Nutrition Treatment for T2D

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National and international guidelines for nutritional and lifestyle recommendations are available, together with protocols to guide weight loss to produce long-term T2D remission. Nutrition treatment becomes extremely challenging since additional determinants of malnutrition may be present, including reduced food intake and/or defective absorption of nutrients and impaired albumin synthesis.

Keywords: behaviour ; diet ; lifestyle ; nutrition supplements ; sarcopenia ; type 2 diabetes

1. Introduction

Diabetes mellitus, namely type 2 diabetes (T2D), constitutes a significant challenge for health systems worldwide. According to the 2019 Diabetes Atlas of the International Diabetes Federation [1], 463 million adults are currently living with diabetes (1 on 11 individuals worldwide, but 1 in 5 are aged over 65). The total number is expected to increase further by 700 million in 2045. The economic impact is huge—driven by the direct costs of treatment and complications, the indirect costs of disability and premature death, and the intangible costs of poor quality of life.

Despite its characterizations as a disease of affluence, nutritional problems are frequent in T2D. Unhealthy lifestyles expressed by overnutrition and/or scarce physical activity, leading to overweight and obesity, add to genetic defects in the pathogenesis of the disease. Dietary restrictions are prescribed to reduce the incidence of T2D as well as to improve metabolic control [2], but weight loss is burdened by the loss of muscle mass [3] and sarcopenia adds to age-dependent muscle wasting [4], increasing frailty [5]. These two opposite needs make a correct nutritional approach mandatory to reduce disease burden, improve metabolic control, limit pharmacologic treatment and reduce the risk of impending cardiovascular disease.

2. Medical Nutrition Therapy for Type 2 Diabetes

Additionally, recommendations on protein intake do not differ from the general population (1.0–1.2 g/kg body weight or corrected body weight for patients with overweight/obese); protein intake should be reduced to 0.8 g/kg body weight in subjects with chronic diabetic nephropathy [6]. At present, there is some inconsistency across guidelines from different countries as to protein sources (some do not limit animal proteins) and as to allowed maximal amount of protein intake (1.2–1.5 g/kg/day) [7]. A recent meta-analysis of 54 RCTs (4344 participants) showed a significant effect of moderate high-protein diets (20–45% of total energy) vs. low-protein diets (10–23%) on weight loss and weight loss maintenance, total fat mass reduction and cardiometabolic risk [8]. The effects might also be due to the blood-pressure-lowering effect of bioactive peptides that inhibit the angiotensin-converting enzyme activity observed in protein isolates [9].

The recommendations have largely focused on the quality of the diet and the importance of a healthy eating pattern that contains nutrient-rich foods, with less attention to the percentage of specific nutrients, with a reduction in daily caloric intake (250–500 kcal) for subjects with overweight and obesity [10]. Several dietary patterns have been studied and proposed, but no single dietary pattern should be preferred [11]. Individual preferences and treatment goals will determine the long-term use of these models; systematic reviews and meta-analyses have shown that a Mediterranean-style dietary pattern significantly improves hard outcomes such as glycaemic control, systolic blood pressure, total cholesterol, HDL-cholesterol and triglycerides [12]. The Mediterranean diet is characterised by a moderate-to-low carbohydrate intake, entirely covering the micronutrient needs [13]. Additionally, a low fat diet, i.e., the DASH-diet, promoted in the prevention of cardiovascular disease and the treatment of high blood pressure [14], has also reached consensus [15].

Another approach is the so-called intermittent fasting, which has gained increased popularity for treating T2D based on very limited literature [16]. This term encompasses various eating behaviours that avoid (or limit) nutrient and energy intake for a significant amount of time (a full day or a time-restricted feeding between 6 to 8 h) on a regular intermittent schedule. Intermittent fasting is claimed to improve glucose control, insulin resistance and to induce weight loss by generating a

‘metabolic switch’, i.e., a sort of rejuvenation of the metabolic homeostasis, leading to increased health span and longevity [17], but no advantage over conventional caloric restriction has been proven. Moreover, this regimen could carry the risk of hypoglycaemia even when following a medication dose-change protocol and should only be used under strict medical control and/or continuous glucose monitoring [18].

Finally, the use of mobile apps and wearable devices has recently gained consensus to facilitate weight loss. The use of these devices allows a direct analysis of daily calorie intake and physical activity (daily steps), translated into calorie consumption [19]. This provides immediate feedback and is likely to support long-term adherence to well-defined goals [20]. Several commercial apps are available, and have been tested in the prevention and treatment of diabetes in trials mimicking the U.S. Diabetes Prevention trial [21]. Toro-Ramos et al. confirmed a modest efficacy of weight loss for app users after 6 and 12 months of systematic use in subjects with prediabetes compared with usual care [22], and similar studies are available with the most recent apps that also support by tailored messages interactivity [23]. Although all these supports are expected to improve long-term weight loss, and a few patients may really reach impressive results [24], their use is biased by higher attrition rates [25]. Nonetheless, the possibility to reach a larger audience makes this approach a useful opportunity.

