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Review Article:

The Potential Role of Fish Oil/ω-3 Polyunsaturated Fatty Acids Supplementation on Liver Size Before Bariatric Surgery

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ABSTRACT

Background: An enlarged liver, resulting from fatty liver and or steatohepatitis, may cause complications in gastric bypass surgery and increase the risk of liver laceration. Recently, ω-3 polyunsaturated fatty acids (ω-3 PUFAs) have been suggested as a potential intervention to reduce liver inflammation and volume. This review aimed to provide a comprehensive overview of the recent advances on fish oil/ ω-3 PUFAs supplementation to reduce the liver volume before the bariatric surgery.

Methods and Materials: This review summarizes studies investigating the influence of fish oil/ ω-3 PUFA in the liver volume of bariatric surgery candidates. Scopus and PubMed databases were systematically searched up to May 2021 for studies providing knowledge about the effects of ω-3 and or fish oil supplementation on liver size, fatty liver, or steatohepatitis.

Results: Most randomized controlled trials showed that ω-3 PUFA supplementation, primarily due to its anti-inflammatory and antioxidative properties, is a practical and effective treatment for fatty liver. It also decreases Alanine Transaminase (ALT), Aspartate Transaminase (AST), and Gamma-Glutamyl Transferase (GGT). ω-3 Fatty acids as essential regulators of hepatic gene transcription can reduce hepatic steatosis and inflammation markers; they also improve insulin sensitivity. As well, the access to the gastroesophageal junction was reported as simple.

Conclusion: The observed data suggest that preoperative fish oil/ω-3 PUFA supplementation could effectively improve liver function and decrease liver volume before bariatric surgery. However, well-designed randomized clinical trials are needed to confirm these results and determine a clear supplementation protocol regarding the optimal dose and duration before surgery.

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ABS ANNALS OF BARIATRIC SURGERY

1. Introduction

Bariatric surgery is recognized as the most successful long-time therapy for severe and morbid obesity [1]. Enlargement of the liver size due to Non-Alcoholic Fatty Liver Disease (NAFLD) and or Non-Alcoholic Steatohepatitis (NASH) is a prevalent disorder among patients with morbid obesity [2]. An enlarged and fatty liver can impose difficulties in bariatric surgery and increases the risk of hepatic laceration [3]. Several approaches have been used to reduce the hepatic volume in patients before the operation. Among those approaches, ω-3 polyunsaturated fatty acids (ω-3 PUFAs) with their proven benefits in hyperlipidemia and cardiovascular disease have recently been suggested for treating the NAFLD. However, there is significant heterogeneity between studies on these fatty acids. ω-3 PUFAs have recently been suggested to decrease hepatic steatosis and affect lipid metabolism and insulin sensitivity [4]. ω-3 PUFAs are derived from marine sources such as fish oil. They regulate several gene transcription factors, inducing a beneficial impact on different parameters of cardio-metabolic risk factors [5]. Animal and human intervention trials have shown that ω-3 PUFAs could improve the properties of NAFLD in terms of imaging and functional measurements [6].

This review aimed to provide a comprehensive overview of the recent advances on fish oil supplementation, focusing on its use as a potential approach to reduce the liver volume before bariatric surgery.

2. Materials and Methods

This review summarizes studies investigating the influence of fish oil/ω-3 long-chain PUFA on the hepatic status of bariatric surgery candidates. Scopus and PubMed databases were systematically searched up to May 2021, using the MeSH terms of “Obesity Surgery”, “Gastric Bypass”, “Bariatric Surgery”, “Fatty Liver”, “Liver Size”, “Liver Volume”, “Steatohepatitis”, “Polyunsaturated Fatty Acid”, “Fish Oil”, “Omega-3”, “n-3 Fatty Acids” for studies providing knowledge about the effects of ω-3 and or fish oil supplementation on liver size, fatty liver, or steatohepatitis.

