MEDWIN PUBLISHERS
Committed to create value for Researchers

Open Access Journal of Endocrinology
ISSN: 2578-4641

Restricting Carbohydrates in the Diet-A Possible Method of Meeting the Challenges of Increasing Diabesity in Type1 Diabetes along with Meeting Exercise Performances Requirements-A Review

Kulvinder Kochar Kaur*[1], Allahbadia G[2] and Mandeep Singh[3]

[1]Scientific Director, Kulvinder Kaur Centre for Human Reproduction, India

[2]Scientific Director, Rotunda-A Centre for Human Reproduction, India

[3]Consultant Neurologist, Swami Satyanand Hospital, India

Review Article

Volume 3 Issue 1

Received Date: May 22, 2019

Published Date: June 06, 2019

DOI: 10.23880/oaje-16000138

***Corresponding author:** Kulvinder Kochar Kaur, Scientific Director, Kulvinder Kaur Centre For Human Reproduction, 721, G.T.B. Nagar, Jalandhar-144001, Punjab, India, Tel: 91-181-9501358180; Email: kulvinder.dr@gmail.com

Abstract

The incidence of diabetes mellitus (DM) in developing countries like Asia has increased over the past few years. This is secondary to the changing development along with lifestyle of the younger generation who prefer to take up the western style of eating high calorie fast food with minimum exercise. Previously, the rate of DM was very low but is increasing at significant rates which are a cause of concern in Asia. There is not much literature available regarding T1D in Asian countries in view of lack of lower field surveys and absence of quantitative data. However in USA approximately 30% of subjects having T1D don't achieve the aimed glycaemic targets and lot of comorbidities exist which suggest some novel treatment avenues which include lifestyle modifications. Recent nutritional guidelines implicate a flexible approach in carbohydrate intake which is in relation to intensive insulin therapy. Basically these guidelines are meant to get more freedom in nutritional choices but may result in greater calorie intakes and unhealthy eating patterns which are resulting in higher prevalence of obesity and Metabolic Syndrome in people living with T1D, a phenomenon observed worldwide, so that recently the term diabesity got coined to understand the importance of treating the 2 together. Low carbohydrate /day (LCD<130g/day) might be a better way of getting a glycaemic control and metabolic health in subjects with T1D. Recreational exercise on a regular basis or getting a high athletic performance might be of importance in many people living with T1D. Work done on subjects not having T1D implicates that if athletes do training using decreased

carbohydrates enhance adaptation in contrast to that with normal/high carbohydrates. Yet this train low aspect has not been checked in T1D subjects. Further use of low restricted/periodised carbohydrate diets in T1D athletes is discussed.

Keywords: T1D; Diabesity; LCD; VLCD; Exercise Training

Abbreviations: DM: Diabetes Mellitus, LCD: Low Carbohydrate Diet, T1D: Type1 Diabetes Mellitus, ADA: American Diabetes Association, DAFNE: Dose Adjustment For Normal Eating, VLCD: Very Low Carbohydrate Diets, DKA: Diabetic Ketoacidosis, IR: Insulin Resistance, IMTG: Intramuscular Triglyceride, SGLT2: Sodium Glucose Transporter2, MAPK: Monophosphate Activated Protein Kinase, IMCL: Intra Myocellular Lipids, Qol: Quality of Life, AT: Adipose Tissue.

Introduction

Type1 diabetes mellitus (T1D) is a chronic inflammatory autoimmune disease where the insulin producing cells within the pancreas get destroyed [1]. This results in lifelong dependency on exogenous insulin and need for managing glucose profiles through diet and exercise. Following a diagnosis of T1D control of blood glucose levels remains challenging, with a continuous risk of severe hypoglycemia and severe hyperglycemia along with keto acidosis lifelong [2]. In long-term people with T1D have an enhanced risk of micro as well as macro vascular complications in view of exposure to improper glucose throughout life [3,4]. The American diabetes association (ADA) treatment guidelines suggest a target Hb A1c of <7.0% (53mmol/mol in adults with T1D (7.5%) for youth with TID to reduce the risk of long term diabetes related complications [5]. Recent data from the T1D Exchange of 22,697 people with T1D in the USA showed that only 17% of children and adolescents under 18years, and only 21% of adults at age >30years are achieving their Hb A1c targets. Rather than improving, it has been found that Hb A1c levels are deteriorating, despite development of technologies like continuous glucose monitoring devices and insulin pumps. The high proportion of subjects not achieving Hb A1c targets with current therapies implicate need for novel intervention strategies urgently to decrease this deterioration in glycaemic control in this patient population. Evidence is emerging that dietary manipulation and in particular low carbohydrate intake (<130g per day) by using a proper strategy for many people especially if weight loss and prevention of hyperglycemia and hypoglycemia are a concern [6].

Many people who live with T1D, especially those ones who participate in physical activity on a recreational basis or achieving a high level of athletic performance is important to get a balance between glycaemic control and nutritional intake to fuel performance that is pivotal for these subjects. Different studies carried out in people without T1D have shown the efficacy of periodic ''train low, compete high'' paradigm where selected sessions are undertaken deliberately with decreased carbohydrate availability to activate molecular pathways, to augment skeletal muscle adaptation [7,8]. Endurance training with decreased muscle glycogen stores (training low) has been demonstrated to enhance the expression of various genes encoding for mitochondrial enzymes protein content and activity, and increase the rates of lipid oxidation during submaximal exercise when compared to training with normal or high glycogen stores [9,10]. In case of athletes having TID, training with decreased carbohydrate availability might also represent a strategy which benefits glycaemic control in day to day life and training-induced increases in skeletal muscle oxidative capacity, which may have benefits both in endurance performance and body composition (i.e., reduced fat mass, enhanced lean mass). But the long term effects of training and decreased carbohydrate availability along with consumption of low carbohydrate diets on skeletal muscle insulin sensitivity, metabolic health, training adaptation, exercise performance, and glycaemic control during and after exercise are yet to be investigated in people with TID.

Thus aims of this review are

a. to know the pros and cons of low carbohydrate diet (LCD) in people having T1D
b. discuss if there is any potential for low and/or restricted carbohydrate diets in recreationally active individuals with T1D
c. Plan carbohydrate restriction strategies for elite or recreational athletes with T1D as means to improve training adaptation besides improving glycaemic control.

Previous History of Restriction of Carbohydrates in T1D Patients

Prior to insulin availability carbohydrate and calorie restriction as ''Starvation diets'' used to be the most advanced treatment for T1D [11]. For this Frederick Allen and Joslin E Proposed use of low carbohydrate restrictive diets, since this was the only way of delaying death from ketoacidosis [12]. Following the discovery of insulin in 1922, this practice of dietary restriction continued, to some degree and carbohydrate liberalization was introduced with a lot of caution. Over the next 50 years diet advice for people with T1D still focused on limited moderate-carbohydrate consumption with restriction of refined sugars. Meal plans to be followed strictly got calculated and exchange systems got developed, where food portions, especially carbohydrates got weighed carefully and measured.

This concept on diet got challenged in 1960's, with concerns raised regarding the risks of a low carbohydrate diet, high saturated diet in an atherogenically disposed individuals. Thus recommendation moved to decrease fat intake (<3 5% of energy) and increasing carbohydrates to approximately 50-55% of total energy intake, but with the instructions that most carbohydrates had to be taken at mealtime and snacks had to be taken from complex food sources. Gradually sucrose got introduced into these recommendations at an intake of no greater than 10% of the total energy intake. Once faster acting meal time insulin's along with sophisticated delivery devices like insulin pens and pumps got introduced, the tailoring to precise doses to food intake preferences using carbohydrate counting and insulin dose calculators could be utilized. This concept of matching insulin to carbohydrate intake, instead of matching food intake to estimated energy needs and insulin dosages, became the standard practice for T1D management. E.g. self-management programs like Dose Adjustment for normal Eating (DAFNE) have permitted greater dietary flexibility with the provision of including potentially all foods. Hence for past years, low fat and high carbohydrate diets have been the recommendation and promoted for healthy eating for people with DM along with for the general population [13,14]. On analysis of the food pattern during this more recent ''obesity epidemic'' revealed that an increase of calories was almost entirely due to greater carbohydrate intake [15]. In this modern day incidence of obesity, Heart disease and DM have become the highest than any other times [16], and the obesity prevalence in T1D has reached very dangerous levels, partly because of this liberalization of diet and general sedentary life led by this patient population.

Low Carbohydrate Diets-Definition

In 2018 the ADA Standards of Medical Care recommended 15-20% of total energy from dietary protein, 20-35%energy from fats that leaves a balance of 45-60% energy from carbohydrate [17]. These guidelines are same for children along with adolescents having T1 D [18]. No universal definitions that have been agreed by all regarding ''low carbohydrate diet'' exist; still <130g of carbohydrate /day or <26% of total energy has been proposed [19] which will vary based on certain factors including age, sex, and activity levels. Some reports show that very low carbohydrate diets (VLCD), as defined that 25-50g of carbohydrate/day may decrease in HbA1c as low as 5.3% [20] in people with T1D, besides some stray reports regarding positive effects of VLCDs for glycaemic control [21,22]. Although lowering HbA1c is beneficial [23], not much evidence exists regarding any additive benefit of getting HbA1c that is lower than 7.0% in T1D when consider total premature risk of morbidity and mortality [24], thus it may be unnecessary to promote these extreme VLCDs, especially if there is a higher risk of hypoglycemia or diabetic ketoacidosis(DKA) [25]. Some reports show that subjects with T1D who had a week low carbohydrate/day (≤50g/d) were at a risk of impaired response to glucagon rescue during mild hypoglycaemia [26], possibly due to decreased liver glycogen content. Normally VLCDs are not recommended by certified diabetes educators and nutritionists for T1D subjects taking into account the theoretical concerns over potential DKA, hypoglycaemia, dyslipidaemia, nutritional deficiencies and difficulty maintaining such diets over long term [27]. Irrespective of whether VLCD's are efficacious in preventing glucose rise and for controlling weight, it appears to be an unrealistic approach for most of T1D patients, as compliance is expected to be very low. While it is possible that an LCD (50-130g of carbohydrate/day) might be a realistic target which is not that restrictive and still might offer potential benefits.

