Fat intake and Glycemic Controltes

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Nutrition therapy is a cornerstone of type 1 diabetes management. Glycemic control is affected by diet composition, which can contribute to the development of diabetes complications. The specific role of macronutrients is still debated, particularly fat intake.

Keywords: fat intake ; diet ; nutrition ; type 1 diabetes ; glycemic control ; cardiovascular diseases

1. Introduction

Type 1 diabetes (T1D) is one of the most common chronic diseases of childhood [1][2]. Glycemic control, nutrition therapy and physical activity are the three cornerstones of T1D management. The main goals of the therapy are the maintenance of blood glucose within a proper range, close to normoglycaemia, with as low frequency of hypoglycemic and hyperglycemic episodes as possible, and reduction of macro- and micro-vascular complications [3][4][5][6].

Even though clinical manifestations of cardiovascular diseases (CVDs) generally appear in adulthood, the vascular damage might start early in T1D and evidence of subclinical CVD can be detected in adolescence [7]. In addition, youth affected by prediabetes or diabetes have an increased risk of metabolic disorders in adulthood, such as hypertension, dyslipidemia, and metabolic syndrome, predisposing to CVD [8]. Therefore, the prevention and early detection of cardiovascular risk factors are mandatory in young with T1D, as assessed in the American Diabetes Association (ADA) and the International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines. Periodical screening and eventually proper treatment for hypertension, dyslipidemia, smoking and nephropathy are recommended [6][9].

The most important cardiovascular risk factor in T1D is glycemic control, also adjusting for potential confounders [10]. Glycemic control is affected by diet and, in particular, diet composition, which contributes to the development of complications in individuals with T1D [11]. Nevertheless, the specific role of the intake of different nutrients is still a matter of debate, in particular fat intake [12][13][14][15][16].

2. Nutrition Guidelines and Adherence in Children and Adolescents with T1D

Current dietary recommendations for people with diabetes reflect guidelines for healthy eating for the general population. The ADA and ISPAD guidelines for children and adolescents with diabetes underline the importance of an individualized assessment of nutrition therapy and the related best distribution of macronutrient, aiming at improving glycemic control and lower cardiovascular risk [4][6]. ISPAD recommendations give the following thresholds as a guide: carbohydrate intake should be 45–50% of total daily energy intake, fat intake no greater than 30–35% (saturated fat < 10%), and protein intake 15–20%. Energy intake should be appropriate for optimal growth in children and adolescents and keeping an ideal body weight. Diet should be assorted with healthy foods, such as fruits, vegetables, dairy, whole grains, legumes and lean meat. Thus, great emphasis is given to the quality of nutrients consumed. Healthy sources of carbohydrate foods, foods with high content of fibers, the replacement of saturated fat with polyunsaturated and monounsaturated fat and finally low-fat animal-derived and vegetable protein sources should be encouraged, according to current guidelines. Instead, restrictions in one macronutrient are discouraged, due to the risk of growth compromising and nutritional deficiencies [4].

Several studies from different countries demonstrated a low adherence in meeting nutrition recommendations among T1D children and adolescents, and particular concern emerged regarding high total fat and saturated fatty acid (SFA) intake [17][18][19][20][21][22][23][24][25][26]. Whether people with T1D were closer to guidelines than controls is debated, since contrasting results are described [13][18][21][23]. A lower adherence to recommendations was associated to poorer glycemic control, i.e., glycated hemoglobin A1c (HbA1c) levels, and therefore to the potential CVD risk and complications [11][22][23]. Of note, following a regular meal pattern was associated with better glycemic outcomes [18]. Moreover, a recent study showed how diet has changed in a 10-year period, showing that children and adolescents with T1D consume a higher amount of

protein and fat and a lower amount of carbohydrate and fiber compared to 10 years ago [27]. Noteworthy, this study was conducted in Italy and therefore results may not be exported in other populations with different nutritional habits. Nevertheless, rapid changes and a deterioration of dietary habits, especially among youth, have been reported worldwide [28].

Nutritional variations seen in youth with T1D tend to follow the changes in the eating habits of the general population and, in particular, of their peers, who frequently do not meet the recommendations either [27][28]. Finally, it is worth mentioning that the food intake is frequently misreported, and especially under-reported, by children and adolescents with T1D and this should be considered when addressing the matter [29].