3. Results

The significance of reducing liver volume in bariatric surgery patients is obvious. An inflamed and enlarged liver size restricts the operating space, bleeds easily, and damages exposure of the gastroesophageal junction, hiatus, and its angle. So all these problems complicate bariatric surgery [7].

Various methods have been advocated to reduce liver volume. Low-Calorie Diet (LCD) and or very low-calorie diet (VLCD) are assumed as such methods. Using the LCD or VLCD is easily administered, widely practiced, and shows a proven influence on liver size reduction in obese individuals waiting for bariatric surgery [8]. But, some critics of VLCD believe that there is no consensus on standardization of the VLCD, and it usually has been linked to poor patient compliance. A dietary restrictions failure rate of 13%–20% has been reported in recent studies since the patients lack the reasonable will to comply and adhere to this dietary advice fully. Another downside of the LCD/VLCD approach is its high cost and burdensome for the patients who are the candidate of bariatric surgery [9]. Moreover, typical side effects of such a highly restricted diet are stomach discomfort, sometimes nausea, vomiting, and constipation. Another serious drawback of this method is that LCD/VLCD for multiple weeks may persuade a catabolic state, which could be a serious disadvantage for post-operation recovery of bariatric surgery [10].

On the other hand, ω-3 PUFAs supplements have become considerably popular over the recent years. It has been considered a more compliance-friendly method to achieve the desired liver volume reduction before obesity surgery as it does not require strict caloric restriction [11]. ω-3 PUFAs supplements have already and widely been used to prevent and treat various cardio-metabolic, neurological, immunological, and psychological disorders. ω-3 PUFAs dietary supplement showed a positive effect on the liver fat content of patients with NAFLD [12]. The supplemented NAFLD patients show a significant reduction in triglyceride serum levels (TG) and alanine aminotransferase enzyme (ALT). Also, the ultrasonographic liver pattern of the patients shows significant benefits, in terms of regression of bright echotexture and increase of DPI (Doppler Perfusion Index), compared with baseline features. The DPI, measured by echo-Doppler, indicates improved liver blood flow TG due to reduced intrahepatic fat accumulation [13]. Most randomized controlled trials showed that ω-3 PUFA supplementation, primarily due to its anti-inflammatory and antioxidative properties, is a practical and effective treatment for fatty liver and decreases ALT, aspartate aminotransferase (AST), and TG and increases high-density lipoprotein cholesterol (HDL-C) [14]. Additionally, ω-3 PUFAs have a beneficial effect on alkaline phosphatase (ALKP), gamma-glutamyl transferase (GGT), and low-density lipoprotein cholesterol (LDL-C). Based on animal studies, ω-3 PUFA as essential regulators of hepatic gene transcription can reduce hepatic steatosis and inflammation markers, also improve insulin sensitivity

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[15]. Use of various doses (1500, 2000 to 2700 mg/d) and duration (from 1, 6 to 12 months) of supplementation in the literature revealed its therapeutic effects on fatty liver improvement and reduction of nutritional hepatic steatosis [16].

Ianelli et al. assessed the influence of ω-3 PUFA on liver volume and finally found a volume reduction of 20% of the left hepatic lobe. These results are promising because they confirmed that it could be a practical approach to reduce hepatic volume without the need for severe dietary and calorie restrictions [17]. ω-3 PUFA supplements to decrease plasma TG may be associated with glycemic control, as shown in a study of NASH patients with diabetes [18]. In addition, McKenney et al. recommend ω-3 PUFA supplementation at a daily dose of 2–4 g to patients with hypertriglyceridemia, which is a common comorbidity with fatty liver [19]. Moreover, Saravanan et al. found that ω-3 PUFA could act as beneficial agents to prevent cardiovascular disease effectively by conducting a review of numerous clinical trials [20]. American Heart Association recommends supplemental therapy with 1 g per day of ω-3 PUFA to those with myocardial infarction [21]. So, the preoperative ω-3 PUFA supplementation could ameliorate the fatty liver, liver volume, and some cardiometabolic risk factors simultaneously and eventually decrease the intra- and peri-operative risk of gastric bypass surgeries [12].