Right now it is not clear whether restricting carbohydrate/day may be very restrictive for active individuals who have T1D like in case of athletes, nutritional requirements would get influenced by the metabolic demands of the sport for which they are training for along with the periods of their training schedule for competitive sports. Hence currently this realization is made regarding use of carbohydrate/day according to a sliding scale for active or athletic T1D

subject [28] and hence needs adjustment day by day and further meal by meal based on the training and competition schedule as reported by Impey, et al. [8]. Nevertheless, subjects with T1D often make claims in various social platforms that they can still be physically active and train while still adhering to a LCD. La-Fountain et al. observed that a 12weeks VLCD (<50g carbohydrate/day) did not affect the physical performance as compared to a mixed diet in military personnel without T1D. This study also showed improved insulin sensitivity along with body composition following the VLCD alongside high adherence. In elite endurance athletes (like cyclicists, runner, long distance swimmers) lot of confusion exists both in acamedicians and athletic circles regarding the correct terminology for use to refer to the variety of periodised carbohydrate schedules which are now commonly used for elite athletes [29]. For extreme cases of highly trained endurance athletes that don't have T1D, like Chris Froome, was given a daily carbohydrate plan which gave >6500Kcal and 18g carbohydrate/kg body weight by support nutrition consultant, author JPM of the article, during one very challenging solo ride over mountains terrain during his victory in the 2018 Giro d 'Italia [30]. Personal observations of the athletes, coauthor JPM [31], showed that elite professional cyclicists might adjust their daily carbohydrate intake from 2-10g/kg body mass during training depending on the goals of the particular training phase. Having personal experiences with professional cyclicists having T1D (Team Novo Nordisc) by author SNS, suggest that the athletes with T1D also adjust their daily intake based somewhat on daily expenditures, although these athletes must also consume carbohydrate on the ride to avoid hypoglycemia. Further research will need to evaluate the effect of such high (and periodised) carbohydrate intakes on daily glycaemic profiles and long term metabolic health in endurance athletes with T1D.

T1D and Low carbohydrate Diets

A flexible approach to carbohydrate intake matched with intensive insulin therapy is suggested by current ADA guidelines [32] that are facilitated by programmes like DAFNE [33]. Concern remains that a higher calorie intakes along with potentially unhealthy eating patterns in general, contribute to the high obesity prevalence and the metabolic syndrome in people having T1D. Moreover research has revealed that subjects with T1D are mostly inaccurate when trying to estimate the carbohydrate content of their food, especially when the carbohydrate content is high [34]. It gets complicated by the fact that subcutaneous insulin absorption rate might vary by as much as 30%,when insulin dosages levels are high [35], suggesting that lower carbohydrate meals and hence thus decreased insulin needs might help to decrease this variability in insulin absorption rates. There is a mismatch between carbohydrate absorption and insulin action especially after large meals in individuals with T1D, particularly with larger carbohydrate meals, that ≥ glucose fluctuations with excessive increase in insulin increasing the risk of hypoglycemia [36]. LCD's might enable more correct estimates of carbohydrate content at a mealtime, and further exogenous insulin needs, for subsequently decreasing glucose variability along with incidence of hypoglycemia.

Very few studies show promise regarding LCD's in T1D subjects , though sample size were small [37]. The effect of low vs. higher carbohydrate diets on variety of T1D outcomes.; like Hb A1c, total daily insulin, incidence of hypoglycemia, and BMI, was not determined with conclusions in a review by Turton, et al. [38], because of the marked heterogeneity of studies. A small study was carried out by Kreb's, et al. to give evidence that a LCD might be possible for people with T1D who were restricted to 100g of carbohydrate/day. They randomized 10 people having T1D for either LCD or a carbohydrate counting course. After this intervention the carbohydrate restricted group had a markedly decreased Hb A1c from 7.9mmol/L to 7.2 mmol/L and daily insulin use also decreased on average, from 64 units to44 units/day. But continuous glucometer data showed no change in glycaemic variability with the low carbohydrate intervention in contrast to carbohydrate counting. An online survey with the use of social media platform to evaluate glycaemic control among adults and parents of children with T1D was done by Lennerz, et al. which reported a mean carbohydrate intake of 36±15g/day. The data was collected from 316 people who responded (42%were parents of children with T1D) suggested excellent glycaemic control (mean HbA1c was 5.67±0.66%) with low rate of side effects. But there are lots of limitations in this study that include questions over how generisable this sample population was to the rest of population and difficulties of using self-reported data [39]. E.g 36g of carbohydrate /day is probably an underestimation of their actual carbohydrate intake from all dietary sources. A case study was done in an adult female consuming 30-50g of carbohydrate/day by Eiswirth, et al. whose HbA1c decreased from 7.5% to 5.3% in 4 mths and average daily blood glucose readings reduced from 10.4 mmol/L to 6.1mmol/L, with a reduced blood glucose variability. They found no rise in hypo or hyperglycaemic episodes. But this is just a case report on

just one probably highly motivated subject, following a strict insulin regimen with frequent blood glucose checkups, so this might not apply to the broader T1D population. Our example diets show how difficult it would be for majority of people to follow such diets safely and effectively over a long time. Short term effects of VLCD's (<50g carbohydrate /day) vs a high carbohydrate diet (≥250g carbohydrate/day) in 10 individuals with T1D was studied by Ranjan, et al. [40]. No difference in mean glucose levels between the interventions was found but glycaemic variability was lower following the VLCD, which meant that participants spent more time in euglycaemia. The biggest positive evidence that LCD's can decrease glycaemic variability, body weight and time spent in hyperglycemia comes from a recent article by Schmidt, et al. [41]. They compared the effect of 12weeks of LCD (<100g carbohydrate/day) to 12weeks of a high carbohydrate diet to (>250g carbohydrate/day) in 14 people with T1D utilizing a randomized crossover design. No difference was found in time spent in glycaemic target range (3.9-10.0mmol/L) between conditions; yet time spent in hypoglycaemia (<3.9mmol/L) and glycaemic variability were lower in the LCD condition. Though some positive effect is seen with LCD's for people having T1D, requirement is for longer time high quality interventions. Moreover, effects of LCD's on metabolic response during exercise needs to be investigated

Expected benefits of LCD in T1D Subjects

Obesity is being found very commonly in T1D subjects [42], of which most subjects don't maintain a healthy body mass or meet physical activity guidelines [43]. The Pittsburgh Epidemiology of Diabetes Complication Study results revealed that a seven fold increased prevalence of obesity from 3% to23% over an 18 year follow up between 1988-2007. This showed that a dramatic weight gain occurred in this population. In large scale studies like the Swedish National Diabetes Registry found that among the 21,000 adults with T1D on their record, obesity was associated with increased incidence of heart failure significantly [44], while Price, et al. [45] found that obesity was associated with retinopathy along with macro vascular disease. These statistics are really cause for concern on combining this with recent data that show the glycaemic control in people with T1D is getting worse.

That LCD's represent an effective strategy for weight loss irrespective of the population was concluded by Feinman et al. though this still needs to be checked in people with T1D. i) As carbohydrate content of the diet is decreased, the relative proportion of energy derived from protein and /or fat is increased that ≥ increased satiety, often ≥ decreased calorie intake. The common forms of LCD's like the Atkins Diet [46] (20g carbohydrate/day with a gradual rise to 50g/day) or protein Powder [47] (≤100g carbohydrate/day) imposed no formal limit on caloric consumption because of assumption that higher satiety of fat and protein will control caloric intake [48].

Further the increase in overweight and obesity might be related to intensive insulin therapy in addition to a positive energy balance. Insulin being an anabolic hormone, stimulates lipogenesis along with slowing the basal metabolism [42,49,50], thus resulting in fat deposition. This is further increased by the fact that exogenously administered insulin circulates systemically initially so it disproportionately affects muscle and adipose tissue (AT) when compared to hepatic tissue. This is in contrast to healthy non diabetic people, where endogenous insulin has to pass through the portal vein initially to the liver where it suppresses neoglucogenesis, and then only 40-50% of insulin moves into the systemic circulation to act on the peripheral muscle and fat tissue to increase peripheral uptake along with suppress lipolysis. Weight gain means a barrier to compliance of insulin therapy and DM control. This was emphasized by Bryden, et al. [51] who kept a follow of 65 young patients with T1D from adolescence to young adulthood and discovered that 30% of the women admitted to underdoing their insulin to manipulate their weight .Restricting carbohydrate/day in diet might be helpful in managing weight in T1D subjects, as calorie intake might decrease with which insulin dosage would decrease automatically. Research on dietary approaches for optimising weight and glycaemic control in T1D is still required.

Another potential factor affecting weight gain is hypoglycaemia. Since acute hypoglycemia is associated with food cravings, especially for carbohydrates to resolve the hypoglycaemia, that may cause disinhibited eating behaviors [52]. Most importantly, individuals having T1D often take intake of carbohydrates greater than that which is recommended to treat hypoglycemia and often unnecessarily treat with foods which also contain protein and fat [53]. Further the impact of regular intake oh high carbohydrates either in snacks or meals was demonstrated by Russell, et al. who found that healthy, normal weight individuals who took an oral glucose challenge (50g glucose) experienced a 1.5 times higher rise in blood glucose concentration, as compared to when they underwent a mixed meal challenge (21.7 g protein, 4.8g fat, 41.0g carbohydrates). On contrast

enhanced ultrasound it was seen that forearm muscle micro vascular blood volume and flow increased following the mixed meal but reduced after the glucose challenge inspite of similar levels of hyperinsulinemia between the 2 conditions [54]. This implies that high glycaemic meals impair skeletal muscle micro vascular blood flow that might limit glucose disposal into the skeletal muscle. If LCD's decrease the incidence of hypoglycemia, this would decrease the input of corrective carbohydrates, and finally help in managing weight and thus potentially decrease the risk of microvascular insulin resistance (IR).

IR is common in T1D individuals with the incidence rising [52,55]. IR is an independent risk factor for microvascular (neuropathy, nephropathy, retinopathy) along with macrovascular (coronary and peripheral vascular disease) complications in people having T1D [55-58]. Overlap is possible in mechanisms of IR in T1D and T2DM, including an increase in intramuscular triglyceride (IMTG) content [59] and mitochondrial dysfunction [60]. But hyperglycemia is unable to explain the high prevalence of IR seen in T1D [61]. It may be possible that chronic exogenous use of insulin might be responsible for the same, as human basal insulin like insulin detemir or glargine have been shown to cause more IR, oxidative stress, skeletal muscle ectopic fat collection along with mitochondrial impairments in contrast to hypoglycemia alone [62]. Studies are there that implicate that higher insulin dose (i.e. IR) is associated with greater mortality in T2DM subjects [63], though a cause and relationship remains to be made. Since LCD's are accompanied with decreased insulin doses in T1D subjects, possibly due to decreased carbohydrate intake [37,64], this decrease in insulin exposure at least theoretically might improve insulin sensitivity as supported by limited animal and observational studies [65]. More studies are needed which examine specifically this relationship of LCD's on insulin sensitivity using insulin clamp methods and/or meal tolerance tests in subjects having T1D.

