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Mini Review

Low Carbohydrate Diet: Where do We Stand?

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Abstract

The diabetic burden in 20-79 years age group is expected to rise to 629 million people by year 2045. Nutrition as a vital factor for preventing obesity & Type 2 Diabetes has sought great attention, however there is lack of proper evidence-based data defining best dietary approach suited for various metabolic conditions. There is some evidence suggesting carbohydrate reduction as a useful strategy for weight reduction and improving glycaemic control in patients with type 2 diabetes. However, there is insufficient data for long term efficacy, sustainability, and safety of this strategy. In this review, we attempt to explore the various evidence, probable mechanisms and adverse effects associated with low carbohydrate diet in treatment of various metabolic disorders.

Keywords: Low carbohydrate diet; Type 2 diabetes; Obesity; Diabetic diet; Nutrition

Introduction

Global obesity prevalence has nearly tripled since 1975. Previously considered a problem of high-income countries, overweight and obesity today are on rise in countries of low and middle income, particularly in urban landscapes. Overweight and obesity are associated with more deaths worldwide than underweight.

By 2030, 1 in 5 women and 1 in 7 men are predicted to be obesity (BMI>30kg/m^2) and over 1 billion people globally. The fundamental mechanism of obesity and overweight is an imbalance in energy between consumed calories and utilised calories. Obesity is a major risk factor for non-communicable diseases such as cardiovascular diseases (mainly ischemic heart disease and stroke), diabetes, musculoskeletal disorders (osteoarthritis), some cancers (endometrial, breast, ovarian, prostate, liver, gallbladder, kidney, and colon). Obesity is preventable as well as treatable. Lifestyle modifications, pharmacotherapy and bariatric surgery are three important modalities of treatment. Amongst them bariatric surgery has the most supportive evidence in long-term weight loss in patients with obesity [1]. Newer Treatments like incretin-based therapies have also gained attention given the important role of incretins in satiety suppression and in obesity management [2]. Lifestyle modification for obesity, though considered generally as an early weight loss strategy, is the foundation in a weight loss plan. It is applicable throughout the course of management of obesity and is complementary to all other strategies. It is the most easily accessible, available, affordable & applicable form of management for weight loss. Lifestyle modifications include diet (which is the central component), exercise, and behaviour therapy which includes smoking cessation, sufficient & quality sleep, optimal mental and emotional health, etc. Dietary habits are the most prominent player in maintaining a healthy lifestyle. Lot of diet plans are available, based on different protocols. Variables may be regarding components of macronutrients, timing of food, chewing time, cooking procedure etc. These diet plans can be Intermittent fasting, Plant-based diet, Low-carb diet, Paleo diet, Low-fat diet, Mediterranean diet, WW (Weight Watchers), DASH diet, etc. Various diets with a low carbohydrate (CHO) content have been proposed, such as the Atkins diet, the Zone diet, the South Beach diet and the Paleo diet. Amongst all available diet plans, the Low-Carbohydrate Diet (LCD) has a significant role in

the management of obesity, metabolic syndrome, type 2 DM and also Type 1 DM. This article will highlight the physiology, metabolic evidence, safety issues of LCD in obesity, type 2 DM and also in type 1 DM.

History of LCD

Before insulin discovery, carbohydrate restriction was one of the main treatment modalities for type 1 DM. But the original LCD, conceptualized in 1921 as treatment for intractable epilepsy in children owing to its ketogenic property and comprised of diet relatively high in dietary fat and protein [3,4]. Now it is extended to include adult population who don't respond to multiple antiepileptic drugs and also are not appropriate surgical candidates [4]. However, the underlying mechanisms of improvement in intractable epilepsy remain unclear. Several proposed hypotheses include effects of ketone bodies on mitochondrial function, in neuronal function and neurotransmitter release, and inhibition of mammalian Target of Rapamycin (mTOR) etc [4,5]. LCD was designed mainly for treatment of epilepsy in the first half and in the second half it was for reduction and maintenance of weight. After 1970, the concept of weight loss was given by Dr. Robert C Atkins [6]. So, the spectrum of use of LCD includes the management of intractable epilepsy to weight reduction in obese, type 2 dm and metabolic syndrome and extend up-to glycaemic control in type 1 DM at present.

Definition

Low-carbohydrate diets are defined as per the American Diabetes Association (ADA) classification of less than 130g/day or 26% Total Energy Intake (TEI) from carbohydrate [7]. But most widely used definition of LCD is based on total daily calories percentage, with <20% calories intake from carbohydrates, a relatively high daily caloric intake from fats (55-65%) and protein (25-30%) [8]. However, the definition of LCD varies between studies.

