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ORIGINAL ARTICLE

Advances in Exercise and Nutrition as Therapy in Diabetes

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Introduction

This year, we surveyed 2200 potentially eligible titles on PubMed and other common search engines for manuscripts on ''exercise, nutrition, and diabetes'' published between July 1, 2019, and June 30, 2020. This year's articles tended to focus on testing new applications for exercise management, including new insulin treatment approaches, wearables, and new smartphone applications. On the nutrition front, we found several new studies on the role of different diets of various macro- and micronutrient contents on glucose control in type 2 diabetes. The 11 articles below highlight some of the major new publications in the field of exercise, nutrition, and diabetes.

Key Articles Reviewed for the Article

Flexible insulin therapy with a hybrid regimen of insulin degludec and continuous subcutaneous insulin infusion with pump suspension before exercise in physically active adults with type 1 diabetes (FIT Untethered): a single-centre, open-label, proof-of-concept, randomised crossover trial.

Aronson R, Li A, Brown RE, McGaugh S, Riddell MC

Lancet Diabetes Endocrinol 2020; ***8****: 511–523*

The use of a smart bolus calculator informed by real-time insulin sensitivity assessments reduces postprandial hypoglycemia following an aerobic exercise session in individuals with type 1 diabetes

Fabris C, Nass RM, Pinnata J, Carr KA, Koravi CLK, Barnett CL, Oliveri MC, Anderson SM, Chernavvsky DR, Breton MD

Diabetes Care 2020; ***43****: 799–805*

A multidisciplinary evaluation of a virtually supervised home-based high-intensity interval training intervention in people with type 1 diabetes

Scott SN, Shepherd SO, Andrews RC, Narendran P, Purewal TS, Kinnafick F, Cuthbertson DJ, Atkinson-Goulding S, Noon T, Wagenmakers AJM, Cocks M

Diabetes Care 2019; ***42****: 2330–2333*

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Impact of daily physical activity as measured by commonly available wearables on mealtime glucose control in type 1 diabetes

Ozaslan B, Patek SD, Breton MD

*Diabetes Technol Ther 2020; **22**: 742–748*

Prediction of hypoglycemia during aerobic exercise in adults with type 1 diabetes

Reddy R, Resalat N, Wilson LM, Castle JR, El Youssef J, Jacobs PG

*J Diabetes Sci Technol 2019; **13**: 919–927*

Efficacy of the Diabeloop closed-loop system to improve glycaemic control in patients with type 1 diabetes exposed to gastronomic dinners or to sustained physical exercise

Hanaire H, Franc S, Borot S, Penfornis A, Benhamou PY, Schaepelynck P, Renard E, Guerci B, Jeandidier N, Simon C, Hannaert P, Xhaard I, Doron M, Huneker E, Charpentier G, Reznik Y

*Diabetes Obes Metab 2020; **22**: 324–334*

High calcium intake from fat-free milk, body composition and glycaemic control in adults with type 2 diabetes: a randomised crossover clinical trial

Gomes JMG, de Assis Costa J, Ribeiro PVM, Alfenas RCG

*Br J Nutr 2019; **122**: 301–308*

A carbohydrate-reduced high-protein diet improves HbA1c and liver fat content in weight stable participants with type 2 diabetes: a randomised controlled trial

Skytte MJ, Samkani A, Petersen AD, Thomsen MN, Astrup A, Chabanova E, Frystyk J, Holst JJ, Thomsen HS, Madsbad S, Larsen TM, Haugaard SB, Krarup T

*Diabetologia 2019; **62**: 2066–2078*

Effects of a Mediterranean eating plan on the need for glucose-lowering medications in participants with type 2 diabetes: a subgroup analysis of the PREDIMED trial

Basterra-Gortari FJ, Ruiz-Canela M, Martínez-González MA, Babio N, Sorlí JV, Fito M, Ros E, Gómez-Gracia E, Fiol M, Lapetra J, Estruch R, Serra-Majem L, Pinto X, González JI, Bulló M, Castañer O, Alonso-Gómez Á, Forga L, Arós F for PREDIMED Study Investigators

*Diabetes Care 2019; **42**: 1390–1397*

Vitamin D supplementation and prevention of type 2 diabetes

Pittas AG, Dawson-Hughes B, Sheehan P, Ware JH, Knowler WC, Aroda VR, Brodsky I, Ceglia L, Chadha C, Chatterjee R, Desouza C, Dolor R, Foreyt J, Fuss P, Ghazi A, Hsia DS, Johnson KC, Kashyap SR, Kim S, LeBlanc ES, Lewis MR, Liao E, Neff LM, Nelson J, O'Neil P, Park J, Peters A, Phillips LS, Pratley R, Raskin P, Rasouli N, Robbins D, Rosen C, Vickery EM, Staten M, D2d Research Group

*N Engl J Med 2019; **381**: 520–530*

Dietary fibre and whole grains in diabetes management: systematic review and meta-analyses

Reynolds AN, Akerman AP, Mann J

*PLoS Med 2020; **17**: e1003053*

Flexible insulin therapy with a hybrid regimen of insulin degludec and continuous subcutaneous insulin infusion with pump suspension before exercise in physically active adults with type 1 diabetes (FIT Untethered): a single-centre, open-label, proof-of-concept, randomised crossover trial

