Nutritional Dietary Approach for NAFLD: Carbohydrate Restriction or Fat Restriction

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Abstract

The increasing prevalence of nonalcoholic fatty liver disease (NAFLD) in many countries, especially the developed ones, has raised attention for the needs to cope with this disease. It has been reported that NAFLD patients have characteristic overloads of carbohydrate and lipid intake, and that their restriction improves the patient’s disease status. Then, which of the two has a better effect: carbohydrate or lipid intake restriction? This review will summarize the pros and cons in assessing NAFLD by carbohydrate or lipid restriction, and will discuss about the proper nutritional intake for NAFLD.

Keywords: Nonalcoholic Fatty Liver Disease; Nutrition Assessment; Energy Restriction; Whole Grain; N-3 Polynsaturated Fatty Acids;

Introduction

Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease in developed countries [1-3], an emerging major health problem in the Asian region [4]. Its increasing prevalence has no relation with race, gender, or age [5-9], and is a problematic issue in many countries. NAFLD patients are known to have an overload of carbohydrate or lipid [10-15]. Indeed, it has been reported that hepatic fat increases in proportion with excess intake of glucose [16], fructose [16, 17], or lipid [17-19]. Moreover, the expression level of lipid synthesis genes in the liver differs between carbohydrate or lipid intake [20], and thus the development of NAFLD depends on the specific nutrient. On the other hand, carbohydrate or lipid restriction has been reported to improve NAFLD with their order of merit [21, 22]. This review will focus on the effects as well as problematic issues about carbohydrate or lipid restriction in NAFLD patients, and discuss on the adequate nutritional treatment to assess NAFLD.

Carbohydrates

Carbohydrates can be found in grain, fruits, vegetables, dairy products, and is a major source of energy. It is a polymerized product of a minimum monosaccharide unit and can be categorized by chemical and physiological characteristics as shown in Table 1 [23]. In addition, the extent of digestibility to digestive enzymes categorizes carbohydrates into “available carbohydrates” and “dietary fiber”. Protein and lipids that bind to carbohydrates are also categorized into carbohydrates, and such compounds are called “complex carbohydrates”, while others are called “simple carbohydrates”. Moreover, the so called “invert sugar”, a product invented by scientific evolution,

Table 1: The major dietary carbohydrates [23]

<table>
<thead>
<tr>
<th>Class (DP*)</th>
<th>Subgroup</th>
<th>Principal components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sugars</td>
<td>Monosaccharides</td>
<td>Glucose, fructose, galactose</td>
</tr>
<tr>
<td></td>
<td>Disaccharides</td>
<td>Sucrose, lactose, maltose, trehalose</td>
</tr>
<tr>
<td></td>
<td>Polyols (sugar alcohols)</td>
<td>Sorbitol, mannitol, lactitol, xylitol, erythritol, isomalt, maltitol</td>
</tr>
<tr>
<td>Oligo- and polysaccharides (3-9): short-chain carbohydrates</td>
<td>Malto- and oligosaccharides (α-glucans)</td>
<td>Malto-dextrins</td>
</tr>
<tr>
<td></td>
<td>Non-α-glucan oligosaccharides</td>
<td>Raffinose, stachyose, fructo and galacto oligosaccharides, polydextrose, inulin</td>
</tr>
<tr>
<td>Polysaccharides (≥10)</td>
<td>Starch (α-glucans)</td>
<td>Amylose, amylopectin, modified starches</td>
</tr>
<tr>
<td></td>
<td>Non-starch polysaccharides</td>
<td>Cellulose, hemicellulose, pectin, arabinoxylans, β-glucan, glucomannans, plant gums and muclilages, hydrocolloids</td>
</tr>
</tbody>
</table>

*Degree of polymerization or number of monomeric (single sugar) units.
Carbohydrate restriction for NAFLD patients: how to take carbohydrate effectively?

