparison to the ingestion of EPA, according to a recent study. In addition, a scientific study that involved a group of young adults who were overweight and who consumed fatty fish for eight weeks showed that those who had higher basal amounts of DHA in red blood cells showed the most significant decline in diastolic blood pressure. The study's results indicated a negative association between elevated levels of DHA in serum phospholipids and diastolic blood pressures measured during clinic visits, at rest, and over a 24-hour period. The efficacy of ω-3 in enhancing cardiovascular health has been demonstrated in individuals undergoing cardiac surgery who received omega-3 fatty acid supplementation prior to the procedure. The study presented findings suggesting a reduction in the duration of hospitalization by up to 2.4 days, attributable to the anti-inflammatory and anti-arrhythmic qualities of ω-3 [8].

Ω-3 are found in fish oil and various other dietary sources. The three primary types are ALA, EPA, and DHA [8]. Since the body cannot synthesize ALA, its dietary intake is crucial. ALA can be sourced from leafy greens, flaxseed, soybeans, linseed, canola, and walnuts. Fish and fish oil provide EPA and DHA, while marine algae serve as a DHA supplement. Enzymatic processes involving carbon chain elongation and desaturation slowly and somewhat inefficiently convert ALA into DHA and EPA. Their metabolic pathway is illustrated in Fig 1.

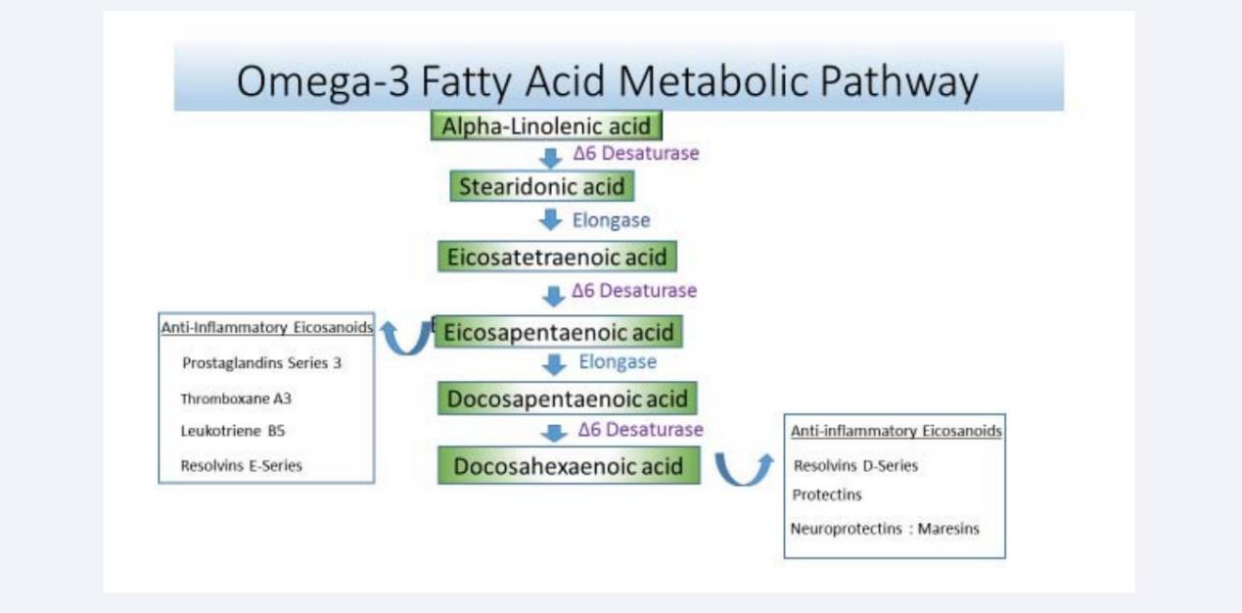

Figure 1. Metabolic pathway of ω-3 [8].

In the absence of ALA production, ω-3 from fish or fish oil supplements are effectively synthesized. Following ingestion, the small intestines break down ω-3 for absorption and transport. EPA and DHA are transported to organs and tissues via lipoproteins or albumin. Phospholipids are crucial components of all cell membranes for both biological and structural functions. Omega-3 fatty acid supplements lead to increased levels of plasma, organ, and tissue EPA and DHA in both humans

and animals. EPA and DHA lipid mediators possess anti-inflammatory, anti-arrhythmic, and vasodilatory properties, offering cardioprotective benefits [8].

3. Hypertension and SCFAs

The synthesis of SCFAs in the gastrointestinal tract primarily occurs through bacterial fermentation in the colon [9]. This process accounts for approximately 90% of SCFA production, with the remaining portion obtained from the consumption of dietary protein and other metabolites. Intestinal bacteria are essential for the digestion of raw food and the production of SCFAs. SCFAs are efficiently and swiftly absorbed in the gastrointestinal tract, resulting in limited excretion in the feces, estimated to be around 5-10% of the total quantity [9]. They play crucial roles in various physiological processes, including inhibiting HDACs, regulating chemotaxis and phagocytosis, and participating in the production of ROS. The main SCFA in the peripheral circulatory system, acetate, has the capacity to pass the blood-brain barrier and regulate the central nervous system to reduce appetite [9].

SCFAs is also connected with hypertension. Scientists have extensively studied the impact of SCFAs on hypertension, and a wealth of research consistently supports the favorable effects of these fatty acids on human hypertension.