Aronson R[1], Li A[1], Brown RE[1], McGaugh S[1], Riddell MC[1,2]

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*Lancet Diabetes Endocrinol 2020; **8**: 511–523*

Background

Individuals with type 1 diabetes who use continuous subcutaneous insulin infusion (CSII) sometimes remove their pump before exercise and sport for a variety of reasons (1). This habit may result in a rise in glucose level and perhaps a greater risk for elevated ketone production if the pump is off for too long (2). The use of a long-acting or an ultra-long-acting basal insulin analog, by once daily needle administration, theoretically could be used to maintain some insulin in circulation during prolonged pump disconnect in these individuals who tend to otherwise prefer CSII therapy. This study aimed to assess the efficacy and safety of this hybrid approach, in which basal insulin delivery was divided between CSII and a daily injection of insulin degludec.

Methods

Physically active adults with type 1 diabetes ($n = 31$), who were all initially using traditional CSII therapy, were randomized to complete various in-clinic and at-home exercise sessions over two 4-week observation blocks using two separate basal insulin strategies (traditional CSII vs hybrid CSII). For the hybrid CSII approach, the delivery of the participant's usual daily basal insulin dose was split (50% delivered by CSII and 50% delivered by a once-daily morning injection of 100 U/mL insulin degludec). The therapy was not masked to the investigators or the participants. For each intervention, participants completed a moderate-intensity and a high-intensity in-clinic exercise session in the first week, followed by four high-intensity and two moderate-intensity home-based exercise sessions in the subsequent 3 weeks. Insulin pumps were suspended or disconnected 60min before exercise and reconnected immediately after exercise during both treatment regimens to simulate pump disconnect behaviors. The time spent in the target glucose range of 4.0–10.0 mmol/L during and after high-intensity exercise and moderate-intensity exercise as measured by continuous glucose monitoring (CGM) in a 6-h window was assessed.

Results

A total of 24 of the 31 participants (77%) completed both study phases for the analysis of 302 total exercise days (48 of the days were in-clinic exercise, while the remaining 254 days were at-home exercise days). Compared with the usual CSII regimen, participants on the hybrid CSII regimen had a significantly longer time in range (TIR; 4.0–10.0 mmol/L) during the 6-h period from the start of both moderate-intensity (mean difference 86min [95% confidence interval (CI) 61–147], $P = 0.005$; percentage TIR 64% [SD 35] vs 40% [35]) and high-intensity in-clinic exercise session (60min [11–109], $P = 0.01$; 66% [32] vs 50% [27]). Participants on the hybrid CSII regimen also showed a higher TIR during home-based exercise sessions (mean difference 23min [95% CI −1 to 46], $P = 0{\cdot}055$), with significantly lower time spent in hyperglycemia than when participants were on the usual CSII regimen (mean difference 25min [2–48], $P = 0{\cdot}04$).

Conclusion

The hybrid regimen of using a proportion of basal insulin (i.e., 50%) via an ultra-long-acting insulin (degludec) once-daily injection, while maintaining a modified CSII basal insulin delivery (i.e., 50%), except for pump removal during exercise, appears to be safe and effective for glycemic control in adults with type 1 diabetes who exercise regularly.

Comment

It has long been preached by many healthcare providers to try to keep your insulin pump on at all times, even during exercise and sport. This recommendation is sometimes hard to follow for active patients living with type 1 diabetes who engage in forms of exercise (or competition) for which it is best to take the pump off (like mixed martial arts, swimming, most contact sports, etc.). This study helped to answer a number of questions related to prolonged pump removal for exercise—a phenomenon that appears to be frequent in some segments of the patient population according to various online patient community forums. First, is pump removal for prolonged exercise (∼2h) detrimental for glycemic control in type 1 diabetes? Should basal insulin be delivered via other means when the pump is expected to be removed for sport and/or exercise? If so, what approach might work? The authors demonstrate in this article that superior glycemic control can be achieved on exercise days when this 50% basal by pump, 50% basal by ultra-long-acting insulin analog approach is used. Originally, this approach was coined the "untethered regimen" by Dr. Steven Edelman in 2004, and you can read more on that here: https://childrenwithdiabetes.com/un-tethered-regimen/. This type of regimen, while allowing for prolonged pump removal for whatever reason, does place extra burden on the patient since they are obliged to take a dose of basal insulin via needle injection. Interestingly, in this study, participants were asked whether they found the hybrid CSII approach useful, and 68% of them rated it as "somewhat" or "very" useful. When asked how "bothersome" the addition of a daily basal insulin injection was, only 18% of the participants rated it as "somewhat" or "very" bothersome. After study completion, 45% of the participants felt that they would be "somewhat likely" or "very likely" to continue using the untethered approach. Thus, overall, this hybrid CSII approach may serve to help a select few who prefer to exercise with their pumps off.

The use of a smart bolus calculator informed by real-time insulin sensitivity assessments reduces postprandial hypoglycemia following an aerobic exercise session in individuals with type 1 diabetes

Fabris C[1], *Nass RM*[2], *Pinnata J*[1], *Carr KA*[1], *Koravi CLK*[1], *Barnett CL*[1], *Oliveri MC*[1], *Anderson SM*[1], *Chernavvsky DR*[1,3], *Breton MD*[1]

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Diabetes Care 2020; ***43****: 799–805*

Background

Minute-by-minute insulin needs in type 1 diabetes are variable not only because of food intake, but also because of changing insulin sensitivity (IS) caused by various metabolic and psychobehavioral factors, such as stress, illness, and exercise. This research examined the incorporation of exercise information into a meal bolus calculator that estimated changes in whole body IS caused by aerobic exercise in adults with type 1 diabetes.

