Advances in Exercise, Physical Activity, and Diabetes Mellitus

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Introduction

IN 2015/2016, A NUMBER OF PAPERS were published on the challenges of exercise management for patients living with diabetes. A big focus was on testing how the artificial pancreas might function during exercise, with or without activity announcements and the addition of glucagon. Moreover, several papers revealed barriers to exercise participation for people living with type 1 or type 2 diabetes. A few papers demonstrated that many of the tools for the preservation of glucose control during and after exercise in type 1 diabetes are not being used. This year, we selected 10 papers to highlight the field of exercise and diabetes, with an emphasis on “technology” rather than on the possible mechanisms for exercise action. Our initial search was restricted to human studies and primarily on studies in which patients with diabetes served as subject participants. We screened over 150 papers on the topic that were found on Pubmed and other common search engines published between July 1, 2015 and June 30, 2016. The following 10 papers, we think, represent some of the highlights.

Key Articles Reviewed for the Article

Algorithm that delivers an individualized rapid-acting insulin dose after morning resistance exercise counters post-exercise hyperglycaemia in people with type 1 diabetes

Turner D, Luzio S, Gray BJ, Bain SC, Hanley S, Richards A, Rhydderch DC, Martin R, Campbell MD, Kilduff LP, West DJ, Bracken RM

Diabet Med 2016; 33: 506–510

Randomized trial of dual-hormone artificial pancreas with dosing adjustment during exercise compared with no adjustment and sense-augmented pump therapy

Jacobs PG, El Youssef J, Reddy R, Resalat N, Branigan D, Condon J, Preiser N, Katrina Ramsey, Jones M, Edwards C, Kuehl K, Leitschuh J, Rajhbeharrysingh U, Castle J

Diabetes Obes Metab 2016; 18: 1110–1118.

Metabolic effects of exercise training among fitness-nonresponsive patients with type 2 diabetes: the HARTD study

Pandey A, Swift DL, McGuire DK, Ayers CR, Neeland IJ, Blair SN, Johannsen N, Earnest CP, Berry JD, Church TS

Diabetes Care 2015; 38: 1494–1501

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Insulin-based strategies to prevent hypoglycaemia during and after exercise in adult patients with type 1 diabetes on pump therapy: the DIABRASPORT randomized study

Franc S, Daoudi A, Pochat A, Petit MH, Randazzo C, Petit C, Martine Duclos M, Penfornis A, Pussard E, Not D, Heyman E, Koukoui F, Simon S, Charpentier G

Diabetes Obes Metab 2015; **17**: 1150–1157

Impact of physical activity on glycemic control and prevalence of cardiovascular risk factors in adults with type 1 diabetes: a cross-sectional multicenter study of 18,028 patients

Bohn B, Herbst A, Pfeifer M, Krakow D, Zimny S, Kopp F, Melmer A, Steinacker JM, and Holl RW, for the DPV Initiative

Diabetes Care 2015; **38**: 1536–1543

Do youth with type 1 diabetes exercise safely? A focus on patient practices and glycemic outcomes

Roberts AJ, Yi-Frazier JP, Aitken KE, Mitrovich CA, Pascual MF, Taplin CE

Pediatr Diabetes 2016; Jul 6. [Epub ahead of print] DOI 10.1111/pedi.12402

General practitioners' barriers to prescribe physical activity: the dark side of the cluster effects on the physical activity of their type 2 diabetes patients

Lanthers C, Duclos M, Guttmann A, Coudeyre E, Pereira B, Ouchchane L

PLoS One 2015; **10**: e0140429.

Effects of high-intensity interval exercise versus moderate continuous exercise on glucose homeostasis and hormone response in patients with type 1 diabetes mellitus using novel ultra-long-acting insulin

Moser O, Tschakert G, Mueller A, Groeschl W, Pieber T, Obermayer-Pietsch B, Koehler G, Hofmann P

PLoS One 2015; **10**: e0136489

Classification of physical activity: information to artificial pancreas control systems in real time

Turksoy K, Paulino TM, Zaharieva DP, Yavelberg L, Jamnik V, Riddell MC, Cinar A

J Diabetes Sci Technol 2015; **9**: 1200–1207

One week of bed rest leads to substantial muscle atrophy and induces whole-body insulin resistance in the absence of skeletal muscle lipid accumulation

Dirks ML, Wall BT, van de Valk B, Holloway TM, Holloway GP, Chabowski A, Goossens GH, van Loon LJC

Diabetes 2016; **65**: 2862–2875.

