

Effects of Aerobic Exercise and Whole Body Vibration on Glycaemia Control in Type 2 Diabetic Males

Lale Behboudi¹, PhD Candidate; Mohammad-Ali Azarbayjani^{1*}, PhD; Hamid Aghaalinejad¹, PhD; Mahyar Salavati², PhD

Authors' Affiliation:

1. Department of Exercise Physiology, Faculty of Physical Education and Sports Science, Islamic Azad University, Central Tehran Branch, Tehran, Iran
2. Iranian Research Centre on Aging, University of Social Welfare and Rehabilitation, Tehran, Iran

* Corresponding Author;

Address: Department of exercise physiology, Faculty of Physical Education and Sports Science, Islamic Azad University, Central Tehran Branch, Tehran, Iran

E-mail: m_azarbayjani@iauctb.ac.ir

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Abstract

Purpose: aerobic exercise has been identified as the main treatment for type 2 diabetic patients. Such an exercise, however, is usually repined by some of patients who suffer from lack of stamina. Therefore, whole body vibration has recently been introduced as a passive intervention. The present study aimed at comparing how aerobic exercise and whole body vibration affect glycaemia control in type 2 diabetic males.

Methods: Thirty diabetic males were divided into three groups, namely aerobic exercise (AE), whole body vibration (WBV), and control. Aerobic exercise schedule consisted of three walking sessions a week, each for 30-60 minutes and in 60-70% of maximum stock heartbeat. Vibration exercise was composed of 8-12-min stand-up and semi-squat positioning in frequency of 30 Hz and amplitude of 2 mm. Concentrations of fasting glycosylated hemoglobin, fasting glucose, and insulin were measured in the beginning of the trial, after the fourth week, and after the eighth week.

Results: After 8 weeks of exercise, no significant difference was detected in concentrations of fasting glycosylated hemoglobin and insulin between the groups ($P=0.83$, $P=0.12$). There were no significant differences in any of the variables between AE and WBV ($P>0.05$). But a more significant decrease in fasting glucose was observed in exercise groups (AE and WBV) compared with control group ($P=0.02$).

Conclusions: The present study showed that AE and WBV identically stimulate metabolic system. Thus, it can be concluded that type 2 diabetic patients lacking stamina for aerobic exercise can opt for vibration exercise as an effective substitute.

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INTRODUCTION

As a heterogenic group of metabolic diseases, diabetes mellitus is broadly known with chronic increase in glucose level of blood. Previous studies

have shown careful control of glucose level of blood and also attainment of plasma glucose within a normal range to prevent acute short- and long-term adverse effects of diabetes [1]. Along with pharmacological treatment and losing weight, physical exercise has been

identified as a controlling factor in glycaemia. Among the effects of various exercising methods on diabetes markers [2], aerobic exercise is considered as the main strategy to treat type 2 diabetic patients [3]. Despite positive outcomes of aerobic exercise, majority of diabetic patients suffer from several troubles such as obesity and articular complications in addition to adverse effects of diabetes. Consequently, they cannot readily take part in such exercise programs [4].

Compared to aerobic exercise, whole body vibration takes lesser time and wider variety of patients can make use of it. Therefore, the method can be utilized, especially by passive patients. Patients performing vibration exercise, who are aroused more by daily activities [5], have been reported to have gravity loads of higher than 14 gr [6]. On the other hand, the method involves nearly 100% of body muscles [5], while regular exercise methods involve only 40-60% of them. Vibration exercise activates muscle spindles through stimulation of tendons and muscles, which causes a kind of muscle flexion called "Tonic Vibration Reaction". This reaction has been reported to activate more motor neurons and muscle spindles and consequently, to increase all bridges between actin and myosin and also to activate more motor units leading to a higher muscular strength [7]. The muscle flexion enhances permeability of myocytes' membranes to glucose and causes a pseudo-insulin effect [8]. More investigations, however, should be performed to evaluate how vibration exercise metabolically affects diabetic markers.

