PREVENTIVE EFFECTS OF EXERCISE ON THE OCCURRENCE OF GESTATIONAL DIABETES MELLITUS

PREVENTIVNI UČINAK VJEŽBANJA NA NASTANAK GESTACIJSKOG DIJABETES MELLITUSA

Iva Šklempe Kokić,1 Marina Ivanišević2

Introduction

Gestational diabetes mellitus (GDM) is impaired glucose tolerance of various degrees first manifested during pregnancy. Prevalence amounts to 1–14% of all pregnancies, with an increasing trend parallel to the increase of obesity and type 2 diabetes mellitus rates (T2DM).1–4

Pregnancy is a condition that brings about many metabolic changes, one of the most significant being insulin resistance caused by hormones and placental cytokines, including tumor necrosis factor alpha (TNF-α), human placental lactogen (HPL), placental growth hormone (PGH), cortisol and progesterone.5,6 Apart from providing increased quantities of glucose for the fetus, insulin resistance also results in adaptive increase in pancreatic β-cells function and increased insulin secretion. In susceptible individuals, insulin resistance leads to slow progressive insulin secretion failure.7 Reduced adaptation of pancreatic β-cells is the major causal factor for...
GDM\(^6\) which occurs due to inhibited insulin secretion,\(^8\) when insulin secretion is insufficient in relation to insulin resistance.\(^5\)

The risk of GDM is influenced by different factors, which may be classified according to whether or not they can be influenced.\(^9,10\) Risk factors that can be influenced include body mass index over 25, lack of physical activity and sedentary lifestyle, low-fibre and high GI diet.\(^11–13\) Increase of body mass index by merely one unit is accompanied by the increase of GDM prevalence by 0.92%.\(^14\) Risk factors that cannot be influenced are pregnancy over the age of 35, affiliation to particular ethnic groups, family history of diabetes mellitus, and woman’s weight at birth, high parity, previous birth of macromomonic infant, GDM during previous pregnancy and polycystic ovary syndrome.\(^13,15,16\)

GDM is related to complications during pregnancy and birth, higher morbidity rates for pregnant women and newborns, as well as certain long-term health risks for the mother and child. In the short term, there is an increased risk of developing preeclampsia and an increased rate of induced labour and caesarean deliveries.\(^17,18\) There is an increased possibility of large-for-gestational-age (LGA) newborns, macrosomia, cephalopelvic disproportion, uterine rupture, shoulder dystocia and perineal laceration.\(^19\) Newborns of mothers suffering from GDM become hypoglycaemic and lethargic, and have larger amounts of adipose tissue. Even lower degrees of hypoglycaemia in pregnant women may be related to adverse outcomes.\(^18,20\) There is an increased risk of numerous perinatal complications, whereas in the long-term children of mothers suffering from GDM face a higher risk of obesity and type 2 diabetes. LGA newborns have a higher risk of developing metabolic syndrome during childhood, adolescence and adulthood.\(^21,22\) GDM triggers and transmits obesity, diabetes and metabolic syndrome from one generation to the next.

Mothers with GDM face a 7–8 times higher risk of developing T2DM,\(^23,24\) whereas the cumulative incidence of T2DM after GDM varies from 2.6 to over 70%, after monitoring within a range of 6 weeks and 28 years after birth.\(^25\) The larger the number of previous pregnancies with GDM, the higher the risk of GDM recurrence in subsequent pregnancies, with recurrence rates ranging from 35 to 80%.\(^26\)

The principal goals of treatment are to optimize glycaemic control and improve pregnancy outcomes.\(^27\) The first instance of treatment consists of changes in diet and lifestyle.\(^28,29\) Insulin is introduced if necessary, whereas recently oral hypoglycaemic agents are introduced as well. As part of treatment, it is recommended to continue or initiate exercising with moderate intensity, provided there are no contraindications.\(^29,30\) Considering high efficiency of conventional treatment of GDM, it could be difficult to find additional modalities for improvement of perinatal and neonatal outcomes.\(^31\) Prevention of GDM could be the key to avoiding adverse health outcomes.

Although the risk factors and possible GDM outcomes are well known, there are not many findings on GDM prevention. There are indications that exercise before and during pregnancy may be effective in GDM prevention, without much evidence, however, from randomized controlled trials. Available data has mostly been obtained in cohort studies.

