ORIGINAL ARTICLE

Advances in Exercise, Physical Activity, and Diabetes Mellitus

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Introduction

IN 2014 AND 2015, several new articles were published on the health and fitness benefits of regular physical activity in various patient populations of diabetes and prediabetes. Moreover, a number of studies were conducted on ways to improve both exercise adherence and glucose control in patients. This year, we have chosen nine articles to represent the field, from an initial literature search of approximately 100 published articles, between July 1, 2014, and June 30, 2015.

Key Articles Reviewed for this Article

Renal function is associated with peak exercise capacity in adolescents with type 1 diabetes

Bjornstad P¹, Cree-Green M^{2,3}, Baumgartner A³, Maahs DM^{2,4}, Cherney DZ⁵, Pyle L¹, Regensteiner JG^{3,6}, Reusch JE^{3,7}, Nadeau KJ^{2,3}

Diabetes Care 2015; **38**: 126–31

Impact of different training modalities on glycaemic control and blood lipids in patients with type 2 diabetes: a systematic review and network meta-analysis

Schwingshackl L¹, Missbach B¹, Dias S², König J¹, Hoffmann G¹

Diabetologia 2014; **57**: 1789–97

Light physical activity determined by a motion sensor decreases insulin resistance, improves lipid homeostasis and reduces visceral fat in high risk subjects

Herzig K-H^{1,2}, Ahola R³, Leppäluoto J¹, Jokelainen J⁴, Jämsä T³, Keinänen-Kiukaanniemi S^{4,5}

International Journal of Obesity 2014; **38**: 1089–96

Circulating miR-192 and miR-193b are markers of prediabetes and are modulated by an exercise intervention

Párrizas M^{1,2}, Brugnara L^{1,2}, Esteban Y^{1,2}, González-Franquesa A^{1,2}, Canivell S^{1,2}, Murillo S^{1,2}, Gordillo-Bastidas E³, Cussó R⁴, Cadefau JA⁴, García-Roves PM^{1,2}, Servitja J-M^{1,2}, Novials A^{1,2}

J Clin Endocrinol Metab 2015; **100**: E407–15

A low-glycemic index meal and bedtime snack prevents postprandial hyperglycemia and associated rises in inflammatory markers, providing protection from early but not late nocturnal hypoglycemia following evening exercise in type 1 diabetes

Campbell MD¹, Walker M², Trenell MI², Stevenson EJ¹, Turner D³, Bracken RM³, Shaw JA², West DJ¹

Diabetes Care 2014; **37**: 1845–53

‘Exercise snacks’ before meals: a novel strategy to improve glycaemic control in individuals with insulin resistance

Francois ME¹, Baldi JC², Manning PJ², Lucas SJE^{1,3,4}, Hawley JA^{5,6}, Williams MJA², Cotter JD¹

Diabetologia 2014; **57**: 1437–45

Physical activity and sedentary behaviors associated with risk of progression from gestational diabetes mellitus to type 2 diabetes mellitus: a prospective cohort study

Bao W¹, Tobias DK², Bowers K³, Chavarro J^{2,4}, Vaag A⁵, Grunnet LG⁵, Strøm M⁶, Mills J¹, Liu A¹, Kiely M¹, Zhang C¹

JAMA Intern Med 2014; **174**: 1047–55

Clinical trial demonstrates exercise following bariatric surgery improves insulin sensitivity

Coen PM^{1,2}, Tanner CJ³, Helbling NL¹, Dubis GS³, Hames KC¹, Xie H⁴, Eid GM⁵, Stefanovic-Racic M¹, Toledo FGS¹, Jakicic JM², Houmard JA³, Goodpaster BH¹

J Clin Invest 2015; **1**: 248–57

Increase in physical activity is associated with lower HbA1c levels in children and adolescents with type 1 diabetes: Results from a cross-sectional study based on the Swedish pediatric diabetes quality registry (SWEDIABKIDS)

Beraki Å¹, Magnuson A², Särnblad S^{3,4}, Åman J^{3,4}, Samuelsson U⁵

Diabetes Res Clin Pract 2014; **105**: 119–25

Renal function is associated with peak exercise capacity in adolescents with type 1 diabetes

Bjornstad P¹, Cree-Green M^{2,3}, Baumgartner A³, Maahs DM^{2,4}, Cherney DZ⁵, Pyle L¹, Regensteiner JG^{3,6}, Reusch JE^{3,7}, Nadeau KJ^{2,3}

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Diabetes Care 2015; **38**: 126–31

Background

Individuals with type 1 diabetes are at an increased risk for developing cardiovascular disease (CVD) and diabetic nephropathy (DN). DN and CVD are strongly linked in adults

with type 1 diabetes, perhaps because of shared pathophysiology, yet little is known about this relationship in adolescents prior to the onset of detectable complications. This study aims to investigate the interactions between kidney function, cardiopulmonary fitness, and insulin sensitivity in otherwise healthy adolescents with type 1 diabetes.