Randomized Clinical Trials (RCTs) that analyzed the effect of carbohydrate restriction (some studies do not show whether the restricted nutrient is carbohydrate or sugar, so we designate both as carbohydrate-restricted meals, here) show each study has a different definition of carbohydrate restriction: some state carbohydrate restriction as ketogenic meals less than 20 g per day [40] or as energy ratio down to 8% [41]; others as weak restrictions like energy ratio down to 30% [42-44] or 40% [22, 45-48]. In addition, the target population of these randomized controlled trials in these meta-analysis studies shows that while carbohydrate restriction has a significant effect on reducing the intra-hepatic lipid content, it shows no effect on lowering the elevated liver enzyme levels [49], and concluding the effect is marginal. A meta-analysis that summarized 19 RCTs studying the effect of carbohydrate on obese subjects show a comparison of low carbohydrate group (1364 subjects) and control group (1406 subjects). Almost all studies showed that changes in body weight is less than 2 kg and the difference of the total average is less than 1 kg, with almost no effect of carbohydrate restriction [50]. Decreasing intake or energy ratio of carbohydrate would result in a relative increase of the ratio of protein or lipid. This increase of the amount or ratio of lipid is a high-risk factor of NAFLD. Moreover, restriction of carbohydrates would result in shortage of whole grain such as dietary fiber or unprocessed grain that may improve the pathological state in NAFLD. Nonetheless, it should be noted that the effective amount or ratio of low carbohydrate diet is not clear, with issues such as the quantity or quality of carbohydrates, as well as effect, safety, and long term prognosis, questionable.

Lipids

Lipids are an important source of metabolic energy, material necessary for synthesizing compounds (essential fatty acids), regulators of gene expression, and are precursors of other nutrients such as fat-soluble vitamins in gastrointestinal region and plasma. Lipids are water-insoluble and soluble in organic acid [51]. They can be categorized to simple, compound, and derived lipids (Table 2) [52] and those with important nutritional roles are fatty acid, neutral fat, phospholipid, glycolipid, and sterol. Fatty acids have a carboxyl group at the end of a hydrocarbon chain (consisted of only hydrogen and carbon) made of 4-36 of carbons. Energy metabolism is done through the carboxyl group, as a source of energy, and also a component of the cell membrane. Fatty acid is consisted of: saturated fatty acid; no double bonds between the carbons, monounsaturated fatty acid; one double bond between carbons, and polyunsaturated fatty acid (PUFA); two or more double bonds between carbons. PUFA can be categorized into n-3 and n-6 fatty acids depending on the location of the first double bond from the methyl group terminal. Unsaturated fatty acids with double bonds have geometric isomers of Trans and cis. In nature, almost all the unsaturated fatty acids are cis, and only few are Trans [53].
Good and bad lipids for NAFLD

Excess or inappropriate intake of fatty acid induces insulin resistance, activation of lipoprotein lipase in adipose tissue by insulin stimulation, decomposition of triglycerol in blood through many genetic alterations in the fatty acid metabolic pathway, and free fatty acid uptake by adipocytes increasing triglycerol storage. This induces increase of lipid storage in the muscle, increase of triglycerol in the liver, an increase of cholesterol-ester [13]. Among the fatty acids, excess intake of saturated fatty acid is implicated in possible increase of insulin resistance and morbidity of type 2 diabetes mellitus that are directly involved in the disease status of NAFLD [54, 55]. The insulin resistance in adipose tissue induces increase of NEFA [25] which induces hyperinsulinemia that stimulates de novo lipogenesis in the liver [26]. Epidemiological studies have shown that NAFLD patients have excess total intake of saturated fatty acid. Musso et al. have used a seven-day dietary recording method to compare nutritional intake between non-alcoholic steatohepatitis (NASH) patients and normal controls, and found that NASH patients have a significantly higher intake of saturated fatty acids [14]. Moreover, the investigation of Toshimitsu et al. has shown that intake of lipids and saturated fatty acid was higher in both NASH and NAFLD patients [56]. Vilar et al. have reported that the percentage of lipid energy intake and saturated fatty acid intake was 37.5% and 10.1%, respectively, in NASH patients. Since this was significantly higher than that in NAFLD patients, they reported that these lipids may be one of the causes of transition from NAFLD to NASH [57]. Conversely, a crossover comparison study of pre-menopause obese women and obese middle-age men for intervention of lipids and saturated fatty acid showed that it decreased liver fat [58, 59]. The energy per kg of lipids is 4 kcal/kg. It is believed that this influences obesity, but animal studies show that when the total energy intake per day is the same, the higher proportion of fat increased the tendency to induce obesity [60]. Ha et al. have shown that high-fat diet for a certain period resulted in an increase in body weight, liver fat composition, blood sugar level, and liver inflammation along with the increase of percentage of lipid energy in mouse studies [61]. Other studies have shown that high-fat diet induces liver fat and insulin resistance [62], increase of TNF-α and inflammation [63]. In other words, excess lipid intake easily induces obesity despite the same energy level. The possible mechanism is due to differences in the nutrition resorption pathway and conversion to triglycerol. On the other hand, reports have shown that n-3 PUFA may improve the pathogenesis of NAFLD. A study where n-3 PUFA was administered for 12 months, liver function and various blood serum markers for NAFLD improved [64]. In addition, a random comparison study of adolescent NAFLD patients administered of n-3 PUFA and improvement of eating habits (carbohydrate 50%, protein 20%, and lipid 30%) for 12 months improved liver steatosis and liver function compared to placebo [65]. In addition, a two-group randomized control study showed that the administered group had significantly improved levels of liver function, lipid metabolic markers, inflammation marker [C-reactive protein (CRP) level], oxidative stress level [malondialdehyde (MDA)] and liver fibrosis markers (Type IV collagen, pro-collagen type III pro-peptide) [66]. On the other hand, a 12-month double-blind randomized placebo-controlled clinical trial study of NASH complicated of type 2 diabetes mellitus showed that PUFA administration does not contribute to the improvement of NASH pathogenesis [67]. Taken together, lipids are deeply involved in NAFLD, but it must be kept in mind that some induce or exacerbate diseases as others may improve them.

