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PUBTEXTO

Accumulating clinical evidence for predominance of low carbohydrate diet (LCD)

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Abstract

The clinical problem of low carbohydrate diet (LCD) vs. calorie restriction (CR) has been discussed for a long time. After Atkins and Bernstein started LCD, authors et al. in Japan initiated LCD development socially through the Japan LCD Promotion Association (JLCDPA). Clinical controversies include in vitro, in vivo, type of diabetes, diabetic complications, and protocol. Medical experiments using mice for rodent species are not necessarily consistent with those of humans. Alternate Healthy Eating Index (AHEI) would be useful for diabetic research. From the United Kingdom Prospective Diabetes Study (UKPDS), the legacy effect has been known and will be more taken into consideration in the future.

Keywords: Low carbohydrate diet (LCD); Japan LCD Promotion Association (JLCDPA); Alternate Healthy; Eating Index (AHEI); United Kingdom Prospective Diabetes Study (UKPDS); Legacy effect

Commentary

For decades, diabetes has been increasing worldwide and causing large burdens from medical, clinical, social, and economic points of view [1]. The total expense would be about $413 billion for diagnosed patients, of which $307 billion for direct costs and $106 billion for indirect costs are estimated [2]. Among several problems, the debate over a low-carbohydrate diet (LCD) versus calorie-restriction (CR) has been ongoing for years. This issue has received much attention, and various opinions have been expressed. Since the problem shows different aspects of complex issues, discussions for the commentators are not proceeding smoothly.

What is the reason for this situation? Some axes can be suggested for solving the problems [3]. The first one would be the experimental data based on in vitro. The second is the results from in vivo, where the discussion exists about humans or rodents used in animal experiments. Third, are the data obtained from all diabetes, type 2 diabetes (T2D), T1D, slowly progressive insulin dependent diabetes mellitus (SPIDDM), or healthy individuals [4]? These three axes seem to be the main conceptions. Furthermore, we can add some categories for detailed conditions. The fourth point would be the condition of the subjects. Is it from young to elderly people? Each patient has different comorbidities, such as obesity, hypertension, dyslipidemia, hyperuricemia, and macroangiopathy, including cerebral vascular accident (CVA), coronary artery disease (CAD) and peripheral artery disease (PAD). The fifth point concerns the method. For example, do they have regular meals in their home, or are they given certain formulated meals or medicines every day? As mentioned above, these factors should be considered when understanding the content of each medical paper on diabetes. It would be required to evaluate what aspect or axis the report shows for a novel result in the field of diabetic research.

From a historical standpoint, the general process and development of LCD would be briefly summarized. Dr. Atkins and Dr. Bernstein initiated LCD in the late 20th century [5,6]. At that time, medical fundamental information was not so well known that only carbohydrates could raise postprandial blood glucose among the three main nutrients. However, kinesiologists had already emphasized that energy derived from ketone bodies (KBs) was more important than glucose. In the early 21st century, Dr. Ebe in Japan started LCD [7], and Shai reported the well-known LCD paper for comparison with LCD, CR and the Mediterranean diet in 2008 [8]. ADA did not adopt LCD as the guideline for diabetic care in 2006 [9], but adopted LCD as the recommended method [10]. After that, the European Association for the Study of Diabetes (EASD) also followed the guidelines [11].

Concerning the clinical effects of LCD, impressive two consecutive reports were found. The research is from the Nurses' Health Study (NHS) and the Health Professionals Follow-up Study (HPFS). This group started a prospective cohort study in 1976 and 1986 with enormous data. As to the results in 2010, the participants were 85168 females and 44568 males without diabetes, cancer or heart disease [12]. They were followed up on for 26 years. As a result, LCD from animal sources showed higher all-cause mortality in both sexes, whereas vegetable-based LCD showed lower all-cause and cardiovascular disease mortality rates. On the other hand, later research in 2023 showed different contents. The subjects were selected who were all newly diagnosed with T2D until 2018. The analyzed number was limited to 7224 females and 2877 males. In conclusion, the patients taking fewer carbohydrates revealed decreased mortality [13]. From these two reports, the analysis of applicants, methods, results and discussion would be different.

In diabetic research, several experiments have been reported using mice or rodent species. However, controversies have been found between humans and rodents [14]. LCD usually contributes to lower energy intake and improved metabolism in humans. However, a higher ratio of fat seems to be attractive in mice, leading to increased appetite and fat deposits through obesogenic mechanisms. Thus, different responses may be present. For a possible perspective, rodents have two positions in the insulin-related gene, and a higher intake of carbohydrate may be suitable for metabolism [15].

Another impressive report included several types of nutrition therapies. Totally nine kinds of dietary approaches were found, including 4937 participants, which are low-carbohydrate, moderate-carbohydrate, low-fat, Mediterranean, high-protein, vegetarian, low GI/GL, Palaeolithic and control [16]. For decreasing HbA1c, LCD was elected as the first dietary approach (84%), followed by Mediterranean (80%) and Palaeolithic (76%) in comparison with control. By network analysis, all types contributed decreased HbA1c and fasting glucose significantly. Among them, the Mediterranean diet seemed to have the most balanced clinical effectiveness.

Regarding dietary guidelines, the Healthy Eating Index (HEI) was presented by the US Department of Agriculture. It seemed to have some relationship with chronic disease risk. Recently, two novel measures have been proposed, which are the Alternate Healthy Eating Index (AHEI) and the Recommended Food Score (RFS) [17], which may predict the risk of chronic disease more effectively. By applying the cases of NHS (n = 67271) and HPFS (n = 38615), relative risk (RR) was analyzed. When comparing the highest and lowest quintiles, AHEI showed the RR of reduction as 0.80/0.89 in males and females. In particular, CVD risk reduction was 0.61/0.72 in males and females.

After the United Kingdom Prospective Diabetes Study (UKPDS), the legacy effect has been known for indicating the importance of glucose control in the early stages [18]. For a cohort study, newly diagnosed T2D patients were followed up for 13.0 years (n = 34737) [19]. As a result, cases with HbA1c ≥6.5% for a 0–1 year period showed increased micro- and macro-vascular events compared with those with HbA1c <6.5%, with a hazard ratio (HR) of 1.204. Consequently, the development of diabetic complications would be influenced by previous glucose variability in the early period, just after the diagnosis. Such factors should be involved in the general evaluation of diabetic cases.

As mentioned above, lots of medical reports have certain subjects or patients in the protocol. There are often misunderstandings about the results between subjects, results, and evaluation. Then, it would lead to the wrong conclusion or inadequate recommendation. They include obesity, T2D with or without complications, healthy subjects, the young generation, the elderly with or without frailty or sarcopenia, and older people with or without a healthy daily life with a satisfactory ikigai feeling [20]. Consequently, physicians and medical staff should recommend an appropriate meal style according to each patient.

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