Algorithm that delivers an individualized rapid-acting insulin dose after morning resistance exercise counters post-exercise hyperglycaemia in people with type 1 diabetes

Turner D^{1,2}, Luzio S^{2,3}, Gray BJ^{1,2}, Bain SC^{2,3}, Hanley S¹, Richards A³, Rhydderch DC³, Martin R⁴, Campbell MD⁵, Kilduff LP¹, West DJ⁵, Bracken RM^{1,2}

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Diabet Med 2016; **33**: 506–510

Background

In type 1 diabetes, weight training and other forms of anaerobic exercise can acutely increase blood glucose levels. How to manage postexercise hyperglycemia safely and effectively in this patient population is currently unclear. The goal of this study was to test an insulin dose adjustment algorithm that delivers an individualized dose of rapid-acting insulin analog after morning resistance exercise to counter postexercise hyperglycemia in individuals with type 1 diabetes.

Methods

Eight people with type 1 diabetes (6 men; 2 women, all on multiple daily insulin injections (MDI)), in fair glycemic control ($8.7\% \pm 1.1\%$, mean $\pm$ standard error) attended two morning laboratory sessions in a fasted state, having taken their usual basal insulin the previous evening. They performed a resistance exercise session comprising of six exercises for two sets of 10 repetitions at 60% of the maximum amount of force that was generated in one maximal contraction. In a counterbalanced order, the subjects were administered either an individualized dose of rapid-acting insulin ($\sim 2 \pm 1$ units, range 0 to 4 units) based on a modification of their own hyperglycemia correction factor (reduced by 50%) or were not administered insulin in recovery. Venous blood glucose concentrations were measured up until 125 min following resistance exercise.

Results

Pre-exercise blood glucose averaged 11.2 ± 1.2 in both sessions. Participants had a rise in blood glucose in both sessions (insulin session increased to 13.0 ± 1.6 vs. no-insulin session increasing to 12.7 ± 1.5 mmol/L; $P=0.834$). The decline in blood glucose concentration between the peak glucose and 125 min mark after exercise was greater in the insulin administered session than in the no-insulin session (3.3 ± 1.0 vs. 1.3 ± 0.4 mmol/L; $P=0.015$). There were no episodes of hypoglycaemia during that same time frame in either session.

Conclusions

These authors propose that the administration of rapid-acting insulin according to an individualized algorithm reduces hyperglycemia after morning resistance exercise without causing hypoglycaemia in the 2 h postexercise window in people with type 1 diabetes.

Kingdom show here that a conservative insulin dose post exercise [i.e., 50% of the typical “correction factor,” based on the total daily insulin dose algorithm calculation, as described by Davidson et al. (6)] is a safe and effective way to gradually bring glucose levels into control after exercise if hyperglycemia develops. The main limitation of this pilot study is that other insulin dose administration protocols were not tested (e.g., 100% correction, bolus before the exercise starts) and the subjects were not followed all that long in recovery (just 120 minutes).

Randomized trial of dual-hormone artificial pancreas with dosing adjustment during exercise compared with no adjustment and sense-augmented pump therapy

Jacobs PG¹, El Youssef J², Reddy R¹, Resalat N¹, Branigan D², Condon J¹, Preiser N¹, Ramsey K³, Jones M², Edwards C², Kuehl K⁴, Leitschuh J¹, Rajhbeharrysingh U¹, Castle J²

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Diabetes Obes Metab 2016; **18**:1110–1118.

Background

Individuals with type 1 diabetes (T1D) have impaired insulin secretion and dysfunctional glucagon secretion, making them particularly susceptible to hyper- and hypoglycemia. It is generally held that artificial pancreas (AP) systems will help mitigate risk of dysglycaemia. In this system, hormone delivery is determined using an algorithm, however, with exercise, insulin sensitivity is significantly altered and adjustments are likely required. This study aimed to determine the optimal adjustments of insulin and glucagon dosing with exercise to prevent exercise induced hypoglycemia.