Table 2: Classification of lipids [52]

<table>
<thead>
<tr>
<th>Class</th>
<th>Subgroup</th>
<th>Principal components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple lipids</td>
<td>Triacylglycerol (mono-, di-, tri-acylglycerol)</td>
<td>Fatty acid, glycerol</td>
</tr>
<tr>
<td></td>
<td>Wax</td>
<td>Fatty acid, higher aliphatic alcohol</td>
</tr>
<tr>
<td></td>
<td>Sterol ester</td>
<td>Sterol, fatty acid</td>
</tr>
<tr>
<td>Compound lipids</td>
<td>Phospholipid Glycerophospholipid</td>
<td>Fatty acid, glycerol, phosphate, base</td>
</tr>
<tr>
<td></td>
<td>Sphingophospholipid</td>
<td>Fatty acid, sphingosine, phosphate, base</td>
</tr>
<tr>
<td></td>
<td>Glycolipid glycerolipid sphingoglycolipid</td>
<td>Fatty acid, glycerol, saccharide</td>
</tr>
<tr>
<td>Derived lipids</td>
<td>Fatty acid</td>
<td>Fatty acid, sphingosine, saccharide</td>
</tr>
<tr>
<td></td>
<td>Sterol ester</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Aliphatic alcohol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fat-soluble vitamin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fat-soluble pigment</td>
<td></td>
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<tr>
<td></td>
<td>Hydrocarbon</td>
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</tr>
</tbody>
</table>

Lipid restriction for NAFLD patients: what is effective lipid intake?

It has been shown that extremely-low lipid diet (energy: 1200 kcal, carbohydrate: 50%, protein: 43%, fat: 7%, dietary fiber 12 g) by a liquid dietary formula decreases hepatic triacylglycerol content in type 2 diabetes mellitus complicated NAFLD patients [68]. Utschneider et al. have reported that hepatic fat level significantly decreased in obese elderly subjects by LSAT diet (lipid: 23%, saturated fatty acid: 7%, glycemic index: 55), but not by HSAT diet (lipid: 43%, saturated fatty acid: 24%, glycemic index: >70), in a 4-week random assignment study [69]. NAFLD patients with a 3-day diet of 30% lipid energy have been reported that 14.9% of hepatic triacylglycerol is directly used from dietary fat [70]. On the other hand, an 8-week intervention of NAFLD patients by a 30% lipid diet modified from the DASH diet (carbohydrate: 52-55%, protein: 16-18%, total fat: 30%; originally designed to be rich in fruits, vegetables, whole grains, and low-fat dairy products and low in saturated fats, cholesterol and refined grains) improved high-sensitivity CRP, MDA, nitric oxide (NO) and glutathione (GSH) as well as liver function and glucose and lipid metabolic markers [71]. These RCTs analyzed small target populations but show that NAFLD may be improved by extremely-low or mildly-low lipid restrictions, but leaving the appropriate lipid intake level unknown. In addition, the specific lipid and the food taken together may have changed the effect. Moreover, the choice of high-protein or normal-protein intake on this low-fat diet may also have had an effect [72].

Lowering fat energy intake would mean to proportionally increase the energy level or percentage of carbohydrate or protein intake. Especially, the increase of carbohydrate level or percentage is known as a risk-factor for NAFLD. If fat is restricted, the n-3 PUFA that may improve NAFLD may also become of shortage. Nonetheless, the present consensus is that the effect of fat restriction on NAFLD is limited, and it should be noted that many issues are left to be answered such as the effective level or percentage of fat, or whether level or percentage is more important.