3. Fat intake and Glycemic Control in people with T1D

3.1. Food Intake and Postprandial Glycemic Control

Postprandial glycemic control is affected by food intake. It is mainly influenced by the amount of carbohydrate intake, along with insulin availability [30]. For this reason, guidelines recommend early nutrition education of individuals with T1D, including carbohydrate counting (CC), a meal planning approach based on the importance of carbohydrate in affecting postprandial glycaemia, used as a tool to improve glycemic control and facilitate flexible food choices [4][31][32]. Thus, insulin dosing at meals is generally decided upon the carbohydrate amount, often using insulin-to-carbohydrate ratio [31]. The importance of carbohydrate in affecting glycaemia has been known for long, however the impact of other diet macronutrients should also be considered. According to recommendations, to optimize postprandial glucose levels, other variables should be considered, including glycemic index, fat, protein and fiber intake [4]. It has been demonstrated that meals with high content of fat or protein lead to a delayed and prolonged increase in postprandial glycaemia, from 2 to 6 h after the meal, with small variations in ranges depending on the study considered [33][34][35][36]. An additive effect was reported when consuming high fat and high protein meals together [33]. Instead, early glycemic peak is reduced with high fat and high protein meals [37][38]. Based on these findings, new methods to establish a more accurate need of insulin that would consider the complexity of the meal were required. Indeed, some studies showed a better glycemic control when using algorithms for calculating insulin dose that account also for protein and fat intake, besides carbohydrate [39][40]. However, more frequent episodes of hypoglycemia were reported when using supplementary fat/protein counting than CC [39]. To note, the Food Insulin Index (FII) is a new algorithm in which foods are sorted by the insulin response to an isoenergetic reference food in healthy people. Since food energy is used as the constant, all foods and their metabolic interactions could be included in the algorithm, allowing a broader assessment of insulin demand [41]. Its use has been compared to CC in adult studies, showing a better control in postprandial glycaemia in subjects with T1D using FII [42][43], also specifically for protein-containing food [41]. However, no significant changes in HbA1c levels and relatively high rates of mild hypoglycemia with both methods were described [41][43]. The efficacy of novel counting methods in children and adolescents with T1D need further studies to be established, since no clear benefit among one method to another was reported up to now [44]. Considering the variation of glycaemia after high fat and/or high protein meals, insulin dose adjustments are recommended [4]. Additional dose of insulin in dual wave bolus and/or the increase in percentage of insulin dose were studied [36][45][46][47][48], even if determining what strategy is more efficient in glycemic control must be further assessed. Thus, it is recommended to adapt meal insulin dose to counterbalance the delayed hyperglycemia resulting from high protein and high fat meals. To the best of our knowledge, available hybrid closed-loop insulin pumps do not have algorithms for fat and/or protein dosing. Considering the wide inter-individual differences in insulin dose demand for fat and protein, it is therefore important to individualize the treatment [4].

3.2. Fat Intake and HbA1c

As indicated in the latest ADA recommendations [6], HbA1c target levels must be individualized, but on a general level it has been shown that a HbA1c target of 6.5% (48 mmol/mol) gives a higher number of patients that achieve a good metabolic control with a higher percentage of glucose values in time in range (3.9–10 mmol/L) and time in target (4.0–8.0 mmol/L) without more episodes of hypoglycaemia [49].

Considering the role of fat intake on HbA1c, mixed results have been reported. Some studies did not find any association between total fat intake and glycemic control [50][51], while, on the contrary, other studies showed that the consumption of fat is associated with HbA1c levels. In particular, a cross-sectional study in 252 young people affected by T1D reported that there was a higher risk of having a suboptimal HbA1c between insulin pump users consuming the highest quartile of fat intake [12]. Another cross-sectional study among 114 children and adolescents with T1D showed that HbA1c levels were positively correlated with lipid intake and SFA and negatively correlated with monounsaturated fatty acid (MUFA) intake. Interestingly, when increasing the SFA intake of 1% of total energy, the risk of having HbA1c >7.5% increases by 53% [13]. A more recent study confirmed the results on MUFA intake, showing that a higher MUFA intake lowered the risk

of having a HbA1c higher than 7.5%, independently from confounders [27]. The prospective Diabetes Control and Complication Trial showed an association between higher HbA1c concentrations and higher SFA, MUFA, and total fat intakes. Moreover, higher HbA1c concentrations were seen when substituting fat for carbohydrate intake, even though this association weakened after adjusting for baseline HbA1c and concurrent insulin dose [14]. In a behavioral nutrition intervention study in 136 adolescents with T1D, as regard lipids, a better glycemic control, i.e., lower HbA1c, was associated with lower percentage of energy from unsaturated fat intake, while no significant associations were found for total fat and SFA [52]. Another study reporting data from 1000 adults with T1D showed that MUFA intake was associated with higher variability in blood glucose measurements. When analyzing the macronutrient substitution, favoring fat intake over protein or favoring SFA over either MUFA or polyunsaturated fatty acids (PUFA) were associated with higher mean self-monitored blood glucose concentrations. However, these effects were no longer significant after adjusting for fiber intake. After that adjustment, it resulted that favoring either carbohydrate or fat over protein or favoring carbohydrate for fat were associated with higher glycemic excursions [53]. Finally, in adults with T1D, fat intake negatively correlated with time spent in euglycemia and positively correlated with time spent in hyperglycemia. To note, it was not correlated with time spent in hypoglycemia [15]. In this regard, the type of fat intake has shown different impact on hypoglycemic risk. In fact, while there was no correlation between daytime non-severe hypoglycemia and total or SFA intake, unsaturated fat was found to be protective of daytime hypoglycemia. Of note, when adjusting for total daily insulin dose per kilogram these associations were lost [54].

