**Long Term Effects of Daily Postprandial Physical Activity on
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Abstract

Previous studies have shown that a bout of moderate or light postprandial physical activity effectively blunts the postprandial increase in blood glucose. The objective of this study was to test whether regular light postprandial physical activity can improve glycemia in persons with hyperglycemia or with high risk of hyperglycemia.

We randomized 56 participants to an intervention or a control group. They were diagnosed as hyperglycemic, not using anti-diabetics or categorized as high-risk individuals for type 2 diabetes. The intervention group was instructed to undertake minimum 30 minutes of daily light physical activity, starting maximum 30 minutes after a meal, in addition to their usual physical activity for 12 weeks. The control group remained with usual lifestyle. Blood samples were taken pre and post.

40 participants completed the study and are included in the results. Self-reported increase in daily physical activity from before to within the study period was higher in the intervention group compared to control (41 ± 25 vs. 2 ± 16 min, $p < 0.001$). Activity diaries and accelerometer recordings supported this observation. The activity in the intervention group started earlier after the last meal compared to control (30 ± 13 vs. 100 ± 57 min, $p = 0.001$). There were no within or between group differences in any glycemic variable from pre to post test.

In conclusion, the present study does not seem to support the notion that regular light postprandial physical activity improves blood glucose in the long term in persons with hyperglycemia or with high risk of hyperglycemia.

Keywords

Exercise, physical activity, walking, blood glucose, postprandial, hyperglycemia, glycemic, carbohydrate, lifestyle.

Introduction

The prevalence of diabetes is increasing, and is expected to exceed 600 million people before 2040 (IDF 2015). This "epidemic" of diabetes and its co-morbid conditions can be reduced by a healthy lifestyle. It is therefore a need to develop simple and effective strategies for diabetes prevention and treatment, which can be implemented in everyday living.

Postprandial glycemia is the blood glucose level in the absorptive phase after food ingestion. Several studies have shown a strong relationship between the magnitude of postprandial glycemia and cardiovascular disease (Cavalot et al. 2011; Cavalot et al. 2006; Chiasson et al. 2003; Coutinho et al. 1999; DECODE 1999; DECODE 2001; DECODE 2003; Hanefeld et al. 2004; Nakagami et al. 2006; Sasso et al. 2004; Sorkin et al. 2005; Temelkova-Kurktschiev et al. 2000). Postprandial glycemia do show a stronger correlation to disease and mortality than fasting blood glucose (Cavalot et al. 2011; Cavalot et al. 2006; DECODE 1999; DECODE 2001; Sasso et al. 2004; Temelkova-Kurktschiev et al. 2000). The largest risk for cardiovascular disease is observed in persons with postprandial blood glucose values defined as "diabetes" or "impaired glucose tolerance". However, the association between postprandial blood glucose levels and cardiovascular disease shows no threshold level and starts well below the area of hyperglycemia, i.e. an elevated risk is present in the upper areas of "normal blood glucose" (Coutinho et al. 1999; DECODE 2003; Levitan et al. 2004).

The positive effect of physical training on blood glucose is well documented (Boule et al. 2001; Snowling and Hopkins 2006; Thomas et al. 2006). However, the timing between food ingestion and exercise affects the acute influence of exercise on postprandial glycemia, with the most pronounced effect observed when physical activity is performed short time after food ingestion (Aadland and Høstmark 2008; Bailey and Locke 2015; Caron et al. 1982; Colberg et al. 2014; Dipietro et al. 2013; Dunstan et al. 2012; Gillen et al. 2012; Hashimoto et al. 2013; Hostmark et al. 2006; Larsen et al. 1997; Larsen et al. 1999; Lunde et al. 2012; Nelson et al. 1982; Nygaard et al. 2009; van Dijk et al. 2013a). Even very light or small amounts of postprandial physical activity have the ability to blunt postprandial increases in glycemia effectively (Aadland and Høstmark 2008; Bailey and Locke 2015; Dipietro et al. 2013; Dunstan et al. 2012; Lunde et al. 2012; Nygaard et al. 2009; van Dijk et al. 2013a). However, little is known about the long-term effect of such activity. Light activity as for example walking is inexpensive, without adverse effects and almost everyone can do it (Morris and Hardman 1997).

