



## Vegetarianism and type 1 diabetes in children

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### ABSTRACT

Type 1 diabetes (T1D) is a chronic autoimmune disease characterized by an absolute deficiency of insulin secretion. T1D management rests on three pillars: insulin therapy, correct diet and physical exercise. The aim is to focus the attention on diet and mainly on vegetarian diet, in order to evaluate if this kind of food style can offer the correct supply of nutrients, necessary for growth and well control glycaemic management. This paper is a short commentary on vegetarianism in the pediatric and adolescent population with Type 1 Diabetes. In all non-omnivorous diets there is a risk of a lack of some nutrients, as B12 vitamin and n 3 fatty acids which must therefore be measured. It is also important to monitor eating disorders especially in adolescent girls. About vegan diet, attention must be paid to the possible injury on growth brain already at risk, in diabetic children compared to the general population, due to insults related to frequent glucose variability (periods of prolonged hyperglycaemia alternating with hypoglycaemic episodes).

In conclusion, vegetarian diet could be suitable for children with type 1 diabetes; vegan diet could be too restrictive but with appropriate additions can be followed by these patients.

### 1. Introduction

Type 1 diabetes is a chronic autoimmune disease characterized by the destruction of pancreatic beta cells and consequent need for lifelong administration of exogenous insulin. Insulin can be administered or with multiple daily insulin injections (MDII) or by continuous subcutaneous insulin infusion (CSII). Physical exercise and correct diet are the other two therapeutic pillars. It is well known that the nutritional care of children with diabetes is complex. Diabetes management is set within the context of the family and social environment, and is influenced by issues of non-adherence, peer pressure, refusal of certain foods, desire for independence and for self-management. Maintaining the quality of life requires a deep understanding of the relationship between treatment regimens and ongoing physiological requirements, including growth, fluctuations in appetite associated with changes in growth velocity, varying nutritional requirement and physical activity. But what if the family context is vegetarian or vegan? What are the main difficulties in managing children Type 1 Diabetes (T1D) nutrition? In this commentary, we aim to briefly summarize the burden of any nutrient deficiencies in a vegetarian or vegan diet and the strategies to make them suitable for children with T1D.

### 2. Current status of knowledge about vegetarian and vegan diets

Vegetarian diet is often considered a simple diet, free of animal products. Actually the concept is much broader and the diet patterns are different. The most common is the lacto-ovo vegetarian diet (LOV) which excludes the consumption of meat and fishery products (including molluscs and shellfish) and includes milk, eggs and derivatives, and it is what we will refer to when talking about the vegetarian diet. But there are also other forms of vegetarianism, such as pesco-vegetarian, where fish are allowed, or the lacto-vegetarian and the ovo-vegetarian one, which excludes eggs and milk respectively. Finally, there is the vegan diet that rejects animal by-products, including honey. It represents the vegetarian diet "strictly speaking". The prevalence of restrictive diets, mainly vegetarian and vegan, is markedly increased in Europe and other Western countries. About 4.3–10% of the whole population in Germany are estimated to be vegetarians, whereas the number of vegans is estimated at 1.6%. Switzerland, Italy, Austria and the UK have a similar number of vegetarians as Germany (9–11%). The proportion of vegans is substantially lower. In the United States, only 5% of the population is considered vegetarian, however, this is still more than 16 million people [1]. There is no epidemiological data in children. In general, vegetarian diets are presumed to be healthy; nevertheless, there are concerns as to whether the dietary specifications required during infancy, childhood,

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and adolescence can be met and there is no clear evidence that a vegetarian diet started in early childhood confers a lasting health benefit. While some scientific societies, that deal with nutrition, consider the LOV diet suitable for all phases of life [2], given the advantages that it seems to bring towards the prevention of certain diseases such as T2D, hypertension, obesity, cancer (as well as a varied and balanced omnivorous diet), a vegan diet is viewed with skepticism because of the associated deficiency risks.