Risks of LCD in subjects having T1D

Few reports document that VLCD's (30-40g carbohydrates /day) in adults having T1D can cause decreases in HbA1c to as less as ~5.5%. But these studies included either case reports or very small sizes of possibly dedicated individuals who are not the proper representative of the broader population, and the other report is a large online survey of select cohorts where no controls were used. Moreover no additional beneficial effect is there of getting HbA1c under 7.0% on either overall health or mortality [66], especially if there is greater risk of hypoglycemia [67] that suggests these diets are extreme unnecessarily. Normally VLCD's are not recommended in T1D subjects in view of the risks of DKA and oxidative stress, dyslipidemia, nutritional deficiencies and difficulty in maintaining such diets over long periods. Importantly VLCD's which have ketogenic effects might increase the risk of DKA especially in individuals taking sodium glucose transporter2 (SGLT2) inhibitors since total daily insulin intake decreases remarkably [68] and thus a risk of euglycaemic DKA. Further there may be risk for more frequent along with more severe hypoglycemia with VLCD, at least in theory. Still with the increased use of continuous glucose monitoring with alerts to warn of impending hypoglycemia might help to facilitate a LCD or VLCD [69]. Increased ketones in an insulin deficient state in people having T1D are known to elicit oxidative stress and inflammatory responses that play a pivotal role in the development of complications [70]. Concerns were raised by Ranjan, et al. regarding VLCD's in people having T1D in a study showed that one week of an isocaloric VLCD, diet defined as ≤50g/day, decreased the treatment effect of glucagon response to glucagon to the VLCD condition might be due to decreased hepatic glycogen stores, Moreover in VLCD condition, the 1st glucose bolus led to significantly greater increase in free fatty acids and ketone body concentrations compared to the high carbohydrates diet condition, implicating that the VLCD might increase the risk of ketogenesis under certain conditions which raise glucagon levels like in prolonged exercise. Thus one can propose that glucagon's efficacy when used as a rescue treatment in severe hypoglycemia would be impaired with VLCD, Still more research in required for testing it.

Another concern of LCD/VLCD's is that dietary carbohydrates is decreased, the intake of saturated fat will likely increase for maintaining calorie intake. A study where11 adults having T1D on a VLCD (<55g carbohydrates /day), 82% were found to have increased total and LDL cholesterol and increased total: HDL ratio as seen in 64% of participants with 27% experiencing increased serum triglycerides [71]. On same basis 62% of participants in the observational study of a VLCD (mean intake of 36±15g carbohydrates day) in adults and children with T1D were shown to have dyslipidemia (increased total and LDL cholesterol). The impact of LCD on blood lipids in the nondiabetic population is controversial; yet more studies gave evidence of positive than negative effects [72-74]. Inspite of concerns, the levels of increased cholesterol is not of much clinical

relevance, mainly if the diet decreased risk of complications due to improved glycaemic control.

Another point that bothers with a VLCD is the potential of nutritional deficiencies. Though high carbohydrates containing foods mostly contain ingredients high in sugar or refined starches with little or no nutritional quality, carbohydrates rich foods also have a broad range of nutritionally valuable options like fruits, vegetables, whole grains, milk, yogurt and legumes. Not consuming these latter foods might not be ideal from a healthy eating perspective, as they often contain valuable nutrients and fibre. Dairy consumption has been shown to have various health promoting effects in DM, possibly by probiotic actions [75]. But though yogurt consumption, as one e.g can be beneficial to health, products can vary widely in sugar control and is common for the carbohydrate content of low fat yogurts to be over 10% due to the addition of low cost fructose syrup [76]. Further it is dangerous to consume regular high fructose syrup in some yogurts and fizzy drinks, especially in children, for the risk of obesity, IR, cardio vascular disease (CVD), fatty liver disease and dental caries [77]. Further a LCD does not differentiate between a higher quality and lower quality food choices. E.g on analysis it was found that Atkins for life VLCD (20-40g carbohydrates/day) was insufficient in delivering Reference daily Intake for 12 of the 27micronutrients [78]. A hypothetical design for a case study, low carbohydrates (<130g/day), high fat diet was found to meet all minimum micronutrient thresholds besides iron in the female meal plans, that achieved 86-98% of the threshold [79]. Further evidence exists that a HFD, as a function of VLCD, can cause iron deficiency. 3 out of 7 men on a VLCD had low hemoglobin as per Leow, et al. [71]. Thus evaluation and monitoring of vitamin and mineral status in subjects with T1D following LCD need to be encouraged along with recommending multi-vitamin supplements might help In decreasing the risk of deficiencies. Special concern regarding VLCD is on bone health with insufficient calcium and Vitamin D intakes. For T1D this is more important, as suboptimal glycaemic control seems to be related to bone mineral density, and almost 20% of people with T1D between 20-56 years meet the criteria of osteoporosis [80]. Though limited data on the long-term effects of a LCD in T1D subjects, after a ketogenic diet results in decreased bone mineral content in children with epilepsy [81,82]. Moreover, despite marked evidence that low glycaemic index carbohydrates are of benefit in management of post pandial glycaemia, in T1D [83], recent trend is emphasizing regarding quantity of carbohydrates in the diet over quality. This seems to be simplification since restriction of poor quality, the refined carbohydrates high in sugar and low in dietary fibers is of benefit for overall health but some high-quality carbohydrates are possibly health promoting, as they often have essential micronutrients and other potentially nutraceuticals that are of benefit. Guidelines regarding diet that includes ADA's Standard of Medical Care in Diabetes recommend nutrient dense carbohydrates sources which are high in fibre, including vegetables, fruits, legumes, whole grains, along with dairy products [84].

Thus a diet that is rich in nutrients, which meets energy, vitamin and mineral needs is essential regarding normal growth and development, if these requirements are not met, it may be especially harmful in children. A series of case studies implicating that carbohydrates restriction in growing children might ≥ anthropometrical and maturation deficits with increased CVD risk profile because of increased fat intake was published by de Bock, et al. [85]. But if compensatory energy is not provided in the form of increased fat and protein, carbohydrates restriction will cause total energy decrease along with weight loss which has potential negative impact on growth in children and adolescents. Thus role of a specialist dietician in determining the overall diet for ensuring all needs are met is believed to be important for subjects living with T1D. ISPAD Clinical Practice Consensus guidelines on nutritional management in children and adolescents with DM gives further information on nutritional management, what correct energy intake is to develop optimal body weight, growth and development. VLCD's, generally are not recommended for youth with T1D and one needs to emphasize the timing and amount of carbohydrate intake around exercise and physical activity that is an additional challenge for the child along with their family. Right now extra carbohydrate-based snacking is advocated for prolonged activities to help in minimizing hypoglycemia risk.

Thus in management of T1D marked effort is paid to food selection along with portion size. If extra dietary restriction is added, risk of food preoccupation gets raised. In Contrast to people who don't live with DM, T1D subjects are at a higher risk of developing eating disorders. Further long term LCD's intake has given different results. Studies that are long term on LCDs are far and few, yet a retrospective audit of dietary compliance (<75g carbohydrate/day) carried out by Nielson, et al. showed that a dropout rate of 52%waspresent. Besides initiating, maintaining the diet restriction is most vital. Hence it may be difficult to

manage these diet restrictions both in short and long term with different cultural factors, role of food in celebrations, and other situations like in restaurants or while travelling. This LCD diet may isolate the subject in context of society and increase risk of disordered eating behaviors. This explains why social media pages that tout VLCD are common even in T1D community.

How to Remain Active on a LCD

Exercise puts special metabolic challenge for subjects with T1D, since it markedly raises the risks of hyper or hypoglycemia, based on umpteen variables [86] To achieve an optimal glucose concentration, during and following a bout of exercise, to get the best performance and training adaptation is a balancing act between the right insulin dosing strategy and carbohydrate intake. Keeping a control on carbohydrate metabolism during endurance exercise is based on how much endogenous and exogenous stores are available, how much transport proteins are there including their activity which transport substrates across plasma and mitochondrial membranes and activity of enzymes involved in metabolic pathways [87]. Exericise intensity, its duration, nutritional status and training status all impact the substrate utilization during exercise and risk of glycaemic disturbances for individuals with T1D. Other factors might also play a role like on board insulin concentrations, etc. Optimising the time and amount of carbohydrate intake might impact largely on performance, blood glucose management along with weight control.

Strategies of Carbohydrate Restriction for Endurance Athletes with T1D-Practical Options

Although low carbohydrate training is a very hotly debated subject amongst athletes, coaches and sports scientists, very little published research is available that is specific for athletes with T1D. Carbohydrate needs are based on training status and the event for which the person is training for. More factors might influence the blood glucose concentrations in athletes with T1D that makes estimation of carbohydrate needs complex (Table 1). Lot of scientific evidence suggest role of high carbohydrate diet in endurance performance athletes along with nonathletes in people without T1D [88,89]. But periodically doing endurance training with decreased carbohydrate available, but still doing competition without carbohydrate restriction (i.e. training low but competing high) has been shown to promote superior training adaptations in skeletal muscle when compared with high carbohydrate availability in athletes without DM. Most of the studies suggest increased cell signaling, gene expression and training induced increases in the oxidative capacity of skeletal muscle (Figure 1). Yet these adaptations always do not translate to improved exercise performance [12,90]. To develop a nutritional strategy for a high level or elite athlete having T1D is very complex because of the number of factors which need to be taken into consideration, besides the task of controlling blood glucose levels which is already tough in daily life. More carbohydrate is needed by athletes to fuel every training session for being able to complete at intensity essential for eliciting adaptation, and there may be need to decrease fat mass and retain or raise lean mass to prepare for competition [91]. There is need for both athlete and their training coach regarding training loads and competition schedule that means carbohydrate intake will vary from day to day. Enough carbohydrate is required to restore muscle glycogen stores between sessions, which are particularly important for athletes who undertake long duration or high intensity training sessions and competing more than one in a short span of time [92]. To control weight might be difficult for athletes having T1D since high levels of insulin would raise the carbohydrate requirements during exercise and decrease the use of endogenous fuel stores. One has to keep this in mind when competing in particular events like long distance running, cycling where idea is to improve power to weight ratio; or sports that entail particular weight categories, needs have to be met like in boxing, martial arts along with horse racing (Figure 2). A low carbohydrate diet used chronically is possibly not suitable in high level athletes having T1D in view of energy needed to fuel their heavy training load. Yet a number of ''train low, compete high'' strategies have been investigated, past exercise carbohydrate restriction, and sleep low, train low strategies; some of which might or might not be of benefit for people with T1D (Figure 3). Athlete having T1D has to make sure that training intensity is not compromised when creating a metabolic milieu that helps in facilitating endurance phenotype along with maintaining a blood glucose concentration which is safe and does not interfere with performance. Training with low glycogen stores has some problems in athletes without T1D s demonstrated by Bartlett, et al. [7]. E.g doing exercises in a low exogenous carbohydrate might be difficult to maintain the training intensity, and hence impairs adaptation. Moreover, regular exercise with or without low exogenous carbohydrate might affect the ability to oxidize the further exogenous carbohydrate when increase in intake is implemented [93].