Methods

This study was a randomized crossover controlled study comparing dual hormone AP with adjustments (APX), versus dual hormone AP without adjustments (APN) and sensor augmented pump (SAP). Twenty-one T1D patients ages 18 to 45 stayed in a hospital overnight and had standardized meals. Postbreakfast, exercise consisted of running at 60% of HR max for 45 min on a motorized treadmill. The exercising dosing algorithm reduced insulin and increased glucagon during and postexercise for 1.5 h. APN

Comment

A large percentage of patients with type 1 diabetes have postexercise hyperglycemia following intense exercise (anaerobic and intense aerobic), likely because of sustained increases in hepatic glucose production that exceeds glucose uptake into muscle that is now finished contracting (1,2). This phenomenon may be more common in patients on MDI than on continuous subcutaneous insulin infusion (CSII) (3), although it can happen in any patient who does intense exercise, particularly if there is heightened competition stress (4). High blood sugars in recovery can be prolonged (5) and can be frustrating since it may promote dehydration and compromise overall A1c levels if it is a frequent occurrence. Some athletes complain that hyperglycemia after exercise makes them feel sluggish and may compromise their capacity to recover from the activity and may wish to bolus insulin to counter these effects. However, bolusing insulin after exercise is a worry since it may increase risk for late-onset hypoglycaemia, another frustrating side effect of exercise. Our colleagues from the United

was unadjusted for exercise and SAP manually managed hormone delivery by patients.

Results

Despite similar baseline values, APX promoted significantly less time in hypoglycaemia postexercise compared to APN (0.3% APX vs. 3.1% APN, $P=0.001$). The APN trial had a reduced percent of time spent in hyperglycemia postexercise than both APX and SAP, although these differences did not reach significance. In the overnight period APN spent significantly less time spent in hyperglycemia than APX (8.7% vs. 17.2%, $P=0.04$).

Conclusions

This study highlights the importance of adjusting insulin and glucagon doses at the onset of exercise to limit hypoglycaemia. APX performs similarly to SAP when insulin was adjusted prior to exercise.

Comment

With T1D, the body's ability to produce insulin is lost and glucagon production becomes dysregulated. As such, maintaining euglycaemia during exercise requires a lot of monitoring, manual adjustments to insulin delivery and carbohydrate snacking. For this reason, the development of the dual hormone AP for the daily monitoring and regulation of blood glucose levels is a novel and exciting branch of research for improving glycemic control in individuals with T1D. In a state of exercise, the rate of change in glycemia occurs more rapidly and in order to counteract this, the dual hormone AP system must be able to measure exercise and possibly make adjustments to both hormones. This study found that when AP was adjusted at the onset of exercise, exercise-associated hypoglycaemia was significantly reduced when compared to nonadjustment AP. SAP also resulted in relatively good glucose control, but a limit to its use is that it requires a lot more manual adjustment, which is a burden and not always feasible, especially with long, sustained exercises. Although this study was beneficial in manipulating the AP to reduce the incidences of hypoglycemia, it did not detect the onset of exercise automatically. Future research from the same group is currently aiming to incorporate an exercise detection component into the AP-algorithm by using accelerometers and heart rate inputs (7) in order to advance the field towards utilizing this technology for day-to-day use.

Metabolic effects of exercise training among fitness-nonresponsive patients with type 2 diabetes: the HART-D study

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Diabetes Care 2015; 38: 1494–1501

Background

Physical activity is closely associated with cardiorespiratory fitness (CRF), yet some individuals are nonresponsive to exercise and do not experience these expected improvements (termed “nonresponders”). This study examined how type 2 diabetes (T2D) patients respond to exercise training, focusing on changes in CRF, hemoglobinA1c (HbA1c) levels and other metabolic parameters.

Methods

This study analyzed data from patients who participated in the Heath Benefits of Aerobic and Resistance Training in Diabetes (HART-D) study. There were 202 participants assigned to supervised training protocols for 9 months. The groups consisted of a nonexercise control group that received stretching and relaxation classes, an aerobic-training group (3 to 5 days/week, 50% to 80% of maximal aerobic capacity [VO₂max]), a resistance-training group (3 days/week, 10 to 12 reps of each activity), and a combination-training group receiving both resistance and aerobic training. Greater than 5% increase in peak oxygen uptake was considered a meaningful improvement in CRF, otherwise, they were considered nonresponders.