An adequate comparison between the abovementioned studies is difficult to obtain since they sometimes express results in different ways. However, it seems reasonable to assess that there is a relationship between lipid intake and glucose control in individuals with T1D. In particular, higher HbA1c levels have been more frequently reported by individuals having a high fat and SFA intake, while contrasting data are reported for unsaturated fatty acids. Further prospective studies are needed to clarify this issue.

3.3. Low-Carbohydrate (High-Fat) Diets

When addressing glycemic control, restrictive diets and particularly low-carbohydrate diets are worth mentioning, especially if considering the current arousing interest for such approaches. The rationale behind these diets is that several studies showed a worse glycemic control with higher carbohydrate intake in people with T1D and vice versa, i.e., better glycemic control with lower carbohydrate intake or lower glycemic-index diets [51][53][55][56][57]. However, in the general population it was demonstrated that both high and low percentages of carbohydrate diets were associated with increased mortality, with the lowest risk reported at 50–55% energy from carbohydrate [58].

There is no univocal definition of low-carbohydrate diets, since the term refers to different nutrition regimens that can be gathered as follows. Low-carbohydrate diets generally contain less than 100 g of carbohydrate per day, with macronutrient distribution amounting to 50–60% of fat, less than 30% of carbohydrate and 20–30% of protein. Very-low carbohydrate diets, with generally less than 50 g of carbohydrate per day, are ketogenic diets in which energy production depends on burning fat and the production of ketone bodies [59]. To guarantee energy requirements, a reduction of carbohydrate intake should be compensated by an increase of protein and lipid intakes. In detail, the individual needs to satisfy the energy requirement to maintain energy balance. The proportion of the different macronutrients may change but the total energy intake should guarantee total energy requirements. Therefore, if the amount of carbohydrate is reduced, an increase of fat and/or protein is necessary for compensating the energy reduction due to the lower carbohydrate intake. This may lead to a high-fat intake.

Recent reviews summarized the pros and cons of low-carbohydrate diets in people with T1D. Possible benefits of these diets are the improvement of glycemic control, the reduction of Hb1Ac levels and insulin requirement that may help to improve psychological outcomes, e.g., reducing diabetes distress and depressive symptoms [59][60][61][62]. In addition, low-carbohydrate diets may be a strategy for weight loss, if total energy intake is lower than the requirement [61]. Worth mentioning is a large online survey in youth and adults with self-reported T1D who followed a very-low carbohydrate diet (mean self-reported daily carbohydrate intake of 36 ± 15 g). The study reported HbA1c levels of 5.71% ± 0.58% in the pediatric age group, well below the ADA recommended target, and low rates of adverse diabetes-related medical events [63]. However, it is important to interpret those results with caution, mostly because of the self-selected sample and the self-reported data of carbohydrate intake and HbA1c levels [60][64]. Nevertheless, caution is needed with low-carbohydrate diets, and especially with very-low carbohydrate diets, because of the possible negative effects, such as the potential risk of diabetic ketoacidosis and oxidative stress, hypoglycemia and the reduced glucagon effect during hypoglycemia, the increase in saturated fatty acid consumption to maintain caloric intake and dyslipidemia, nutrient deficiencies and difficulties in maintaining these diets for long [59][60][61][62]. In growing children, low-carbohydrate diets may also negatively impact growth [59][61]. The unphysiological delivery of external insulin into the subcutaneous tissue instead of directly into the liver as in the non-diabetes situation leads in low-carbohydrate diets to more or less lack of insulin in the liver with e.g.,

less IGF-1 stimulation. Moreover, low-carbohydrate diets, as restrictive diets, may have adverse psychological outcomes, such as greater diabetes distress and augmented risk of eating disorders [60].

In summary, although low-carbohydrate diets and very-low carbohydrate diets may be effective in improving glycemic control, because of the potential important negative consequences of these diets, especially in children, we do not recommend the use of these diets for treating T1D, and caution is important when addressing to the topic [4][6][64].

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