Methods

In all, 82 adolescents were recruited for this study—69 had type 1 diabetes and 13 were nondiabetic controls. Data was collected on individual fitness, insulin sensitivity, and body composition, and measures kidney function, including their albumin to creatinine ratio as well as cystatin C levels, which were used to calculate their estimated glomerular filtration rate (eGFR). Subjects were assessed using Tanner Staging to determine pubertal development (Tanner stage >1 included). Their activity levels were also determined. Subjects had 3 days of restricted physical activity and a fixed diet before tests of kidney function, insulin sensitivity, and aerobic fitness (VO₂peak) were performed.

Results

Type 1 diabetics had a significantly reduced exercise capacity when compared with age-matched controls (VO₂peak/lean kg 43.7 ± 7.0 vs. 51.0 ± 8.6 mL per kg lean mass per min, *P* = 0.007); however, once adjusted for eGFR, sex differences,

and Tanner stage, the differences between groups were not significant. A significant negative correlation between eGFR and VO₂peak in type 1 diabetic subjects existed ($r = -0.55$, $R^2 = 30.22\%$, $P = 0.002$), a relationship that was significant even when adjusted for insulin sensitivity, systolic blood pressure, and levels of HbA1c and LDL cholesterol. No significant relationship was found in control subjects. When stratified into tertiles, subjects with the highest eGFR levels had the lowest VO₂peak, when expressed per kilogram mass or per kilogram lean mass.

Conclusion

The main finding of this study is that eGFR is negatively associated with cardiopulmonary fitness in adolescents with type 1 diabetes. This association is independent of insulin sensitivity and blood lipid profile in this patient population. As such, a potential interaction between renal function and cardiac exercise capacity, independent from atherosclerosis and coronary heart disease, may exist in type 1 diabetes.

Comment

Type 1 diabetes is associated with a shortened life span, cardiac disturbances, and vascular dysfunction, independent of coronary artery disease (1). Aerobic fitness, endurance capacity, and muscular strength can all be suppressed in young patients with type 1 diabetes (2). These authors have previously demonstrated that a lower insulin sensitivity is correlated with a reduced VO₂peak in adolescents with type 1 diabetes (3), suggesting that insulin resistance may be linked to poor aerobic fitness. Reduced exercise capacity and its association with renal health, as highlighted in this article, taken together with the established relationship between aerobic fitness and premature CVD mortality, may provide an alternative and novel pathway explaining the premature mortality of subjects with type 1 diabetes. This study is important as it shows that a lower aerobic capacity might be a marker of poor renal function and an early predictor of diabetes-related complications. It should be noted, however, that aerobic capacity is trainable in adolescents with type 1 diabetes (4) and determining if an improvement in (or perhaps a failure to improve) VO₂peak is associated with alterations in renal function is warranted.

Impact of different training modalities on glycaemic control and blood lipids in patients with type 2 diabetes: a systematic review and network meta-analysis

Schwingshackl L¹, Missbach B¹, Dias S², König J¹, Hoffmann G¹

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Diabetologia 2014; 57: 1789–97

Background

Lifestyle interventions, such as diet and exercise, are useful tools to improve the prognosis of type 2 diabetes;

however, the best type of exercise to prescribe is still unclear. Both the American Diabetes Association and The American College of Sports Medicine have listed combination training (aerobic plus resistance-type exercises) as the most effective form of exercise to improve glycemic control, but most of the analysis conducted to date compared the various training modalities (aerobic only, resistance only, combined) to data collected from sedentary controls (rather than comparing aerobic vs. resistance *per se*). This is the first systemic review that examines how glycemic control and blood lipid profile are affected both directly and indirectly by various training modalities in patients with type 2 diabetes.

Methods

The literature search for this meta-analysis was limited to randomized control trials using supervised exercise interventions in type 2 diabetic subjects. Studies were published between 2003 and 2013. Out of the initial 9,477 trials, 14 fit these restrictions and were eligible in the study, cumulating a total of 915 subjects (49–62.5 years, BMI 27.1–43.8 kg/m²). All subjects were ≥ 19 years of age and exercise interventions lasted for at least 8 weeks. Studies compared aerobic training (AET), resistance training (RT), or combined training (CT) and assessed at least one of the following: HbA1c, glucose levels, body weight, blood pressure, lipid levels (total cholesterol [TC], LDL, HDL, or triglyceride [TG] levels). A pairwise and network meta-analysis were used to determine the pooled relative effect of each modality.

