

Comparison the effects of aqua aerobic and resistance training on blood sugar and insulin resistance in women with gestational diabetes mellitus

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Abstract

Introduction: The purpose of this study was to comparison the effects of aqua and resistance training on insulin resistance and homeostasis model assessment of β -Cell function in women with gestational diabetes mellitus.

Material and Methods: For this purpose, 34 women with gestational diabetes voluntarily participated which were selected from the available sampling pool. The subjects were simple random assigned in three groups. 12 subjects participated in an aqua aerobic training group (3 days/week, 30-45 min/day, 50-70% maximum heart rate) and 11 subjects participated in an aqua resistance training group (3 days/week, 2-3 set of 15 repetition, 50-70%maximum heart rate), and 11 subjects were in control group who did not participate in any exercise program during the study period.

Results: The results indicated that HOMA- β increased and fasting glucose decreased in the aqua resistance training ($P < 0.05$), however no significant differences were observed between three groups. For fasting insulin and insulin resistance no significant differences observed after the intervention.

Conclusions: It seems likely that aqua resistance training is more effective in comparison to aqua aerobic training in improving diabetes risk factors in women with gestational diabetes.

Key words: Insulin resistance, Insulin sensitivity, Pregnancy, Gestational diabetes.

1. Introduction

Gestational diabetes mellitus (GDM) is a type 2 diabetes (T2DM) which initiates or diagnosed during pregnancy (1). Pregnancy causes insulin resistance, an impairment which will disappear after childbirth. Pancreatic β -cells normally increase their insulin secretion during pregnancy to compensate for the insulin resistance. As a result, changes in circulating glucose levels over the course of pregnancy are quite insignificant in comparison to the huge changes in insulin sensitivity. Thus, robust plasticity of β -cells function as the progressive insulin resistance is the trademark of normal glucose regulation during pregnancy (2,3).

In women where pancreatic β -cells function is less than normal, secretion may not be enough to compensate for this resistance and this may cause gestational diabetes (2). Insulin resistance and defective pancreatic β -cells are characteristics of gestational diabetes, which will cause an abnormal increase in the liver's glucose production and on the other hand, cause a decrease in glucose uptake of muscle and adipose tissues (1).

GDM is related to numerous complications and adverse outcomes during pregnancy and delivery such as; preeclampsia, prolonged labor and higher rate of cesarean section, macrosomia, cephalopelvic disproportion,

uterine rupture, shoulder dystocia, and perineal laceration (4,5). Even a mild degree of hyperglycemia can create adverse outcomes (5-7). In the long term, GDM carries risks for the mother and child. Newborns of women with GDM are exposed to higher risk of obesity, glucose intolerance, metabolic syndrome and T2DM (8-10) Women with GDM in their medical history are 7-8 times at higher risk of developing T2DM (11,12).

Adequate glycemic control of patients with GDM is necessary to minimize the complications. In this respect, diet therapy is the first method of intervention, if it is unsuccessful, it should be accompanied by insulin treatment. Although it is effective in reducing the risk of fetal macrosomia, but it does not have any effects on the origin of problem (i.e., increased peripheral resistance to the action of insulin in the second half of gestation) (3). In addition, the aggressive use of insulin may result in an increased incidence of small-for-gestational-age infants (13).

Nowadays, the positive role of exercise and physical activity in prevention and control of different diseases has been proven. Physical activity increases the translocation rate of glucose transporters (GLUT-4) to skeletal muscle cell surfaces, independent of insulin's function. Muscle contractions also increase the ratio of AMP/ATP and creatinine to phosphocreatine which quickly activates the Adenosine Monophosphate Kinase (AMPK) 1. AMPK is the key intermediary in fatty acid oxidation and glucose transportation in mammalian cells and it seems that during muscle contraction it causes GLUT-4 translocation (2). Regular physical activity in non-pregnant individuals results in numerous health benefits, such as; improvements in glucose homeostasis and insulin sensitivity. The beneficial effects of physical activities are due to an increased responsiveness of muscle uptake to insulin which is related to an increase in GLUT-4 expression (14).

Until a few decades ago, it was believed that physical activity during pregnancy would cause damages or have adverse effects in mothers and their fetus (13). However, clinical and epidemiological studies have shown that mild and moderate physical activities have no negative effects on mothers and their fetus. At the moment, pregnant women are encouraged to participate in regular aerobic exercise without any medical

consequences (14). The American colleges of obstetricians and gynecologists and the American diabetes association (ADA) have recognized exercise as a complementary treatment for GDM. A lot of evidence show that women who participate in physical activities are less likely to get GDM (15,16). Participating in any kind of physical activity during the first 20 weeks of pregnancy will decrease the risk of GDM by about 50% (15). Exercise can provide benefits to women with GDM which insulin cannot provide (17-20). Exercise has shown to decrease peripheral insulin resistance and may be more acceptable to many women rather than daily insulin injections (19-21).