Previous studies have delved into the influence of SCFA on blood pressure regulation in various animal models, investigating alterations in SCFA levels. Broadly, elevated levels of controlled SCFA are correlated with lower blood pressure [10]. While butyrate significantly enhanced intestinal barrier function in a mouse model of hypertension, Jin et al. discovered increased inflammation and permeability in the gut in hypertensive individuals [10]. However, a recent study indicated that excess butyrate might exacerbate hypertension [11]. The modified microbial composition impacts SCFA levels in plasma, consequently influencing blood pressure homeostasis. Remarkably, even low concentrations of SCFA in the intestine can impact blood pressure [12]. Another recent study revealed that exogenous SCFA prompted vasodilation and a subsequent decrease in blood pressure [13].

Recent research has also demonstrated that supplementation with fiber and acetate can enhance gut ecology, potentially exerting a preventive effect on cardiovascular disease [14]. Moreover, supplementing propionic acid has shown effectiveness in reducing hypertension, inflammatory response, mitigating heart damage, and restoring vascular function. Furthermore, diets low in fiber, characteristic of a Westernized eating pattern, might contribute to hypertension due to inadequate SCFA production. Therefore, microorganisms responsible for SCFA production play a pivotal role in maintaining cardiovascular health.

Numerous studies illustrated the connection between hypertension and the microbial composition of the gastrointestinal tract [9]. Notable discrepancies in the intestinal microbiota were observed between SHRs and WKY control rats, the latter exhibiting normal blood pressure levels [15]. The study revealed a reduced prevalence of Actinomycetes and Bifidobacteria in SHRs. The proportion of bacteria that produce lactate, on the other hand, varied significantly between SHRs and the control WKY rats. Additionally, WKY rats had a higher prevalence of bacteria known for their butyrate-producing capacity compared to SHRs. The F/B ratio showed a significant correlation with hypertension development. Another study involving 99 subjects with essential hypertension, 56 individuals with prehypertension, and 41 healthy controls found enriched fecal microbiota in patients. However, diversity was reduced. Moreover, the microbiome characteristics of the prehypertensive group closely resembled those of the hypertensive group [16]. Furthermore, Kim et al. demonstrated that modifications in the gut bacteria's makeup resulted in intestinal inflammation by compromising the integrity of the gastrointestinal barrier [10]. Prior research indicated potential influences of some bacteria on gut barrier function and the initiation of intestinal inflammation, which correlated with elevated SBP. Conversely, some bacteria exhibited a regulatory effect on inflammation and demonstrated an inverse correlation with SBP.

Numerous studies have yielded significant insights into the effect of hypertension on the composition and diversity of gut microbiota. Previous research has suggested that the restoration of microbiota, which improves gut health, may have the potential to mitigate hypertension in affected individuals. However, it remains uncertain whether improvements in hypertension are achieved through effects on SCFA. Further research endeavors will provide a comprehensive understanding of the principal bacteria associated with hypertension [9].

4. Diets and Hypertension

In recent years, the DASH diet and the Mediterranean diet (Med-diet) have emerged as crucial dietary guidelines in the context of hypertension. Previous investigations have indicated that key components of both diets are correlated with reduced mortality from hypertension and can significantly contribute to the prevention of cardiovascular disease. These dietary approaches emphasize the consumption of more vegetables, fish, and whole grains. When combined with previous analyses, researcher can infer their potential mechanisms of action on hypertension.

Fish, particularly rich in EPA and DHA, has been consistently associated with lower blood pressure in prior studies. Additionally, both diets advocate for lower consumption of red meat, which has been linked to various forms of inflammation. Instead, they emphasize anti-inflammatory components like polyphenols, which may influence gut inflammation and enhance gut barrier function, consequently improving blood pressure.

Vegetables and whole grains serve as important sources of dietary fiber. Dietary fiber plays a critical role in supporting the intestinal flora. It is not only essential for their survival, but also serves as a crucial raw material for the production of SCFAs. Countless research has highlighted the negative impacts of inadequate dietary fiber intake, underscoring the significance of increasing fiber consumption in the management of high blood pressure.

Both the DASH and Med-diet are relatively straightforward to implement in households and hold considerable potential for widespread adoption and long-term adherence.

5. Conclusion

In summary, it can be concluded that both ω-3 and SCFAs exert influences on hypertension, but they operate through different mechanisms. Research indicates that EPA and DHA within ω-3 possess direct antihypertensive effects, alongside anti-inflammatory and antiarrhythmic properties. Regarding SCFAs, previous studies demonstrate that SCFAs can ameliorate inflammation, enhance intestinal barrier integrity, and promote vasodilation, thus aiding in alleviating high blood pressure. However, it's worth noting that excessive intake may lead to contrary effects. Moreover, alterations in the composition of intestinal flora have been observed in hypertensive patients compared to healthy individuals. Although the precise mechanism is not fully elucidated, it has been established that in some cases, shifts in the intestinal flora composition led to changes in SCFA intake, thereby influencing hypertension. Presently, there is evidence pointing to the association between fatty acids and hypertension, though a more precise mechanism is yet to be fully understood. Further research efforts are warranted to attain a comprehensive and deeper comprehension of this area, particularly in terms of the impact of gut microbiota.

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