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Editorial

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Current Controversies around Carbohydrate Restriction and the Risk of High-Protein Diets

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LOW CARBOHYDRATE DIET AND FRUCTOSE-RICH CORN SYRUP

Recently, a Low carbohydrate (LCH) diet has been recommended by many doctors to control hyperglycemia and overweight. Unlike a traditional calorie-restricted diet, a carbohydrate-restricted diet typically contains less than 15% of the total energy intake from carbohydrates and about 30% from proteins. High glycemic index carbohydrates are the only cause of the glucose spike, so the main benefit of a LCH diet is not to cause postprandial hyperglycemia, which is considered to be the most serious risk factor for arteriosclerosis in diabetic patients. Life With Diabetes[1] says that all absorbable carbohydrate foods turn to glucose in the blood, while fats and proteins do not, at least directly. Compared to a calorie-restricted diet, a carbohydrate-restricted diet accelerates fat metabolism yielding to ketogenic energy and helps gluconeogenesis in the liver, resulting in a more effective control of weight.

The recent movie "That Sugar Film" seems to expose the dangers of eating sugar for the society. Inspired by "Super Size Me", the antecedent of "That Sugar Film", Gameau relates how he experienced on his own body for 60 days, and indulged in taking healthy foods containing sugar. The experiment caused fatty liver, an excess of 10 cm of visceral fat around his waist, mood swings, and metabolic changes which could lead to coronary disease. Gameau actually consumed the typical Australian amount of 40 teaspoons of sugar (160 g) a day, maintained physical exercise, took the same amount of kilojoules as in his usual diet, and only ate food items perceived to be healthy. The latter include cereal, smoothies, muesli bars, and low-fat yoghurt. For Gameau, the worst effects of the diet were on his cognition, mood and ability to concentrate.

Food companies are convincing people that these foods might actually be good for them. At the same time, these products are replete with cheap additives, and premium prices are charged to make consumers believe that they are purchasing something healthy. In 2015, World Health Organization (WHO) recommended to reduce the intake of free sugars throughout the life course.[2] For both adults and children, WHO recommends reducing the intake of free sugars to less than 10% of total energy intake. WHO suggests a further reduction of the intake of free sugars to below 5% of the total energy intake. However, the problem is not only caused by refined sugars, but also by syrup hidden in processed foods. The sweetness of fructose is 1.5 times stronger than sucrose. Because high fructose corn syrup is cheap and easy to handle, it is frequently added to many industrial foods.

The average dietary intake of fructose, largely derived from sweeteners based on high-fructose corn syrup, has been estimated to increase by 20-40% over the last three decades. Compared to glucose, fructose is more potent in the stimulation of de novo hepatic lipogenesis and Very Low Density Lipoprotein (VLDL) secretion, which subsequently impact on systemic energy metabolism and insulin sensitivity. Fructose is absorbed by enterocytes through Glucose Transporter or Fructose Transporter (GLUT5), a fructose-specific hexose transporter, and reaches the liver through the portal vein. In the liver, fructose enters the glycolytic pathway downstream of phosphofructokinase, a rate-limiting enzyme of the glycolysis, and generates carbons for the synthesis of fatty acids and triglycerides. Fructose intake also activates the expression of lipogenic genes, which involves the induction of Sterol Regulatory Element Binding Proteins (SREBP), particularly SREBP1c, a major transcriptional regulator of lipogenic

gene expression.[3] High-fructose corn syrup is certainly not a healthy alternative to sucrose.[4]

Recently, sweetened fruit (soft) drinks have received considerable attention as popular high-energy beverages potentially related to the prevalence of obesity among young children. Wright et al[5] performed a secondary analysis of the data from the National Health and Nutrition Examination Survey (NHANES) 1999-2002. Twenty-four percent of the children were overweight or at risk for overweight, and more than 80% children drank fructose-rich high-calorie drinks.

Thus, the sources of excessive intake of fructose and glucose are mostly processed foods, fruit drinks, and soda, where sweeteners are added to cause taste addiction. Fruit sugar (fructose, the sweeter half of sucrose or cane sugar) is poisonous to the liver in sustained large quantities. Excessive intake of apple juice and other fruit juices is not part of a healthy diet. Abid et al[6] reported that the consumption of soft drinks is associated with fatty liver disease, independently of the presence of a metabolic syndrome.

HYPERKETONEMIA FROM LOW CARBOHYDRATE DIET

Low-carbohydrate diet relies on alternate energy sources for the human body. Some specialized cells, for example in the brain, retina, gonadal germinal epithelium, and erythrocytes require glucose as the primary energy source. Carbohydrate-restriction diet increases the concentration of β-hydroxy butyrate (BHB) and other ketones in the blood. Cahill[7] studied the glucose metabolism of people who voluntarily fasted for 40 days. He reported that in starving human adults, BHB and aceto-acetate were produced in the liver from long-chain fatty acids and released into the blood. BHB can rise to approximately 6 mM during starvation, but newly produced amounts of acetyl-CoA from fat cannot be metabolized in the Krebs cycle and it is diverted towards ketone body synthesis. The reference range of BHB is less than 0.4-0.5 mmol/L in healthy persons, but it may exceed 1 mmol/L as a consequence of a carbohydrate-restricted diet.[8]