Methods

Adults with type 1 diabetes ($n=15$) on continuous subcutaneous insulin infusion (CSII) with continuous glucose monitoring (CGM) completed two 24-h admissions in a hotel setting. In both admissions, participants performed early afternoon exercise (45min of cycling), after which they received a standardized dinner ($\sim$0.75–0.85 g/kg carbohydrates). The dinner bolus was computed using a standard bolus calculator or smart bolus calculator informed by real-time IS estimates. Glucose control was assessed using CGM in the 4-h following dinner and compared between the two admissions.

Results

The use of the IS-informed bolus calculator promoted a reduction in postprandial hypoglycemia, as quantified by the low blood glucose index (2.02 vs 3.31, $P=0.006$) and percent time <70 mg/dL (8.48% vs 15.18%, $P=0.049$), without increasing hyperglycemia. The number of hypoglycemic rescue events was reduced from 14 to 7 (of the 14 who completed both visits) with the use of the IS-informed bolus calculator.

Conclusion

The study shows that the proposed IS-informed dinner bolus calculator is safe and effective in reducing postprandial hypoglycemia without promoting hyperglycemia in adults with type 1 diabetes who have completed a 45-minute bout of cycling exercise before the meal.

Comment

The risk of nocturnal hypoglycemia following afternoon exercise is high in individuals with type 1 diabetes (3). The greater risk for hypoglycemia in the hours after exercise is likely related to the increase in insulin sensitivity in the body that can last for several hours (4), thereby potentially reducing dinner bolus insulin needs (5). The challenge of developing delivery systems that account for external factors that impact insulin requirement—for example, exercise—is well recognized. Iterative progress in the algorithms has improved the user experience of insulin delivery devices; however, automated insulin delivery during and following exercise has remained particularly challenging. This study used a novel engineering approach (6) that relies on parameter identification techniques to model specific meal dynamics and a Kalman filter-based state estimation to track individual IS over the period of interest after exercise. The authors found roughly a 30% increase in IS caused by this type of exercise (cycling for 45min at a moderate-intensity), and this information was then used to temper the meal bolus to help reduce hypoglycemia while still maintaining excellent postprandial control. Although not all events of hypoglycemia were eliminated, the IS-informed calculator cut hypoglycemic events by half. This work demonstrates both exciting and encouraging potential for exercise-smart bolus calculators in diabetes devices such as smart pumps or other decision-support tools.

A multidisciplinary evaluation of a virtually supervised home-based high-intensity interval training intervention in people with type 1 diabetes

Scott SN[1], *Shepherd SO*[1], *Andrews RC*[2], *Narendran P*[3], *Purewal TS*[4], *Kinnafick F*[5], *Cuthbertson DJ*[6], *Atkinson-Goulding S*[1], *Noon T*[1], *Wagenmakers AJM*[1], *Cocks M*[1]

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Diabetes Care 2019; ***42****: 2330–2333*

Background

High-intensity interval training (HIT) is recommended for people living with diabetes as an optional exercise strategy to improve cardiometabolic fitness (7). However, much of the data demonstrating efficacy and safety of HIT in type 1 diabetes has been collected from carefully supervised and highly controlled in-clinic experiments. This study used a multidisciplinary approach to evaluate a novel, virtually monitored home-based HIT (Home-HIT) intervention in adults living with type 1 diabetes.

Methods

Eleven individuals with type 1 diabetes (7 women; age 30 ± 3 years [mean ± SD]; duration of diabetes 10 ± 2 years; HbA1c

8.0 ± 0.6% [64 ± 7 mmol/mol]; BMI 27.3 ± 1.6 kg/m^2; daily insulin dose 0.31 ± 0.06 IU/kg/day) completed six weeks of Home-HIT. A heart-rate monitor and mobile phone application were used to provide feedback to the participants and research team on exercise intensity (compliance) and adherence. Participants performed repeated 1-min bouts of high-intensity exercise (calisthenics, with a target heart rate of ≥ 80% of their age-predicted maximum) interspersed with 1min of rest. They were advised to train three times per week in a fasted state and complete six 1-min intervals per session in weeks 1–2, increasing to eight intervals in weeks 3–4 and 10 intervals in weeks 5–6.

Results

Adherence to the Home-HIT prescription was 95% (ranging from 83%–100%). Blood glucose remained stable during and after exercise, while carbohydrate consumption to treat hypoglycemia was rare (in 10 of 188 sessions) as was the need for corrective insulin bolus postexercise (3 of 188 sessions). Aerobic fitness (VO_{2peak}) increased by 7% ($P = 0.017$), while there was a 13% decrease ($P = 0.012$) in short-acting insulin use. Mean glucose levels, as measured by a 7-day, 8-point diary, and body mass index did not change.

Conclusion

This study shows that virtually monitored Home-HIT is a safe, effective, and acceptable strategy for supporting exercise in people with type 1 diabetes.