Physiology

Excess of calories stored as compared to the expenditure is the basis of obesity. The concept of LCD in promoting weight loss comes from Carbohydrate Insulin Model (CIM), in which there occurs high insulin secretion after a high carbohydrate diet. Amongst all the stimulus for secretion of insulin, carbohydrate in diet is the most potent one, and it varies as per the amount as well as type of carbohydrates [9]. High-carbohydrate diets stimulate post-prandial hyperinsulinemia which in turn promotes deposition of calories within fat cells, rather than the alternate fate of oxidation within lean tissues, thereby causing weight gain. Protein also stimulates the secretion of insulin, but the effect is counterbalanced by the concomitant glucagon secretion to some extent and fat in diet too has some direct effect on the secretion and insulin release [9]. Following a high carbohydrate meal, post prandial insulin secretion will be more, which favours adipogenesis and leads to obesity and metabolic dysfunctions like T2 DM. The basic metabolic processes after the adaption of LCD are mainly gluconeogenesis and ketogenesis [10].

In LCD, there is reduced glucose supply to muscles, liver and brain as a result of reduced synthesis and storage of glycogen that also leads to reduced glycolysis. Alternate to this process is gluconeogenesis [10] which utilizes amino acids like alanine, glycerol and glutamine, lactic acid as substrates for producing glucose [11]. But the process of gluconeogenesis is of a short time due to the limited supply of substrates. Ketogenesis occurs thereafter causing ketone bodies synthesis, which is the alternate energy source [10]. Relative insulin deficiency in LCD cause lipolysis with elevated fatty acid levels, thereby causing its conversion to ketone bodies like acetone, acetoacetic acid and beta hydroxybutyrate [10]. LCD may reduce plasma insulin levels, thereby promoting oxidation of ingested calories in lean tissues with low fat storage, which is the basic physiological pillar, which is applied for entire spectrum starting from the management of obesity to pre diabetes, metabolic syndrome and type 2 DM. It has beneficial effect on appetite as well. High carbohydrate diet stimulates appetite through hedonic mechanism where as in LCD, it was absent. To understand the metabolic benefits of the LCD, it can be interesting to discuss the metabolic effects of adopting a High Carbohydrate Diet (HCD) which results in augmented insulin secretion, that in turn diverts energy away from oxidation towards storage such as fat deposits within adipose tissue.

In response to brain's perception of 'cellular internal starvation', there is increase of appetite and suppression of metabolic rate. However, an alternate explanation for weight gain with a HCD simply invokes the pleasant taste of sweetness and its inherent hedonic effects that in turn drives us to eat more. The underlying mechanisms that link the HCD with resultant weight gain may implicate appetite control, the hedonic centres, metabolic rate, insulin-mediated energy partitioning or a combination of all of these factors. Whatever the actual mechanisms, the literature provides clear consensus on the metabolic effects of diets according to carbohydrate content: HCDs promote weight gain and metabolic dysfunction, and LCDs promote weight loss (at least in the short-term) and optimization of metabolic functioning. To summarize this section, the LCD is defined as a diet that has a low proportion of daily calories (<20%) derived from carbohydrates. LCDs therefore also contain a relatively high proportion of calories derived from dietary fat and protein, which hampers any attempt to explore the effects of low dietary carbohydrate ingestion in isolation. Although originally conceived as a treatment for intractable epilepsy, the primary application of the LCD currently is to facilitate weight loss and metabolic improvements in people with obesity, including obesity-related co-morbidities such as T2D. In this review, we focus on the metabolic effects of the LCD in these scenarios. Ultimately, there is individualization of the implementation of dietary interventions such as the LCD, according to their rationale and purpose. It is important to consider carefully the available evidence when choosing appropriate dietary interventions such as the LCD, including metabolic efficacy and safety.