Comparing how aerobic exercise and whole body vibration affect glycemic short- (fasting glucose level of blood) and long-term (glycosylated hemoglobin) indices and also blood insulin rate, the present study intended to know whether whole body vibration can

be considered as a modern measure to control glycaemia effectively, even as a more effective method in comparison to aerobic exercise.

METHODS AND SUBJECTS

Subjects:

Eighty two type 2 diabetic males, who were under treatment in the clinic of Bus System Company in Karaj City, Iran, formed available community of the present study. Face-to-face interview and personal-medical questionnaires were used to choose 30 patients as subjects of the study. They were 45-65 years old without acute and/or chronic symptoms of diabetes and less than 250 mg/dl blood fasting glucose level. Before signing letters of consent, the subjects were given necessary information about the study and possible risks orally and in writing. The subjects were promised that their information would be kept confidentially and they were allowed to change their mind about participating in the study whenever they intended. All of the above-motivated steps were verified by Ethical Committee of Central Azad University of Tehran. It is noteworthy that the subjects have not been smoking and participating in regular exercise programs. Afterwards, the subjects were randomly divided into three groups, namely aerobic exercise (AE), whole body vibration (WBV), and control, each was comprised of 10 patients.

The subjects were asked not to change their nutritional and pharmacological programs during the study. General characteristics of the subjects are presented in Table 1.

Table 1: General characteristics of the subjects

	Control	Aerobic training	Vibration	F	P value
Age (year)	52.30 (6.17)	53.10 (6.57)	49.20 (3.94)	1.31	0.285
Weight (kg)	76.43 (9.22)	82.24 (12.33)	75 (10.92)	3.08	0.062
Height (cm)	165.60 (4.99)	172.60 (8.14)	168.40 (5.44)	1.31	0.285

The data are given based on mean values (Standard Deviation)

Physiological assays:

Maximum oxygen consumption ($V_{O_{2max}}$) was estimated through one-mile track walk test^[9] to assess aerobic strength using thoracic heartbeat-meter (Beurer PM65). Body Mass Index (BMI) of the subjects was measured via dividing weight (kg) by the square of height (m). Body fat percentage was also estimated using a caliper (Harpenden, CEO120, England) and Sirri formula^[10].

Blood drawing:

In order to evaluate halting levels of glycosylated hemoglobin, glucose, and insulin, 10 cc blood was drawn from anti-cubital vein in a time less than 1 min following bandaging with tourniquet in a sitting position after 12 hours of fasting in the beginning of the trial (pre-test), at the end of the fourth week (mid-test), and at the end of the eighth week (post-test). All samples were drawn at 8 A.M. the subjects were asked to avoid any physical activity during 24 hours before blood drawing except for daily routine activities.

Biochemical assays:

Concentrations of glycosylated hemoglobin, insulin, and glucose were measured through immunoturbidimetric method (using quantifying kit made by Pars Azmoon Company-Iran with internal measurement degree of 1.36 and sensitivity of 3%), ELISA method (using insulin kit made by Diametra Company-Italy with internal measurement degree of 2% and sensitivity degree of 2 micIU/mL, and GOD Photometric Method (using glucose kit made by Pars Azmoon Company-Iran with internal measurement degree of 1.28 and sensitivity of 5 mg/dl) respectively.

Aerobic exercise protocols:

AE group participated in an 8-week increasing aerobic exercise program with 3 sessions per week. The subjects exercised for 30 minutes (5-min running with 60-70% of stock heartbeat and 5-min active rest with 30-45% of maximum stock heartbeat), 42 minutes (7-min running with 60-70% of stock heartbeat and 7-min active rest with 30-45% of maximum stock heartbeat), and 60 minutes (10-min running with 60-70% of stock heartbeat and 10-min active rest with 30-45% of maximum stock heartbeat) in the first week to the third week, the fourth week to the sixth week and the

seventh week to the eighth week respectively. Exercising sessions were comprised of warming up (stretching, turning joints, and walking slowly), the main program (aerobic running), and cooling down (stretching, turning joints, and walking slowly). In order to prevent hypoglycemia and thirst, the subjects were asked to drink 100 ml of water before onset of the exercise and to carry syrup (containing 5% sugar, ml/kg/min). All exercise sessions were performed in 50-70-min periods.