Results

Only 36.6% of exercisers were considered CRF responsive (improvements in VO₂max <5%). Both responders and nonresponders in the exercise groups had significantly decreased in HbA1c from baseline (−0.26% [95% confidence interval (CI) −0.5 to −0.01], −0.26% [95% CI −0/45 to −0.08]). Additionally, both responders and nonresponders had reduced waist circumference (WC) and percent body fat (−2.6 cm [95% CI −3.7 to −1.5] vs. −1.8cm [95% CI −2.6 to −1.0]), (% body fat −1.07% [95% CI −1.5 to −0.62] vs −0.75% [95% CI −1.09 to −0.41]). Lastly, both responsive and nonresponsive exercisers tended to report a reduced use of diabetes-related oral agents compared to controls (36% vs. 20.5%; $P=0.08$).

Conclusions

Exercise is associated with significant improvements in glycemic control, reductions in percent body fat/waist circumference, independent of the cardiorespiratory response to training. Based on this study, it is recommended that exercise be prescribed to T2D patients to decrease their risk of diabetes related comorbidities and improve their glucose control, with little regard to if the exercise makes their cardiorespiratory system more fit or not.

Comment

Metabolic parameters such as cardiorespiratory fitness and waist circumference are inversely associated with insulin resistance (8,9,10). Regular exercise is known to improve these factors, but for some, termed “nonresponsive” individuals, improvements in these factors are not seen, even with supervised and regular exercise. This is the first study to compare the effects of chronic moderate-intensity activity on T2D patients in responders versus nonresponders.

This was a large study ($n=202$) with long-term supervised training interventions. It was found that in their population of only T2D adults, a surprising 63% of the subjects were considered fitness nonresponsive, a value that was quite high, especially when compared to the general population. In a recent study, only 17.6% of obese and otherwise healthy subjects were considered nonresponders after undergoing an exercise program with frequent low intensity exercise sessions (11). The reason for the increased prevalence of nonresponders with T2D requires further investigation. The lack of improvement in fitness may be discouraging for individuals and may influence exercise compliance and commitment to an exercise program. However, despite no clinical improvements in CRF, exercise is independently associated with improved glucose control, reduced insulin resistance and less body fat, thus validating that exercise is still a beneficial therapy for diabetes treatment (8).

Insulin-based strategies to prevent hypoglycaemia during and after exercise in adult patients with type 1 diabetes on pump therapy: the DIABRASPORT randomized study

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Diabetes Obes Metab 2015; **17**: 1150–1157

Background

Aerobic exercise is known to cause hypoglycemia in T1D. Previous studies have primarily focused on the optimal doses of bolus and basal insulin for prolonged exercise in athletic

patients on CSII, but the guidelines for short, exercise sessions in nonathletic patients have not been determined. This study aimed to define optimal adjustments to insulin dosing for 30 min of exercise performed 3 h (Part 1) or 90 min (Part 2) following a meal (lunch) in patients on CSII.

Methods

This was a randomized control crossover trial with 20 adult T1D patients. Subjects attended multiple sessions where they exercised 3 hours postlunch; 1 rest session, 2 moderate exercise sessions (one with a 50% and the other with a 80% basal rate (BR) reduction), and 2 intense exercise sessions (one with an 80% BR reduction and the other with the pump stopped). All BR adjustments were made during exercise and remained for 2 h following exercise (except for the pump stopped session, where the infusion rate was re-established after exercise). Subjects returned for 2 postlunch exercise sessions that occurred 90 min postmeal in order to assess differences between adjusting bolus vs. basal insulin delivery. For all exercises, patients assessed their perceived intensity using the Borg scale.

Results

For the late exercise sessions, there were no overall differences in the occurrence of hypoglycemia with exercise versus rest. In the afternoon, there were significantly more hypoglycemic events with the milder reductions at both exercise intensities compared to rest (moderate exercise; 50% BR reduction vs. rest, $P=0.03$; intense exercise, 80% BR reduction vs. rest, $P=0.028$). For the early exercise sessions, there was a trend towards fewer hypoglycemia events with bolus versus BR reduction, but this did not reach significance ($P=0.07$). When asked about perceived intensity, 90% of subjects accurately rated the 50% VO_2max exercise as moderate, while the 75% VO_2max exercise was only accurately perceived as intense 60% of the time.

Conclusions

In adults with T1D, it is possible to exercise for 30 min, 3 h postlunch without increasing the risk of hypoglycemia by reducing the BR by 80% for moderate exercise and by stopping the pump altogether for intense exercise. If exercising shortly after a meal, reducing the bolus insulin dose by 50% appears to be sufficiently effective in preventing hypoglycemia.