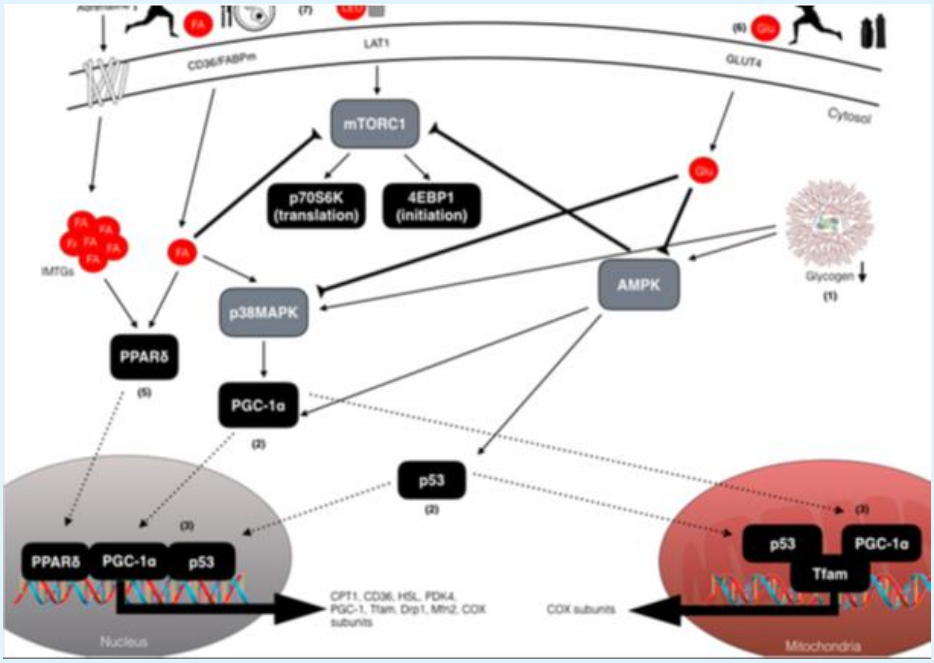

Figure 1: Courtesy ref no- 31 Schematic overview of the exercise-nutrient-sensitive cell signalling pathways regulating enhanced mitochondrial adaptations associated with training with low carbohydrate availability in people without Type 1 diabetes (T1D). Adapted with permission from [8]. (1) Reduced muscle glycogen enhances 50 AMP-activated protein kinase (AMPK) and p38 mitogen-activated protein kinase (p38MAPK) phosphorylation resulting in (2) activation and translocation of peroxisome proliferator-activated receptor gamma coactivator 1-_ (PGC-1_) and p53 to the mitochondria and nucleus. (3) Upon entry into the nucleus, PGC-1_ co-activates additional transcription factors (i.e., NRF1/2) to increase the expression of cytochrome c oxidase (COX) subunits and mitochondrial transcription factor A (Tfam), as well as auto regulating its own expression. In the mitochondria, PGC1_ co-activates Tfam to coordinate regulation of mtDNA, and induces expression of key mitochondrial proteins of the electron transport chain; e.g., COX subunits. Similar to PGC-1_, p53 also translocates to the mitochondria to modulate Tfam activity and mtDNA expression and to the nucleus where it functions to increase expression of proteins involved in mitochondrial fission and fusion (i.e., dynamin-related protein 1 and mitofusion-2) and electron transport chain proteins. (4) Exercising in conditions of reduced carbohydrate availability increases adipose tissue and intramuscular lipolysis via increased circulating adrenaline concentrations. (5) The resulting elevation in free fatty acids (FFA) activates the nuclear transcription factor, peroxisome proliferator-activated receptor _, to increase expression of proteins involved in lipid metabolism. (6) However, consuming pre-exercise meals rich in carbohydrates and/or carbohydrate during exercise can downregulate lipolysis (thereby negating FFA-mediated signalling), as well as reduce both AMPK and p38MAPK activity, thus having negative implications for downstream regulators. It is important to note that these signalling responses are likely different in athletes with T1D due to dependence on exogenous insulin that will suppress lipolysis and activation of the PPARs, which in turn may impair adaptations in mitochondrial proteins and oxidative enzymes following exercise. This may suggest a mechanism for enhanced adaptation with fasted exercise in athletes with T1D, but this hypothesis needs to be tested. (7) High fat feeding can also modulate PPAR_ signalling and upregulate genes with regulatory roles in lipid metabolism and down regulate carbohydrate metabolism.

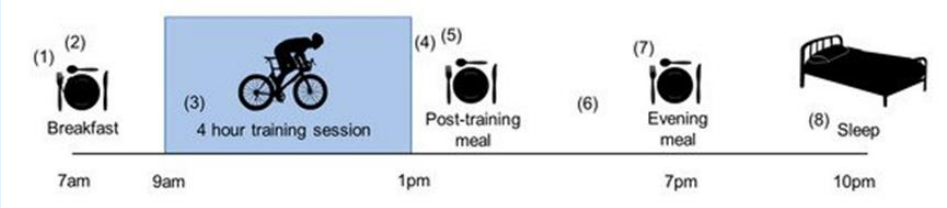

Figure 2: Courtesy ref no.31 An example day in the life of a high-level endurance athlete living with Type 1 diabetes. This is a simplified schematic to demonstrate the complexity of managing the many factors that the athlete must take into account to achieve optimal nutrition for training, recovery and to spend as long as possible in the target glycaemic range. These factors will vary between and within athletes, depending on training schedule and nutrition requirements. (1) Upon waking, liver glycogen levels will be low, therefore breakfast should be planned with the morning training session in mind to ensure the athlete is fuelled and blood glucose levels are in the target range to complete the session. (2) Reduced insulin dose with breakfast, by 25-75%, is an important consideration in order to minimize a drop in blood glucose concentration during training. (3) In ride nutrition needs to be planned in accordance with their workload, pre-exercise blood glucose concentration, and training conditions (e.g., if session is at altitude and/or high ambient temperature). The aim is to ensure that the athlete is not at risk of hypoglycaemia or hyperglycaemia while taking on carbohydrates to maintain carbohydrate availability to promote training intensity (carbohydrate intake can be low, simply to reduce risk for hypoglycaemia, moderate if insulin dose reductions are performed, or can be as high as 60-75g per hour to maximize performance. Hydration is also important, with fluid consumption matched to water loss from sweat and respiration. (4) Post training nutrition is important to capitalize on glycogen storage, which is particularly important if they plan on training on the same or following day. (5) The athlete may consider adjusting their insulin dose post-training depending on their blood glucose levels. Typically less basal insulin is required for active days]. (6) Snacks containing carbohydrates may be consumed throughout the rest of the day to maintain fuelling and to prevent hypoglycaemia. (7) The macronutrient content of the evening meal and insulin bolus is important to ensure refuelling glycogen stores following the training session. (8) It is also important that the athlete gets enough undisturbed sleep to recover, which can be a challenge if glucose control is compromised overall and because late day activity may compromise sleep quality since nocturnal hypoglycaemia risk increases. The risk of nocturnal hypoglycaemia can be increased following certain training sessions. Therefore, the athlete should consider adjusting their insulin dose overnight to increase the time in target and reduce the risk of disrupted sleep. Continuous glucose monitoring is a useful tool for the athlete to monitor difficult areas throughout their daily schedule to reduce the time spent in hyper or hypoglycaemia, and to help ensure that their nutrition is adequate for their training schedule.

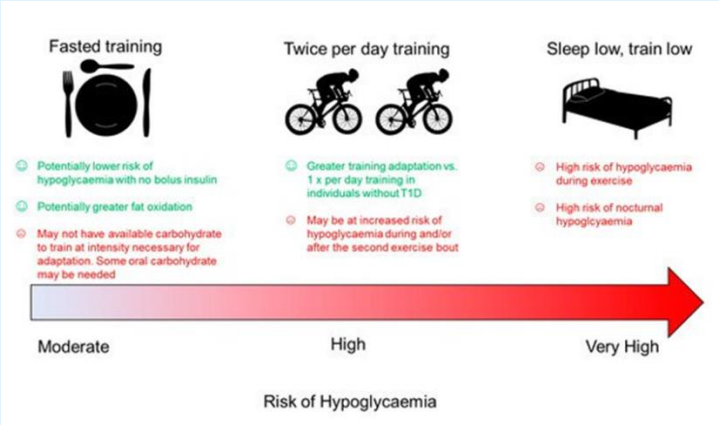

Figure 3: Courtesy ref no.31-Summary of presumed hypoglycaemia risk and benefit to training adaptation in people with Type 1 diabetes using 'train low' strategies.

Factor	Comments	Implications for the athlete with T1D
Exercise modality and protocol	Exercise modality, duration and intensity can all affect muscle glucose uptake and both liver and muscle glycogenolysis.	Carbohydrate requirements will be greater with greater training loads. The type of exercise influences the change in glycaemia [86].
Environmental conditions	Training/competing at high temperatures and/or at altitude increases the risk of hypoglycaemia.	Extra consideration is needed, especially if they are accustomed to lower temperatures.
Antecedent hypoglycaemia and/or moderate intensity exercise	Counter regulatory responses may be impaired during subsequent exercise bouts and increase the risk of hypoglycaemia	Following recent hypoglycaemia, carbohydrate requirements during subsequent training sessions may be greater than usual.
Pre-exercise blood glucose levels	There is evidence that blood glucose drops more when starting exercise with higher blood glucose concentration.	If blood glucose is elevated, carbohydrate feeding may need to be delayed until blood glucose has lowered. However, when pre-exercise blood glucose is low, high glycaemic index carbohydrate may need to be consumed.
Time of day	Exercising late in the afternoon may increase the risk of nocturnal hypoglycaemia. Early morning exercise may reduce risk of hypoglycaemia due to the 'dawn effect'.	The athlete may require more vigilance after an afternoon exercise session to reduce the risk of nocturnal hypoglycaemia.
Hormonal factors	Menstrual cycle phase in women and possibly competition stress (i.e., insulin resistance during early luteal phase and a rise in glucose level during competition stress associated with cortisol and/or catechol amines)	Adrenaline release before competition may cause blood glucose levels to rapidly rise. Blood glucose responses during training may be very different during high stress competition settings.