Whole body vibration:

WBV group participated also in an 8-week increasing aerobic exercise program with 3 sessions per week. Each exercise session was performed through 30 Hz of frequency and 2 mm of amplitude. The subjects stood on a whole body vibrator (Star Sport-Taiwan) and they were vibrated in a 110° squat positioning (the degree was adjusted using a goniometer). The subjects exercised for 16 minutes (1 min vibration with 8 iterations and 1 min break between each iteration), 20, and 24 minutes in the first week to the third week, the fourth week to the sixth week, and the seventh week to the eighth week respectively. It should be noted that the control subjects were asked to do their routine activities and to participate only in biochemical and physiological assays.

Statistical analysis:

Two-way iterative analysis of variance (ANOVA) was adopted to analyze simultaneous changes in the groups and measure time (interactive effect of time and group, considering time as iteration). The mean values of each blood index were compared in different times between the groups. In this regard, variance analysis of iterative values and Bonferroni test were adopted. Then, variance homogeneity was assessed through Lon test. Variance analysis and Tukey test (if necessary) were used in the case of homogeneity. Otherwise, the Welch test to compare the group simultaneously and also Games-Howell (if necessary) were adopted for binary test of mean values of the groups. In order to assess the effect of the groups in mid-test and post-test on ununiformed basic values, covariance analysis and Bonferroni test were adopted based on modified mean values. Significance level was considered to be $p < 0.05$

for all tests. All the statistical analyses were performed using SPSS Software version 13.

RESULTS

Table 2 shows changes in V_{O2max} , BMI, and fat percentage following aerobic exercise and whole body vibration compared to the control group. Eight weeks of aerobic exercise had a significant effect on V_{O2max} ($P<0.001$ and $F_{(2,18)}=31.191$). V_{O2max} increased significantly after 4 weeks of exercise compared to the beginning of the trial ($P=0.006$). This increasing procedure continued until the end of the eighth week, so that V_{O2max} was higher than that of pre-test ($P=0.01$) and mid-test ($P=0.01$) (during the second four weeks, $P=0.01$) after eight weeks ($P<0.001$).

Vibration exercise showed not to affect V_{O2max} significantly ($P=0.3$). Besides, after 8 weeks of aerobic exercise and whole body vibration, no significant change was detected in BMI ($P=0.5$) and fat percentage ($P=0.3$) of the subjects ($P>0.05$).

Although no significant change was observed in concentration of fasting glucose after 8 weeks of aerobic exercise and whole body vibration ($P=0.3$ and $F_{(1.49,40.24)}=1.03$), the concentration was significantly

($P=0.02$ and $F_{(2)}=4.42$) higher in control group than that of AE and WHB. No significant difference, however, was observed between AE and WBV ($P=0.9$).

Eight weeks of aerobic exercise ($P=0.08$ and $F_{(1.49,40.24)}=3.50$) and whole body vibration ($P=0.9$ and $F_{(1.49,40.24)}=0.04$) had no significant effect on concentrations of insulin and glycosylated hemoglobin.

DISCUSSION

AE and WBV diminished fasting glucose insignificantly. The decrease in AE might be associated with glucose uptake by active muscles in absence of insulin^[11]. The increasing procedure of glucose uptake by skeletal muscle in non-diabetics and type 2 diabetic patients during physical activity continues until more than 48 hours only after 1 exercise session. The response has been known as a consequence of increasing sensitivity to insulin and also endogenic influence of GLUT4 carriers rise on sarcolemma of muscle filaments^[12]. The endogenic effect in skeletal muscle can be attributed to glycogen synthesis in muscle which can continue for more than 5 hours. Increasing sensitivity to insulin caused by physical

Table 2: Changes in V_{O2max} , BMI, and fat percentage following aerobic exercise and whole body vibration compared to the control group