Results

Reductions in HbA1c levels were more significant in AET protocols when compared to RT; however, CT proved to be significantly better at reducing HbA1c than the other modalities, with the most significant reductions seen in long-term studies, or in studies on obese diabetic subjects (mean difference -0.17% [-1.87 mmol/mol]; 95% CI -0.31 to -0.03 ; $p = 0.02$, $I^2 = 21\%$, 9 trials, 493 participants). When comparing AET and RT, it was found that AET showed significant reductions in fasting glucose levels (mean difference -0.90 mmol/L; 95% CI -1.71 , -0.09 ; $p = 0.03$, $I^2 = 72\%$, 8 trials, 245 participants), but there were no significant differences when looking at body weight, blood pressure, or cholesterol levels (total cholesterol, HDLs, LDLs, or TGs). CT proved most effective in reducing fasting glucose (mean difference -1.99 mmol/L; 95% CI -3.07 , -0.90 ; $p = 0.0003$, $I^2 = 61\%$, 3 trials, 99 participants), as well as all measured forms of cholesterol, systolic blood pressure, body weight, and TG levels. CT was 75% probable for being the best modality at improving most outcomes.

Conclusion

All exercise training modalities proved to have some benefits in improving metabolic and cardiovascular risk profile outcomes in patients with type 2 diabetes. Resistance-type exercise was useful for enhancing insulin sensitivity, perhaps by increasing muscle mass, while aerobic-type exercise was proven to be very effective at reducing HbA1c and fasting glucose levels. However, after considering all of the data that was analyzed, it appears that combined aerobic plus resistance training is the most effective method for improving

glycemic control and related factors, including reduced levels of HbA1c, as well as improving the management of fasting glucose levels, HDL cholesterol, TGs, diastolic blood pressure, and body weight. When combining exercises, it is recommended that both AET and RT exercises are utilized on different days for optimal benefits in glycemic control.

Comment

The debate of which training modality is the most effective in improving glucose control in type 2 diabetics is ongoing. Many studies have found that combination training is the ideal method for improved fitness, metabolic and cardiovascular risk profile (5); however, other meta-analysis fail to support one mode of training over another (6). This study was an extensive meta-analysis incorporating various randomized control trials adding power to this research question. As pointed out by these authors, aerobic exercise may be more effective in reducing HbA1c and glucose levels when compared with resistance-only exercise. However, the interpretation of these findings with respect to their clinical relevance is limited by the overall low to moderate quality of some of the studies included, the lack of information on the clinical importance of the outcomes measured, and the limited information on the adverse effects of the various types of exercise performed.

Light physical activity determined by a motion sensor decreases insulin resistance, improves lipid homeostasis and reduces visceral fat in high risk subjects

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International Journal of Obesity 2014; **38**: 1089–96

Background

Type 2 diabetes (T2D) is on the rise globally and is a serious concern for many nations worldwide. Physical activity (PA) has consistently been shown to reduce T2D risk in persons at risk for developing the disease. Based on studies in prediabetes, current guidelines recommend 150 minutes per week of moderate to vigorous aerobic exercise (7), but objective and practical guidelines for patients with known T2D have yet to be fully established. Daily walking is an activity that is easy to implement and is known to be beneficial for improving the prognosis of T2D. This study utilized accelerometers to record the number of steps taken when walking (or running) in order to provide accurate PA thresholds. The purpose of this study was to examine the effects of a short-term walking intervention on fasting and 2-hour glucose,

insulin concentration, as well as lipid homeostasis in overweight subjects with abnormal glucose tolerance.

Methods

Participants were recruited from an outpatient diabetic clinic in Oulo Deaconess Hospital in Finland. The FINDRISC questionnaire and oral glucose tolerance tests were used to evaluate T2D in subjects. In total, there were 78 eligible subjects identified with abnormal glucose tolerance. Baseline anthropometric measurements were taken along with an ECG, blood pressure measures, oral glucose tolerance, and fasting and 2-hour glucose measures. A questionnaire was distributed to subjects to record baseline PA, measured in metabolic units (METS). Subjects were assigned to an exercise or control group. The exercise intervention consisted of 60-minutes of walking three times a week (i.e., 180 minutes per week) for 3 months. The accelerometer recorded the amount of vertical accelerations at a rate of 400s⁻¹, with levels from 0.3–9.9 g (gravitational acceleration; standing at 0g) and was sealed so subjects were blinded to their results.

Results

The total amount of daily steps recorded was higher in the intervention group than in the controls (median 5,576 vs. 4,004 steps per day, respectively). The intervention group experienced significant decreases in fasting (−3.4 mUI⁻¹, $P=0.035$) and 2-hour insulin (−26.6 mUI⁻¹, $P=0.003$), whereas the control group experienced no change in these markers of insulin sensitivity. Interestingly, body weight decreased in both groups; however, a reduction in visceral fat area of 16 cm² was only experienced in the intervention group when daily steps exceeded 6,520, ($P=0.030$). Also, when daily steps exceeded this threshold, the exercise group demonstrated significant decreases in LDL cholesterol of 0.7 mmol l⁻¹ (95% confidence interval 0.1–1.2 mmol l⁻¹, $P=0.008$).