Table 1: Factors to consider when calculating carbohydrate intake requirements for the active patient with Type 1 diabetes (T1D).

Lastly, any increased muscular adaptations using these 'train low' strategies might have further metabolic benefits in people having T1D in view of improved overall skeletal health. Importance of this is highlighted by the fact that skeletal muscle health has been shown to be impaired in people with T1D (like mass, function metabolism) and thus represents a therapeutic target [60,94]. A hypothesis that T1D is a type of increased ageing in skeletal muscles due to impairments in mitochondrial structure and function potentially accelerating the decline in muscle health was emphasized by Monaco, et al. Thus it might be important to improve skeletal muscle health in view of increased mitochondrial protein expression for athletes with T1D, irrespective of any performance benefits for improved glycaemic control along with metabolic health that would implicate that one needs to investigate if the effects of train low strategies is really worthwhile. E,g increased cell signaling ≥ improved mitochondrial structure and function might be of benefit for performance and/or metabolic health knowing that mitochondrial structure is impaired in people with T1D. Bur since this is just a speculation it requires proper exploration.

What are the adaptations to exercise under carbohydrate restricted conditions have not been tested in people with T1D, hence most of the further section s on the bases of trying to extrapolate which mechanisms possibly occur in people having T1D. Though focus is on endurance athletes, it is still a very simple approach since even among elite athletes, training loads can differ as much as 10-12h / week with individual training sessions lasting between 1-6h for cyclists and triathletes. To conduct any research in this field, it is important that glycaemic control during and after exercise and overall metabolic health are given just as much attention as performance outcomes while studying dietary needs and interventions for subjects with T1D. Importance lies in conducting studies which characterize the 24h glucose profiles, changes in lipid metabolism, body composition

and HbA1c following predisposition training strategies in subjects with T1D.

Training twice /day

Training twice in a day is other training approach which is designed so that athletes finishes a morning training session followed by lot of hours of decreased carbohydrate intake so that the 2nd training session is started with decreased muscle glycogen (i.e depleted training glycogen). In subjects without T1D, 3-10 weeks of twice /day training increases oxidative enzyme activity as demonstrated earlier [89,95]. Whole body composition, and intramuscular lipid utilization, aerobic capacity and performance [96] vis a vis once/day training. Initially Hansen, et al. [95] used a one legged kicking model for comparison of once training vs twice a day training every alternate day. Which meant that the second bout in the twice /day condition was done with low muscle glycogen. These positive findings of twice /day training were then shown on a whole –body level by others.

Though still to be tested in a research setting twice /day training is going to be technically challenging for subjects with T1D.

a. Antecedent exercise blunts the counter regulatory responses on further exercise that would increase the rise of hypoglycaemia [97].
b. twice /day training would need continuous glucose checking throughout training days and increase watch overnight to prevent nocturnal hypoglycemia compared to a single session. Still under correct conditions, athletes might be able to do twice /day training if they take some carbohydrates at the 2nd training session to prevent hypoglycemia along with use continuous glucose monitoring.

Exercise in Fasting conditions in T1D Athletes

Exercise in Fasting conditions when breakfast is taken following morning training sessions, is a simpler model for training low which might ≥ training in the fed state [98]. Exercise in overnight fasted conditions in people without DM has been associated with a lot of responses which may translate to long term improvements in lipid and glucose metabolism [99]. On exercising during fasting, increase fat utilization, improved plasma lipid profiles and increased activation of the molecular signaling pathways increased mitochondrial content and capacity to oxidize fat while suppressing glucose metabolism in contrast to fed exercise [100,101]. 5'Adenosine monophosphate activated protein kinase (MAPK) activity, Ca MK, and p38MAPK are the kinases involved, While exercising these kinases translocate from the cytosol in to the nucleus where they activate transcription factors controlling the expression of nuclear genes known to control mitochondrial biogenesis and genes encoding for fatty acid transport into skeletal muscle, the capacity of the carnitine shuttle and the β-oxidation enzymes. Feeding prior to exercise lowers post exercise adipose tissue gene expression of pyruvate dehydrogenase kinase isozyme 4, adipocyte triglyceride lipase, hormone sensitive lipase, GLUT4 and insulin receptor substrate 2 compared to the fasted state. Undertaking moderate to high intensity steady state exercise (70%WMAX in the fasted state increased fatty acid availability augmented AMPKThr172 phosphorylation and Increased PDK4mRNA expression compared to the same exercise bout in the fed state. Carbohydrates intake before and during exercise stimulates a contribution of blood glucose to the metabolic substrate intake before and during exercise stimulates a contribution of blood glucose to the metabolic substrates pool fuelling muscle and inhibits fat oxidation due to higher glycolytic flux and pyruvate oxidation by the pyruvate dehydrogenase complex [102,103]. This attenuated lipid utilization during exercise, mainly due to higher insulin concentrations, that help lipolysis both of the AT stores (reducing plasma NEFA concentrations) and the IMTG stores [104]. The high insulin concentration, as typically occurs in the post meal state especially if carbohydrates are consumed will also suppress liver glyconeogenesis, meaning that glucose production by the liver will not match oxidation by the muscle, thus blood glucose falls [105]. In comparison to fed state exercise, during fasted exercise, an increase in mobilization of triglycerides reserves from AT and reduced re-esterification of NEFA and insulin concentrations will be low, that a rise in concentrations of circulating NEFA in the plasma and thus more lipid provisions to the muscle for oxidation [106]. Low insulin levels will also decreased blood glucose oxidation and muscle glycogen breakdown, as well as liver glucose production via glycolysis and gluconeogenesis. Subjects with T1D can slightly change the fuel selection during exercise on the basis of the time exercise is done, in relation to their bolus insulin administration and how much basal and bolus insulin is present in circulation at the time of body's reliance on carbohydrates as fuel [107]. But withholding insulin can itself dramatically increase glycaemia and ketone production during exercise [108].

Evidence is coming forward regarding T1D's who train regularly in a fasted state is of benefit for metabolic adaptations. The effects of six weeks of supervised endurance training under tight dietary control on

metabolic adaptations to exercise was studied by Van Proeyen, et al. in which half of the participants trained consistently in the fasted state and the other half were fed carbohydrate before and during each training session. Histology of the muscle revealed that fasted training increased the contribution of intramyocellular lipids (IMCL) to energy provision, but these changes were not found in the fed group. This implicates that training in a fasted state stimulates adaptations in muscle cells to shift fat fuel selection towards a higher fraction of ICML utilization, But though the study suggested that training in the fasted state is a more potent stimulus than fed training to increase muscle oxidative capacity, the increased oxidative capacity in fasted training did not translate to any better performance in the 60'time interval. Thus particularly for T1D individuals, these findings implicate the importance of decreasing insulin dose before exercise to increase the contribution of lipid oxidation to fuel the exercise bout that might help in decreasing fat mass and prevent a decrease in blood glucose concentration. To decrease insulin in an effective way those on insulin pumps, aggressive basal rate decrease (by 80%)~90 min pre-exercise is needed and the effect of lipid utilization might just be marginal [109].

That training during fasting but not fed training prevented the decrease in glucose concentrations induced by exercise during a bout of fasted exercise that was done post training was interesting in Van Proeyen's, et al. study [110]. They proposed that regular exercise in the fasted state might stimulate adaptations in the liver to facilitate glucose production via gluconeogenesis. If the same adaptation also occurs in people with T1D, regular fasted training might be a method of preventing the drop in blood glucose during moderate intensity exercise hence decreases the risk of hypoglycemia. Counter to this, fasted training might help in consistent rise in blood glucose level if the exercise was very vigorous. Also what was of interest was Stannard's, et al. results, who demonstrated that training five times/week for 4 weeks in an overnight fasted state increased muscle glycogen storage greater than fed training . Increase in resting muscle glycogen stores was only 3% in fed training condition in contrast to 55% in fasted state, implicating increased training adaptations occur in T1D subjects as well, if done regularly fasted training might improve metabolic adaptations and improve glycaemic control as well and decrease the risk of hypoglycemia over the 24h period. The effects of regular long-term training in the fed vis a vis fasted state has not been studied in T1D subjects however.

In T1D subjects , blood glucose levels have been found to have greater stability after exercise done in fasted condition in morning [111], opposite to the decrease in blood glucose levels found in late day (fed state) aerobic exercise [112-117] and high intensity training. It might be because of more reliance on fat oxidation while fasted exercise which might offset the fall in blood glucose level and decrease the risk of hypoglycemia. Greater small sessions of intensive high intensity interval type exercise might even cause a marked rise in blood glucose levels that needs insulin correction prior to 1st meal [118]. Still it is not clear if exercising in the fasted state would be helpful when going through training sessions of >30', that makes this knowledge impossible to relate to elite athletes that usually train for >6hrs. Several explanations are possible for these changes observed during fasted exercise. 1st, lower circulating insulin during fasted exercise prevents the suppression of hepatic glycogenolysis and thus increases blood glucose level during exercise. 2nd, subjects with T1D might experience the so called ''dawn phenomenon'', if the exercise is done in early morning, where an early morning increase in blood glucose level is probably secondary to a higher circulating growth hormone [119,120]. Although these theories are unconfirmed, one can still suggest that people who are struggling with hypoglycemia during exercise and or those who are trying to prevent use of extra carbohydrates to help in weight management might have greater success with early morning /fasted exercise than they would when exercise is done later in the day. Generally potential for overnight fasted exercise for promoting better metabolic health is highlighted by these studies than regular fed exercise, still there is limited work in this area, particularly in T1D subjects. Still it seems fasted exercise might be a good strategy for T1D subjects, since it might decrease the risk of exercise induced hypoglycemia besides improving adaptation, and needs to be studied deeply.