Aerobic exercises are among recommended activities for weight gain prevention and maintaining cardiovascular fitness (13). Many researches have shown that, resistance training increases glucose transporter (GLUT-4) levels in skeletal muscles, as well as, muscle glycogen synthesis and hexokinase levels that result in glucose uptake and phosphorylation in response to insulin's stimulation (19). Regular physical activities can improve blood glucose control, lipid profile, cardiovascular fitness and body composition in patients with T2DM. Two randomized studies have provided evidence that aerobic training will lower blood glucose levels consistently in women with GDM. Results of these studies demonstrated that aerobic exercise with a frequency as low as three times per week may eliminate the need for insulin therapy in women with GDM (19).

In the meantime, it seems that resistance training is increasingly becoming popular as a suitable way to improve overall health, metabolism and to decrease the risk of diabetic pathogens and side-effects in patients. Resistance training increases the glucose uptake and muscle strength and mass, and can be considered as an effective tool in controlling and treating several diseases (21,22). Appropriate resistance training, like aerobic exercises, will cause an increase in insulin sensitivity, energy costs and improved quality of life (21). Studies on the effects of resistance training have shown a positive relation between resistance training and diabetes control. Moreover, it was shown that appropriate resistance training can decrease pro-inflammatory cytokines in individuals with diabetes (23). In general, advantages of exercise in pregnant women include; increase of GLUT-4 and its translocation in

skeletal muscles, increased insulin sensitivity, metabolism adjustment, and the increase of energy plus higher consumption of oxygen after training (1). Due to importance of pregnancy period and at the same time reduction of physical activity caused by sedentary life and the prevalence of gestational diabetes, studying the effects of resistance and aerobic training on gestational diabetes should be considered as an important issue. Thus, considering different training mechanisms of resistance and aerobic exercise in diabetes, in this research we have compared the effects of these exercises on gestational diabetes and have tried to resolve the mechanisms which have created this deficiency. We have tried to choose the appropriate form of physical activity for these individuals by applying exercise as a complementary treatment.

2. Material and Methods

Subjects

The present researches methodology is interventional. This study, which is registered in the Iranian clinical trials base with the ethical code number IRCT = 2014031717035, was performed during November 2014 until January 2015 in Shiraz. The statistical population of the present study was all the mothers with gestational diabetes who went to the primatology clinic of Hafez educational hospital and the Motahari clinic affiliated with the Shiraz University of Medical Sciences. Sampling was done after getting a written informed consent from each individual who participated in this study. All participants performed these exercises under the supervision of the senior author. Statistical samples were 34 inactive pregnant female with gestational diabetes in their 24th week of pregnancy and under insulin treatment that had no history of physical activity within the past year, systemic diseases and no medical complications in order to do any kind of physical activity. NPH insulin was prescribed for control blood sugar in the morning (before breakfast) and half an hour before dinner; Regular insulin was added at meals to improve the glycemic control if the exclusive use of NPH insulin was not sufficient to maintain the glycemia at adequate levels. The female's gestational age was calculated based on the first day of the last stated and regular menstrual period (LMP) and the ultrasound images of the early stages of pregnancy. These individuals were identified during daily

visits to the Hafez clinic. The participants filled out a questioner that asked about their physical activity levels using the authentic International physical activity questionnaires (IPAQ), and their personal information and medical history was obtained. The subjects were simple random assigned in three groups: aqua aerobic training group (n=12); aqua resistance training group (n=11) or control group (n=11).

Exercise Training Protocol

According to the recommendations and guidelines on women's exercise during pregnancy and the characteristics of aerobic and resistance training programs and the resources at hand, the non-athletic pregnant women's training program was performed during a 6 week period (17-20). The training program included 6 weeks of aqua aerobic and aqua resistance training with moderate intensity (maximum heart rate of 50-70 %), which was done 3 days a week (15,19). The aqua aerobic training started from 30 minutes during the first session and gradually it was raised to 45 minutes per session, in the last sessions. The training consisted of general warm up, stretching exercises outside water and slow walking in water, aerobic exercises with moderate intensity in the water and then slowly walking towards recovery (1,15,19).