The purpose of the present study was to test the hypothesis that regular light postprandial physical activity can improve glycemia of persons with hyperglycemia or with high risk of hyperglycemia.

Materials and methods

Participants and recruitment process

We recruited the participants from Lillehammer, Oslo and the surrounding area in Norway, using information in media, posters, local diabetes associations, mosques, temples and community events. Recruitment started in May 2010 and data collection was completed in June 2014. We included hyperglycemic persons (independent of origin) treated with lifestyle change only and south Asian immigrants with high risk of type 2 diabetes according to Ramachandran's risk score for Asian Indians. Hyperglycemia was defined as previously measured fasting venous plasma glucose $\geq 6.1 \text{ mmol L}^{-1}$ and/or 2 hour glucose tolerance $\geq 7.8 \text{ mmol L}^{-1}$, and a cut off >21 was used for the risk-score according to Ramachandran's recommendations (Ramachandran et al. 2005). Originally, only hyperglycemic persons were included, but due to a low number of participants (in 2010 and 2011) we changed eligibility to also include Asian immigrants with high risk of diabetes type 2 (from 2012). We considered medication or illnesses directly affecting glycemia (other than hyperglycemia per se) as exclusion criteria.

We chose HbA1c, fasting glucose and 2 hour glucose as primary outcome measures. In power calculations we considered a 5% improvement in the primary outcomes; HbA1c or glucose as clinical relevant. We expected a standard deviation of 5% on the change. Accordingly, 20 participants in each group would be enough to detect a clinical relevant improvement with a two-sided test, $\alpha=0.05$ and power=80%. Interested persons were given detailed written information. A total of 56 persons were randomized to a control group (CON) or an intervention group (INT), of which 16 dropped out after inclusion (Fig. 1). Randomization was done in accordance with the random allocation rule (Lachin 1988). To ensure equal group sizes of $n=20$, the lot from a participant that dropped-out were replaced in the lottery. To limit

interchange of information from INT to CON, family members or close friends that enrolled at the same time were randomized to the same group. Four persons dropped out between randomization and pre-test (Fig. 1), 12 persons dropped out during the intervention period, whereas 40 persons completed the post-tests with 20 persons in each group. Baseline characteristics of the participants who completed the study are given in table 1.

Ethics Statement

The Regional Ethics Committee (REK Sør-Øst, Norway) approved the study, and all subjects gave their written informed consent. The trial and all related studies are registered at clinicaltrials.gov. ID: NCT02536066, URL:

<https://clinicaltrials.gov/ct2/show/NCT02536066?term=h%C3%A5vard+nygaard&rank=2>.

The authors confirm that all ongoing and related trials for this intervention are registered. The trial was not registered prior to enrollment because we were not aware of this requirement.

Intervention

Participants in INT underwent a individual motivation session. Everyone were instructed to add >30 minutes of physical activity each day, starting <30 minutes after a meal, during the 12 week intervention. However, they were free to do more than 30 minutes, and everyone developed individual targets for the level and pattern of postprandial physical activity during intervention. Individual targets were based on each participant's motivation, wishes and possibilities for performing activity after meals. Our intention was to increase the level of postprandial physical activity as much as possible for each individual in INT. The intervention was "home-based", and they were free to do whatever type of activity they wanted, as long as it involved the legs. Prior to target-setting they were given information about the acute effects of postprandial physical activity on blood glucose (Aadland and

Høstmark 2008; Caron et al. 1982; Colberg et al. 2014; Colberg et al. 2009; Derave et al. 2007; Dipietro et al. 2013; Dunstan et al. 2012; Hashimoto et al. 2013; Hostmark et al. 2006; Larsen et al. 1997; Larsen et al. 1999; Lunde et al. 2012; Nelson et al. 1982; Nygaard et al. 2009; Peddie et al. 2013; van Dijk et al. 2013a). They were free to choose which of the daily meals that should be followed by physical activity, but they were informed that the effect was anticipated to be largest after meals with largest carbohydrate intake. Furthermore, the participants in INT were told to maintain their usual diet and live as usual. The participants in CON were instructed to maintain their usual lifestyle habits. We contacted the participants in INT by telephone every 2 – 3 week during the study period to help them maintain motivation for the intervention.