An effective diet therapy for NAFLD: carbohydrate vs. fat restriction

We have shown the effect of carbohydrate and fat restriction on NAFLD patients, but which of the two has the better effect? Haufe et al. have conducted a 6-month intervention random assignment comparison study on 170 overweight and obese subjects for low-carbohydrate diet (carbohydrate ≥ 90 g, protein 0.8 g/kg, fat ≥ 30%) or low-fat diet (fat ≥ 20%, protein 0.8 g/kg). A total of 102 subjects completed the study with proper intake of each group, and resulted in improved body weight, AST and ALT levels, intra-hepatic lipids, whole body insulin resistance, and hepatic insulin resistance. Both low-carbohydrate or low-fat diet showed the same result that decrease of energy intake and good compliance would improve obesity that induces NAFLD and other diseases [21]. Sacks et al. divided 811 obese subjects into 4 groups (group A; carbohydrate 60 %, fat 20 %, protein 15 %, group B; carbohydrate 55 %, fat 20 %, protein 25 %, group C; carbohydrate 45 %, fat 40 %, protein 15 %, group D; carbohydrate 35 %, fat 40 %, protein 25 %) taking the predetermined nutritional intake for 2 years and checked for change in body weight. The results of this carefully designed study showed that body weight did not change when the energy intake was equal despite the source [73]. Comparison by meta-analysis of 48 randomized trials using diet methods without dietary intervention targeted to 7286 subjects of obese overweight patients showed that low-carbohydrate and low-fat correlated well with bodyweight reduction, but no difference between dietary methods. These results showed that a diet method with good compliance should be recommended to a patient [74]. In addition, the influence of low-carbohydrate, low-fat (in comparison to Mediterranean diet) on bodyweight reduction was analyzed by four meta-analysis trials (13-24 trials) and found that adherence to the predetermined diet and exercise correlated most well with bodyweight reduction and improvement of disease [72, 75-77]. There was almost no difference between various dietary restrictions on bodyweight reduction ratio, and since the results were not consistent, some people even say that the “low-carbohydrate vs. low-fat” has no meaning [78]. In other words, before conducting restriction of a specific nutrient, managing the biological, behavioral, and environmental factors related to improving dietary and exercise adherence of lifestyle is the most important issue to be followed [78]. Nonetheless, the routine lipid restriction for patients with excess carbohydrate intake or carbohydrate restriction for patients with excess fat intake would be inappropriate from the aspect of disease pathogenesis or nutritional balance of dietary intake.

We propose that before mechanically conducting a choice between carbohydrate or fat restriction, a “nutritional diagnosis” based upon nutritional assessment of each patient should be made. Then, restriction of the excess nutrient should be corrected by this “nutritional diagnosis”. The speed of eating [79, 80], the extent of mastication [81, 82], and the order of eating [83, 84] have also been shown to change bodyweight and metabolism, making the effect of a specific nutrient or active ingredient not the sole issue of argument. In addition, restricting carbohydrates or fat should concern the subjects’ eating habits, dietary culture, local tradition, dietary environment or accessibility to purchased food (how easily the subject can purchase food). According to the “Nutrition Therapy Recommendations for the Management of Adults with Diabetes” of 2013 [85], personal and cultural preferences, lifestyle, therapeutic goals are different between patients, and thus nutrition therapy must also be conducted differentially, and that no standard evidence-based meal plan exists. The importance of nutrition therapy is that it fits with each lifestyle of personal habitual preferences. This applies to all diseases including diabetes where nutritional and dietary therapy is necessary. Taken together, nutritional and dietary therapy of NAFLD should be based upon assessment, nutritional diagnosis, and understandings of personal preferences, with concomitant settings of a nutritional care plan where energy intake can easily be decreased.
Conclusions

We have discussed here the effect, the problems, and the limitations of carbohydrate and lipid restriction of nutritional therapy for NAFLD patients. Nutritional approaches focusing on one sole nutrient such as carbohydrate or lipid can sometimes be inappropriate and unsuitable for a patient. Nutritional approaches of NAFLD patients must be initially done by a thorough nutritional assessment of the patient’s life history, with a subsequent nutritional diagnosis, and a total care approach must be conducted thereafter to improve the pathogenic condition of the patient’s disease.

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References

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