The purpose of this article is to provide an overview of preventive effects of physical activity and exercise before and during pregnancy on the occurrence of GDM. It provides an overview of current evidence on the relation between physical activity and development of GDM, as well as the possibility of using exercise programmes in GDM prevention.

Comprehensive database search within Pubmed, OvidSP and ClinicalTrials.gov was performed during May 2012 in order to find articles on preventive effects of exercise programmes on GDM occurrence. The search was not limited with respect to trial design and time when article was published, apart from using exclusively articles related to GDM prevention. The key terms and their combinations used for the search were: »pregnancy«, »gestational diabetes mellitus«, »GDM«, »prevention«, »exercise«, »physical activity«, »insulin resistance«, »hyperglycaemia« and »glucose tolerance«. The procedure was concluded by using references found in all relevant papers. The search did not take into consideration the trials dealing with short-term effects of exercise, or therapeutic effects of exercise after GDM has already been diagnosed.

Preventive value of exercise

The effects of exercise before and during pregnancy on the prevention of GDM are specified mainly in cohort studies and a small number of randomized controlled trials, with discrepant and contradictory results. Studies relate higher levels of physical activity before and during early pregnancy with a lower risk of developing GDM.\(^32\) Only one randomized trial studied the effects of exercise on the prevention of GDM and insulin resistance in the general population of healthy pregnant women.\(^33\) Another two randomized controlled trials studied the effects of exercise in healthy pregnant women on glycaemic control parameters (insulin resistance, blood glucose and insulin levels),\(^34,35\) but due to small samples were not sufficiently statistically powerful to measure GDM prevalence as an outcome.

Stafne and associates\(^33\) conducted a randomized controlled trial including the total of 855 healthy pregnant women (experimental group BMI: 24.7 +/- 3.0; control group BMI: 25.0 +/- 3.4) with gestational age ranging between 18 and 22 weeks. The experimental group underwent a standard 12-week exercise programme, whereas the control group received standard prenatal health care. The exercise programme adhered to the guidelines for exercise during pregnancy\(^36\) which consisted of a combination of moderate and high-intensity exercises for three or more days a week. The programme
included aerobic, strength and balance exercises, where-
as supervised 60-minute training was applied once a
week. Furthermore, women were encouraged to follow
a written 45-minute exercise programme consisting of
30 minutes of endurance training and 15 minutes of
strength and balance exercises, at least twice a week.
The primary studied outcomes included the occurrence
of gestational diabetes and insulin resistance. The anal-
ysis included data on 375 women from the experimen-
tal group and 327 women from the control group. For
the women between the 32nd and 36th week of pregnancy
there were no statistically significant differences in
GDM prevalence between groups (25/375 (7%) for
the intervention group vs. 18/327 (6%) for the control
group, p=0.52). Likewise, there were no statistically
significant differences with respect to insulin resistance.
Only approximately 55% of women in the experimental
group managed to follow the recommended exercise
protocol. Women in the experimental group exercised
twice a week on average with moderate or high inten-
sity, whereas only approximately 10% of pregnant
women in the control group exercised three times a
week with moderate or high intensity i.e. pregnant
women in the control group exercised on average 0.7
days a week. Pregnancy outcomes were similar for both
groups. The authors of the trial concluded that execut-
ing a 12-week exercise programme during the second
half of pregnancy does not help prevent gestational dia-
betes, nor does it improve insulin resistance in healthy
pregnant women.

Hopkins and associates34 conducted a randomized
controlled trial examining the effects of aerobic exer-
cise programmes on maternal insulin sensitivity and
neonatal outcomes in 84 healthy pregnant women (47
within the experimental group and 37 within the control
group), during their second half of pregnancy. The exer-
cise programme included the use of exercise bicycle at
home from the 20th gestational week to birth. The pro-
grame allowed the maximum of five 40-minute train-
ings a week and aimed at achieving a moderate exercise
intensity of approximately 65% VO2max. It is recom-
ended to maintain exercise until at least 36th gesta-
tional week, preferably until the very birth. The percentage
of women adhering to the exercise protocol amounted
to 75 +/- 17% of the total number of set trainings. In-
fants of women in the experimental group showed lower
birth-weight values (p=0.03) and lower BMI after birth
(p=0.04), however, without statistically significant dif-
fences in maternal insulin sensitivity.