Conclusion

Daily light PA consisting of >6,520 steps with an acceleration of 0.3–0.7g is shown in this study to be clinically beneficial for overweight and obese individuals with a high risk of T2D.

Comment

Exercise is a useful tool to reduce the risk of developing T2D and does not need to be vigorous to be effective. It is clear from this study that light PA can assist in lowering the risk factors for T2DM by reducing visceral fat mass, blood cholesterol, and insulin resistance. This study demonstrated that a simple intervention (walking) is likely enough to bring about significant decreases in T2DM risk, although it is unclear how much less CVD risk patients were at post-intervention. At the very least, this study successfully translated the number of steps to be taken daily, and the pace to take them at, to better inform walking guidelines. Based on this study, people at risk for developing T2D should attain a daily step count of over 6,520 at acceleration levels similar to

~30–35% of one's maximal aerobic capacity (2–3 METS, or very light intensity). The use of an accelerometer should be deemed a good way to provide precise and accurate prescription for daily exercise. Although this study was limited to a 3 month exercise intervention in just 38 subjects, it was still able to provide evidence that daily walking for a moderate distance (~3 miles) can decrease various CVD risk factors in high-risk prediabetic subjects.

Circulating miR-192 and miR-193b are markers of prediabetes and are modulated by an exercise intervention

Párrizas M^{1,2}, Brugnara L^{1,2}, Esteban Y^{1,2}, González-Franquesa A^{1,2}, Canivell S^{1,2}, Murillo S^{1,2}, Gordillo-Bastidas E³, Cussó R⁴, Cadeñau JA⁴, García-Roves PM^{1,2}, Servitja J-M^{1,2}, Novials A^{1,2}

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J Clin Endocrinol Metab 2015; **100**: E407–15

Background

With the prevalence of type 2 diabetes on the rise, early detection of prediabetes is of the utmost importance in order to implement intervention strategies that will delay or prevent its progression, in turn reducing the likelihood of complications. Unfortunately, most cases of type 2 diabetes go undiagnosed until they progress to an advanced stage. Profiling MicroRNAs (miRNAs) has recently been deemed helpful for early detection of other conditions and even for various forms of diabetes, but has not been studied in prediabetic patients. miRNAs are noncoding RNAs involved in regulation of cells and are critical in states of stress and are therefore expected to be altering in a prediabetic state, as the uncontrolled hyperglycemic excursions disturb metabolic balance. The purpose of this study was to profile critical miRNAs in prediabetic patients with the intention of identifying novel therapeutic tools. This study will also examine how the levels of miRNAs altered after the completion of an exercise intervention.

Methods

In the first cohort, 92 serum samples from the Hospital Clinic-IDIBAPS Biobank were used. Subjects were all males; 29 were healthy controls while the remainder had various degrees of glucose intolerance established by ADA guidelines (22 prediabetic with IFG, 21 prediabetic with isolated IGT, 20 newly diagnoses T2D). c-miRNAs were extracted from 46 representative samples and their abundance was profiled using RT-PCR analysis. Once significant miRNAs were determined,

the remaining samples were analyzed. In the second study, a cohort of 12 controls and 6 prediabetic subjects underwent a 16-week exercise intervention. The program consisted of one aerobic and one resistance session each week. Aerobic exercise was performed on a cycloergometer at 60–80% of VO₂max. For the resistance exercise, subjects performed 3–5 sets with 8–15 repetitions at 50–70% of their 1 repetition maximum (1RM). For the last 8 weeks it was increased to 4–5 sets with 4–12 repetitions at 70–80% 1RM. Serum samples were analyzed both pre- and post-intervention. The intervention was 16 weeks long and occurred twice a week, cycling at an intensity of 60–85% VO₂ max as well as resistance training with increasing intensity. An animal model inducing glucose intolerance in mice was also used to assess miRNA and the impact of exercise training.

Results

In the first cohort, those recognized as having prediabetes exhibited significantly increased levels of mi-RNA 150, mi-RNA 192, and mi-RNA 193b when compared to the other groups. There also appears to be a relationship between the fatty liver index and mi-RNA 192 and mi-RNA 193b abundance, indicating these microarrays may play a role in liver pathogenesis. In the second cohort, it was found that at baseline, these same markers tended to be higher in prediabetic subjects compared to the control subjects. Following the intervention, mi-RNA 192 and mi-RNA 193b were reduced to levels comparable to the control group. These results were replicated in the animal model where glucose intolerant mice also had elevated levels of these miRNA, but were reduced after the exercise intervention (treadmill running 5 days a week for 1 hour with speeds up to 22 m/min).