Measurements

The participants were instructed not to do intense or exhausting exercise during the last three days leading up to pre or post-test. Light activity (the intervention included) was allowed. Time from the most recent activity bout to post-test was 2 ± 3 days for CON and 1 ± 0 days for INT (median $\pm$ interquartile range, IQR).

Venous blood samples were analyzed commercially by Furst Medical Laboratories, Oslo. HbA1c was analysed by HPLC- G8, Tosoh Bioscience. Glucose, triglycerides and all cholesterol levels by Advia 2400 Chemistry system, Siemens Healthcare Diagnostics Inc, and insulin and c-peptide by immunoassays, Advia Centaur XP, Siemens Healthcare Diagnostics Inc.

The original protocol included measures of HbA1c and fasted values of glucose, insulin, triglycerides, HDL cholesterol and LDL cholesterol, as well as 2 hour glucose (75 g glucose challenge), systolic BP, diastolic BP, body weight, waist circumference, dietary recordings, accelerometer recordings and questionnaires. After the 8th participant we also added fasting

and 2 hour c-peptide, 2 hour insulin and finger sticks with capillary glucose measurements every 15 minute during the 2 hour oral glucose tolerance test. All data were collected by the first author.

In three subjects the 2 hour insulin value exceeded the upper measurement range of the analysis instrument (all three at the pre-test and two of them at post-test), which were 2080 pmol·L⁻¹. Those values were set to 2080 pmol·L⁻¹ in the analysis. Blood pressure is presented as mean of two measures; one in the fasting state after 5 minutes rest and the other 1 hour after start of glucose intake.

To measure the level of physical activity we used questionnaires, activity diaries and accelerometer recordings. In the questionnaire at the pre-test, the participants were asked about the level of physical activity, defined as walking, bicycling or more intense activity during the 3 months prior to the study. In the questionnaire at the post-test, they were asked about the magnitude of change in such activity from before the study to within the study period. During the entire study period they kept an activity diary which included type of activity, duration, perceived exertion (Borg 1982), and time from end of last meal to start of activity. In the diary, physical activity was defined as all activity involving the legs and lasting >10 minutes. Accelerometers were used to estimate the level of physical activity pre study and during study. Before the study, the participants used the accelerometers (ActiGraph GT3X, ActiGraph. LLC, Pensacola, FL, US) for four consecutive days at home; 3 weekdays and 1 day during the weekend. The accelerometers were carried at the right hip, while awake (Troost et al. 2005). This procedure was repeated on the same weekdays in the middle of the study period. The accelerometers registered vertical acceleration 30 times per second in units called counts. Mean count values were stored in 10-second intervals. We downloaded the data to the ActiLife software provided by the manufacturer (ActiGraph, LLC). To control for the influence of wear-time on the total amount of counts we used wear-time computed by the

software. This was defined as total registration time minus all time with at least 60 consecutive minutes with zero counts, with allowance for up to 1 minute with counts greater than zero. Such accelerometer recordings is regarded as a preferred method for assessing free living physical activity level and the correlation to other methods (e.g. indirect calorimetry) is in the range $r=0.45 - 0.90$ (Hansen et al. 2014; Trost et al. 2005).

To assess dietary habits, the participants also performed dietary recordings. They did this registration simultaneously as the accelerometer recordings. Every component of every meal was carefully registered by a digital kitchen scale and noted in the diary during this four-day period. Dietary assessment data were analyzed using a nutrient analysis program (Mat på Data 5.0, The Norwegian Food Safety Authority, Oslo, Norway).

Statistics

We did the statistical analyses with IBM SPSS statistics, version 22.0. Analysis of within group changes and comparisons between groups of within group changes were done with a linear mixed model. Participant number was used as the “repeated subject variable” with random intercept. Group and time (pre, post) were used as fixed factors. The effect of intervention was defined as the group*time interaction. Residuals were checked for normality and homogeneity. Between group comparisons of data sampled only on one time point was done with independent t-tests. Correlations were done with Pearson's r . However, there were some exceptions since the residuals for the comparison of the pre and post values for 2 hour insulin (CON and INT) and LDL cholesterol (INT) were indistinctly skewed. We performed both parametric and nonparametric tests (Wilcoxon) for the within group comparisons, and chose to report the highest p value for each variable. However, choose of method did not affect whether any difference was significant or not. The level of physical activity prior to