Callaway and associates35 conducted a randomized
controlled trial examining the feasibility of exercise
programmes aimed at preventing GDM in obese preg-
nant women. The trial included 50 pregnant women, 25
in the experimental group and 25 in the control group.
73% of women within the experimental group (16 out
of 22) burned more than 900 kcal a week during exer-
cise activities, as opposed to 42% of women in the con-
trol group (8 out of 19) (p=0.047). There was a statisti-
cally significant difference in fasting glucose levels in
the 28th week of pregnancy (p=0.03), as well as fasting
insulin levels in the 36th week (p=0.05), with no signifi-
cant differences, however, between groups with respect
to insulin resistance (HOMA-IR). Authors of the trial
explain these findings as a result of potentially insuffi-
cient differences in physical activity levels between
groups i.e. conclude that exercise may not be a suffi-
ciently effective means of influencing insulin resistance,
and that HOMA-IR may not be the best method of es-
timating the effects of exercise on insulin resistance,
because it provides a better insight on hepatic insulin
resistance than peripheral insulin resistance, whereas
exercise probably reduces peripheral insulin resistance.

Redden, Lamonte, Freudenheim and Rudra37 con-
ducted a cross-sectional study on the relation between
recreational physical activity before pregnancy and
GDM. The study included 1051 women with GDM and
10351 women who did not develop GDM during preg-
nancy. By means of structured interviews a postpartum
estimate was made of recreational physical activity for
the period of three months prior to pregnancy. When
compared to women who exercised less than twice a
week, women who exercised more than five times a
week had a 31% less chance of developing GDM (aOR
0.69, 95% CI 0.46–1.03). Women who exercised 1–4
times a week had a 7% less chance of developing GDM
(aOR 0.93, 95% CI 0.72–1.19). Authors of the study did
not establish a statistically significant relation between
the level of physical activity prior to pregnancy and the
risk of developing GDM, whereas the findings are con-
sistent with previous observational studies. Observed
trends do, however, suggest that physical activity may
play a role in the prevention of GDM.

The results of prospective cohort studies indicate that
the risk of GDM decreases by 20–55% in women who
have engaged in physical exercise of various duration
and intensity, before and during pregnancy.38–40 The
meta-analysis conducted by Tobias and associates32 in-
dicates that there is a 55% lower risk of GDM for the
women in the quintile of highest physical activity be-
fore pregnancy, as opposed to those in lower quintiles
(OR 0.45, 95% CI 0.28–0.75, p = 0.002), as well as a
24% lower risk for women who were the most active
during early pregnancy (OR 0.76, 95% CI 0.70–0.83,
p<0.0001).

The Viva project39 studied the relation between physi-
cal activity and watching television before and during
pregnancy, and the risk of developing GDM and abnor-
mal glucose tolerance. The trial included 1051 women,
(OR 0.45, 95% CI 0.28–0.75, p = 0.002), as well as a
24% lower risk for women who were the most active
during early pregnancy (OR 0.76, 95% CI 0.70–0.83,
p<0.0001).

The Viva project39 studied the relation between physi-
cal activity and watching television before and during
pregnancy, and the risk of developing GDM and abnor-
mal glucose tolerance. The trial included 1051 women,
engaged in strenuous physical activities before pregnancy, and continued with mild or moderate physical activities during pregnancy had an even lower risk of developing GDM (OR 0.49, 95% CI 0.24–1.01) and abnormal glucose tolerance (OR 0.70, 95% CI 0.49–1.01), as opposed to women who were physically inactive in those periods. Walking and overall physical activity produced moderate benefits, whereas watching television could be related to neither GDM, nor abnormal glucose tolerance.