Comment

For many, starting a new vigorous exercise training regimen under the supervision of a trainer can be intimidating and costly. Moreover, many trainers in fitness centers have little knowledge of the unique circumstances that people with diabetes often face when they exercise. Hypoglycemia, hyperglycemia, fear of a loss in glucose control, and body image issues are frequent challenges for people living with diabetes. Learning how to perform the activities at the correct pace can be an additional challenge. During the ongoing COVID-19 pandemic, many people with diabetes are trying (or should be trying) to get some exercise while at home. This innovative study by Scott and colleagues clearly shows that high-intensity interval training at home can be achieved with good success by adults living with type 1 diabetes. The reduction in total bolus insulin needs by 13% in this article is worth noting, as are the improvements in aerobic fitness gains by 7%. The finding that the virtually monitored home-HIT protocol is an impressive training approach is in-line with what has been published previously in a supervised clinic study of type 1 diabetes (8), but the current study is a much more cost-effective approach and elicited good safety results. If the exercise modalities could be digitized into an app with more advanced training options, along with better strategies for glucose control, then perhaps exercising at home could end up being safer and more effective than joining a gym!

Impact of daily physical activity as measured by commonly available wearables on mealtime glucose control in type 1 diabetes

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*Diabetes Technol Ther 2020; **22**: 742–748*

Background

Research shows that increasing levels of daily physical activity can lead to improved health benefits (9,10). In contrast, with structured physical activity or exercise, glycemic disturbances due to daily unstructured physical activity in individuals with type 1 diabetes are largely under-researched and treatment recommendations are limited. The purpose of this retrospective analysis was to determine the impact of daily physical activity, as measured by an off-the-shelf activity tracker, on postprandial blood glucose control in individuals with type 1 diabetes in free-living conditions.

Methods

Data was captured from two clinical trials with identical data collection protocols and retrospectively analyzed. A total of 37 individuals with type 1 diabetes were included in this analysis. The data collected included 4 weeks of continuous glucose monitoring, carbohydrate intake, insulin injections, and activity that was assessed via wearable activity tracker in free-living conditions. Five-hour glucose area under curves (GAUC) after the last meal bolus of each day were calculated to determine the postprandial glucose excursions, and relations with corresponding antecedent physical activity was analyzed using linear mixed effects regression models, accounting for meal, insulin, and current blood glucose state.

Results

A total of 845 days of data was collected from 37 subjects (22.8 ± 11.6 days/subject). The postmeal GAUC was negatively associated with total daily physical activity measured by step count ($P = 0.025$), and total time spent performing higher than light-intensity activity ($P = 0.042$). Subjects with higher median total daily physical activity had lower average postprandial GAUC ($P < 0.01$).

Conclusion

This analysis found that daily physical activity assessed by commonly available activity trackers is significantly associated with reduced glucose exposure following an evening meal. Thus, quantitative assessment of daily physical activity patterns may aid in mealtime treatment decisions.

Comment

Physical activity in individuals with type 1 diabetes has many health benefits, including improvements in cardiovascular and mental health, better weight management, and increased insulin sensitivity (2). However, following a bout of afternoon exercise, individuals with type 1 diabetes are at heightened risk of late-onset (11) or nocturnal hypoglycemia (12,13). In this study, Ozaslan et al. examine the impact of daily physical activity, using a commercially available activity tracker, on postprandial glucose control and to explore how available information from activity trackers can help improve glycemic control in type 1 diabetes. Importantly, and often overlooked, is the impact of unstructured or daily activity and the impact it may have on blood glucose levels in individuals with type 1 diabetes. The results of this study demonstrate at least two important findings: (1) there is an inverse association between daily physical activity levels and postprandial glucose exposure, and (2) commercially available activity trackers can be used to better estimate insulin needs to manage postprandial glucose control. Using these activity trackers, future studies can now focus on the incorporation of various activity metrics, such as activity volume, intensity, and timing of daily habitual activity on insulin dosing adjustments.

Prediction of hypoglycemia during aerobic exercise in adults with type 1 diabetes

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*J Diabetes Sci Technol 2019; **13**: 919–927*

Background

Although guidelines strongly recommend regular physical activity for individuals with type 1 diabetes (2,7), a primary barrier to exercise is the fear of hypoglycemia (14,15). The integration of accelerometers and physical activity trackers into artificial pancreas (AP) systems has allowed better detection of activity to avoid exercise-associated hypoglycemia. This article presents two new algorithms to better predict and identify the risk of hypoglycemia at the onset of exercise.

Methods

The two developed algorithms are referred to as Model 1, which is a decision tree model, and Model 2, which is a random forest model. Data was compiled from three different randomized clinical trials at Oregon Health & Science University and both models were trained using a metadata set based on 154 exercise observations in 43 adults with type 1 diabetes. Participants used either sensor-augmented pump therapy, automated insulin delivery therapy, or automated insulin and glucagon therapy. Both models were validated with 90 exercise observations collected from 12 new adults with type 1 diabetes.

Results

Heart rate and glucose at exercise onset were identified as two critical features of predicting hypoglycemia during exercise in Model 1. Hypoglycemia was predicted with 80% accuracy if glucose at exercise start was less than 182 mg/dL and if heart rate rose greater than 121 bpm during the first 5 minutes of exercise. With additional features and higher complexity in Model 2, hypoglycemia was predicted with 87% accuracy.