Comment

The benefits of exercise are well known, but with fear of hypoglycemia being one of the major barriers to exercise in type 1 diabetes, there is an increased requirement to develop specific strategies to limit its likelihood of occurring. Most studies use well trained athletes, but with a significant percent of the general population being physical inactive ($\sim 36.1\%$) (12), a percentage that only increases in the T1D population ($\sim 63\%$) (13), specific guidelines for a nonathletic population are required. This study used insulin pumps as opposed to multiple daily injections and one of the major benefits to this with exercise is that adjustments can be made at the onset of

exercise, making an employable strategy if activity cannot be foreseen in advance. This study successfully determined optimal dose adjustments of nonathletic individuals performing short bouts of exercise (30 min) that would be representative of daily leisure or work activity. Based on this study, an aggressive reduction of basal insulin delivery (i.e., 80%–100%) might be most effective, as the 50% BR reduction did not fully prevent hypoglycemia. This adjustment was found to be in agreement with a study by McAuley and colleagues, where a 50% BR reduction was not sufficient to reduce circulating insulin levels even when it was performed an hour before the start of the activity (14).

Impact of physical activity on glycemic control and prevalence of cardiovascular risk factors in adults with type 1 diabetes: a cross-sectional multicenter study of 18,028 patients

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Diabetes Care 2015; **38**: 1536–1543

Background

Various studies have demonstrated the positive effects of physical activity on a multitude of diseases including cardiovascular disease, T2D and some cancers, yet studies on T1D tend to be smaller and meta-analyses have shown conflicting results for exercise recommendations. For this reason, this study aims to examine the influence of exercise on glycemic control and cardiovascular risk factors in 18,028 patients with T1D.

Methods

Subject information was provided by the Diabetes Patienten-Verlaufsdokumentation (DPV) database in Germany and Austria, which documented diabetes care strategies and their outcomes from 18,028 patients aged 18 to 80 years. Data reported included self-reported physical activity (PA), measured as frequency per week (PA2; 2 or more times per week, PA1; 1 time a week, and PA0; inactive), HbA1c values, body mass index (BMI), hypertension and the use of anti-hypertensive drugs, dyslipidemia, diabetic ketoacidosis (DKA), and events of severe hypoglycemia and hypoglycemia

resulting in a loss of consciousness. Data were stratified by group size and further stratified by age and gender.

Results

Frequency of PA ranged between 0 and 9 times per week. The number of subjects who reported exercising more than two times per week (PA2) was 3212 (17.8%), 3459 subjects (19.9%) reported to be physically active one to two times (PA1), and 11,357 (63.0%) were inactive (PA0). Women were more often inactive compared with men (PA0: 66.0% vs. 60.5%, respectively) and the percentage of inactive individuals increased with age in both genders. PA had an inverse association with total daily insulin levels and HbA1c levels, independent of age and gender ($P < 0.0001$). Additionally, physical activity was inversely associated with DKA, BMI, and dyslipidemia ($P < 0.0001$ for all). Rates of severe hypoglycemia were lowest in the moderately active group. In addition to having the highest rates of hypoglycemia, the least active group had the highest incidence of retinopathy and microalbuminuria.

Conclusions

Physical activity has a beneficial effect on T1D patients in terms of improving HbA1c levels and associated comorbidities. Despite this, an increased percentage of subjects were reported to be inactive (63% versus approximately 34% in the general population) and more research should focus on encouraging participation in physical activity in this patient population.

Comment

This multicenter cross-sectional study from Germany and Austria is the largest to date to demonstrate the beneficial impact of exercise on T1D. Overall, high levels of PA were associated with a lower daily insulin dose, a lower HbA1c and reduced diabetes-related complications. However, with T1D, the potential for developing exercise-induced hypoglycemia is one of the greatest barriers to participating in exercise (15). In this large study, it was found that in women and in the oldest age-group (45 to 80 years), the rate of severe hypoglycemia increased with PA, whereas in other subgroups, there was an inverse association. This finding should caution health-care providers about prescribing exercise for older women living with type 1 diabetes, whose rates of hypoglycemia are already elevated when compared to younger women (16).

Do youth with type 1 diabetes exercise safely? A focus on patient practices and glycemic outcomes

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Background

Various insulin adjustment strategies have been tested to help reduce glycemic excursions during and after exercise, but little is known about their use in youth with type 1 diabetes. These authors aimed to assess the typical exercise management practices in youth with type 1 diabetes and examine the associations between key behaviors and glycemic control.