study and during study were markedly skewed (both CON and INT) and p values were obtained with Mann Whitney U. The α -level was set at 0.05 and a p value <0.1 was considered as a tendency towards statistical significance. The data are presented as means $\pm$ SD except from physical activity prior to and during study, which are presented as median $\pm$ IQR. The result section is based upon the 40 participants that completed the study, unless intention-to-treat or otherwise are stated. All 40 are included, regardless of whether they did all the recommended activity or not, unless otherwise stated. Missing values in the intention-to-treat analysis (post-test results of dropouts) were replaced by the baseline values.

Results

Dietary recordings

12 participants in CON and 17 in INT completed the dietary registration. All 11 participants who did not complete the dietary registration reported that they were not on a diet low on carbohydrates. Data from the recordings are given in table 2. Between groups analysis showed that the fat consumption decreased in INT compared to CON from pre to midway ($p=0.010$), and dietary fiber decreased in CON compared to INT ($p=0.015$).

Level of physical activity

Activity levels reported in questionnaires are shown in table 3. Prior to the study the participants in CON reported 12 minutes more physical activity per day for the last three months than INT (defined as walking, bicycling or more intense activity, $p=0.001$). The

participants in INT reported an increase in activity level from before the intervention to within the intervention period of 41 ± 25 minutes per day, while CON reported an increase of 2 ± 16 ($p < 0.001$ between groups). Results from accelerometer measurements are presented in table 4. INT had $44 \pm 70\%$ increase in accelerometer counts from before intervention to within intervention. The corresponding value in CON was $5 \pm 56\%$. However, the difference between INT and CON was only borderline significant ($p = 0.061$). One subject reported swimming as main activity during INT (without the accelerometer). Results from activity diaries showed that INT performed 1.3 ± 0.8 bouts of physical activity per day during intervention (table 3). Each bout lasted 56 ± 21 minutes, with an intensity of 11.3 ± 1.0 on Borg RPE scale (physical activity was defined as all activity involving the legs and lasting >10 minutes). The total amount of activity performed per day tended to be higher than in CON (1.0 ± 0.7 bouts per day with duration 53 ± 36 minutes per bout, $p = 0.085$). The activity of INT started 30 ± 13 minutes after the last meal, which was earlier than the corresponding value in CON (100 ± 57 minutes after meal, $p = 0.001$). The pattern of physical activity in INT is shown in figure 2 in relation to the blood glucose curve during the glucose tolerance test. The predominant activity during intervention in INT was walking, but there was also registered some bicycling, gardening and swimming.

Health related outcomes

One of the participants reported some flatulence as a result of the intervention, otherwise no side effects was reported. Results from blood samples, anthropometry and blood pressure are shown in table 5. Neither intention-to-treat analysis, nor analysis with only the participants that completed the study revealed any effect of intervention on HbA1c, glucose, insulin or c-peptide measures. There was no significant interaction between the effect of intervention and

carbohydrate intake or ethnicity. Blood glucose curves during the 2 hour oral glucose tolerance test are shown in figure 2. There was no significant correlation between the baseline values and the pre to post change in the glycemic variables.

The change in level of physical activity reported by questionnaire or measured by accelerometer did not correlate significantly with change in any glycemic variable in INT. Correlation coefficients to HbA1c, fasting and 2 hour glucose were 0.302, -0.071 and 0.262 for change in physical activity based on questionnaire results and 0.236, 0.005 and -0.003 for the change in physical activity based on accelerometer counts. A subgroup analysis in INT after exclusions of the participants that did report a change in physical activity level of <30 minutes per day, showed that the participants who added more than 30 minutes of activity each day (n=14) did not have any effect of the intervention on HbA1c or glucose values. Accelerometer data confirmed the increase in activity level in this group, with a mean increase from pre to midway by $55 \pm 77\%$ ($p < 0.001$). An additional exclusion (per protocol analysis) of the participants that started activity >30 minutes after the last meal did not change this result (n=9). Accelerometer data confirmed the increase in activity level also in this group, with a mean increase from pre to midway by $61 \pm 70\%$ ($p < 0.001$).