Aqua resistance training was performed with an elastic band. The Resistance training consisted of circuit type resistance training, elaborated in such a way that the main muscle groups of the patients would get exercise (chest, back, biceps, triceps, deltoid, quadriceps, thigh, and calf muscles). A circuit series was defined as a sequence of these eight exercises (stations). The women performed 15 repetitions of each exercise (station), with a minimum resting period of 30 seconds and maximum of 1 minute between each set. During the first and second week of follow-up the women underwent 2 circuit series, followed by 3 circuit series from the third week of inclusion in the study till the end of study (24). The intensity of the trainings were controlled based on the Rating of Perceived Exertion (RPE) (21,24) using Polar's heart rate monitor made in Finland. ACOG and Canadian guidelines recommend the use of ratings of perceived exertion (RPE) in addition to heart rate (23). Borg's conventional 6-20-point scale is recommended with 12 to 14 (a rating of 13 corresponds to a subjective rating of "somewhat hard")

identified as the RPE range to apply in pregnancy (23). Hence, 90 minutes after a meal, before participating in a session, each sample's blood sugar levels were measured with a glucometer; if the glucose level was between 100 and 250 mg/dl, the participant would have permission to exercise (24). The experimental groups spent 6 weeks exercising; while the control group did not participate in any training programs.

Measurements

Anthropometric and body composition measurements

At the beginning of the research, heights of the candidates were measured and using their pre-pregnancy weights which were acquired via self-reporting, their body mass index (BMI) was calculated based on kg/m^2 (23,24).

Biochemical analyses

Blood samples were referred to the laboratory for a fasting blood test. 24 hours before the training started and in basic conditions, in order to measure blood variables, blood was taken from the samples between 7 and 8 in the morning and in fasting conditions; then the samples were randomly assigned to three groups of aqua resistance training group, aqua aerobic training group and the control group. 48 hours after the end of this course, we took blood samples from each candidate for the purpose of measuring the variables. In order to measure blood factors, venous blood was taken from the patients after 8-12 hours of fasting. Blood was separated from serum in order to determine the glucose levels; during the 2-3 hours after sampling, the serum's glucose level was measured with the glucose oxidase method (using Hitachi auto-analyzer and Pars Azmoon kits). The serum's insulin levels were measured with the ELISA method using the laboratory kit that was bought from IZOTOPES Ltd Company in Hungary.

HOMA-IR, an index insulin resistance, was calculated as fasting glucose (mg/dl) multiplied by fasting insulin ($\mu\text{U}/\text{ml}$) divided by 405. Homeostasis model assessment of β -cell function (HOMA- β) an of insulin secretion, was calculated as 360 multiplied by fasting insulin ($\mu\text{U}/\text{ml}$) divided by (fasting glucose (mg/dl) - 63).

Statistical Analysis

In order to see if data distribution was normal we used Shapiro-wilks's test. Considering the low number of samples in each group, some variables were not distributed normally. Thus, we used the nonparametric Wilcoxon signed rank test to analyze these variables, and for the intragroup comparisons of normal variables we used the Paired sample t-test. Kruskal-wallis test was used for between group comparisons. The data was analyzed using the SPSS-23 software and the significance level was set $P < 0.05$.

3. Results

The sample consisted of 34 patients who were equally divided into the 3 groups. The samples' descriptive characteristics are presented in the Table 1. The groups were similar in terms of the variables measured at the time of inclusion in the study.

Table 1. Samples personal information in the initial condition

Variables	Aqua aerobic	Aqua resistance	Control	P value
Age (years)	28.9 ± 3.6	30.2 ± 4.1	29.1 ± 4.3	0.70
Height (cm)	164.3 ± 3.3	166.2 ± 4.6	162.7 ± 2.6	0.80
Weight (Kg)	68.5 ± 6.9	73.1 ± 10.1	63.8 ± 11.2	0.07
Pre-pregnancy BMI (Kg/m ²)	25.3 ± 1.7	26.3 ± 2.4	24.2 ± 3.8	0.15
Amount of Insulin required (u/kg)	0.5 ± 0.2	0.6 ± 0.2	0.6 ± 0.04	0.46

Changes of biochemical parameters of the subjects in three groups are presented in the Table 2.

The results indicated that fasting glucose decreased after 6 weeks aqua resistance training ($P < 0.05$); however fasting glucose had not significant changes after aqua aerobic training. No significant differences were observed in fasting glucose between aqua resistance training, aqua aerobic training and control group. For fasting insulin and insulin resistance demonstrated with HOMA-IR no significant changes were observed after aqua aerobic training and aqua resistance training.