Conclusion

This study provides evidence with the validation models that algorithms can accurately identify and possibly prevent hypoglycemia associated with exercise. As a rule of thumb, the simple Model 1 can use the 180/120 rule; Model 2 is more complex and uses additional features but with greater accuracy in predicting hypoglycemia.

Comment

Although exercise consensus guidelines and position statements have been well established for type 1 diabetes (2,7,16), these suggestions generally serve as starting points and often require tailoring for individualized needs. In addition, the current guidelines are primarily targeted toward blood glucose management strategies for open loop therapy. With the increasing use of closed-loop systems in type 1 diabetes, less is known around guidance and strategies for glycemic control during physical activity. Reddy and colleagues acknowledge the complexity of insulin kinetics and dynamics related to exercise and as such, developed two algorithms to predict hypoglycemia at exercise onset in the present study. The data was compiled from three different randomized clinical studies including 154 exercise observations. The two models were (1) decision tree and (2) random forest. In this study, the simple decision tree model (180/120 rule) describes avoidance of hypoglycemia based on heart rate and glucose at exercise onset. The random forest model uses additional features and requires computational resources to capture nonlinear interactions between the input features. Overall, Model 2 (random forest) was able to more accurately predict hypoglycemia versus Model 1 (decision tree) with 87% vs 80% accuracy, respectively. In conclusion, this study provides evidence that the validated models using pre-exercise glucose levels and exercise intensity (i.e., heart rate) can accurately identify and possibly prevent exercise-associated hypoglycemia in most cases. Further research is required in this area, particularly using real-life exercise settings rather than exercise from a controlled inpatient environment.

Efficacy of the Diabeloop closed-loop system to improve glycaemic control in patients with type 1 diabetes exposed to gastronomic dinners or to sustained physical exercise

Hanaire H[1], Franc S[2], Borot S[3], Penfornis A[2,4], Benhamou PY[5], Schaepelynck P[6], Renard E[7], Guerci B[8], Jeandidier N[9], Simon C[10], Hannaert P[11], Xhaard I[12], Doron M[13,14], Huneker E[15], Charpentier G[2], Reznik Y[16]

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*Diabetes Obes Metab 2020; **22**: 324–334*

Background

Automated insulin delivery or closed-loop (CL) systems have been shown to effectively and safely reduce blood glucose variability in individuals with type 1 diabetes (17,18). The Diabeloop single-hormone CL system runs a model predictive control algorithm and has also been proven to be safe and effective in prior studies (19). This study compared open-loop (OL) vs CL systems on blood glucose control in adults with type 1 diabetes that were exposed to challenging, real-life situations (i.e., gastronomic dinners or sustained physical activity).

Methods

This was a randomized, 72-h crossover pilot trial that included 38 adults with type 1 diabetes comparing glycemic control using an open vs CL device. The three conditions included: (1) large (gastronomic) dinners; (2) sustained and repeated bouts of prolonged aerobic exercise (with uncontrolled food intake); and (3) control (rest). This study assessed glucose time in ranges (4.4–7.8 mmol/L and 3.9–10.0 mmol/L) and time in hypo- and hyperglycemia.

Results

Overnight, the time spent in the tight range (4.4–7.8 mmol/L) was longer with CL (mean: 63.2% vs 40.9% with OL; $P \leq 0.0001$). During the day, time in range (3.9–10.0 mmol/L) was also longer with CL (79.4% vs 64.1% with OL; $P \leq 0.0001$). In addition, during the day, participants using the CL system spent less time in hyperglycemia (> 10.0 mmol/L) vs OL (17.9% vs 31.9%; $P \leq 0.0001$). Time spent with hyperglycemia during the day for those using CL in the gastronomic dinner and physical exercise groups were similar to those in the control group (18.1 ± 6.3%, 17.2 ± 8.1%, and 18.4 ± 12.5%, respectively). Lastly, time spent in hypoglycemia was not significantly different among groups.

Conclusion

In summary, when individuals with type 1 diabetes were exposed to gastronomic dinners or exercise followed by uncontrolled food and carbohydrate intake, the CL system more effectively reduced hyperglycemia compared to OL.

Comment

The increase in blood glucose turnover during exercise, in addition to consumption of large meals, can both lead to disturbances in glycemic control (20). CL systems are often limited by their inability to detect the type and intensity of physical activity being performed, both of which would better determine the necessary insulin requirements for exercise (21). In this multicenter study, 38 adults with type 1 diabetes were randomized to either Diabeloop CL system first, follow by OL, or vice versa. Hanaire et al. investigated the real-life impact of large (gastronomic) dinners or sustained exercise on glycemic control with the use of CL versus OL insulin delivery systems. Participants were divided into three groups, including (1) rest (control), (2) gastronomic dinners, and (3) sustained exercise, followed by uncontrolled food and carbohydrate intake. Overall, the Diabeloop CL system led to 23.9% longer time in range (3.9–10.0 mmol/L) versus OL. Time spent in hypoglycemia was < 5% and not significantly different across all groups. The CL system also led to marked reductions in hyperglycemia following both gastronomic dinners and sustained exercise. These types of studies provide valuable and promising data toward overall improvements in glycemic control in the short-term; however, future studies are needed in real-life settings with a variety of exercise types and for longer periods of study.