Among the lipoproteins (table 5) there was a difference between groups in the change of LDL cholesterol from pre to post ($p = 0.036$). Waist circumference and body weight were reduced in INT compared to CON ($p = 0.031$ and $p = 0.009$ respectively).

Discussion

The main finding in this study is that the addition of daily postprandial physical activity for 12 weeks did not improve glycemia in the participants who was either hyperglycemic or defined as persons with high risk for type 2 diabetes.

The results from the questionnaires and accelerometers confirm that the participants in the intervention group actually increased their level of physical activity. The accelerometer results may though have underestimated the increases in activity level, since some of the participant in the intervention group practiced swimming (without the accelerometer) and bicycling as regular activities during intervention. Bicycling is poorly registered by accelerometer worn on the hip (Hansen et al. 2014). Results from the activity diary that were recorded during the study also suggest that the intervention group increased their level of physical activity, since the reported activity level tended to be higher than in the control group. However, the results from the activity diaries are difficult to interpret, since there is no baseline data, and as suggested by the results from the questionnaires, there may have been a higher baseline activity level in the control group than in the intervention group. The increased activity level in the intervention group induced a reduction in body weight and waist circumference. The body weight and waist circumference reductions were however just modest. It might therefore be speculated that the reported changes in activity level is overestimated, or that a dietary compensation to the increased activity level have occurred. Such a dietary compensation is however not supported by the results from the dietary recordings. The intensity and duration of the added activity may therefore have been too low to cause major reduction in fat mass.

Independent of the level of activity performed it seems convincing that the intervention group had changed their activity pattern with regard to timing to the preceding meal. A start of

activity 30 minutes after the last meal was much earlier than the control group and the variability in this time was low between the participants in the intervention group. This timing between food intake and onset of physical activity has been suggested to be ideal for lowering postprandial glycemia in diabetic persons, due to a high insulin-to-glucagon ratio at this point (Chacko 2014). A high insulin-to-glucagon ratio would in turn inhibit the counter regulatory increase of hepatic glucose output that will occur when exercise is done at other times. In accordance with this, it has been shown that the glucose lowering effect of physical activity depends on the glucose level at onset of activity. If the glucose level is high, the subsequent decrease during physical activity will be larger (Gaudet-Savard et al. 2007). It is very likely that glycemia is at its highest 30 minutes into the postprandial phase in persons with moderate glycemia (Derave et al. 2007; Dipietro et al. 2013; Dunstan et al. 2012; Little et al. 2014; Lunde et al. 2012; Nelson et al. 1982). Thus, the lack of improvement in glycemia was present despite changes in activity patterns that should be ideal for blunting of glycemic excursions. The reported duration of the light activity bouts in the intervention group is also long enough to blunt postprandial glycemia substantially (Dipietro et al. 2013; Dunstan et al. 2012; Lunde et al. 2012; Nygaard et al. 2009). An alternative could have been to do shorter activity bouts after a higher number of meals (Dipietro et al. 2013). It is however, not known if such an approach would have been more successful, and it might have been harder to carry out for the participants.

Some of the participants in the intervention group did not add >30 minutes of physical activity each day, and did not start <30 minutes after a meal which they were told to do. However, the exclusion of these participants in the analysis did not affect the results. Furthermore, there was no significant correlation between the amount of postprandial physical activity added during intervention and the effect on glycemia. Indeed, if any relationship was

present, it was in disfavor of the hypothesis. This observations reinforce our findings of lack of chronic effect of the intervention on glycemic response.

One might question whether the results is influenced by the fact that the sample was rather heterogeneous. There was however no significant correlation between the severity of hyperglycemia and the effect of intervention. Heterogeneity between groups might also have influenced the results. The most pronounced difference between groups were observed in baseline physical activity, with a higher level in the control group compared to the intervention group. It is however hard to interpret this as a possible explanation of lack of effect in the intervention group, since a low level of physical activity intuitively should enlarge the potential for an effect of an activity intervention. A corresponding reasoning can be done for glucose tolerance that appear to have been most impaired in the intervention group. In addition, there is a lack of positive effect also within the intervention group. This reinforce the impression that the lack of differences between groups is not a result of baseline characteristics in the intervention group.

