Benefits of Omega-3 Polyunsaturated Fatty Acids to Patients with Oral and Metabolic Diseases

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Running title: mega-3 Polyunsaturated Fatty Acids

**Abstract**

Human body cannot produce omega-3 fatty acids and must obtain it from diet. There are three types of omega-3 fatty acids that are needed by the human body, namely α-linolenic acid (ALA), docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). Although studies have shown that omega-3 fatty acids cannot prevent or treat diabetes or heart diseases, it did improve the condition of insulin resistance and the level of triglycerides in the body. It is well known that overweight leads to insulin resistance, which in turn leads to metabolic syndrome. Many animal experiments have already confirmed that long-chain omega-3 polyunsaturated fatty acids (n-3 PUFA) are beneficial in promoting insulin sensitivity. It inhibits nuclear transcription factor kappa B (NFκB), which is a key transcription factor for gene expression of inflammatory cytokines. On the other hand, studies have also pointed out that omega-3 polyunsaturated fatty acids do not improve the function of kidney’s endothelial cells and high blood pressure in patients of type 2 diabetes.

Keywords: Metabolic disorders; Dysglycemia; Insulin resistance; Oral disease; Long-chain omega-3 polyunsaturated fatty acids

**Introduction**

Type 2 diabetes is a metabolic disease characterized by hyperglycemia. It is estimated that the worldwide prevalence will increase from 171 million in 2000 to 366 million in 2030 [1]. Omega-3 fatty acids, in fish oil or linseed oil, can improve the sub-health status of patients with diabetes or dyslipidemia, such as insulin resistance, serum TG, HDL (high-density lipoprotein), etc., and regulate prostaglandin production [1]. Although the anti-inflammatory effect and triglyceride-lowering properties of long-chain omega-3 polyunsaturated fatty acids (n-3 PUFA) have been clinically proven, its inhibitory effect on body weight and the improvement on metabolic syndrome remain controversial [1-3]. The mechanisms by which n-3 PUFA may improve body composition and inhibit metabolic changes associated with obesity include regulating lipid metabolism, regulate fat or muscle hormones, such as adiponectin, leptin, etc., and reducing inflammation caused by adipose tissues. DHA (docosahexaenoic acid) and EPA (eicosapentaenoic acid) in omega-3 fatty acids cannot be produced by the human body and must be supplemented in the diet through fish or linseed oil, as well as nuts and other foods. Long-chain omega-3 polyunsaturated fatty acids can prevent inflammation by inducing the production of adiponectin. But studies have shown that supplementing fish oil for healthy group does not improve insulin sensitivity. For the population of sub-health status, such as having metabolic syndrome, such supplement will increase insulin sensitivity [1,3].

Clinically, diabetic patients may experience other common oral conditions such as gingivitis, periodontal disease, dental caries, dry mouth, angular cheilitis, burning sensation of oral mucosa or tongue, fungal infection, lichen planus, etc. The symptoms include burning sensation, dryness, bad odor and dysfunctional taste perception. Beside common signs of periodontitis and tooth loss, there is a decrease in salivation that leads to a constant feeling of high temperature (burning) in the mouth, all of which are indication of poor glycemic control. The delayed healing of wound is also common in the oral cavity of diabetics, not to mention tooth hypersensitivity with paresthesia and gingival decay. Diabetic patients may experience disturbance in the taste function. Fungal or bacterial infection is also common, as well as observing lichen planus-like lesions or angular cheilitis. All symptoms, such as periodontal disease, are more severe in the patients of diabetes than healthy people, which is probably due to higher A1C. Given these patients with poor immune function, the accumulation of late-stage product of glycation process in the body will trigger the inflammatory cells to systematically produce cytokines and cause a body-wide response. Dental plaque will increase under this condition and is observed by an increase of inflammation of soft tissues around the teeth. These biofilms of microorganisms will further invade the gums and alveolar bones to cause the necrosis of tissues in the cavity[4].

**Definition of Metabolic Disorders**

Dysfunctional metabolism is often categorized as metabolic syndrome, encompassing a variety of early conditions of some chronic diseases, such as hypertension, coronary heart disease, diabetes, dyslipidemia, obesity, gout, etc. Some studies have pointed out that insulin resistance and hyperinsulinemia are closely related to metabolic dysfunction [5,6]. The blood in adipose tissues is generally filled with abundance of free fatty acids, which inhibits the activities of insulin in the muscles and reduces the use of glucose; thus, elevating the level of blood sugar in the body. The rapid increase of glucose will force pancreas to secrete more insulin to compensate, but unfortunately, fats are highly resistant to insulin, leading to a vicious cycle of hyperinsulinemia, a condition of increased insulin in blood. Both conditions will contribute to abnormal level of blood lipids, blood pressure and systemic inflammation response, all of which may well lead to the final formation of atherosclerotic plaques to clog the blood vessels to cause myocardial infarction or ischemic cerebral infarction. Other associated metabolic diseases include fatty liver and diabetes.