''Sleep low Train Low''

This means doing a bout of exercise in the evening, restrict carbohydrate intake overnight and then exercise in the fasted state the next morning [121]. Low here points to muscle glycogen stores and not to hypoglycaemia. The anticipated benefit of this model is that the collective total time spent in a state of decreased muscle glycogen can be as long as 12-14h based on the time and duration of the training sessions along with sleep periods. Studied that have used this model of ''Sleep low Train Low'' demonstrate increased activation of AMPK, p38AMPK and p53 signaling [122]. The effects of

1-3 weeks of sleep low training in the elite level cyclists and triathletes without DM on a stimulated triathlon race performance was studied by Marquet and others [123,124]. Increased cycling efficiency, 20km time trial performance and 10km running performance was found by them as compared to traditional high carbohydrate training. Still no trials have studied ''Sleep low Train Low'' in subjects with T1D. Still irrespective of ''Sleep low Train Low'' augmenting training adaptation, this strategy does not seem to be a viable option for T1D subjects in view of high risk of nocturnal hypoglycaemia.

Conclusion/Future Research Suggestions

With the modern trend of rising obesity rates and impaired metabolic control in type1 diabetics, inspite of improved insulin quality and technology. Earlier we have reviewed on TID aetiopathogenesis and concerns regarding diabesity [125,126] so here we have concentrated on ways that could be possible in preventing diabesity. Some novel lifestyle changes that can be achieved are required. LCD's that consist of <130g of carbohydrate/day might be a strategy to better glycaemic control along with metabolic health in T1D subjects. The /day demands imposed on a person with T1D for controlling their glucose are complex, hence strategies proposed should be achievable, better the quality of life (QoL) and make sure the person enjoys his food taking social and psychological factors into account. Guidance regarding nutrition in T1D should be based on proper research with good methods. Although limited work has been done regarding LCD's they seem to be a good option for increasing glycaemic control along with metabolic health in T1D, which would raise the time in target glycaemia in view of decreased risk of hypo and hyperglycaemia. Further large body of evidence suggests that LCD would help in bettering total body composition along with insulin needs that is of benefit for overall cardio metabolic health. Still there are no properly done randomized controlled trials to state this for sure that degree of carbohydrate restriction which is safe, practical and has efficacy over a long period in people with T1D. Most of the published research have been cross sectional studies where no control groups have been used or case reports in this topic from highly motivated subjects who have been self-selected, the one's that follow intensive insulin management treatments and thus are not representative of the general subjects having T1D. Moreover a lot of LCD studies are based on self-report diet taken which has its own limitations. For the elite athlete who is recreationally active having T1D, even lesser research is available in this field. Although work done on individuals without T1D implicates "train low" methods might be of benefit for metabolic adaptations as compared to when training with high carbohydrate present. Still in athletes having T1D these methods need testing and some of them might have extra challenges that makes them unsuitable for athletes having T1D, irrespective of any potential efficacy in the performance. Thus this research needs further attention in people living with T1D.

References

1. Atkinson MA, Eisenbarth GS (2001) Type 1 diabetes: New perspectives on disease pathogenesis and treatment. Lancet 358(9277): 221-229.

2. Foster NC, Beck RW, Miller KM, Clements MA, Clements MA, et al. (2019) State of Type 1 diabetes Management and outcomes from the T1D exchange in 2016-2018. Diabetes Technol Ther 21(2): 66-72.

3. Chimen M, Kennedy A, Nirantharakumar K, Pang TT, Andrews R, et al. (2012) What are the health benefits of physical activity in Type 1 diabetes mellitus? A literature review. Diabetologia 55(3): 542-551.

4. Livingstone R, Boyle JG, Petrie JR (2019) How tightly controlled do fluctuations in blood glucose levels need to be to reduce the risk of developing complications in people with Type 1 diabetes?. Diabetes Med.

5. Nathan DM (2014) The Diabetes control and complications trial/epidemiology of diabetes interventions and complications at 30 years: Overview. Diabetes Care 37(1): 9-16.

6. Corbin KD, Driscoll KA, Pratley RE, Smith SR, Maahs DM, et al. (2018) Obesity in Type 1 diabetes: Pathophysiology, Clinical Impact and Mechanisms. Endocr Rev 39(5): 629-663.

7. Bartlett JD, Hawley JA, Morton JP (2015) Carbohydrate availability and exercise training adaptations: Too much of a good thing?. Eur J Sports Sci 15(1): 3-12.

8. Impey SC, Hearris MA, Hammond KM, Bartlett JD, Louis J, et al. (2018) Fuel for the Work Required: A Theoretical Framework for Carbohydrate Periodization and the Glycogen Threshold Hypothesis. Sports Med 48(5): 1031-1048.

9. Jeukendrup AE (2017) Periodized nutrition for athletes. Sports Med 47(Suppl1): 51-63.

10. Stannard SR, Buckley AJ, Edge JA, Thompsen MW (2010) Adaptations to skeletal muscle with endurance exercise training in the acutely fed versus overnight-fasted state. J Sci Med Sports 13(4): 465-469.

11. Mazur A (2011) Why were ''starvation diets'' promoted for diabetes in the pre-insulin period?. Nutr J 10: 23.

12. Thomas B (2004) Nutritionally Advance for people with Diabetes: Past, Present, What Next?. Pract Diab Int 21(2): 69-72.

13. Dietary Guidelines Advisory Committee Report of the Advisory Committee on the Dietary Guidelines for Americans 2015.

14. Dietary Guidelines Advisory Committee Report of the Advisory Committee on the Dietary Guidelines for Americans 2010.

15. Centres for Disease Control and Prevention (CDC) (2004) Trends in intake of energy and macronutrients-United States, 1971-2000. Morbid Mortal Wkly Rep 53(4): 80-82.

16. Merger SR, Kerner W, Stadler M, Zeyfang A, Jehle P, et al. (2016) Prevalence and comorbidities of double diabetes. Diabetes Res Clin Pract 119: 48-56.

17. Talmadge K, Philipson L, Reusch J, Hill-Briggs F, Youssef G, et al. (2018) American diabetes association standards of medical care in diabetes 2018. Diabetes Care 41: S38-S50.

18. Smart CE, Annan F, Higgins LA, Jelleryd E, Lopez M, (2018) ISPAD Clinical Practice Consensus Guidelines 2018: Nutritional management in children and adolescents in diabetes. Paediatr Diabetes 19(27): 136-154.

19. Accurso A, Bernstein RK, Dahlquist A, Drazrin B, Feinman RD, et al. (2008) Dietary carbohydrate restriction in type 2 Diabetes mellitus and metabolic syndrome: Time for critical appraisal. Nutr Metab 5: 9.

20. Feinman RD, Pogozelsky WK, Astrup A, Bernstein RK, Fine EJ, et al. (2015) Dietary carbohydrate restriction is the first approach in diabetes management: Critical review and evidence base. Nutrition 31(1): 1-13.

21. Eiswirth M, Clark E, Diamond M (2018) Low carbohydrate diet and improved glycaemic control in a patient with type1 diabetes. Endocrinol Diabetes Metabol Case Rep.

22. Lennerz BS, Barton A, Bernstein RK, Dikeman RD, Diulus C, et al. (2018) Management of type1 diabetes with a very low carbohydrate Diet. Paediatrics 141(6): e20173349.

23. Diabetes Control and Complications Trial Research Group, Nathan DM, Genuth S, Lachin J, Cleary P, et al. (1993) The effect of intensity treatment of diabetes on the development and progression of long term complications in insulin dependent diabetes mellitus. N Engl J Med 329(14): 977-986.

24. Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Intervention and Complications (EDIC): Study Research Group. Mortality of type1 diabetes in the DCCT/EDIC Versus the General Population. Diabetes Care 2016 39(8): 1378-1383.

25. Seckold R, Fisher E, DeBock M, King BR, Smart CE (2018) The ups and downs of Low carbohydrate diets in the management of type1 diabetes: A review of clinical outcomes. Diabetes Med 36(3): 326-344.

26. Ranjan A, Schmidt S, Damm-Frydenberg C, Steineck J, Clausen TR, et al. (2017) Low carbohydrate diets impair the effect of glucagon in the treatment of insulin induced mild hypoglycemia: A randomized crossover study. Diabetes Care 40(1): 132-135.

27. Kanikarla-Marie P, Jain SK (2016) Hyperketonaemia and ketosis increase the risk of complications in type1 diabetes. Free Radic Biol Med 95: 268-277.

28. Thomas DT, Erdman K, Burke LM (2016) American College of Sports Medicine Joint Position Statement. Nutrition and Athletic Performance. Med Sci Sports Exerc 48(3): 543-568.

29. Burke LM, Jeukendrup AE, Jones AM, Mooses M (2019) Contemporary Nutrition Strategies to Optimize Performance in Distance Runners and Race Walkers. Int J Sports Nutr Exec Metab 29(2): 117-129.

30. Fordyce T, Chris Froome (2018) Team sky's Unprecedented Release of Data Reveals How British Riders Won Giro d'Italia.

31. Scott NS, Anderson L, Morton JP, Wagen makers AJM, Riddell MC (2019) Carbohydrate Restriction in type1 diabetes: A realistic Therapy for Improved Glycaemic Control and Athletic Performance?. Nutrients 11(5): 1022.

32. Chiang JI, Kirkman MS, Laffel LMB, Peters AL (2014) Type 1 diabetes through the lifespan: A position Statement of the American Diabetes Association. Diabetes Care 37(7): 2034-2054.

33. DAFNE Study Group (2002) Training in flexible, intensive management to endure dietary freedom in people with type1 Diabetes: Dose adjustment for normal eating (DAFNE) randomized controlled trial. BMJ 325(7367): 746.

34. Meade LT, Kushton WE (2016) Accuracy of Carbohydrate Counting in adults. Clin Diabetes 34(3): 142-147.

35. Heinemann J (2008) Variability of Insulin action: Does it matter?. Insulin 3(1): 37-45.

36. Gingras V, Talen N, Roy-Fleming A, Lenault L, Rabasa-Lhoret R (2018) The challenges of delivering postprandial glucose control using closed –loop systems in patients with Type 1 diabetes. Diabetes Obes Metab 20(2): 245-256.

37. Krebs JD, Strong AP, Cresswell P, Reynolds AN, Hanna A, et al. (2016) A randomized trial of the feasibility of a low Carbohydrate diet vs standard Carbohydrate counting in adults with type 1Diabetes taking body weight into account. Asia Pac J Clin Nutr 25(1): 78-84.

38. Turton JL, Raab R, Rooney KB (2018) Low Carbohydrate diets for Type 1 diabetes mellitus: A systematic review. PLoS ONE 13(3): e0194987.