Glucose, BHB, and aceto-acetate are used as energy sources for the brain of people put on a low-carbohydrate diet. However, the brain requires 80 g glucose a day by gluconeogenesis, with the following daily synthesis: 15-20 g glucose from lactic acid and glycerol, 20 g from pyruvate reuse, 35-40 g from ketone bodies, and 10-11 g from the degradation of proteins. The liver accounts for two-fifths, and the kidney for three-fifths of the glucose production.[9] A low-carbohydrate diet inevitably requires high-fat high-protein diet. An example of high-fat diet is the keton formula in which 70% of energy comes from fat, and 30% from proteins. The keton formula is usually given for 2 years to epileptic children, and long-term effects are unknown. The effects of dietary composition on energy expenditure during the maintenance of weight loss have been shown in recent studies.[10]

RISKS OF HIGH PROTEIN, LOW CARBOHYDRATE DIET

Ebbeling et al[10] conducted a cross-over study on the effects of three different diet regimens administered for 4 weeks: isocaloric low-fat diet (60% of energy from carbohydrates, 20% from proteins); low-glycemic index diet (40% from carbohydrates, 20% from proteins); and very low-carbohydrate diet (10% from carbohydrates, 30% from proteins). Compared with the baseline prior to weight loss, the resting and total energy expenditure were increased in the very low-carbohydrate/high protein group. Urinary corticosteroids and C-reactive protein were also high. These observations would suggest that metabolic changes caused by a 3-weeks intake of low-carbohydrate/high protein diet resulted in stress and inflammation of the body.

Altogether, the above data suggest that longer-term human studies are necessary to determine the ideal balance between major nutrients, carbohydrate, protein and fat associated with a healthy longevity. The low carbohydrate/high-protein diet used in the Swedish women's cohort study showed that low carbohydrate/high protein diets are associated with an increased risk of cardiovascular diseases after an average of 15.7 years of follow-up.[11] The longest follow-up study is the US physician and nurse's cohorts, in which 44,548 males and 85,168 females were followed up for 20 years and 12.6 years respectively.[12] The total number of deaths among males was 8678, including 2746 cardiovascular deaths and 2960 cancer cases. Those among females were 1255 total deaths, 2458 cardiovascular deaths and 5780 cancer cases. The relative risk of high protein low carbohydrate diet was estimated at 1.23 for total deaths, 1.14 cardiovascular deaths, and 1.28 cancers. Other studies have shown similar trends.[13,14] The risk of chronic kidney diseases has not been described, but the risk of high-protein diet for kidney has been shown in many studies. We conducted a cross-sectional study on Chronic Kidney Disease (CKD) patients with very low protein diet (protein <0.5 g/kg/day). We found that they remained healthy for more than 6.7 years on average without clinical manifestation, starting from more than 5-6 mg serum creatinin/dl.[15]

IDEALLY BALANCED HEALTHY DIET AND DIETARY HABITS

Solon-Biet et al[16] compared three regimens varying in protein to carbohydrate ratio under both Calorie Restriction (CR) and

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ad libitum conditions. These diets were classified as low-protein (5%), Low-protein high-carbohydrate (LPHC), medium-protein (33%), medium-carbohydrate and high-protein (60%), low-carbohydrate. Fat content was fixed at 20% of the total energy intake for all three diets. Ad libitum LPHC diets offered similar benefits to CR in terms of levels of insulin, glucose, lipids, and Homeostatic model assessment (HOMA), despite an increased energy intake. CR on LPHC diets did not provide additional benefits relative to ad libitum LPHC.

Whereas HPLC diets do not sustain optimal cardio-metabolic health in later ages, it is important to note that nutritional requirements change with age, and higher P:C diets are required to support reproduction rather than to sustain a maximal lifespan.[17,18] You can prevent very severe health risks by improving your diet with an appropriate carbohydrate content, by exclusively eating natural foods with plenty of green vegetables, and by avoiding meat. Most of us know more or less what we should eat in order to feel well and have the weight which suits us. Fruits and vegetables should be part of our everyday meals. And whatever we eat should conform with our hunger and satiety.

Nettleton JA et al[19] recently reported a meta-analysis investigating associations between healthy diet, fasting glucose, insulin levels, and genetic loci associated with glucose homeostasis. They utilized data from 15 USA and European cohort studies comprising 51,289 persons without diabetes to test whether genotype and diet interact to influence glucose or insulin concentration. Genome-wide association studies focusing on genomic regions of diabetes and obesity did not show statistically significant associations.

Thus, dietary and other lifestyle habits are important for a healthy live. We all know these basic rules, but many of us are intoxicated by the food industry and so called ‘specialist’ messages. Rational thinking and emotions are disconnected . Brownell et al[20] argue in favour of a tax system that could promote good nutrition and help the nation recover health care costs associated with the consumption of sugar-sweetened beverages. Such integrative approaches should be effective to make our world a healthier place.

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