Conclusion

This study indicates that these specific markers, miRNA-192 and miRNA-193b, can be used as markers for prediabetes before overt symptoms occur. Interestingly, both prediabetic groups, IFG and IGT, showed similar levels of mi-RNA 192 and mi-RNA 193b despite stemming from distinct etiologies, while this pattern was not seen in the T2D group. Exercise interventions normalized mi-RNA 192 and mi-RNA 193b back to levels comparable to the control. It is likely that the improved levels of these biomarkers are an indirect effect of the intervention, influenced by the improvements in the metabolic phenotype rather than a direct effect of exercise itself.

Comment

Early detection of prediabetes is critical for implementing interventions to reduce the risk of developing complications, yet many cases go undetected. This study offers a new form of early metabolic dysregulation/detection using miRNA from serum to detect prediabetes. It also provided additional validation of the efficacy of exercise interventions. Exercise is known to improve the prognosis of nearly all forms of diabetes, and it was found after an exercise intervention that exercise reduced levels of 2 specific miRNAs associated with prediabetes, thereby limiting its progression. This study, while perhaps costly,

may be applied clinically as an alternative to current diagnostic tests, although it is unclear from the present study if exercise has a direct or indirect effect on these miRNAs.

A low-glycemic index meal and bedtime snack prevents postprandial hyperglycemia and associated rises in inflammatory markers, providing protection from early but not late nocturnal hypoglycemia following evening exercise in type 1 diabetes

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Diabetes Care 2014; 37: 1845–53

Background

Regular exercise for type 1 diabetes has been proven beneficial; however, it exposes patients to increased risk for iatrogenic hypoglycemia. This is of particular concern when exercising in the afternoon/evenings because it makes individuals with type 1 diabetes more susceptible to nocturnal hypoglycemia. Lowering the dose of bolus insulin in the meal before exercise is useful in attenuating exercise-associated hypoglycemia, however, dietary choices in the meals surrounding exercise should also be considered. More specifically, the influence that the glycemic index of foods consumed post-exercise has on glucose dynamics requires more study. This study aimed to determine the influence of the glycemic index on glucose control and metabolism, with the authors hypothesizing that a low glycemic index (LGI) snack will be absorbed at slower rates than high glycemic index (HGI) snack, thereby reducing the risk of both early post-exercise hyperglycemia and late onset hypoglycemia.

Methods

Ten male subjects, aged 18–35 years with type 1 diabetes (HbA1c < 8.0) were recruited. Subjects all exercised regularly and were treated with a basal-bolus insulin regimen. Fifty percent of patients injected basal insulin glargine in the morning, while the others took it late evening or at bedtime. Subjects came in for three sessions. The first session assessed peak cardiorespiratory capacity in an incremental treadmill exercise. The order of the other two sessions was randomized and included a 45-minute treadmill run at 70% of their peak aerobic capacity (VO₂peak), followed by consuming either a LGI or HGI meal (1.0 g carbohydrate/kg body mass along with 50% less rapid-acting insulin analog) in the early evening after exercise. In all trials, subjects replicated their habitual diets and insulin regimen prior to exercise. Continuous glucose monitors were used throughout the study and venous blood was also collected prior to exercise, as well as periodically throughout each stage.

Results

During the exercise, there was a significant effect of both time and the condition on blood glucose concentration. No subjects developed hypoglycemia during exercise or in early recovery. Following exercise, insulin peaks were similar 60 minutes following the LGI and HGI meals. Following the postexercise meal, the HGI meal induced hyperglycemia in all patients (mean $\pm$ SD glucose 13.5 $\pm$ 3.3 mmol/L) and marked increases in TNF- α and IL-6 levels, whereas relative euglycemia was maintained with the LGI meal (7.7 $\pm$ 2.5 mmol/L) without inflammatory cytokine elevation. Although both meal types protected from early hypoglycemia, both were also associated with a drop in glucose levels throughout the night, with some individuals experiencing late-onset hypoglycemia (n = 5 for each meal/trial). Glucose levels were not significantly different between groups the following day.

Conclusion

LGI food was found to improve early post-prandial glycemia and acute postexercise inflammation; however, subjects were still at risk for nocturnal hypoglycemia following the 45 minutes of heavy aerobic exercise. Importantly, however, the LGI meal depressed the levels of inflammatory markers relative to the HGI group. Most of the subjects where in a euglycemic state before bed when they consumed the LGI meal, whereas the HGI meal was associated with bedtime hyperglycemia. Despite the initial benefits in glycose dynamics of the LGI meal, both conditions were comparable after about 3 hours from the consumption of the meal. Surprisingly, when subjects were given an excess of carbohydrates to counter the excess energy used in exercise and the increased insulin sensitivity postexercise, nocturnal hypoglycemia was still evident. This suggests that although consuming an LGI snack is useful, the dose and timing of the basal insulin needs to be investigated further to optimize postworkout regimens for active patients with type 1 diabetes.