39. Mayer-Davis EJ, Laffel LM, Buse JB (2018) Management of Type 1 diabetes with a very-low-Carbohydrate diet: A word of caution. Paediatrics 142(2): e20181536B.

40. Ranjan A, Schmidt S, Damm-Frydenberg C, Holst JJ, Madsbad S, et al. (2017) Short term effects of a low-Carbohydrate diet on glycaemic variables and cardiovascular risk markers in patients with Type 1 diabetes: A randomized open-label crossover trial. Diabetes Obes Metab 19(10): 1479-11484.

41. Schmidt S, Christensen MB, Damm- Frydenberg C, Jensen JEB, Floyel T, et al. (2019) Low versus High Carbohydrate diet in Type 1 diabetes: A 12week randomized open label crossover study. Diabetes Obes Metab.

42. Conway B, Miller RG, Costacou T, Fried L, Kelsey S, et al. (2010) Temporal patterns in overweight and obesity in Type 1 diabetes. Diabetes Med 27(4): 398-404.

43. Makura CB, Niranthakumar K, Girling AJ, Sarvanan P, Narendran P (2013) Effect of physical activity on the development and progression of micro vascular complications in Type 1 diabetes: Retrospective analysis of the DCCT study. BMC Endocr Disord 13: 37.

44. Vestberg D, Rosengren A, Olsson M, Gudbjornsdottir S, Svensson AM, et al. (2013) Relationship between overweight and obesity with hospitalization for heart failure in 20,985 patients with Type 1 diabetes: A population-based study from the Swedish National Diabetes Registry. Diabetes Care 36(9): 2857-2861.

45. Price SA, Gorelik A, Fourlanos S, Colman PG, Wentworth JM (2014) Obesity is associated with retinopathy and macrovascular disease in Type 1 diabetes. Obes Res Clin Pract 8(2): 178-182.

46. Atkins R (2002) Dr Atkin's New Diet Revolution; Harper Collins: New York, NY, USA.

47. Eades M; Eades M (1997) Protein Powder: The High Protein/Low Carbohydrate Way to lose Weight, Feel Fit and Boost Your Health-In just weeks! 1st ed'Bantam: New York, NY, USA.

48. Astrup A, Meinert-Larsen T, Harper A (2004) Atkins and other Low Carbohydrate diets: Hoax or an effective tool for weight loss?. Lancet 364(9437): 897-899.

49. Russell-Jones D, Khan R (2007) Insulin-associated weight gain in diabetes-causes, effects and coping strategies. Diabetes Obes Metab 9(6): 799-812.

50. Szadkowska A, Madej A, Ziolkowska K, Szymanska M, Jezioorny K, et al. (2015) Gender and age dependent effect of Type 1 diabetes on obesity and altered body

composition in young adults. Ann Agric Environ Med 22(1): 124-128.

51. Bryden KS, Neil A, Mayou RA, Peveler RC, Fairburn CG, et al. (1999) Eating habits, body weight and insulin misuse, A longitudinal study of teenagers and young adults with Type 1 diabetes. Diabetes Care 22(12): 1956-1960.

52. Strachan MWJ, Ewing FME, Frier BM, Harper A, Deary IJ (2004) Food craving during acute hypoglycemia in adults with Type 1 diabetes. Physiol Behav 80(5): 675-682.

53. Savard V, Gingras V, Letoux C, Bertrand A, Desjardins K, et al. (2016) Treatment of hypoglycaemia in adults patients with Type 1 diabetes: An Observational Study. Can J Diabetes 40(4): 318-323.

54. Russell RD, Hu D, Greenaway T, Sharman JE, Rattigan S, et al. (2018) Oral glucose challenge impairs skeletal muscle microvascular blood flow in healthy people. Am J Physiol Endocrinol Metab 315(2): 307-315.

55. Kilpatrick FS, Rigby AS, Atkin SL (2007) Insulin resistance, the metabolic syndrome and complication risk in Type 1 diabetes: "double diabetes'' in the Diabetes Control and Complications Trial. Diabetes Care 30(3): 707-712.

56. McGill M, Molymeaux L, Twigg SM, Yue DK (2008) The metabolic syndrome in Type 1 diabetes: Does it exist and does it matter?. J Diabetes Complications 22(1): 18-23.

57. Chaturvedi N, Sjolie AK, Porta M, Aldington SJ, Fuller JH, et al. (2001) EURODIAB Prospective Comlications Study. Markers of insulin resistance are strong risk factors for retinopathy incidence in type1 diabetes. Diabetes Care 24(2): 284-289.

58. Tesfaye S, Chaturvedi N, Eaton SFM, Ward JD, Manes C, et al. (2005) EURODIAB Prospective Complications Study. Vascular risk factors and diabetes neuropathy. N Engl J Med 352: 341-350.

59. Perseghin G, Lattuada G, Danna M, Sereni LP, Maffi P, et al. (2003) Insulin resistance, intramyocellular lipid content, and plasma adiponectin in patients with type1 diabetes. Am J Physiol Endocrinol Metab 285(6): 1174-1181.

60. Monaco CMF, Hughes MC, Ramos SV, Varah NE, Lambertz C, et al. (2018) Altered mitochondrial biogenetics and ultrastructure in the skeletal muscle of young adults with type1 diabetes. Dibetologia 61(6): 1411-1423.

61. Bergman BC, Howard D, Schauer IE, Maahs DM, Snell-Bergeon JK, et al. (2012) Features of hepatic and skeletal muscle Insulin resistance unique to type1 diabetes. J Clin Endocrinol Metab 97(5): 1663-1672.

62. Liu HY, Yehuda-Shnaidman E, Hong T, Han J, Pi J, et al. (2009) Prolonged exposure to insulin suppresses mitochondrial production in primary hepatocytes. J Biol Chem 284(21): 14087-14095.

63. Gamble JM, Simpson SH, Eurich DT, Majumdar SR, Johnson JA (2010) Insulin use and increased risk of mortality in type 2 diabetes: A cohort study. Diabetes Obes Metab 12(1): 47-53

64. Nielsen J, Gando C, Joensson E, Paulson CE (2012) Low Carbohydrate diet in type1 diabetes, long term improvement and adherence: A clinical audit. Diabetol Metab Syndr 4(1): 23.

65. Shanik MH, Xu Y, Skrha J, Dankner R, Zick Y, et al. (2008) Insulin resistance and Hyperinsulinemia: Is Hyperinsulinemia the cart of the horse?. Diabetes Care 31(Suppl2): 262-268.

66. Shoenkar DAJM, Simon D, Chaturdevi N, Fuller JH, Soedamah-Muthu SS (2014) Glycemic control and all-cause mortality risk in type1 diabetes: The EURODIAB Prospective Complications Study Group. J Clin Endocrinol Metab 99(3): 800-807.

67. Subramaniam S, Hirsch IB (2018) Intensive Diabetes treatment and Cardiovascular Outcomes in type1 diabetes Mellitus: Implications of the Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Intervention and Complications Study Group 30-year Follow-up. Endocrinol Metab Clin N Am 47(1): 65-79.

68. Danne T, Biesler T, Kordonouri O (2018) Combined SGLT1 and SGLT2 Inhibitors and their role in Diabetes care. Diabetes Technol Ther 20(S2): S269-S277.

69. Puhr S, Derdzinski M, Welsh JB, Parker AS, Walker T, et al. (2019) Real world hypoglycemia avoidance with a Continuous glucose Monitoring System's Predictive Low glucose alert. Diabetes Technol Ther 21(4): 155-158.

70. Stentz FB, Umppierres GE, Cuervo R, Kitabchi AE (2004) Proinflammatory cytokines, markers of cardiovascular risks, oxidative stress and lipid peroxidation in patients with hyperglycemic crises. Diabetes 53(8): 2079-2086.

71. Leow ZZX, Guelfi KJ, Davis EA, Jones TW, Fournier PA (2018) The glycaemic benefits a very-low carbohydrate ketogenic diet adults with type1 diabetes Mellitus may be opposed by increased hypoglycaemia riskand dyslipidaemia. Diabet Med 35: 1258-1263.

72. Gardner CD, Kiazand A, Alhassan S, Kim S, Stafford RS, et al. (2007) Comparison of the Atkins, Zone, Ornish and LEARN diets for change in weight and related risk factors among overweight premenopausal women. The A to Z Weight loss study. A randomized trial. JAMA 297(9): 969-977.

73. Shai I, Schwarzfuchs D, Henkin Y, Shahai DR, Witkow S, et al. (2008) Weight loss with a low carbohydrate, Mediterranean or low fat diet. N Engl J Med 359: 229-241.

74. Nordmann AJ, Nordmann A, Briel M, Keller U, Yancy WS, et al. (2006) Effects of low carbohydrate vs low fat diets on weight loss and cardiovascular risk factors. A meta-analysis of randomized controlled trials. Arch Int Med 166(3): 285-293.

75. Salas-Salvado J, Guash-Ferre M, Dian-Lopez A, Babio N (2017) Yogurt and Diabetes: Overview of Recent Observational studies. J Nutr 147(7): S1452-S1461.

76. Moore JB, Harts A, Fielding BA (2018) Evaluation of the nutrient content of yogurts: A comprehensive survey of yogurt products in the major UK supermarkets. BMJ Open 8(8).

77. Moore JB, Fielding BA (2016) Sugar and metabolic health: Is there still a debate?. Curr Opin Clin Nutr Metab Care 19(4): 303-309.

78. Calton JB (2010) Prevalence of micronutrient deficiency in popular diet plans. J Int Soc Sports Nutr 7: 24.

79. Zinn C, Rush A, Johnson R (2018) Assessing the nutrient intake of a low carbohydrate –high fat (LCHF) diet: A hypothetical case study design. BMJ Open 8(2).

80. Kalaitzoglou E, Popescu I, Bunn RC, Fowlkes JL, Thrailkill KM (2016) Effects of type1 diabetes on Osteoblasts, Osteocytes, and Osteoclasts. Curr Osteoporos Rep 14(6): 310-319.

81. Sunderraghavan V, Mazur MM, Evans B, Liu L, Ebraheim NA (2017) Diabetes and bone health: Latest evidence and clinical implications. Ther Adv Muskuloskelet Dis 9(3): 67-74.

82. Bergqvist AGC, Schall JL, Stallings VA, Zemel BS (2008) Progressive bone mineral content loss in children with intractable epilepsy treated with the ketogenic diet. Am J Clin Nutr 88(6): 1678-1684.