Generally, vegetarian and especially vegan diets provide relatively large amounts of cereals, pulses, fruits and vegetables. In terms of nutrients, these diets are usually rich in carbohydrates, n-6 fatty acids, dietary fiber, carotenoids, folic acid, vitamin C, vitamin E and Mg, and relatively low in protein, saturated fat, long-chain n-3 fatty acids, retinol, vitamin B12, iron and Zn; vegans may have particularly low intakes of calcium and vitamin B12 because no food of vegetable origin contains enough of this vitamin. Vitamin B 12 deficiency develops slowly, as the liver stores sufficient quantities to last several years. It should be remembered that the blood level of vitamin B12 is not sufficient to rule out its deficiency, also because vegetarian/vegan diets are typically characterized by a high content of folate which is able to mask the haematological signs of vitamin B12 deficiency. High folate, however, cannot prevent the deleterious effects of vitamin B12 deficiency on the nervous system. Therefore, in vegetarians vitamin B12 status is optimally assessed using homocysteine, holotranscobalamin II and methylmalonic acid as markers. Even greater attention should be paid to vegetarian subjects with T2D under metformin therapy, because metformin reduces vitamin B12 absorption by interaction with Intrinsic Factor/B12 complex, ileal endocytic receptor cubilin and impaired calcium availability.

In literature there are not many manuscripts that reported the relation between type 1 diabetes and vegetarianism, and some of them are dated. T1D children who live in a vegetarian family or T1D adolescents who choose to be vegetarian have complex nutritional needs because of their continued physical growth and development, their participation in physical activities, and their need to consume sufficient carbohydrates to match their insulin doses, but diabetic vegetarian children and adolescents have not been extensively studied. Indeed, studies on vegetarian or vegan diets during childhood, not only in T1D subjects but in general population, are highly heterogeneous, mostly cross-sectional, of small sample sizes, and outdated.

The elimination of meat or fish proteins can lead to the consumption of a largely carbohydrate diet. In order to control the plasma glucose-raising, it is certainly useful to consider the glycaemic index (GI) and glycaemic load (GL) of the carbohydrates intake. However, postprandial glucose excursions may also depend on other factors such as tissue sensitivity to insulin, the fat/fiber content of meals, time spent consuming meals, method of cooking food, intestinal microbiota, consuming vegetables before carbohydrates when eating, and others. Any use of more carbohydrates requires adjustment of insulin doses, either through MDI or CSII modality, and this could lead to overweight.

About proteins, all plant foods contain the 20 amino acids, including the 9 indispensable amino acids even if the amino acid distribution profile is less optimal than in animal foods. Protein quality is determined by digestibility and amino acid content [3]. Lysine is present in much lower than optimal proportions for human needs in grains, but is plentiful in most pulses and similarly the sulfur containing amino acids (methionine and cysteine) are proportionally slightly lower in legumes, but in developed countries plant proteins are mixed and consequently deficiencies are uncommon. About quantity, protein intake in vegetarian diets is usually adequate. Some studies have reported trends toward differences in protein metabolism, such as a lower postprandial decrease in protein breakdown when vegetarian diets are consumed. This is probably due to the presence of fibers; in fact, vegetal proteins digestibility is conditioned by the presence of fibers and antinutritional factors, so it seems to be slower than that of animal proteins, especially compared to milk. Microalgal food supplements represent another

source of protein, iron and bioavailable forms of vitamin B12, but they can contain cyanotoxins and elevated concentrations of toxic metals and inorganic arsenic species; in any case, food supplements should not be used as a substitute for a varied diet [4].