Comment

A limited amount of research has been conducted to try to ameliorate postexercise hyper- or hypoglycemia in patients with type 1 diabetes. Taplin and colleagues found that a 20% basal rate reduction at bedtime in adolescents on insulin pump therapy helps prevent late-onset nocturnal hypoglycemia following afternoon exercise (8). For patients on MDI therapy, adjusting basal insulin at bedtime after exercise is more challenging since patients may find themselves with higher than desired blood glucose the next day. As expected in this study, a LGI meal after exercise was associated with less postexercise hyperglycemia when compared to a HGI meal. Surprisingly, however, the LGI meal did not help prevent nocturnal hypoglycemia. It was also interesting to note in this study that inflammatory markers increase postexercise in type 1 diabetes, particularly if an HGI meal is consumed. More studies are needed, however, to help prevent that nagging risk for postexercise, late-onset hypoglycemia in this patient population.

‘Exercise snacks’ before meals: a novel strategy to improve glycaemic control in individuals with insulin resistance

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Diabetologia 2014; 57: 1437–45

Background

The prognosis for type 2 diabetes and insulin resistance has been shown to be manageable for some individuals through lifestyle modification (i.e., moderate caloric restriction and regular physical activity). Yet this form of treatment is vastly underutilized, despite being one of the easiest and safest to recommend. Exercise has not only been shown to improve glycemic control in patients with T2D, but also reduce the risk of complications. High-intensity interval training (HIT) is a form of exercise in which participants exercise vigorously in short bouts (at ~90% of their maximal heart rate). HIT-type exercises have been proven effective in helping control blood glucose levels in patients with prediabetes or T2D (9, 10) and is deemed preferable for some patients because of the shorter time commitment. This study used the phrase “exercise snack” as a brief bout of intense exercise premeal. This study aimed to investigate the potential benefits of using an intense exercise snack prior to a meal as a tool to help regulate blood glucose, hypothesizing that the HIT will attenuate postprandial glucose levels and improve glycemic control.

Methods

This was a crossover study that recruited 16 subjects (18–55 years, nonmedicated for blood glucose or elevated blood pressure) through advertising. Subjects performed an oral glucose tolerance test and it was found that 9 subjects were either insulin resistant or type 2 diabetic according to the American Diabetes Association criteria. Subjects then performed incremental exercise on a treadmill and their $\text{VO}_{2\text{max}}$ was determined. They were then randomly assigned the order of the interventions. Interventions included traditional continuous exercise (CONT), exercise snacks (ES), and composite exercise snacks (CES). CONT consisted of a 30-minute treadmill run at a moderate intensity prior to eating. ES was the HIT method in which subjects performed 6 bouts of high intensity walking (at 90% of HR_{max}) for 1 minute at a time. CES were 6 one min work bouts, alternating between walking and resistance-based exercise. In all trials, the exercises were performed 30 minutes before breakfast, lunch,

and dinner, and the diet was kept constant across each intervention.

Results

When comparing the ES to the CONT trial, it was evident that ES effectively lowered postprandial glucose area under the curve (AUC) significantly better than CONT following breakfast (CONT AUC = $1,307 \pm 337 \text{ mmol/L} \times 3 \text{ h}$ vs. ES AUC = $1,090 \pm 178 \text{ mmol/L} \times 3 \text{ h}$, $p=0.04$); and dinner (CONT $1,285 \pm 208 \text{ mmol/L} \times 3 \text{ h}$ vs. ES $1,116 \pm 197 \text{ mmol/L} \times 3 \text{ h}$, $p=0.04$). This continued for the following 24 hours when the ES group showed greater glycemic control with reduced variability. Insulin concentrations were found to be similar between the groups.

When comparing between the ES groups (ES and CES), no significant differences were observed. Both had a reduction in their postprandial and 24 hr glucose levels, with similar levels in variability.

Conclusion

A brief, intermittent, high-intensity exercise snack before meals, lasting only about 12 minutes in total duration, reduces postprandial glucose as well as 24 hr glucose when compared to a longer (30-minute) bout of continuous exercise. In addition to reducing this risk of hyperglycemia, HIT exercises have also been shown to reduce the risk of comorbidities such as cardiovascular disease (11). A study by Karstoft *et al.* (12) found that the long-term use of high-intensity exercises were optimal for regulating glucose levels as opposed to continuous exercise. Considering most individuals do not reach the recommended activity levels, HIT exercises may be the ideal due to their time efficiency. Both intermittent walking mixed with resistance-based exercises were also effective at improving glycemic control. When the timing of these exercises were optimized (30 minutes prior to a meal), they proved to be an easy, beneficial tool in managing insulin resistance and type 2 diabetes.