83. Bell KJ, Smart CE, Steil JM, Brand-Miller JC, King B, et al. (2015) Impact of fat protein and glycaemic index on postprandial glucose control in type1 diabetes: Implications for intensive diabetes management in the continuous glucose monitoring era. Diabetes Care 38(6): 1008-1015.

84. American Diabetes Association (2019) 5. Lifestyle Management: Standards Of Medical Care in diabetes-2019. Diabetes Care 42(Suppl1): S46-S60.

85. DeBock M, Lobley K, Anderson D, Davis E, Donaghue K, et al. (2018) Endocrine and metabolic consequences due to restrictive carbohydrate diets in children with type1 diabetes. Paediatr Diabetes 19(1): 129-137.

86. Adolfsson P, Riddell MC, Taplin CE, Davis EA, Fournier PA, et al. (2018) ISPAD Clinical Practice Consensus Guidelines 2018: Exercise in children and adolescents with diabetes. Paeditr Diabetes 19(Suppl27): 205-226.

87. Riddell MC, Gallen JW, Smart CE, Taplin E, Adolfsson P, et al. (2017) Exercise management in type1 diabetes: A Consensus Statement. Lancet Diabetes Endocrinol 5(5): 377-390.

88. Burke LM, Hawley JA (2018) Swifter, higher, stronger: What's on the menu?. Science 362(6416): 781-787.

89. Cermak NM, Van Loon LJC (2013) The use of carbohydrates during Exercise as an ergogenic aid. Sports Med 43(11): 1139-1155.

90. Hulston CJ, Venables MC, Maan CH, Martin C, Philip A, et al. (2010) Training with low muscle glycogen enables fat metabolism in well trained cyclists. Med Sci Sports Exerc 42(11): 2046-2055.

91. Burke LM, Hawley JA, Jeukendrop AE, Morton JP, Stelling werff T, et al. (2018) Toward a common understanding of Diet- Exercise Strategies to Manipulate Fuel Availability for training and competition Preparation in Endurance Sport. Int J Sports Exerc Metab 28(5): 451-463.

92. Burke LM, Collier GR, Hargreaves M (1993) Muscle glycogen stores after prolonged exercise: Effect of the glycaemic index of carbohydrate feedings. J Appl Physiol 75(2): 1019-1023.

93. Cox GR, Clark SA, Cox AJ, Halson SI, Hargreaves M, et al. (2010) Daily training with high carbohydrate availability increases exogenous carbohydrate oxidation during Endurance cycling. J Appl Physiol 109(1): 126-134.

94. Monaco CMF, Gingrich MA, Hawke TJ (2019) Considering type1 diabetes as a form of Accelerated muscle Aging. Exerc Sport Sci Rev 47(2): 98-107.

95. Hansen AK, Fischer CP, Plomgaard P, Andersen JL, Saltin B, et al. (2005) Skeletal muscle adaptation training every second day vs training once daily. J Appl Physiol 98(1): 93-99.

96. Cochran AJ, Myslik F, MacInns MJ, Percival ME, Bishop D, et al. (2015) Manipulating carbohydrate availability between twice-daily sessions of high intensity interval training over 2 weeks improves time trial performance. Int J Sports Nutr Exerc Metab 25(5): 463-470.

97. Galassetti P, Tate D, Neil RA, Richardson A, Leu SY, et al. (2006) Effect of differing antecedent hypoglycaemia on counter regulatory responses to exercise in type1 diabetes. Am J Physiol Endocrinol Metab 290(6): 1109-1117.

98. Wallis GA, Gonzalez JT (2018) Is exercise best served on an empty stomach?. Proc Nutr Soc 78(1): 110-117.

99. Stocks B, Dent JR, Ogden HB, Zemp P, Philp A (2018) Post-exercise skeletal muscle signaling responses to moderate-to high intensity steady state exercise in the fed or fasted state. Am JPhysiol Endocrinol Metab 316(2): 230-238.

100. Chen YC, Travers RL, Walthin JP, Gonzalez JT, Koumanov F, et al. (2017) Feeding influences adipose tissue responses to exercise In overweight men. Am J Physiol Endocrinol Metab 313(1): 84-93.

101. Civtarese AE, Hesselink MKC, Russell AP, Ravussin E, Schrauwen P (2005) Glucose ingestion during exercise blunts exercise-induced glucose gene expression in skeletal muscle fat oxidative genes. Am JPhysiol Endocrinol Metab 289(6): 1023-1029.

102. Akerstrom TC, Birk JB, Klein DK, Erikstrup C, Plomgaard P, et al. (2006) Oral glucose ingestion attenuates exercise-induced activation of 5'-AMP-activated protein kinase in human skeletal muscle. Biochem Biophys Res Commun 342(3): 949-955.

103. Horowitz JF, Mora-Rodriques R, Byerley LO, Coyle EF (1997) Lipolytic suppression following carbohydrate ingestion limits fat oxidation during exercise. Am JPhysiol Endocrinol Metab 273(4 Pt 1): 768-775.

104. Spriet LL (2014) New insights into interaction of carbohydrate and fat metabolism during exercise. Sports Med 44(Suppl1): 87-96.

105. Zimman B, Murray FT, Vranic M, Albisser AM, Leibel BS, et al. (1977) Glucoregulation during moderate exercise in insulin treated diabetics. J Clin Endocrinol Metab 45(4): 641-652.

106. Manghan RJ, Fallah J, Coyle EF (2010) The effects of fasting on metabolism and performance. Br J Sports Med 44(7): 490-494.

107. Krzentowski G, Pirnay E, Pallikarakis N, Luyckx AS, Lacroix M, et al. (1981) Glucose utilization during exercise in normal and diabetic subjects. The role of insulin. Diabetes 30(12): 983-989.

108. Zaharieva DP, McGaugh S, Pooni R, Vienneau T, Ly T, et al. (2019) Improved open loop glucose control with basal insulin reduction in 90minutes before aerobic exercise in patients with type1 diabetes on continuous Subcutaneous insulin infusion. Diabetes Care 42(5): 824-831.

109. Riddell MC, Pooni R, Yavelberg L, Li Z, Kollman C, et al. (2019) Reproducibility in the cardiometabolic responses to high –intensity interval exercise in adults with type1 diabetes. Diabetes Res Clin Pract 148: 137-143.

110. Van Proeyen K, Szlufcik K, Nielens H, Ramaekers M, Hespel P (2011) Beneficial metabolic adaptations due to endurance exercise training in the fasted state. J Appl Physiol 110(1): 236-245.

111. Scott SN, Cocks M, Andrews RC, Narendran P, Purewal TS, et al. (2019) Fasted high intensity interval and moderate intensity exercise do not lead to detrimental 24-hours blood glucoseprofiles. J Clin Endocrinol Metab 104(1): 111-117.

112. Maran A, Pavan P, Bosembiante B, Brugin E, Ermolao AA, et al. (2010) Continuous glucose monitoring reveals exercise nocturnal hypoglycemia after intermittent high intensity exercise in nocturnal patients with type1 diabetes. Diabetes Technol Ther 12(10): 763-768.

113. Guelfi KJ, Jones TW, Fournier PA (2005) Intermittent high intensity exercise does not increase the risk of early post exercise hypoglycemia in individuals with type1 diabetes. Diabetes Care 28(2): 416-418.

114. Iscoe KE, RiddellMC (2011) Continous moderate intensity exercise with or without intermittent high intensity work. Effect on acute and late hypoglycaemia in athletes with type1 diabetes. Diabetes Med 28(7): 824-832.

115. Campbell MD, West DJ, Bain SC, Kinsley MLC, Foley P, et al. (2015) Simulated games activity vs continuous running exercise: Anovel comparison of the glycaemic and metabolic responses in T1DM patients. Scand J Med Sci Sports 25(2): 216-222.

116. Moser O, Tschakert G, Mueller A, Groeschl W, Pieber TR, et al. (2015) Effect of high –intensity interval exercise versus moderate Continuous exercise on glucose homeostasis and hormone response in patients with type 1 diabetes. PLoS ONE 10(8): e0136489.

117. Zaharieva D, Yavelberg L, Ja mnik V, Cinor A, Turksoy K, et al. (2017) The effect of basal insulin suspension at the start of exercise on blood glucose levels during continuous versus circuit based exercise in individuals with type1 diabetes on continuous Subcutaneous insulin infusion. Diabetes Technol Ther 19(6): 370-378.

118. Aronson R, Brown RE, Li A, Riddell MC (2018) Optimal insulin correction factors in post high intensity exercise hyperglycemia in adults with type1 diabetes. The FIT Study. Diabetes Care 42(1): 10-16.

119. Schmidt MJ, Hadji-Georgopoulos A, Rendell M, Margolis S, Kowarski A (1981) The dawn phenomenon an early morning glucose rise: Implications for diabetic intraday glucose variation. Diabetes Care 4(6): 579-85.

120. Edge JA, Mattews DR, Dunger DB (1990) The dawn phenomenon is related to overnight growth hormone release in adolescent diabetes. Clin Endocrinol 33(6): 729-737.

121. Lane SC, Camera DM, Lassiter DG, Areta JL, Bird SR, et al. (2015) Effect of sleeping with reduced carbohydrate availability on acute training responses. J Appl Physiol 119(6): 643-655.

122. Bartlett JD, Louhelainen J, Iqbal Z, Cochran AJ, Gibala MJ, et al. (2013) Reduced carbohydrate availability enhances exercise induced p53 signaling in human skeletal muscle: Implications for mitochondrial biogenesis. Am J Physiol Regul Integr Comp Physiol 304(6): 450-458.

123. Marquet LA, Brisswater J, Louis J, Tiollier E, Burke LM, et al. (2016) Enhanced Endurance Performance by periodization of carbohydrate ‘‘Sleep Low’’ Strategy. Med Sci Sports Exerc 48(4): 663-672.

124. Marquet LA, Hausewirth C, Molle O, Hawley JA, Burke LM, et al. (2016) Periodization of carbohydrate Intake: Short-Term Effect on Performance. Nutrients 8(12): 755.

125. Kulvinder Kochar Kaur, Allahbadia GN, Mandeep Singh (2017) An Update on Etiopathogenesis and Management of Type 1 Diabetes Mellitus. J Endocrinol 1(2): 000107.

126. Kulvinder Kochar Kaur, Allahbadia GN, Mandeep Singh (2019) Importance of Simultaneous Treatment of Obesity and Diabetes Mellitus: A Sequelae tothe Understanding of Diabesity-A Review. Obes Res Open J 6(1): 1-10.