Zhang and associates\(^{40}\) came to similar results in their prospective cohort study ("Nurses’ Health Study II") which included 21 765 women who have given birth at least once between 1990 and 1998. They studied whether the quantity, type and intensity of exercise prior to pregnancy and sedentary lifestyle are related to the risk of developing GDM. In the total population participating in the trial 1428 cases of GDM were documented. After covariance adjustment, a significant inverse relation was established between strenuous physical activity and the risk of developing GDM. The multivariate relative risk (RR) of comparing the highest quintile of strenuous activity with the lowest amounted to 0.77 (95% CI 0.69–0.94, \(p\) (trend)=0.002). Among the women who did not engage in strenuous physical activity, those who used to power walk had a significantly lower risk of developing GDM (RR 0.66; 95% CI, 0.46–0.95), as opposed to those who took slower walks. The women who watched television 20 or more hours a week and did not engage in strenuous physical activities had a significantly higher risk of developing GDM, as opposed to women who watched television less than two hours a week and were physically active (RR 2.30; 95% CI, 1.06–4.97). Authors of the study concluded that there is a strong relation between engaging in physical activity before pregnancy and a lower risk of developing GDM.

Dempsey, Butler and Williams\(^{41}\) established that the risk of developing GDM in women who were physically active during the first 20 weeks of pregnancy was decreased by 48%, as opposed to physically inactive women (OR 0.52, 95% CI 0.33–0.80). Women who engaged in recreational physical activities in the year prior to pregnancy also had a decreased risk of developing GDM, whereas those who were physically active before and during pregnancy showed the highest risk decrease (OR 0.40, 95% CI 0.23–0.68).

An inverse relation was also established between walking before pregnancy and the risk of developing GDM. Women who engaged in long-distance power walking, i.e. > 2 miles a day\(^{41}\) or > 30 min a day\(^{40}\) had a lower risk of developing GDM, as opposed to women who took slower walks or shorter distances, but this relation did not produce any statistical significance during pregnancy. Likewise, stair climbing, i.e. \(≥\) 10 sequences of stairs a day\(^{41}\) or \(≥\) 15 sequences of stairs a day\(^{46}\) before and during early pregnancy is inversely related to the risk of developing GDM.

Liu, Laditka, Mayer-Davis and Pate\(^{42}\) aimed at establishing whether women who were physically inactive prior to pregnancy and have become physically active during pregnancy have a lower risk of developing GDM. The analysis included 4813 women who were physically inactive before pregnancy, had given birth to one child and had not been previously diagnosed with diabetes. GDM was diagnosed in 3.5% of women, whereas 11.8% of the previously physically inactive women began exercising during pregnancy. Women who became physically active had a 57% lower adjusted risk of developing GDM, as opposed to those who remained physically inactive (OR 0.43, 95% CI 0.20–0.93). The women who engaged in power walking also had a lower risk (OR 0.44, 95% CI 0.19–1.02), whereas those with above-median physical activity index had a 62% lower risk of developing GDM, as opposed to physically inactive women (95% CI 0.15–0.96). Authors of the trial concluded that beginning physical activity during pregnancy in otherwise inactive pregnant women is related to a lower risk of developing GDM.

Sopper, Hammond, Giroux, McManus and Mottola\(^{43}\) developed the NELIP prevention programme ("Nutrition and Exercise Lifestyle Intervention Program"), consisting of slow walks (30% \(V_{O_{2}max}\)) combined with food intake control (8350kJ a day, with the maximum of 200 g carbohydrates a day) for women with a higher risk of developing GDM. The results were encouraging and the women who participated in the programme did not develop GDM, body mass increase was prevented, whereas normal glucose tolerance was maintained for two months postpartum.\(^{44}\) In addition, high-risk women included in the programme maintained their insulin sensitivity index similar to that of women with low GDM risk, and not one developed GDM.\(^{45}\) This indicates that low-intensity exercise combined with food intake control does help reduce the risk of developing GDM, regulates blood glucose levels and prevents excessive body mass increase.