Methods

The “Type 1 Diabetes Report of Exercise Practices Survey (T1D-REPS)” was developed and piloted in 100 youth with type 1 diabetes on CSII. Participants completed a 3 day physical activity recall and 30 days of pump/glucose data were collected and analysed.

Results

Eighty-four percent of participants modified their insulin regimen around exercise; only 40% reported adjusting prandial insulin immediately before exercise, while 68% reported some modification (suspension or decrease) of basal insulin during exercise. Following exercise, only 10% reported reducing basal insulin overnight. Those who performed ≥ 5 glucose checks/day adjusted basal insulin during exercise more frequently than those with fewer daily glucose checks (33% vs. 13%, $P=0.05$, $\chi(2)=3.7$), and were more likely to report decreasing insulin dose for the bedtime snack following exercise (50% vs. 17%, $P=0.004$, $\chi(2)=8.2$).

Conclusions

Basal insulin reduction at the time of exercise appears to be the most common approach to reduce the risk of exercise-associated hypoglycemia. Despite research demonstrating that hypoglycemia after exercise is a frequent occurrence in youth, a majority (~90%) are not adjusting insulin overnight after exercise. A tool designed to capture patient practices and provide clinicians with a framework for patient education may lead to improved safety around exercise in this active patient population.

Comment

Over the last several years, a good number of clinical studies have been conducted to help inform insulin dose reductions and/or carbohydrate snacks for aerobic exercise in adolescents with type 1 diabetes (17,18,19,20). Guidelines for exercise management based on these studies have been published (21) and updated (22). For youth on CSII, it should almost be automatic to reduce basal insulin infusion rates overnight by about 20% from bedtime for about 6 hours to help reduce risk for nocturnal hypoglycemia (19). Yet, according to this study, few patients, or their parents, are performing these basic adjustments. Another very recently published study demonstrates that exercise makes glucose control more difficult and that few evidenced-based practices are being used by adults with type 1 diabetes on MDI or on CSII (23). Collectively, these findings may be alarming for those of us who advocate for safe physical activity for youth with diabetes. As these authors point out, automated tools that monitor physical activity levels and then recommend basic insulin dose adjustments at bedtime are urgently needed.

General practitioners' barriers to prescribe physical activity: the dark side of the cluster effects on the physical activity of their type 2 diabetes patients

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Background

This research was conducted to quantify the barriers to physical activity engagement in patients with type 2 diabetes. It also determined if general practitioners (GPs) have any perceived barriers for exercise for their patients that may be impacting their activity levels.

Methods

A cross-sectional study of GPs (n=48) and their type 2 diabetes patients (n=369) measuring respectively barriers to prescribe and practice physical activity was conducted using a self-assessment questionnaire: barriers to physical activity in diabetes (BAPAD). Statistical analysis was performed using a hierarchical data structure. Similar practitioner's patients were assessed using a cluster sharing common patterns approach.

Results

Patients with higher barriers to physical activity were much more likely to declare practicing no physical activity ($P<0.001$) or a lower frequency and duration of activity ($P<0.001$). A high patient's BAPAD score was also associated with a higher risk to have a HbA1c $\geq 7\%$ (53 mmol/mol) ($P=0.001$). The intra-class correlation coefficient between type 2 diabetes patients and GPs was ~34%, indicating a high cluster effect. Thus, when a GP has a high BAPAD score regarding the exercise prescription, it is predictive of a high BAPAD score with their patients, regarding their practice.

Conclusions

Overall, it appears that patients with lower BAPAD score and thus lower perceived barriers to physical activity, have

higher physical activity levels and better glycemic control compared to those with higher BAPAD scores. A deleterious cluster effect between GPs and their patients was also found: the higher the GP's BAPAD score for their patient, the higher the patients' BAPAD score. This important cluster effect might designate GPs as a relevant lever for future interventions regarding patient's education towards exercise and type 2 diabetes management.