High calcium intake from fat-free milk, body composition and glycaemic control in adults with type 2 diabetes: a randomised crossover clinical trial

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*Br J Nutr 2019; **122**: 301–308*

Background

This study by Gomes et al. compared the effects of low-calcium (low-Ca) versus high-calcium (high-Ca) fat-free milk consumption on glycemic control and obesity in adults with type 2 diabetes.

Methods

This was a randomized crossover clinical trial that included 14 subjects with type 2 diabetes and low habitual Ca consumption (< 600 mg/d). Participants completed two 12-week experimental sessions (high-Ca, fat-free milk [HC] or low-Ca control [LC]) separated by 8-week washout. In the laboratory, participants consumed a daily breakfast shake of 700 mg (HC) or 6.4 mg (LC) of Ca. Energy-restricted diets (800 mg of dietary calcium per day [Ca/d]) were prescribed.

Results

Dietary records data indicated the consumption of 1200 mg of Ca/d during HC and of 525 mg of Ca/d during LC. There was a greater reduction in body weight, body fat mass, waist circumference, and waist:hip ratio after HC. After HC, there was an increase in serum 25-hydoxyvitamin D and homeostatic model assessment-2 β-cell function (HOMA2-%B), and decrease in serum uric acid, parathormone (PTH), and glycated Hb (HbA1c) concentrations. The serum uric acid, glucose, HbA1c, and PTH concentrations were lower from baseline, and HOMA2-%B, serum Ca, and 25-hydoxyvitamin D were higher after the HC compared to after the LC.

Conclusion

The authors concluded that consuming approximately three servings of fat-free milk and 1200 mg of dietary Ca/d promoted greater weight loss, improved body composition, and promoted glycemic control in individuals with type 2 diabetes versus low habitual Ca consumption (< 600 mg/d).

Comment

The role of milk consumption in weight regulation has been controversial; in fact, the recent 2020 U.S. Dietary Guidelines Advisory Committee Scientific Report stated that ''Limited evidence suggests that milk intake is not associated with adiposity in adults'' (22). The study by Gomes et al. focused on adults with type 2 diabetes and sought to evaluate the effect of high-calcium, fat-free milk on body composition and glycemic control. Participants were provided with the high-calcium, fat-free milk or a low-calcium control that was similar in macronutrients, vitamin D, sodium, and fiber in the context of energy-restricted diets. Although the sample size was small and the length of the study fairly short, results were promising, both in regard to weight as well as additional markers of metabolic health. Whether calcium supplements or other dietary sources of calcium would have a similar effect is yet to be learned. It will also be important to validate these findings among individuals with type 2 diabetes who are treated with insulin, as well as older adults with diabetes (> 60 years of age). Finally, it is important to note that the intervention was effective among individuals with low habitual calcium intake (< 600 mg/d), which precludes generalizability to individuals who may exceed this daily intake as part of a typical western diet. Overall, this study opens doors to new research to tackle the vexing problems of weight management and glycemic control in type 2 diabetes.

A carbohydrate-reduced high-protein diet improves HbA1c and liver fat content in weight stable participants with type 2 diabetes: a randomised controlled trial

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Background

While overweight adults with type 2 diabetes were once advised to consume a high-carbohydrate/low-glycemic-index diet based on reasonable evidence (23), recent guidelines are putting less emphasis on macronutrient distribution in favor of individualized diets (24,25). This research examined the question of if a carbohydrate-reduced high-protein (CRHP) diet could improve glycemic control as compared to a more conventional diet (CD) that was higher in low-glycemic-index carbohydrates in individuals with type 2 diabetes.

Methods

Twenty-eight adults with type 2 diabetes completed both the CD strategy for 6 weeks and the CRHP diet for 6 weeks in a randomized counterbalance cross-over design. The CD/CRHP diets contained carbohydrate 50/30 energy percent (E%), protein 17/30E%, and fat 33/40E%, respectively. Participants underwent a meal test at the end of each diet period and glycemic variables; lipid profiles; 24-h blood pressure; and ectopic fat, including liver and pancreatic fat content, were assessed at baseline and at the end of each diet period.

Results

The 6-week, highly controlled CRHP diet was shown to improve glycemic control as measured by HbA1c (mean ± SEM: -6.2 ± 0.8 mmol/mol (-0.6 ± 0.1%) vs -0.75 ± 1.0 mmol/mol (-0.1 ± 0.1%); $P < 0.001$), likely by reducing both fasting (-0.71 ± 0.20 mmol/l vs 0.03 ± 0.23 mmol/l; $P < 0.05$) and postprandial (area under the curve $= 9.58 \pm 0.29$ mmol/l $\times$ 240min vs 11.89 ± 0.43 mmol/l $\times$ 240min; $P < 0.001$) glucose levels. Hepatic fat reduction was also greater with CRHP (-2.4% [-7.8% to -1.0%]) as compared to CD (0.2% [-2.3% to 0.9%]; $P < 0.01$) as was pancreatic fat content reduction (-1.7% [-3.5% to 0.6%] vs

0.5% [−1.0% to 2.0%]; $P<0.05$). Changes in other secondary outcomes, that is, 24-h blood pressure and muscle-, visceral- or subcutaneous adipose tissue, did not differ between diets.

Conclusion

A moderate macronutrient shift by substituting low glycemic index carbohydrates with protein and fat for 6 weeks reduces HbA1c and hepatic fat content in weight stable individuals with type 2 diabetes.