Among the participants who were of different ethnicities, there was a variation in carbohydrate intake. A traditional Asian diet represent a higher glycemic load than a traditional European diet (Burden et al. 1994; Hu et al. 2012), and some of the ethnic European participants did in fact report to be on a low carbohydrate diet. Low carbohydrate intake entails smaller postprandial excursions in blood glucose compared to a large intake and may therefore decrease the potential for a glycemic effect of physical activity. There was no statistical relationship between the amount of carbohydrate intake and the effect of the intervention, but it cannot be ruled out that a low carbohydrate intake in some of the participants has decreased the possibility of finding an effect of the intervention.

The positive effect of regular exercise on hyperglycemia is well documented (Boule et al. 2001; Snowling and Hopkins 2006; Thomas et al. 2006). As shown in a meta-analysis by Qui et al. (2014), also light activity like walking has the ability to decrease HbA1c more than what was observed in the present study. However, this meta-analysis included studies on diabetic participants only, and as mentioned earlier, the glucose lowering effect of physical activity may certainly depend on the baseline glycemic status (Aadland and Høstmark 2008; Church et al. 2010; Hordern et al. 2008; Mikines et al. 1988; Nygaard et al. 2009; Snowling and Hopkins 2006; Van Dijk et al. 2013b; Walker et al. 1999). Nevertheless, the amount of light-intensity physical activity measured by accelerometers is associated with glucose tolerance in a population without known diabetes (Healy et al. 2007). Furthermore, Walker et al. (1999) found that a walking program, comparable to the intervention in the present study, entailed a significant reduction in glycemia also in normoglycemic individuals. Based on previous results of low intensity physical activity interventions and the fact that light postprandial physical activity entails considerable acute reductions of postprandial glycemia (Aadland and Høstmark 2008; Bailey and Locke 2015; Dipietro et al. 2013; Dunstan et al. 2012; Lunde et al. 2012; Nygaard et al. 2009; van Dijk et al. 2013a), it was reasonable to expect a reduction in glycemia also in the present study. The lack of effect raises the question whether some of the anticipated adaptations to regular physical activity are blunted as a result of the nutritional status during postprandial activity.

One possible physiological explanation of the lack of positive results of the intervention is related to intramyocellular lipids. Accumulation of intramyocellular lipids is believed to be an important mechanism behind insulin resistance (Pan et al. 1997; Zhang et al. 2010). These lipids are used as an energy source during exercise. Glucose feeding during exercise has the ability to decrease the release of hormone sensitive lipase which is the rate-limiting enzyme in the breakdown of intramyocellular lipids (Watt et al. 2004). A few studies have demonstrated

a larger breakdown of intramyocellular lipids after postabsorptive exercise compared to exercise in the carbohydrate fed state or after exercise with carbohydrate feeding, in healthy participants (De Bock et al. 2005; Van Proeyen et al. 2011). Furthermore, exercise in healthy participants in the fasted state have advantageous effects on insulin sensitivity during a fat-rich high-energy diet compared to exercise accompanied with glucose intake (Van Proeyen et al. 2010).

All types of physical activity, light activity included, is associated with major health benefits both in diabetic populations (Gregg et al. 2003; Hu et al. 2004) and in the general population (Ekblom-Bak et al. 2013; Manson et al. 1999). Despite growing knowledge about exercise as an effective strategy to improve glycemic control, many diabetes patients do not engage in structured exercise programs (Praet and van Loon 2008). Light physical activity like walking, is simple, inexpensive, without adverse effects and may therefore be a good strategy for implementing physical activity (Morris and Hardman 1997). The results of the present study should therefore not be interpreted as if light physical activity does not matter to health. Indeed, health benefits like reduction of body weight, waist circumference and LDL cholesterol were observed in the present study. However, our results do not support the notion that physical activity should be performed just after a meal if the purpose is to improve glycemia. The study should be interpreted with care, with regard to the methodological concerns and potential bias mentioned above. The results contrasts results from a review based on findings in acute studies, which concludes that physical activity should be done in the postprandial state for improving postprandial glycemia, at least if carbohydrates is a main nutrient (Haxhi et al. 2013). Our results may be generalized to people in the upper normoglycemic areas or people with moderate hyperglycemia. Postprandial physical activity may affect glycemia differently in people with severe hyperglycemia. Also type 1 diabetes, which is not caused by insulin resistance, may be a suitable area for future research on

postprandial physical activity. There is a need for a direct comparison of postabsorptive and postprandial physical activity in the long term. Furthermore, the effects on other health parameters in addition to glycemia should be explored. For example, there are indications that postprandial glycemic excursions leads to cardiovascular diseases via several mechanisms that can be assessed (Standl et al. 2011).