About fats, adults and vegetarian children tend to eat more fruits and vegetables and less saturated fat, but this is not always true for those on a LOV diet. The intake of n-6 fatty acids is usually adequate, on the contrary, the intake of n-3 is deficient due to the lack of fish consumption. The only n-3 fatty acid present in useful amounts in plant foods is alfa-linolenic acid (ALA), an essential fatty acid (flaxseeds, chia seeds, walnuts, hemp seeds, seaweeds). But the most important n-3 fatty acids are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), that come mainly from fish. They can be synthesized from ALA but only in a small percentage. EPA and DHA are the components of cell membranes throughout the body and modulate the receptor function in these membranes; they are precursors of hormones that regulate blood clotting, modulate contraction and relaxation of artery walls. Moreover, they are precursors of mediators involved in resolving inflammation (resolvins); n-3 fatty acids reduce the expression of inflammatory cytokines (such as TNF alpha) also in children at high risk for T1D development [5–7]. The combination of n-3 fatty acids and vitamin D at high dosages would seem able to act on the functional reserve of pancreatic beta cells by prolonging the survival of the residual beta cells. This would allow to reduce insulin requirements in patients with recent T1D diagnosis (less than 6 months) and would likely delay or avoid long-term complications [8]. Currently, fish oils represents the most prominent dietary sources of EPA and DHA but these are unsuitable for vegetarians. The content of EPA and DHA in fish oil derives from unicellular algae of the *Schizochytrium* and *Cryptocodinium cohnii* genus. It is possible to directly use algae and not fish for the extraction of the nutrients to be used in any case in the form of supplements [9]. Hence, the importance of adequately supplement n-3 fatty acids especially in T1D children who follow restrictive diets that exclude fish intake.

About micronutrients, plant foods contain good quantities of calcium (nuts, pulses, leafy vegetables) but its bioavailability is affected by oxalate and phytate presence. The deficiency risk is greater in vegans who should therefore take foods that are good sources of calcium, as vegetables low in oxalate and phytate, soy products, calcium-rich mineral water, nuts and seeds. Also the bioavailability of iron is very different. LOV and vegan diets often have an iron content similar to or higher than that of diets omnivore but the bioavailability of iron from plant foods (non-heme iron) is lower than that of iron meat (heme iron). Iron absorption is estimated to be around 14–18% in omnivorous diet and around 5–12% in vegetarian diet. About zinc, in omnivore diet over half comes from animal origin foods. For vegetarians and vegans a good source of zinc are whole grains, cereals, pulses, nuts and seeds, foods that are also rich in phytates however. Zinc absorption in vegetarian/vegan diets is 15–25% vs 33–35% in omnivorous [10]. Micronutrients absorption can be improved by adopting food preparation methods (soaking, germination, fermentation), by using fortified foods and by consuming fruits and vegetables rich in vitamin C, together with iron-rich foods. Vitamin B12 was already mentioned. With regard to vitamin D, it is worth remembering that, in case of deficiency, there are products based on a completely vegetable vitamin D, obtained, for example, from Icelandic lichen and carried by extra virgin olive oil.

About microbiota, diet is a major factor driving the composition and metabolism of the gut microbiota which seems to respond to vegetable-rich diets primarily with: an increased cell motility to access nutrients, an increased catalytic activities for carbohydrates and food proteins, the synthesis/release of bioactive metabolites/proteins and potentially beneficial impacts on human health [11]. The fiber-rich diet is related to the abundance of microorganisms producing short chain fatty acids (SCFA) which have anti-inflammatory, immunomodulatory and anti-carcinogenic properties.

The latest International Society for Pediatric and Adolescent Diabetology (ISPAD) guidelines about nutritional management in T1D

children advise that carbohydrate should be approximate 45%–50% of energy [12]. In case of the percentages tend to be higher, it is advisable to choose carbohydrates with a lower glycemic index (ID), and eat them in combination with fibers, proteins (legumes) or fats. Rye, barley, oats, but also brown rice, parboiled rice, buckwheat which, together with pseudocereals such as quinoa or amaranth, are also suitable. Quinoa and amaranth both have IG 35, contain high biological value proteins, such as those of meat, with the essential amino acid lysine and methionine and are rich in calcium and fiber.