As shown in the Table 2, HOMA- β increased after 6 weeks aqua resistance training ($P < 0.05$); however HOMA- β had not significant

changes after aqua aerobic training. No significant differences were observed in HOMA- β between aqua resistance training, aqua aerobic training and control group.

Table 2. Samples biochemical index changes from before and after the test in experimental and control groups

Variables	Groups	Pre-test	Post-test	Changes	P value	Kruskal-wallis
Glucose (mg/dl)	Aqua aerobic	83.4 \pm 8.4	81.7 \pm 6.8	-1.9%	0.31	0.07
	Aqua resistance	93.8 \pm 8.1	87.0 \pm 8.1	-7.1%	0.01*	
	Control	89.5 \pm 10.2	89.0 \pm 10.5	-	0.39	
Insulin (μ U/ml)	Aqua aerobic	8.1 \pm 2.8	7.8 \pm 2.5	-4.0%	0.68	0.31
	Aqua resistance	9.8 \pm 2.3	10.2 \pm 2.7	4.1%	0.43	
	Control	12.5 \pm 3.4	13.8 \pm 2.9	10.1%	0.14	
HOMA-IR	Aqua aerobic	1.6 \pm 0.5	1.5 \pm 0.5	-7.1%	0.48	0.82
	Aqua resistance	2.2 \pm 0.5	2.1 \pm 0.5	-3.5%	0.50	
	Control	2.7 \pm 0.6	3.0 \pm 0.6	9.0%	0.16	
HOMA- β	Aqua aerobic	166.9 \pm 77.3	180.6 \pm 170.9	8.2%	0.59	0.43
	Aqua resistance	129.1 \pm 70.4	177.3 \pm 99.7	38.9%	0.03*	
	Control	210.3 \pm 129.9	224.1 \pm 163.1	6.5%	0.06	

* Significance differences (P<0.05)

4. Discussion

Pancreatic beta-cell dysfunction is one of the main pathogenetic mechanisms of GDM. Women with GDM have a chronic defect in β -cell function (2). Although this defect is likely to precedes the pregnancy, it is clinically first detected in the form of insufficient β -cell compensation for insulin resistance in late pregnancy. The β -cell defect in women with GDM is still present in the postpartum period (2). Results from the present study shows that HOMA- β levels increased after aqua resistance training. Also, insulin resistance decreases in the intervention groups following the six weeks of aqua aerobic and aqua resistance training, this decrease was insignificant. One of the characteristics of the pregnancy period is the increase of insulin resistance, which is more important in gestational diabetes, because it creates the possibility of being diagnosed with pregnancies with dangerous complications such as; gestational diabetes and also the possibility of getting T2DM in the future. Research

shows that gestational diabetes causes impairments in insulin resistance and defects in pancreatic β -cells (25). There is the possibility that gestational diabetes in women with normal weight is somewhat caused by the defects in pancreatic β -cells, which won't get better by exercise, while in women with extra weight insulin resistance might be the more prominent mechanism at work (26). Evidence shows that the protective effects of exercise in prevention of type 2 diabetes are more among obese individuals, people who are more likely to be insulin resistance. Exercise has more benefits for overweight women with gestational diabetes (27,28). Insulin resistance during a normal pregnancy is multifactorial and includes insulin's reduced ability to phosphorylate insulin receptors, decreased expression of insulin receptor substrate (IRS-1), and the increase of the P85 α subunit from Inositol -3- triphosphate (PI-3) kinase. In this regard, IRS-1 decreases more in women with gestational diabetes and creates higher resistance. However, in women with gestational diabetes, mutual and reverse changes happen in the phosphorylation level of IR and IRS-1's serine and tyrosine, which will block signaling more and will cause a substantial decrease in the translocation of GLUT-4 and less glucose uptake compared to natural pregnancy (29). The changes in insulin resistance levels, although insignificant, could be used as an argument for the effectiveness of physical activity in gestational diabetes.

Data on preventive effects of exercise before and during pregnancy are mainly based on cohort studies and a small number of randomized controlled trials. There was only one randomized trial on the preventive effects of exercise on the occurrence of GDM and insulin resistance which was conducted on healthy pregnant women (30). Although sample was large (N=855), only 55% of women in the experimental group (N=375) managed to follow recommended exercise regimen, a 12-week exercise program during second half of the pregnancy. Pregnancy outcomes were similar in both groups and the authors concluded that; exercise did not help to prevent GDM or improve insulin resistance. Two other trial studies, analyzed the effects of exercise on insulin resistance, blood glucose and insulin levels on healthy pregnant women (31, 32). These trials were conducted on small samples but the results were not reliable to measure GDM incidence as an outcome. Hopkins et al. (2010)

examined the effects of exercise during second half of the pregnancy on maternal insulin sensitivity and neonatal outcomes (32). At the same time, Callaway et al. (2010) studied fasting glucose and insulin levels and insulin resistance (31). Both Hopkins et al. (2010) and Callaway et al. (2010) did not find statistically significant differences in maternal insulin sensitivity (31,32), but Callaway et al. (2010) found a statistically significant difference in fasting glucose and insulin levels during the 28th and 36th week of pregnancy (31).