Comment

Let's face it. Seeing long-term successes on glycemic control and body mass with dietary interventions in diabetes is a challenge (26–28). This study shows, however, that a 6-week intervention of a low-carbohydrate/high-protein meal plan, which was provided free of charge (five meals a day), can profoundly improve glycemic control and lower liver and pancreatic fat stores. The finding that a low-carbohydrate diet can work to improve glucose control in type 2 diabetes largely by reducing meal excursions is in line with previous work looking at acute glucose control (29). While impressive, the reality remains that changing eating habits may be difficult in all subtypes of diabetes, and the adherence of such a low-carbohydrate/high-protein diet in reality may be much more challenging if the food preparation was up to the patient.

Effects of a Mediterranean eating plan on the need for glucose-lowering medications in participants with type 2 diabetes: a subgroup analysis of the PREDIMED trial

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Background

A key component of type 2 diabetes management includes healthy eating patterns, such as the Mediterranean eating plan (Med-EatPlan). Basterra-Gortari et al. investigated the effect of two Med-EatPlans on the need for glucose-lowering medication versus a low-fat control eating plan.

Methods

This study included 3230 participants with type 2 diabetes from the Prevención Dieta Mediterránea (PREDIMED) trial. Participants were randomly assigned to one of the following: (1) Med-EatPlan with added extra virgin olive oil (EVOO), (2) MedEatPlan with mixed nuts, or (3) a low-fat eating plan as the control. Instead of individual randomization, in a subgroup (15%), the allocation was done in small clusters. The following two outcomes were evaluated: (1) introduction of the first glucose-lowering medication (oral or injectable) among participants on lifestyle management at enrollment and (2) insulin initiation.

Results

In a multivariable analysis adjusting for baseline characteristics and propensity scores, after a median 3.2-year follow-up, the hazard ratios (HRs) of starting a first glucose-lowering medication were 0.78 (95% CI 0.62–0.98) for Med-EatPlan + EVOO and 0.89 (0.71–1.12) for Med-EatPlan + nuts, versus the control eating plan. After a median follow-up of 5.1 years, the adjusted HRs of starting insulin treatment were 0.87 (0.68–1.11) for Med-EatPlan + EVOO and 0.89 (0.69–1.14) for Med-EatPlan + nuts versus the control eating plan.

Conclusion

Basterra-Gortari and colleagues found that a Med-EatPlan + EVOO may delay the introduction of new-onset, glucose-lowering medications in individuals with type 2 diabetes. Overall, the Med-EatPlan did not result in a significantly lower need for insulin.

Comment

It is well known that underlying glucose dysregulation generally begins several years before a clinical diagnosis of type 2 diabetes, and that cardiovascular disease (CVD) risk profile is often already substantially compromised by that time. It is also widely appreciated that a healthy diet can improve CVD risk profile. Here, it was shown that the Mediterranean diet pattern supplemented by extra virgin olive oil delayed the need to initiate glucose-lowering medications among individuals with type 2 diabetes in the PREDIMED trial, once again confirming the benefits of healthy dietary patterns. However, we know that type 2 diabetes is a progressive disease, and neither the Mediterranean diet plus EVOO nor the Mediterranean diet plus nuts delayed the need to initiate insulin treatment. Nonetheless, it is important to note that these diets did provide primary protection for individuals both with and without type 2 diabetes against CVD outcomes (30), an independent benefit and a message that ought not be lost. This study, in the context of other results that have been published from the PREDIMED trial, underscores the important role of dietary patterns rather than single nutrient approaches for delaying the progression and complications of type 2 diabetes.

Vitamin D supplementation and prevention of type 2 diabetes

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Background

Observational studies support an association between a low blood 25-hydroxyvitamin D level and the risk of diabetes; however, it is currently unclear whether vitamin D supplementation lowers the risk of type 2 diabetes.

Methods

Participants that met at least two of three glycemic criteria for prediabetes (fasting plasma glucose level, 100–125 mg/dL; plasma glucose level 2 hours after a 75-g oral glucose load, 140–199 mg/dL; and glycated hemoglobin level, 5.7%–6.4%) and no diagnostic criteria for diabetes were randomized to receive 4000 IU per day of vitamin D3 or placebo, regardless of the baseline serum 25-hydroxyvitamin D level. New-onset diabetes was the primary outcome in this time-to-event analysis, and the trial design was event-driven with a target number of diabetes events of 508.

Results

A total of 1211 participants were randomized to the vitamin D group and 1212 to the placebo group. The mean serum 25-hydroxyvitamin D level in the vitamin D group by month 24 was 54.3 ng/mL (from 27.7 ng/mL at baseline), versus 28.8 ng/mL in the placebo group (from 28.2 ng/mL at baseline). After 2.5-year median follow-up, the primary outcome of diabetes occurred in 293 participants in the vitamin D group and 323 in the placebo group (9.39 and 10.66 events per 100 person-years, respectively). The hazard ratio for vitamin D versus placebo was 0.88 (95% CI, 0.75 to 1.04; $P = 0.12$). In addition, there was no significant difference in the incidence of adverse events between the two groups.

Conclusion

Pittas and colleagues found that among individuals at high risk for type 2 diabetes not selected for vitamin D insufficiency, vitamin D3 supplementation at a dose of 4000 IU per day did not result in a significantly lower risk of diabetes versus placebo after a median follow-up of 2.5 years.