Conclusion

The present study does not seem to support the notion that regular light postprandial physical activity improves blood glucose concentrations in the long term in persons with hyperglycemia or with high risk of hyperglycemia.

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Conflict of interest

The authors report no conflicts of interest associated with the manuscript.

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Tables

Table 1. Baseline characteristics of the participants that completed the study

	CON	INT
Participants, n	20	20
Previously diagnosed with hyperglycemia, n	10	13
of which diagnosed with diabetes, n	5	5
Time since diagnosis of hyperglycemia, months	26 ± 27	35 ± 39
Included by Ramachandran's risk score, n	10	7
Asian origin, n	11	12
European origin, n	9	8
Female, n	7	6
Age, years	46 ± 8	53 ± 9
Postmenopausal women, n	5	5
Height, cm	172 ± 10	168 ± 10
Body weight, kg	80.7 ± 17.8	74.4 ± 10.7
BMI, kg·m ⁻²	27.4 ± 4.5	26.3 ± 2.4

Hyperglycemia was defined as previously measured fasting venous plasma glucose ≥ 6.1 mmol·L⁻¹ and/or 2 hour glucose tolerance ≥ 7.8 mmol·L⁻¹. Diabetes was defined as previously measured fasting venous plasma glucose ≥ 7 mmol·L⁻¹ and/or 2 hour glucose tolerance ≥ 11.1 mmol·L⁻¹. A cut off >21 was used for the risk-score according to Ramachandran's recommendations (Ramachandran et al. 2005).

Table 2. Dietary intake per day.

	CON, n=12		INT, n=17	
	Pre	Midway	Pre	Midway
Energy intake, KJ	8279 ± 2150	8043 ± 1819	8231 ± 2216	7364 ± 1602 \$
Protein, g	86 ± 18	83 ± 14	88 ± 24	83 ± 26
Fat, g	78 ± 25	84 ± 28	82 ± 39	66 ± 32 * #
CHO, g	212 ± 87	193 ± 68	199 ± 97	194 ± 88
Mono + disaccharide, g	91 ± 62	85 ± 46	72 ± 39	61 ± 29 \$
Starch, g	117 ± 45	105 ± 36	126 ± 77	131 ± 72
Added sugar, g	36 ± 46	35 ± 26	26 ± 24	21 ± 18
Dietary fiber, g	30 ± 12	22 ± 9 *	23 ± 8	23 ± 8 #

Mean ± SD calculated from four days dietary recordings performed before and during the study period (midway). \$=p<0.1 within group. *=p<0.05 within group. #=p<0.05 between groups, change from pre to during study.

Table 3. Physical activity patterns.

	CON	INT
<u>Questionnaire:</u>		
Physical activity level pre study, min per day (median $\pm$ IQR)	21 $\pm$ 22	2 $\pm$ 17 **
Change from pre to during study, min per day	2 $\pm$ 16	41 $\pm$ 25 **
<u>Physical activity diary:</u>		
Physical activity during study, min per day (median $\pm$ IQR)	38 $\pm$ 48	58 $\pm$ 72 \$
Daily bouts of physical activity	1.0 $\pm$ 0.7	1.3 $\pm$ 0.8
Duration per bout of physical activity during intervention, min	53 $\pm$ 36	56 $\pm$ 21
Time between physical activity and the last meal, min	100 $\pm$ 57	30 $\pm$ 13 **
Perceived exertion (Borg 6-20 scale)	11 $\pm$ 2	11 $\pm$ 1

Mean values $\pm$ SD except from physical activity pre and during study, which are median $\pm$ IQR.