Comment

Glucose management, particularly following a meal, can be a challenge for individuals with T2D. This study utilizes exercise in a unique way as an intervention to help control it. “Exercise snacks” are quick bursts of high-intensity exercise prior to a meal with the goal of reducing post-prandial hyperglycemia. We liked this new terminology for brief bouts of intense exercise. The intervention, lasting only 12 minutes each time, with just six 1-minute bursts of intense walking up an incline, proved beneficial and successfully improved glucose control, even more so than longer aerobic exercises. The short amount of time required to complete an “exercise snack” may be preferable for most individuals to implement, because it does not require a drastic change in lifestyle to make time for it. If this type of exercise is safe for all patients remains unclear, as is one’s motivation to exercise near maximally repeatedly for 1-minute intervals. But we are sure going to give it a try!

Physical activity and sedentary behaviors associated with risk of progression from gestational diabetes mellitus to type 2 diabetes mellitus: a prospective cohort study

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JAMA Intern Med 2014; **174**: 1047–55

Background

Approximately 20 percent of pregnant women develop temporary (gestational) diabetes (GDM), which places them at an increased risk of subsequently developing type 2 diabetes (T2D) (13, 14). This study aimed to examine the independent effect of physical activity levels on the development of T2DM from GDM. It is hypothesized that physical activity will significantly decrease the effect of developing T2DM in the general population.

Methods

The population of interest was composed of women from the Nurse's Health study, an ongoing prospective cohort study consisting of 116,671 female nurses as subjects. Women were determined to be eligible for the study if they had reported in their 1991 questionnaire as having a history of GDM, without T2DM or other serious diseases. Subjects reported the average time spent doing physical activity as well as time spent doing sedentary activities using questionnaires. Covariates such as BMI, diet information, and general body statistics were collected from 1991 to adjust for differences. After receiving reports of T2DM in some participants, they were assessed using the criteria established by the National Diabetes Data group association. The 4,554 total amount of participants were then divided into quartiles based on their median MET-hr/wk level of physical activity.

Results

Amongst the 4,554 women with a history of GDM, 635 incident cases of T2DM were identified (~14%). Women in the lowest quartile of total PA had a 62% increased risk of developing T2DM when compared to those in the highest PA. Each 5 MET hr/wk increment of total PA was related to a 9% total reduction in the risk of T2D (RR 0.91; 95% CI, 0.88–0.94). It was also found that engaging in the minimum recommended amount of PA was related to ~45% reduced risk of progressing from GDM to T2D.

Conclusion

This study showed that increasing PA can lead to a decreased risk in developing T2D in women who previously had GDM. PA has long been shown to improve insulin action, glycemic control and fat oxidation, and storage in skeletal muscle. The loss of visceral fat associated with PA also decreases the risk of developing T2D as it is strongly associated with insulin resistance.

Comment

This study is important because it has a very large number of subjects from one of the largest studies to date—the Nurses' Health study. Although only a questionnaire was utilized to measure activity levels (which may be susceptible to physical activity quantification error or participant bias), this study was able to show that meeting physical activity guidelines lowers T2D risk by about 45% in women previously diagnosed with GDM. This is obviously important news that needs dissemination.

Clinical trial demonstrates exercise following bariatric surgery improves insulin sensitivity

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J Clin Invest 2015; **1**: 248–57

Background

Roux-en-Y gastric bypass (RYGB) is a common surgery used to treat obesity and often results in dramatic weight loss as well as remission of type 2 diabetes (T2D). A modest improvement in insulin sensitivity (S_I) in nondiabetic patients has been noted post-RYGB surgery; however, exercise has been well established to effectively improve peripheral S_I and glucose control as well as glucose effectiveness (S_G , which refers to the ability of glucose per se to stimulate glucose uptake). This is the first randomized control trial that addresses the independent effects of exercise on improving S_I following RYGB surgery. It also examined the additive effect of exercise interventions, along with RYGB, on cardiorespiratory fitness, BMI, weight, and other risk factors following the surgery.

Methods

Subjects were recruited from the University of Pittsburgh Medical Center and East Carolina University bariatric surgery centers in Pittsburgh, Pennsylvania, and Greenville, North Carolina. Eligible participants were between the ages of 21–60 years (BMI < 55 kg/m², completed bariatric surgery 1–3 months prior). After various exclusion criteria were

applied, the total number of subjects was 128 that were further randomized with 66 in the exercise group (EX) and 62 as control (CON). Participants in the EX group were required to complete a minimum of 120 min/wk of semisupervised exercise (treadmill walking or stationary cycling at a moderate intensity) and keep a detailed log of their exercise. Health education sessions were required for both groups. Sessions were held once a month for 6 months and consisted of lectures and demonstrations on medications and nutrition.