Discussion

Taking into consideration that GDM affects a significant number of pregnant women every year with a growing prevalence (1–4) and that it is related to numerous complications and disorders during and after pregnancy and birth, its prevention is necessary. Physical activity is an economically acceptable means of prevention which also brings numerous other benefits for the mother and fetus. It is a known fact that exercise is also effective in preventing T2DM, because it can prevent or postpone disease incidence in persons with high risk of contracting it. For a long-lasting effect, however, exercise must be regular.\(^{46}\)

Exercise also indirectly prevents the development of GDM, because it can prevent excessive weight gain during pregnancy, which increases the risk of GDM. Taking into consideration that approximately only 50% of non-gravid women follow the advice regarding the min-
Physical inactivity is a risk factor for obesity and T2DM which have begun assuming epidemic proportions in today’s society. Obesity and GDM are closely related, leaving obese women with a 17% higher risk of developing GDM, whereas women with high BMI between 25 and 30 have a 1.8–6.5 higher risk of developing GDM than women with normal weight. Likewise, one of the risk factors is sedentary lifestyle, making it a common risk factor for both obesity and GDM, with obesity and GDM being risk factors for T2DM. Projections made in 2000 predict the possibility of a 114% increase in the number of persons afflicted by T2DM and a prevalence increase ranging from 2.8 to 4.4%. thus making every effective form of prevention truly important due to vast health and economic implications of an epidemic of diabetes, obesity and other diseases related to physical inactivity.

Regular exercise before and during early pregnancy may have a more important role in GDM prevention than exercise during the second half of pregnancy. This is probably the result of chronic adaptations to glucose uptake regulation in skeletal muscles, and of better tolerance of metabolic stress during pregnancy. Most findings, however, originate from observational studies, whereas randomized controlled trials, especially of the population with high risk of developing GDM, are yet to be conducted. Randomized controlled trials of exercise effects on GDM prevention are accompanied by a series of methodological issues. Discrepancies in results of the current trials probably resulted from incomplete randomization, small samples, insufficient control of exercise implementation parameters and the withdrawal of some examinees before the end of intervention. When planning future randomized controlled trials the feasibility of exercise programmes should be taken into consideration i.e. what degree of cooperation and adherence to exercise programmes is to be expected from the examined population, due to a history of relatively frequent examinee withdrawal before trial completion, as well as incomplete implementation of interventions.

A definite clinical significance of a prevention exercise programme is yet to be determined, much like the optimal frequency, intensity, type and duration of therapeutic exercise. It must also be determined which period prior to or during pregnancy yields the best results, what is the preventive value of exercise before and during pregnancy on the one hand, and the benefits of beginning exercise during pregnancy for previously physically inactive women on the other. Likewise, it must be precisely determined which pregnant women groups, depending on risk factors, would benefit from particular forms of exercise and what benefits are to be expected.

Conclusion

Considering the preliminary evidence on the preventive effects of exercise and physical activity before and during pregnancy on GDM incidence, additional randomized controlled trials are necessary to determine the optimal frequency, duration, intensity and type of exercise, as well as the optimal time of implementation. Previously conducted randomized trials have not succeeded in confirming the preventive effects of exercise on GDM prevalence and reduced insulin resistance, which can partly be attributed to small samples and methodological issues.

Likewise, it is necessary to determine the benefits of exercise before and during pregnancy, and the benefits of beginning a preventive exercise programme during pregnancy among the population without risk factors, as well as for pregnant women with one or more risk factors. The preliminary data speak in favour of various benefits of exercise implementation during various stages before and during pregnancy.

Physical activity before or during early pregnancy is significantly related to a decreased risk of developing GDM, with the decrease being most prominent in physically most active women. Physical activity level before pregnancy is one of the biggest predictors of physical activity during early pregnancy, making it difficult to determine whether only one or both of these factors contribute to risk decrease, due to their high degree of correlation. On the other hand, physical activity during the second half of pregnancy may not produce such a significant preventive effect on GDM prevalence and insulin resistance, calling for further research, especially in the population with one or more risk factors.

It is currently impossible to suggest a convenient, cost-effective and evidence-based exercise programme with specific guidelines. Considering the fact that T2DM and obesity are assuming epidemic proportions in today’s society, increased incidence of pregnant women suffering from GDM is to be expected, leading to significant health and economic consequences for this generation and those to come. Exercise during pregnancy might be an effective and economically acceptable method of reducing GDM incidence, as well as a means of preventing risks of T2DM, obesity and other diseases related to physical inactivity, and a means of preventing the transmission of morbidity from one generation to the next, but further research is necessary to confirm this hypothesis.

References


Corresponding author: Iva Škleme Kokić, Ilica 128, 10000 Zagreb, e-mail: iskokic@tvevu.hr