Digestion of vegetable proteins is slower due to the presence of fibers which promote a better glycemic control avoiding peaks. However, the high intake of fibers can interfere with the absorption of some minerals, especially iron, zinc and calcium due to the phytates present in cereals and legume seeds. Some experts propose a higher protein intake for vegetarian and vegan children due to the lower digestibility and/or protein quality of plant protein but an excess protein intake during early childhood could cause adverse effects on the kidneys and, through the mechanism of insulin resistance, encourage the development of overweight or obesity later in life. The protein needs of vegetarians are easily met when the diet includes a variety of plant foods, and calorie intake is adequate. Germination of seeds and grains and fermentation of pulses and cereals can improve proteins digestibility so a higher protein intake is not necessary.

Both adults and vegetarian children tend to eat less saturated fat than omnivorous. Indeed, the risk of reduced fat intake exists only for vegans, because in LOV diet eggs and cheese bring cholesterol and saturated fats, unless egg whites, light cheeses, partially skim milk are preferred. In studies done mainly in adult populations, a plant-based diet showed benefits in the reduced risk of chronic diseases such as obesity and cardiovascular diseases and probably the reduction of saturated fat intake is equally useful in T1D subjects.

Both adults and vegetarian children tend to eat more fruits than omnivorous, and therefore, more fructose. Fructose is a monosaccharide metabolized from liver in glycogen and fatty acids. A large intake of fruits could increase obesity and insulin resistance. Patients with type 1 diabetes should match the correct balance between fruit assumption, insulin dosages and weight control and it is advisable to choose fruit with less sugar and less ripe.

As regards to the overall effects of the vegetarian diet on HbA1c and on fasting blood sugar, the average reduction of HbA1c in subjects following a vegetarian diet is significant ( $-0.39\%$ ; 95% CI,  $-0.62$ - $-0.15$ ;  $P = 0.001$ ;  $I^2 = 3.0$ ;  $P$  for heterogeneity = 0.389), when compared to that of subjects following an omnivorous diet. The glucose level was not significantly different [13].

Optimal glycemic control is indeed particularly difficult to achieve in children and adolescents with T1D, despite careful monitoring of insulin dosing, diet, and exercise. Childhood and adolescence are periods of major neuro-developmental change. Dysglycaemia like severe or recurrent or unawareness hypoglycaemia, or chronic hyperglycaemia, or extreme glycaemic variability can cause cellular and structural injury and lead to altered neuropsychological outcomes which could persist into adult life [14,15].

Finally, adolescents with diabetes are at higher risk of eating disturbances, such as dieting for weight loss, self-induced vomiting, excessive exercise, and laxative or diuretic use; these behaviors, although apparently mild and not classified among the true eating disorders (EDs) like anorexia nervosa, bulimia nervosa, binge-eating disorder, pica and rumination, must be closely evaluated because they can evolve into true EDs. One of the warning clinical signs for eating disturbances is precisely the tendency toward vegetarianism [16,17].

Sticking with these key points, subjects with type 1 diabetes can be allowed the vegetarian diet while the vegan one, like all dietary regimes that are too restrictive, could expose to deficiency risks and can only be followed with the appropriate supplements. The vitamin B12 status of vegetarians should be monitored, together with iron, zinc and n-3 fatty acids, especially DHA, at least once a year in all diabetes centers, and

supplementing them if deficient. Their deficiency can cause damage to the central nervous system in a population, such as that of children with T1D, who already has risk factors in this regard. In fact, glucose variability is a characteristic of T1D in children and both hypoglycaemia and hyperglycaemia, but also marked fluctuations in glucose, could result in changes in brain structure and integrity [18].

Finally, special attention must be paid to vegetarian girls with T1D that should be carefully monitored for the adequacy of their diet because they may be at risk of developing an eating disorder.

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## Author' contributions

V.T and F.S designed and conducted research; V.T wrote the paper. All authors read and approved the final manuscript.

## Compliance with ethical standards

This article does not contain any studies with human or animal subjects performed by any of the authors.

## Declaration of competing interest

The authors declare no conflict of interest.

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