Comment

Physical activity is a central component of type 2 diabetes management, but a number of barriers for engagement may exist for patients. Of course, lack of time, lack of resources, poor motivation, and bad weather may all get in the way of being active if you have diabetes (or not), as may challenges with one's own diabetes control. But having your physician not think you can exercise? That is a whole other set of problems. In this study, the perceived barriers for patients with type 2 diabetes were assessed via questionnaire to 48 GPs. The survey also asked about the physicians' own engagement in regular exercise. In general, the GPs promoted regular physical activity (primarily walking) and felt that regular exercise was as important as medications for glycemic control. However, some physicians believed that their own patients were too unfit (and/or too unhealthy) to participate in exercise and that exercise would cause challenges to glucose control. For the patients, those with more barriers to exercise participation tended to have diabetes longer and tended to have higher HbA1c levels compared to those patients who had fewer barriers. Patients' BAPAD score was not linked with practitioner specialty or the physician's level of physical activity levels. But, the higher the GPs' BAPAD score, the higher the patients' BAPAD score. This finding is important, since perceived barriers decrease the likelihood of engaging in health-related behaviors that might otherwise reduce disease risks and improve patient quality of life. This research suggests that some of the barriers to physical activity engagement might be being reinforced through some of the actions of their own GPs. The next step will be to attempt to influence the GPs' perceived barriers for their patients and help them promote physical activity safely and effectively.

Effects of high-intensity interval exercise versus moderate continuous exercise on glucose homeostasis and hormone response in patients with type 1 diabetes mellitus using novel ultra-long-acting insulin

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This manuscript is discussed also in Article on New Insulin, Biosimilars, and Insulin Therapy, page S-42.

Background

Hypoglycemia during exercise can be ameliorated in MDI patients with type 1 diabetes by reducing the prandial insulin dose at the meal before exercise. Post-exercise hypoglycemia can also be managed with this approach by reducing the bolus insulin at the meal after exercise. The purpose of this study was to determine the efficacy of reducing the meal time boluses by 25%, 50%, and 75% for continuous (CON) and intermittent high intensity interval exercise (HIIE) at low, moderate, and high workloads in patients with type 1 diabetes on MDI.

Methods

Seven males with type 1 diabetes, all using insulin degludec (Tresiba/Novo Nordisk, Denmark) as basal insulin, performed either HIIE or CON exercise at one of three different intensities (low, moderate, high) on a cycle ergometer. Before exercise, standardized meals were administered, and short-acting insulin dose was reduced by 25% (low intensity trial), 50% (moderate intensity trial), or 75% (high intensity trial).

Results

Blood glucose (BG) decrease during HIIE was significantly smaller for the moderate intensity exercise ($P=0.024$) and tended to be smaller for the other intensities compared to the CON trials. No differences were found for post-exercise interstitial glucose, acute hormone response, and carbohydrate utilization between HIIE and CON for low, moderate, and high intensity exercise. In HIIE, blood lactate for the low intensity ($P=0.006$) and moderate intensity ($P=0.004$), as well as respiratory exchange ratio for low ($P=0.003$) and moderate intensity ($P=0.003$) were significantly higher compared to CON but not for the high intensity exercise.

Conclusions

Hypoglycemia did not occur during or after HIIE and CON when using ultra-long-acting insulin and when applying a bolus dose insulin reduction for exercise. In general, HIIE tended to be associated with a lesser reduction in glycemia when compared to CON exercise, even with markedly higher peak workloads occurring with the former type of exercise.

Comment

People with type 1 diabetes perform all sorts of different types of exercise. In this study, it was shown that activities that have brief periods of higher intensity effort, called high intensity interval exercise (HIIE) tend to be associated with less risk for hypoglycaemia compared with continuous exercise. This study also shows that, in general, higher intensity aerobic exercise performed for 30 min requires greater reductions in prandial insulin at the meals before and after exercise than milder forms

of activity. Interpreting the findings in this study, the following table below may be useful as a starting point for the mealtime adjustments on days with predictable activity in patients on MDI therapy:

<i>Intensity of CON exercise or HIIE</i>	<i>Preexercise prandial percent insulin reduction</i>	<i>Postexercise prandial percent insulin reduction</i>
Low intensity aerobic exercise	– 25%	– 25%
Moderate intensity aerobic exercise	– 50%	– 50%
High intensity aerobic exercise	– 75%	– 75%

Note: CON, continuous aerobic exercise; HIIE, high-intensity interval exercise.

Overall, a close look at the results section of this study, however, indicates that with higher intensity exercise, the greater the patient variability in the glycemic responses. Some patients actually had a rise in glycemia during the high intensity activity sessions, which might indicate that such aggressive insulin dose reductions should not be employed. In line with this, work from colleagues in Australia recently showed that very little exogenous glucose is required to maintain euglycemia when the exercise intensity is above about 80% of maximal aerobic capacity in patients on pump therapy who do no basal rate insulin adjustments (24).