Results

The EX group performed an average of 147 ± 15 min/wk (mean, SEM) of physical activity (exercise) over the final 12 weeks of the intervention. Lack of adherence to the exercise program resulted in exclusion from analysis. Subjects who performed over 120 min/wk of exercise in the final 12 weeks greatly improved their S_I when compared to the CON group (EX vs. CON; $+2.69$ vs. $+1.57$, $\text{min}^{-1}/\mu\text{U/mL}$, $P=0.019$). There was also an improvement of S_G seen in the EX group (EX vs. CON; $+0.0063$ vs. $+0.0023$ min^{-1} , $P=0.009$). Weight loss was noted across both groups, but there were no significant differences between the two. Cardiorespiratory fitness, measured by VO_2peak , was significantly improved in the EX group when compared to the CON, a finding that was deemed valuable since improved cardiorespiratory fitness is associated with a decreased risk in all-cause mortality (15).

Conclusion

This study indicates that moderate exercise brings about improvements in insulin sensitivity (S_I) and the ability of glucose to stimulate glucose uptake (S_G), as well as cardiorespiratory fitness in subjects who have experienced RYGB surgery. It is clear that obese subjects who participate in physical activity gain additional benefits in glucose metabolism compared to just having the RYGB surgery alone.

Comment

This study's importance lies in that it succeeded in providing an improved prognosis following RYGB surgery with added exercise, with respect to enhanced insulin sensitivity, glucose effectiveness and aerobic fitness. Although the sample was not very diverse (mostly young to middle age women), it was a relatively large sample (128 post RYGB patients). Some limitations lie in that it is unknown if there were benefits of health education as there was no group that did not receive the lectures, and nutritional intake was not monitored. Nonetheless, the study succeeded in providing evidence that increased PA results in overall increased health and is useful for those who have undergone RYGB surgery.

Increase in physical activity is associated with lower HbA1c levels in children and adolescents with type 1 diabetes: Results from a cross-sectional study based on the Swedish pediatric diabetes quality registry (SWEDIABKIDS)

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Diabetes Res Clin Pract 2014; **105**: 119–25

Background

Physical activity (PA) is highly recommended for children with type 1 diabetes (T1D). It has many benefits that include increased insulin sensitivity, improved physical fitness, and improved psychological well being. It is unclear if PA results in decreased levels of glycated hemoglobin (HbA1c) in pediatric type 1 diabetes, since many studies show conflicting results. The purpose of this study was to evaluate the association between physical activity and levels of HbA1c in children with T1D.

Methods

SWEDIABKIDS is the Swedish pediatric diabetes quality registry that contains data from 99% of the children in Sweden with diabetes. In Sweden, children with diabetes visit the clinic a minimum of four times a year, where HbA1c levels are measured along with other variables. In this study, HbA1c levels were analyzed via blood samples. The study grouped the patients into quartiles by frequency of PA lasting at least 30 min on each occasion: PA0, none; PA1, less than once a week; PA2, 1–2 times per week; PA3, 3–5 times per week; and PA4, every day. Data on 4,655 children and adolescents and a total of 16,891 visits remained after excluding those children who had not recorded their PA or HbA1c levels.

Results

After stratifying the groups, a clear association was seen between age and HbA1c levels. In the oldest group (16–19 years), there was a greater increase in HbA1c in girls when compared to boys (3.3 mmol/mol higher in girls; $p<0.001$). Boys were generally more physically active (58% $\geq$ PA3) than girls (53% $\geq$ PA3, $p<0.001$). Weekly physical was also negatively associated with age. The lowest activity groups had the highest HbA1c levels (PA0: $8.8\% \pm 1.5$ [72 mmol/mol ± 16]), whereas the opposite was found for the highest activity group (PA4: $7.7\% \pm 1.0$ [60 mmol/mol ± 11], $p<0.001$). This relationship was found in all groups except for girls' ages 7–10 years. Smokers in particular had a tendency to be less physically active, making up 19% of the PA0 group compared to 1% in the PA4 group. When individuals increased their physical activity frequency over a 1-year period, they were able to decrease their HbA1c levels, further indicating a relationship.

Conclusion

This study demonstrates a clear significant negative association between the amount of physical activity and HbA1c levels in the Swedish pediatric T1D population. This is

expected, but not always observed in some studies (16–19), because PA is known to improve glucose uptake in skeletal muscle and enhance insulin sensitivity. This relationship was seen in both sexes, but interestingly a stronger association was seen in the older age group (15–18 years). Smoking appears to pose a high risk for elevated HbA1c levels, especially when paired with low physical activity. The only negative affect observed with increased physical activity was the tendency to experience severe hypoglycemic episodes more frequently.

Comment

This is a strong study because of the large national (Swedish) pediatric population used and the large amount of information received in its longitudinal design. The use of activity questionnaires may limit somewhat the reliability of these data and a different story may exist in other countries with a more divergent ethnic population. However, the main message that more exercise is better for lowering HbA1c in the pediatric T1D population should now ring loud and clear based on this big study.

Author Disclosure Statement

M.C.R. has been an industry sponsored speaker for Medtronic, Sanofi and Eli Lilly.

A.M.P and N.N. have no competing financial interests.

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