**Discussion**

1.Prevention of metabolic disorders

Excessive adipose tissues in the body, especially around visceral organs, will produce free fatty acids and cause insulin resistance. Therefore, weight loss is a key factor in improving metabolic syndrome. Regular physical activities can improve insulin sensitivity, blood sugar, blood pressure and blood lipids. It also increases the concentration of HDL-C [7]. Omega-3 fatty acids are involved in the synthesis of some hormones that may inhibit inflammation and blood coagulation, as well as suppressing some of the immune responses. Therefore, for patients of immunodeficiency or coagulation disorder, it may instead increase the risk of infection or bleeding. The American Heart Association recommends that the supplement of omega-3 fatty acids to reduce the risk of heart diseases, but it will not help to reduce the mortality of ischemic heart diseases or failure due to type 2 diabetes or pre-diabetic condition, as it has the risk of inducing cerebellar hemorrhage [8]. Although omega-3 fatty acids cannot improve the metabolism of carbohydrates and proteins in diabetic patients, it shows promising result of lowering triglycerides and has been demonstrated in patients of metabolic disorder to have decreased fatty acids due to improved lipolytic enzyme activities.

2. Omega-3 polyunsaturated fatty acids in the oral cavity

According to the American Dental Association, diabetes increases the prevalence of oral diseases and the risk of other dental symptoms. And approximately 1/5 cases of tooth loss were reported to be related to diabetes. The top five factors of oral health in association with diabetes are gum disease, dry mouth, changes in taste, infection, slow healing, and periodontal disease. The International Diabetes Federation (IDF) also recommends that periodontal disease is one of the important complications of diabetes. Current evidence has also confirmed that diabetic patients are 2 to 3 times more likely to have periodontal disease, even when their blood sugar is well-controlled. But the degree of alveolar bone destruction is negatively correlated with the control of blood sugar that the destruction may be 4 to 11 times worse when blood sugar is uncontrolled. Severe periodontal disease will increase the blood sugar concentration in the body, not to mention that oral infection will also increase resistance to insulin. These will lead the patient into a vicious cycle of oral lesions due to diabetes. Diabetes and periodontitis are both chronic inflammatory diseases that significantly affect morbidity and represent a major health problem. However, periodontal disease is more prevalent and is associated with higher A1C value. Studies have shown that patients with periodontal disease have a higher incidence of diabetes. Moreover, periodontitis is associated with macroalbuminuria, end-stage renal disease, atherosclerosis and increased risk of cardiovascular event. Basically, every research has pointed to an unfavorable outcome for the diabetic patients. In a randomized clinical trial, it was found that the treatment group that focused on improving the periodontal disease showed a better control of blood sugar and there was a significant drop in the inflammatory response after 12 months of follow-up. Thus, it proved that the diabetic patients should have routine oral examination and cleaning. As the society is aging in Taiwan, the number of diabetic patients is bound to increase, and the need of health care is becoming more important than ever. Statistically, the prevalence rate of periodontitis in Taiwan is around 29 to 43%, with 25 to 36% as moderate case and 5 to 7% as severe case. Diabetes will further along the progression of periodontitis and related diseases, which contribute to uncontrolled blood sugar and vascular complications in the body. For oral treatment, beside the suggestions to have regular dental examination, good practice of teeth cleaning (once every 6 months) and brushing (following Bayer’s teeth brushing technique), and good eating habit to avoid corrosive foods, it will be wise to also control the blood sugar level.

3. Reduce the systemic inflammatory response

Studies on type 2 diabetes have found that chronic systemic inflammation may lead to insulin resistance because cytokines in the body will induce systemic but low-grade inflammation, which will cause the muscles and adipose tissues to become insulin resistant. When fats accumulate in the liver, it is then referred to as fatty liver and may dysfunction to cause more severe insulin resistance in the body. All these conditions will increase the complications of type 2 diabetes, including periodontal disease, chronic kidney diseases, etc. But proven by experiments, the supplement of omega-3 unsaturated fatty acids can reduce insulin resistance caused by the systemic inflammation [9,10].

Conclusion

Diabetes is a chronic disease with abnormal metabolism. Due to the relative or absolute lack of insulin in the body, or the resistance of muscles and adipose tissues to insulin, the body's ability to use the ingested starch is reduced or completely obliterated. The result is elevated blood sugar, which in turn cause mayhem in the metabolism of carbohydrates, lipids and proteins. Muscles lose mass and are weakened in strength, resulting in the condition of sarcopenia [7,11]. Omega-3 fatty acids increase the oxidation of fatty acids in the liver, adipose tissues, and skeletal muscles and limit their lipid accumulation in these tissues. It also reduces the production and release of adipokines, which promote inflammation. In the skeletal muscles, it promotes protein synthesis. All these activities will help to improve the overall metabolism. It is noted that patients with poor blood sugar control have reduced salivation; thus, oral cleaning is very important, since the bacterial growth will cause dental caries, gingivitis, periodontal disease, etc., in which periodontal disease is the most common oral complication in diabetic patients. The periodontal tissues are usually destroyed by the end products of glycation, causing swelling and bleeding of the gums. The interdental space is also expanded in the process. In some severe cases, patients may even lose their teeth. Therefore, diabetic patients should be supplemented with Omega-3 PUFA and pay attention to their oral health [12-16].

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