Classification of physical activity: information to artificial pancreas control systems in real time

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Background

Exercise has wide ranging effects on glucose concentrations in type 1 diabetes, depending on the type (i.e., aerobic, anaerobic, mixed) of activity performed. This variability in glucose responses to physical activity makes the development of artificial pancreas (AP) systems challenging. Automatic detection of exercise type and intensity, and its classification as aerobic or anaerobic would provide valuable information to AP control algorithms.

Methods

Using a multivariable AP approach where biometric variables were measured and reported to the AP at high frequency, a classification system was developed that identifies, in real time, the exercise intensity and its reliance on aerobic

or anaerobic metabolism. This new technology was tested on 5 persons with T1D and 3 individuals without in a controlled laboratory setting using a variety of common types of aerobic, anaerobic, and mixed activity.

Results

The classifier had an average sensitivity of 98.7% for correctly assessing physiological data collected over a range of exercise modalities and intensities in these subjects.

Conclusions

This new exercise classifier will be added as a new module to the integrated multivariable adaptive AP system to enable the detection of aerobic and anaerobic exercise for enhancing the accuracy of insulin infusion strategies during and after exercise.

Comment

With aerobic exercise, insulin levels need to drop, while with intense anaerobic work, insulin levels may need to rise. This change to insulin needs, based on the type of exercise done, makes the development of the AP a real challenge for exercise. This is the first study to use a tool that can be used to classify exercise as anaerobic, anaerobic or mixed. This may help a number of groups who are currently working on AP development for exercise (25,26,27).

One week of bed rest leads to substantial muscle atrophy and induces whole-body insulin resistance in the absence of skeletal muscle lipid accumulation

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Background

Despite periods of recovery with muscle disuse being necessary following an injury or illness, immobilization results in detrimental physiological effects on glycemic control and muscular health. This study aimed to examine the molecular and metabolic changes that result from 1 week of immobility.

Methods

For this study, 10 healthy recreationally active adult males were recruited (23 ± 1 years, BMI: 23.0 ± 0.9 kg/m²) and were limited to bed rest for 7 days. Dual-energy X-ray absorptiometry assessments, computerized tomography scans, fitness measures, muscle biopsies, and hyperinsulinemic-euglycemic clamps were assessed prior to and after the bed rest treatment.

Results

Bed-rest resulted in $29\% \pm 5\%$ decrease in insulin resistance ($P < 0.01$). Additionally, a decrease was observed in lean tissue (i.e., muscle and bone) mass 1.4 ± 0.2 kg ($P < 0.01$), accompanied with a $3.2\% \pm 0.9\%$ decline in quadriceps cross-sectional area ($P < 0.01$). Impairments in peak oxygen uptake ($\text{VO}_{2\text{peak}}$) were also observed, decreasing by $6.4\% \pm 2.3\%$ ($P < 0.05$), while one repetition max (1RM) was reduced $6.9\% \pm 1.4\%$ ($P < 0.01$). Lipid content, mitochondrial function and capillary density were unchanged in muscle biopsy samples.

Conclusions

Overall, bed rest resulted in significant impairments to metabolic health and the mechanisms for the impairments in glucose tolerance were not associated with those that are typically associated with high-fat diet induced insulin resistance.

Comment

The benefits of exercise on improving overall glycemic control seem to be well understood (28), but this study takes another angle and highlights the detrimental implications of impaired physical activity in the extreme setting of bed rest. A report in 2014 revealed that $\sim 25\%$ of all Americans were not getting any form of leisure physical activity (29). In this study, it is highlighted that after just one week of bed rest, there is a significant detriment in insulin sensitivity, reducing glucose disposal by about 30%. Additionally, in the one week trial, the body went through physiological changes that would take 12 weeks of intensive exercise to revert. It was surprising to find that the expected mechanisms for the impaired insulin sensitivity could not account for the changes they observed. Increases in insulin resistance occurred before changes in key muscle proteins known to regulate glucose uptake, or before any detected changes in lipid profiles or accumulation, or before dysfunction of mitochondria, or reduced capillary density. One potential mechanism may simply be the loss of muscle mass, resulting in a reduced capacity for glucose uptake. Although the precise mechanism remains to be elucidated, this study emphasizes the detrimental effects of inactivity. Future strategies should focus on strategies to limit periods of immobility, specifically with hospitalization, as well as creating programs to encourage physical activity as a proactive treatment to help glycemic control.

Author Disclosure Statement

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