Evidence of Metabolic Consequences

LCD enhances lipolysis, reduces plasma insulin level, causes

greater decrease in body fat mass, improvement in metabolic parameters, although in short term. In a meta-analysis of 14 Randomized Controlled Trials (RCTs) which include >1400 obese individuals, greater reduction in fat mass to the tune of 0.77 Kg was seen in LCD and VLCD groups as compared to low-fat diet groups [12]. Long-term data on LCD with respect to weight reduction is rather disappointing. The advantages of the LCD either disappears or diminishes after 1 year, when it is compared with traditional calories restricted diet [13,14]. Decreased physical activity and fatigue due to decreased glycogen stores [15], with resultant decreased energy expenditure may be the underlying causative factors for less weight reduction in long term. Apart from the weight reduction, some other metabolic benefits are also seen in LCD. There is improvement in future risk of cardiovascular disease amongst type 2 DM and prediabetes [16,17]. LCD also causes improvement in fasting and pre-prandial insulin sensitivity, but the effect of fasting insulin sensitivity decreases with time. There are also limited data regarding post prandial insulin sensitivity. Systemic review of 9 RCTs (LCD vs normal or high carbohydrate diet) that comprised of >700 T2DM subjects revealed glycaemic benefits (0.44% HbA1C reduction) and plasma triglyceride reduction of 0.33mmol/L. There was no significant change in total or LDL cholesterol and in long run no significant effect of the LCD on body weight was appreciated [18]. In obese type 2 patients also, LCD led to improvement in glycaemic parameters, insulin sensitivity, favourable lipid profile and weight reduction, though in short term [19]. A recent meta-analysis with more than 1350 type 2 patients (LCD vs control diets), LCD achieved more weight loss, improvement in fasting insulin sensitivity and triglyceride level at 12 months. Higher rate of remission seen in LCD groups at 6 months [7]. But the data regarding the long-term remission of diabetes is not substantial so far.

Adverse Effects

Nutritional deficiency is one of the major concerns in LCD, which results from restriction of dietary options and calories intake. There may be hypoglycaemia risk which is sometimes severe and resistant to glucagon effect due to the associated glycogen stores depletion, seen in type 1 DM while adapting LCD [20]. In the long run LCD may cause vitamin, minerals and trace elements deficiency which may lead to the decrease in bone health, renal calculi and sometimes growth failure, in young patients [4]. Less intake of dietary fibre in LCD and a relative lack of plant-based foods may cause constipation [21]. Dyslipidaemia is another concern related to high fat intake in LCD [4]. There may be deterioration in renal function in women with mild renal impairment in high protein diet, which is not seen in healthy subjects [8,22,23]. Again, studies show that diet having low or high percentages of carbohydrates predisposes the individual to increased mortality, which is even more in those with lack of plant-based food [24-26]. Ketosis, which was the prime concern in the first half, in the history of LCD, in short term causes gastrointestinal side effects like nausea, vomiting, diarrhoea, pain abdomen, reflux disorder etc [4]. But sustained ketosis for longer duration of time may have effect on calcium stores and thus theoretical risk of osteoporosis and nephrolithiasis [8]. High protein intake may have some adverse effects like dysglycemia and increased Type 2 DM development risk [27,28]. There may be some risk of hyperuricaemia, nephrolithiasis and gouty arthritis from breakdown of purines which is from high protein diet [8,29]. Impact of LCD on gut microbiota leading to gut dysbiosis is also a concern. Long Term LCD is associated with fatigue and decreased athletic performance [30]. Prescribing LCD should also have Emotional, Social and Socioeconomic factors to be considered.

Limitations

Poor adherence to modifications in diet is a major cause for limited efficacy of any diet plan [31]. Adherence depends on its acceptability of the particular plan by the individual. The long-term success also depends on the practical applicability of the diet plan and the enjoyment associated with the adaption of the same. Palatability is reduced in LCD, so as its enjoyment, as carbohydrate (sweet) is an important portion of food for palatability. So non palatable diet is less acceptable in long run by the individual. Severe limitation of food choice is one of the important limiting factors for long term adherence. Inadequate nutrition is also another drawback for long term adherence of LCD [8]. The possibility of impairing the athletic performance is noticed in LCD in few studies [30]. LCD may not be a suitable option in pregnant and lactating women, patients with renal disease or those who are with SGLT2 inhibitor. So, while prescribing LCD, one has to be vigilant.

Conclusion

Diet is an essential component of a healthy lifestyle, and it should include the proper balance of macronutrients like carbohydrates, fats and proteins along with proper quantity of vitamins, minerals and fibre. With The increasing prevalence of metabolic syndrome due to sedentary lifestyle and unhealthy dietary habits, the reassessment of dietary patterns and probable solutions is the need of the time. The goal being to prevent long term metabolic complications associated with Obesity, Diabetes and Metabolic Syndrome. On reviewing various dietary solutions, we came across Pros and Cons of various type of diets. Though there are specific metabolic benefits like improvement of glycaemic control and reduction of body weight etc from LCD, but these benefits are short-lived. The long-term benefits are not only disappointing, but potential safety issues are also a concern.

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