Results from this study showed an insignificant increase of fasting glucose levels in the two groups of aerobic and control and a significant decrease in the resistance group. Exercise increases the available glucose and decreases insulin needs during the training days. In a study done by Oostdam et al. (2012), they showed that an exercise program in the second and third trimesters of pregnancy, does not have a significant effect on fasting blood sugar levels and insulin sensitivity of overweight women who were exposed to gestational diabetes (33). Meanwhile, Jovanovic-Peterson et al. (1989) showed that women who exercised 3 times a week had significantly lower fasting and after-meal blood sugar levels comparing to the diet therapy group (34).

Insulin's ability to prevent lipolysis decreases in the final months of pregnancy and this decrease is higher in GDM, therefore, it leads to a higher increase in FFA, increased hepatic glucose production and increases insulin resistance (22). Resistance training also causes increased access to glucose by increasing FFA without any changes in muscle's inherent capacity to respond to insulin. While aerobic training increases glucose access independent from changes in FFA, fat mass and maximum oxygen intake, which indicates internal changes in muscle's ability for glucose metabolism (24). Probably it is because of having more access to FFA, that resistance training showed a significant effect on fasting glucose levels. The insulin levels had not significant changes after 2 types of training. Marcelo et al. (2010) showed that resistance training causes less insulin consumption in women with gestational diabetes (24), while Brankston et al. (2004) did not observe any significant differences between the training and control group (26). These mixed results may be caused by the differences in patients' characteristics, the intervention, the length of exercises, and the low

number of participants in each group. In this research, unpredictable factors such as; the mother's concern for fetus health, physical limitations and lack of required energy and motivation could have affected the results.

There are few studies about the mechanism and beneficial effects of exercise on GDM. But because of the similarities between GDM and T2DM, their mechanisms are explained the same way. There are two routes which lead to glucose transfer: one is through stimulation by insulin and the other is by active contraction or hypoxia (1). PI3 kinase intervenes in the insulin pathway (not through the contracted pathway), while AMPK participates in the contraction pathways activation responses (34). Insulin stimulates IRS; the stimulated Akt kinase and PI3 kinase's activities by insulin, are defected in overweight people with diabetes and GDM (1).

In conclusion, exercise can offer a solution for patients with diabetes (13). Regular physical activity improves insulin function and glucose tolerance in healthy people, as well as patients with obesity and those who are insulin resistance and diabetes (1). Molecular mechanisms for glucose uptake and insulin sensitivity can be improved by exercising which increases the activity and expression of the signaling proteins and enzymes involved in lipids and glucose metabolism (1,21). GLUT-4 biogenesis is a key enzyme in glucose uptake by the muscles, which will increase in numbers with exercise. Muscle biopsies of pregnant women showed that the increase of GLUT-4 expression occurs as a result of moderate exercises (1). However, the improvement of insulin signaling caused by exercise is not exclusively limited to the expression increase of GLUT-4 protein, for instance its concentrations are similar in the inactive diabetes patients and the insulin sensitive observation group, while exercise increases GLUT-4 protein and its mRNA in diabetes patients. The increase of insulin signaling receptors is the main mechanism which causes GLUT-4 positioning and glucose uptake especially during the final stage of the PI3-K insulin cascade (1). In order to promote exercising to reduce the risk of T2DM in women with GDM scientists and healthcare specialists are encouraged to change women's exercise beliefs, which is beneficial for them. These barriers

should be removed to create a framework for designing an effective diabetes treatment and prevention programs (19).

5. Conclusion

Since the present study is one of the first researches on the effects of exercise and physical activity on women with gestational diabetes in their second trimester. Therefore, we suggest a more comprehensive study to further investigate the mechanisms that influence the changes related to gestational diabetes after the exercise.

6. Limitations

One of the limitations in our study was the number of participants which was multifactorial such as; lack of knowledge, financial limitations. Another limitation which can have altered our results is the lack of motivation to fully participate in the exercises assigned by the senior author. Finally most likely if we had used Hyperinsulinemic-euglycemic clamp technique for measuring HOMA-IR different results might have been achieved, but since this is expensive it was not affordable.

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