3. Nutritional Supplements for Metabolic Control

Vitamin D levels are frequently suboptimal in T2D, probably driven by overweight/obesity, and specifically by visceral adiposity [26], and have been associated with chronic inflammation and insulin resistance, as well as impaired insulin release [27]. Epidemiological studies support the existence of a relationship between low vitamin D levels and the presence of T2D, metabolic syndrome [28][29], nonalcoholic fatty liver disease (NAFLD) [30], cardiovascular risk factors [31] and insulin resistance, also tested by glucose clamp [32]. However, a clear association between vitamin D levels, insulin and glucose metabolism has not been systematically confirmed by intervention studies, and a causal association has never been established [33]. In a subset of the RECORD trial, a placebo-controlled trial of oral vitamin D 3 and/or calcium supplementation for the secondary prevention of osteoporotic fractures in older people, vitamin D 3 at the daily dose of 800 IU with or without 1000 mg of calcium did not prevent the development of T2D and did not reduce the need for glucose-lowering drugs in T2D patients [34]. Although the effects on insulin sensitivity have long been conflicting [35], a recent systematic review with metanalysis confirmed that vitamin D supplementation resulted in a significant improvement in HOMA-IR (standardized mean difference = −0.57; 95% CI: −1.09 to −0.04), particularly when vitamin D was administered in large doses and for a short period of time to nonobese, vitamin D deficient patients, or to individuals with optimal glucose control at baseline [36]. Data have been confirmed in another recent study in vitamin D-deficient adults randomized to high dose vitamin D supplementation. The HOMA value of insulin resistance was significantly reduced, and a lower rate of progression toward diabetes was observed vs. the control group (3% vs. 22%; p = 0.002) [37].

Of note, vitamin D has been extensively used also to treat sarcopenia, considering the role of insulin resistance extending from glucose metabolism to protein and amino acid metabolism, as discussed below.

Insulin modulates the shift of magnesium from extracellular to intracellular space; in turn, intracellular Mg 2+ concentration modulates insulin action, as well as blood pressure [38]; thus, low magnesium induces insulin resistance, and insulin resistance further decreases magnesium levels [39]. In the past 20 years, several epidemiological and clinical studies have demonstrated the protective role of magnesium on the risk of diabetes. In U.S. women aged ≥45 years (Women’s Health Study) with no previous history of T2D, an inverse association was found between dietary magnesium and incident T2D, which was significant among women with increasing grades of overweight/obesity (P for trend, 0.02). It was associated with a progressive decline of insulin levels (P for trend, 0.03) [40]. Data were confirmed in 1122 individuals (20–65 years of age) enrolled between 1996 and 1997 and re-examined about 10 years later. The relative risk of new-onset prediabetes and T2D were increased in the presence of low magnesium levels at baseline [41].

4. Prevention and Treatment of Diabetes-Related Sarcopenia

Optimal energy intake, healthy food choices and sufficient protein intake, coupled with habitual physical activity, especially resistance training, are the cornerstones for metabolic control and the prevention of frailty in T2D. Despite the mounting evidence of the negative impact of sarcopenia on the natural history [42] and quality of life of T2D patients [43], there is a surprising dearth of intervention studies addressing T2D-related sarcopenia. Therefore, we must rely on findings from general intervention studies on sarcopenia and/or sarcopenic obesity.

Resistance training represents the most effective intervention for prevention and treatment and can be safely carried out even in fragile patients [44]. High protein (1.2–1.4 g/kg) hypocaloric diets—either exclusively food-based or including protein supplements, both as an adjunct to resistance training—have proven effective for preventing muscle mass loss

during weight-reduction diets in women with obesity [45]. To reach the anabolic threshold, the protein supplement should be provided at meals rather than between meals in the elderly. The optimal protein dose (including food protein and proteins from supplements) should be 30–45 g of proteins per serving in the elderly [46]. However, high protein load cannot be recommended to T2D patients with chronic kidney disease (CKD) [47].

Whey proteins, rich in the anabolic amino acid leucine, represent the most frequently used protein supplements. Additionally, BCAA supplement or the leucine metabolite β-hydroxy-β-methyl butyrate have been proposed. These supplements are generally ineffective as sole treatment in patients without diabetes [45][48][49] and must be added to resistance training to improve already-established sarcopenia (associated or not to obesity). Leucine has strong insulinotropic properties, and leucine-rich supplements may increase the availability of amino acids for protein synthesis and reduce protein breakdown in the muscle, at the same time enhancing glucose disposal and glycaemic control, but solid data are lacking [50]. A noteworthy issue is that BCAA treatment has proven effective both in preventing and in improving sarcopenia in patients with liver cirrhosis, also independently of physical exercise/resistance training [51][52].

Finally, vitamin D was also proposed as a nutritional supplement to control sarcopenia. The activation of the vitamin D receptor present in muscle cells promotes their differentiation, proliferation and hypertrophy. Vitamin D deficiency is associated with reduced muscle mass and strength in the elderly [53], and vitamin D supplementation increased muscle strength, particularly in vitamin D-deficient cases and in the elderly [53]. Data were not confirmed by a Cochrane review in patients with liver disease; no data are available in T2D [54] and trials are eagerly warranted.

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