Parameter	Group	Pre Test	Mid Test	Post Test
		Mean (SD)	Mean (SD)	Mean (SD)
V_{O2max} (ml.Kg min)	Aerobic	28.30 (8.41)	29.64 (0.52)	31.62 (2.73)
	vibration	31.26 (2.22)	32.80 (2.48)	39.63 (4.93)
	control	37.52 (5.35)	38.80 (6.21)	39.47 (5.56)
Fat percentage	Aerobic	6.61 (2.46)	7.52 (1.20)	7.03 (1.17)
	Vibration	7.18± (2.36)	7.48 (2.43)	7.03 (2.23)
	Control	9.53 (2.23)	9.63 (2.18)	9.68 (2.32)
BMI (m ²)	Aerobic	28.43 (4.00)	27.45 (2.55)	27.23 (2.49)
	Vibration	26.48 (3.62)	26.76 (3.42)	26.79 (3.09)
	Control	27.87 (3.16)	27.91 (3.21)	27.16 (3.06)

BMI: Body Mass Index / SD: Standard Deviation

exercise is higher when muscle mass is more engaged in the exercise.

Nevertheless, when provided amateur individuals (e.g. the subjects of the present study) experience eccentric muscle contraction (e.g. running, weight lifting, and whole body vibration), muscle injury can be inevitable which might bring about temporary decrease in insulin level. The popular long-term influence of physical exercise on environmental glucose consumption and sensitivity to insulin is associated with stimulatory *modus operandi* induced by insulin. Therefore, physical activity can practically mitigate low glucose consumption caused by low insulin^[12]. Besides, during whole body vibration, tonic vibration reflection activates muscle spindles through stimulation of tendon and muscle which causes contact of actin and myosin bridges and also increases activation of more motor units and consequently, mightier contraction. Muscles use glucose in 2-3 hours after each meal when concentration of blood glucose is high and pancreas secretes a lot of insulin. The excessive insulin results in swifter transfer of glucose into muscle cells^[11].

On the other hand, the significant variation in fasting glucose during the assays in both groups may be ascribed to possible agitation during sampling which causes secretion of a lot of epinephrine. The hormone strives against insulin and hinders secretion of insulin and leads to secretion of glucagon which elevates blood sugar^[13].

The current knowledge of vibration exercise mechanism is not that wide. However, the results of the present study showed that vibration exercise (considering its special characteristics such as lower time needed and passiveness of the patients), decreases fasting glucose similar to other exercising methods (e.g. aerobic exercise), even more. Insulin increases glucose transfer into muscle cells either directly or indirectly. Insulin receptors are of membranous receptors and tyrosine kinases. Insulin stimulates tyrosine kinase through connection to the receptors which brings forth auto-phosphorylation of the receptor and formation of intracellular signaling molecules such as insulin receptors types 1 and 2. The substances and other adaptive proteins commence a complex chain of phosphorylation and dephosphorylation which causes

extended metabolic and mitogenic effects of insulin consequently. For instance, activation of phosphatidylinositol-3-kinase (PI-3 kinase) provokes relocation of glucose carriers (e.g. GLUT4) to cell surface. The procedure is of a great importance for glucose uptake by skeletal muscle and fat tissue. Deficiency of insulin, resistance against insulin (hyperinsulinemia), reduced number of the carriers, defect in relocation of the carrier to membrane, and inherited defect of the carrier cause reduced activity of GLUT4^[14].

The main trouble in type 2 diabetes is not necessarily the deficiency of insulin. Indeed, the trouble is usually in target tissues, especially in muscles. Since carbohydrate cannot pass into target cells in type 2 diabetic patients, blood sugar exceeds normal level and as a result, pancreas is stimulated and thus, higher insulin level is formed by beta cells to blood. The process causes higher fasting blood sugar causing hypoglycemia or hyperglycemia^[15].

The subjects of the present study, who were suffering from hyperinsulinemia, showed no significant change during the exercise. The results obtained from AE are consistent with those of Poierer et al. in 2002^[16]. Moreover, the results obtained from WBV are in accordance with those of Di Loreto et al., who are the only authors who studied the effect of one session WBV with the frequency of 30 Hz on endocrine system (insulin, glucagon, cortisol, epinephrine, norepinephrine, growth, IGF-1, and total and free testosterone) in 10 healthy males^[17].