Comment

There has been an explosion of papers in the literature over the last 5+ years on the topic of vitamin D and risk for type 2 diabetes. This long-awaited randomized controlled trial was preceded by studies ranging from basic science and clinical studies to large epidemiological studies focused on the potential role of vitamin D in modulating insulin sensitivity, insulin secretion, and body composition. Results were, frankly, more than a little frustrating for many, with an association in the direction desired, but a *P*-value of 0.12. Moreover, the investigators were not able to identify a particular subgroup—race or ethnicity, sex, age, body mass index, or even geographic latitude—according to baseline serum vitamin D levels for whom vitamin D supplementation was protective against developing diabetes. One limitation to note is that a high percentage of the trial participants had sufficient baseline vitamin D levels, so statistical power was limited to detect differences in the effect of vitamin D supplementation according to baseline level. It remains possible that there exists a subgroup of individuals who, for reasons of genetic drivers of vitamin D metabolism or varying risk determinants for type 2 diabetes, may substantially benefit from vitamin D supplementation; this remains to be seen. While these null results should not preclude the future study of vitamin D for other potential benefits for patients with type 2 diabetes, the trial serves as a reminder of how disparate the results of clinical and epidemiologic studies and randomized trials may be and underscores the importance of careful interpretation of each respective study design prior to drawing conclusions.

Dietary fibre and whole grains in diabetes management: systematic review and meta-analyses

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Background

Fiber is commonly promoted as part of a healthy diet in general and in diabetes management. More specifically, higher intakes of dietary fiber are associated with a reduction in premature mortality and incidence of numerous diseases.

Methods

Reynolds and colleagues conducted a systematic review and meta-analysis of dietary fiber and explored whether it has the potential to improve glycemic control in type 1 diabetes and prediabetes. A total of 8300 adults with type 1 or type 2 diabetes were followed for an average of 8.8 years, and 42 trials including 1789 adults with type 1 diabetes, prediabetes, or type 2 diabetes were identified.

Results

The prospective cohort data indicate an absolute reduction of 14 fewer deaths (95% CI 4–19) per 1000 participants over the study duration, when comparing a daily dietary fiber intake of 35 g with the average intake of 19 g. Increased fiber intakes resulted in reduced HbA1c (mean difference [MD] −2.00 mmol/mol, 95% CI −3.30 to −0.71 from 33 trials), fasting plasma glucose (MD −0.56 mmol/L, 95% CI −0.73 to −0.38 from 34 trials), insulin (standardized mean difference [SMD] −2.03, 95% CI −2.92 to −1.13 from 19 trials), homeostatic model assessment of insulin resistance (HOMA IR; MD −1.24 mg/dL, 95% CI −1.72 to −0.76 from 9 trials), total cholesterol (MD −0.34 mmol/L, 95% CI −0.46 to −0.22 from 27 trials), low-density lipoprotein (LDL) cholesterol (MD −0.17 mmol/L, 95% CI −0.27 to −0.08 from 21 trials), triglycerides (MD −0.16 mmol/L, 95% CI −0.23 to −0.09 from 28 trials), body weight (MD −0.56 kg, 95% CI −0.98 to −0.13 from 18 trials), body mass index (BMI; MD −0.36, 95% CI −0.55 to −0.16 from 14 trials), and C-reactive protein (SMD −2.80, 95% CI −4.52 to −1.09 from 7 trials) when compared with lower fiber diets. Potential limitations included the lack of data in non-European countries and the lack of long-term (≥12 months) studies of increasing fiber intake in adults with diabetes.

Conclusion

In this analysis, Reynolds et al. found that participants in prospective cohort studies consuming higher intakes of dietary fiber had a reduced risk of premature mortality when compared with those with lower fiber intakes. These benefits were apparent across the range of fiber intakes and were not confined to the type of fiber or type of diabetes. Overall, increasing daily fiber intake between 15–35 grams may aid in reducing the risk of premature mortality in adults with diabetes.

Comment

For time immemorial, a wide range of dietary composition and dietary intake patterns have been promoted for health benefits. More specifically, interest has focused on the impact of dietary approaches on disease outcomes. The recommendations for diabetes have changed many times, and the evidence has often been confusing for both healthcare professionals and consumers. It is also difficult to tease out one dietary component and its contribution to health from another. For example, at one time, there was enthusiasm for benefits of high-carbohydrate diets, until it was appreciated the positive outcomes were probably secondary to the high fiber rather than the carbohydrate itself. Those limitations aside, dietary fiber is one dietary element that has long been linked with health benefits, and this article aimed to address the question of health benefit of dietary fiber for people with both type 1 and type 2 diabetes on mortality, cardiovascular risk factors, and glycemic control. A detailed and thorough systematic review and meta-analysis confirms the benefits of dietary fiber across all outcome measures, and benefits do not seem restricted to one particular form of fiber. This is not a surprising finding given the recognized value of fiber for gut health and other conditions. This article reinforces the evidence to encourage consumption of up to 35 grams per day of fiber in those living with diabetes. The bigger challenge is how to implement this knowledge, as poor diet and food insecurity are increasing concerns for many of the families living with diabetes.

Author Disclosure Statement

No competing financial interests exist.

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