ω-3 PUFA supplements are effective in the prevention and reversion of hepatic steatosis by reducing lipogenic gene expression, exerting anti-inflammatory properties, suppressing oxidative stress, increasing insulin sensitivity, and improving glycemic tolerance [22]. These aspects, together with other advantages of the ω-3, could attract the clinicians for more prescription of ω-3 PUFA supplementation. ω-3 PUFAs are natural ligands of peroxisome proliferator-activated receptor-α (eventually decreasing intra- and peri-operative risk of gastric bypass surgeries) [12].

ω-3PUFA supplements can reverse liver steatosis by affecting lipogenic gene expression, anti-inflammatory action, antioxidative properties, increasing insulin sensitivity, and alleviate glycemic control. A group of nuclear receptors that modulate lipid metabolism and stimulates fatty acid oxidation in hepatocytes, i.e., peroxisome proliferator-activated receptor (PPAR) gamma, increases insulin sensitivity, inhibits hepatic lipogenesis, and reduces hepatic reactive oxygen species [23]. Besides, patients with NAFLD have insufficient n-3 PUFAs in the diet than healthy controls, and a higher ω-6/ω-3 ratio in NAFLD patients increased lipogenesis leading to steatosis [24]. Thus, an increase in the ω-6/ω-3 ratio impair PPAR-α activity in the liver and is associated with a higher hepatic uptake of circulating free fatty acids, a decrease of hepatocyte microsomal ω-oxidation, peroxisomal and mitochondrial b-oxidation, reduced synthesis of fatty acid transport proteins (namely very low-density lipoproteins), and an up-regulation of lipogenic transcription factors (namely sterol regulatory element-binding protein-1 [SREBP-1], stimulatory protein-1, and nuclear factor-Y) [25]. Previous experimental studies have shown that diets enriched with ω-3 PUFA increase insulin sensitivity in rats, reduce intra-hepatic triglyceride content and ameliorate steatohepatitis in mice and rats [26]. Although it is commonly reported that refined and concentrated ω-3 PUFA products contain virtually no methyl-mercury and are very low in organochloride contaminants, some less well-controlled preparations can contain appreciable amounts of mercury and other contaminations, which may affect the hepatoprotective properties of fish oil/ω-3 PUFAs [27, 28].

Regarding the safety issue of ω-3 PUFA supplementation, low and optimal doses of ω-3 PUFAs do not show any adverse issues, but some side effects do occur [29]. Some most common reported side effects are a fishy aftertaste, relatively gastrointestinal disturbances, and sometimes nausea. ω-3 PUFA benefits are seen with a consumption of >0.83 g/d. However, because of some side effects of ω-3 PUFA supplementation (such as clinical bleeding, worsening of glycemia in patients with impaired glucose tolerance, or rise in LDL-C in some patients) in doses of 3 g and higher [30], the optimal doses and duration of consumption should be established in future studies.

4. Conclusion

The obtained data suggest that preoperative fish oil/ω-3 PUFA supplementation may improve liver function and decrease liver volume through its role as negative regulators of hepatic lipogenesis and its anti-inflammatory and antioxidative response. So, the preoperative ω-3 PUFA supplementation could ameliorate the fatty liver, liver volume, and some cardiometabolic risk factors simultaneously and eventually decrease the intra- and peri-operative risks of gastric bypass surgery. However, well-designed randomized clinical trials are needed to confirm these results and determine a clear supplementation protocol. Given that the dietary factors, including the status of oxidant or antioxidant and inflammatory or anti-inflammatory compounds, could affect the fish oil/ω-3 PUFA metabolic responses, this matter should be considered in future studies.

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Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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Authors' contributions

Conceptualization and supervision, investigation, writing – original draft, and writing – review & editing: Gholamreza Mohammadi-Farsani and Mahsa Hatami; Methodology, data collection: Saeed Khajavi and Hastimansooreh Ansar.

Conflict of interest

The authors declared no conflicts of interest.

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