Values are calculated from activity diaries of the 12 week study period, except from “Physical activity level pre intervention” and “changes from pre intervention”, which was asked for in questionnaires pre and post intervention. All participants answered the questionnaire, while 16 and 20 fulfilled the activity diary in CON and INT respectively. Note that the definition of physical activity differed in the questionnaires vs the diary. \$=p<0.1 between groups, **=p<0.001 between groups.

Table 4. Accelerometer data.

	CON, n=18		INT, n=20	
	Pre	Midway	Pre	Midway
Wear-time, hours per day	14.4 ± 2.2	13.4 ± 2.7	15.3 ± 1.7	14.2 ± 2.8 *
Counts per day	339026 ± 187319	320632 ± 203603	292602 ± 150506	379281 ± 178849 * \$

Mean ± SD calculated from four days accelerometer recordings performed before and during the 12 week study period (midway). *=p<0.05 within group. \$=p<0.1 between groups, change from pre to during study. 18 in CON and 20 in INT completed the accelerometer recordings.

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Table 5. Main results.

	CON		INT	
	Pre	Post	Pre	Post
HbA1c, %	6.2 ± 0.6	6.1 ± 0.8	6.2 ± 0.5	6.1 ± 0.8
Glucose, fasting, mmol·L ⁻¹	5.9 ± 1.1	6.0 ± 1.5	6.0 ± 1.3	6.2 ± 1.8
Glucose, 2 hour, mmol·L ⁻¹	7.7 ± 3.5	8.6 ± 5.1	8.8 ± 4.0	8.9 ± 4.8
Mean glucose during 2 hour glucose tolerance test, mmol·L ⁻¹	10.5 ± 2.4	9.1 ± 2.5	10.5 ± 3.1	9.5 ± 3.2
Insulin, fasting, pmol·L ⁻¹	94 ± 52	108 ± 75	110 ± 74	98 ± 54
Insulin, 2 hour, pmol·L ⁻¹	634 ± 388	712 ± 415	921 ± 654	907 ± 720
C-peptide, fasting, pmol·L ⁻¹	596 ± 253	622 ± 257	659 ± 197	612 ± 208
C-peptide, 2 hour, pmol·L ⁻¹	2486 ± 790	2508 ± 702	2995 ± 1206	2733 ± 1080
Triglycerides, fasting, mmol·L ⁻¹	1.7 ± 1.1	1.8 ± 0.9	1.4 ± 0.5	1.3 ± 0.6
HDL cholesterol, mmol·L ⁻¹	1.3 ± 0.2	1.3 ± 0.3	1.2 ± 0.3	1.2 ± 0.2
LDL cholesterol, mmol·L ⁻¹	3.5 ± 1.1	3.7 ± 0.9	3.4 ± 1.0	3.2 ± 1.0 #
Waist circumference, cm	97.8 ± 13.8	99.0 ± 12.1	96.2 ± 6.0	94.8 ± 6.0 \$ #
Body weight, kg	80.7 ± 17.8	81.3 ± 17.1	74.4 ± 10.7	73.7 ± 10.4 * #
Systolic blood pressure, mm/Hg	121 ± 18	123 ± 19	125 ± 17	122 ± 14
Diastolic blood pressure, mm/Hg	80 ± 11	80 ± 9	77 ± 10	77 ± 7

Mean values ± SD. \$=p<0.1 within group. *=p<0.05 within group. #=p<0.05 between groups for change from pre to post of the 12 week intervention. n=20 for HbA1c, fasting glucose, 2 hour glucose, fasting insulin, fasting TG, HDL, LDL, Sys BP, Dias BP, body weight and waist circumference in both CON and INT. n=17 for 2 hour insulin, fasting c peptide and 2 hour c

peptide in CON. n=14 for 2 hour insulin and 2 hour c peptide INT. n=15 for fasting c-peptide in INT.

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Figure captions

Fig 1. Participant flow chart

Fig 2. Oral glucose tolerance test in relation to the activity pattern in the intervention group. Curves are blood glucose sampled every 15th minute during pre and post oral glucose tolerance test for CON (left, n=15) and INT (right, n=16). The line with a walking man indicates the pattern of physical activity performed during intervention (Mean: 56 minutes duration, 1.3 times per day with start 30 minutes after a meal, n=20). I.e. physical activity took place when blood glucose was expected to be elevated.