Increased post-receptor messaging of insulin^[18], increased GLUT4 and mRNA carriers^[19], increased activity of glycogen synthase and hexokinase^[20], decreased release and increased scavenging of free fatty acids (FFAs)^[21], increased release of glucose to blood from muscle due to increased capillaries of muscle, and changes in composition of muscle due to elevated glucose uptake can all be considered as the mechanisms which prevent from hyperinsulinemia and increase the effect of insulin (or decrease glucose secretion level) after aerobic exercise. Intergroup comparison in the present study showed no significant difference between AE and WBV. Hence, absence of one of the above-mentioned mechanisms can be claimed to cause insignificant effect of vibration exercise on repetitious insulin measurements.

Aerobic exercise in the present study affected glycaemia control efficiently. Muscle contraction can be claimed to possess a pseudo-insulin effect and to transmit a lot of glucose into the cell as energy fuel. Furthermore, it permits muscle filaments to have a low concentration of glycogen for a rather long time. On the other hand, after completion of physical exercise, muscle cells figure on restoring glycogen reserves. Therefore, blood glucose concentration is low for a few hours after physical activity^[5] and accordingly, glycosylation possibility of hemoglobin decreases.

Insignificant change of glycosylated hemoglobin in pre-test, mid-test, and post-test is consistent with previous studies^[22]. Lack of decreased glycosylated hemoglobin in mid-test (the first four weeks of the exercise) is attributable to long-term (2-3 months) assessment of blood sugar level by HbA_{1c}. Besides, insignificant increase in glycosylated hemoglobin may be a consequence of improper nutrition and glycaemia or inconsistency of controlling systems of body with the exercise.

Moreover, insignificant difference of glycosylated hemoglobin between mid-test and post-test is not consistent with the only work performed in this case by Baum et al^[13]. Insignificant effects of aerobic exercise and WBV on the variable might be owing to incomplete nutrition control of the subjects or insufficient time or intensity of the exercise.

Lower decrease in glycosylated hemoglobin in WBV than that of AE might be due to shorter exercise sessions (one third of AE). Of course, decreased glycosylated hemoglobin has been shown to decrease long-term diabetic adverse effects. This is independent of primary level of hemoglobin. 0.8% decrease of glycosylated hemoglobin from 8 to 7.2 decreases the risk of retinopathy about 43-45% and a 1% decrease in glycosylated hemoglobin from 8 to 7 diminishes the risk of vascular complications around 40%^[3], which offers 15-20% and 37% decrease in cardiovascular problems and microvascular complications respectively^[23]. Variations in glycosylated hemoglobin levels in the present study was claimed to be a consequence of season shifts which is of high clinical importance. Why the variations happen is not clearly known, but it is sometimes attributed to variations of blood glucose level. Longer day hours in the summer

compared to the winter can be assumed to cause higher physical activity which brings about decreased concentration of blood glucose^[24]. There are also evidences which consider levels of the insulin-interactive hormones (e.g. cortisol, glucagon, hydroxycorticosteroid, and thyroxin) affected by season shifts. Epidemiological study by Tseng et al. on 280000 patients inhabiting various climates proved the effect of season shifts on concentration of glycosylated hemoglobin with higher levels in the winter^[24]. Thus, while half of the present study has been performed in winter, glycosylated hemoglobin level can be assumed to be lower (even significant) in the summer. Glycosylated hemoglobin level is not only affected by blood glucose level, but also by survival of red globules. Young erythrocytes have been shown to contain lower glycosylated hemoglobin in comparison with aged ones^[25]. Besides, stress and excitement can elevate glycosylated hemoglobin via increasing glucose level (thank to secretion of insulin-interactive hormones)^[26].

On the other hand, decreased glycosylation level of red globules leads to raised oxygen delivering to muscle cells during the exercise and increased $V_{O_{2max}}$ in type 2 diabetic patients. As hemoglobin glycosylation causes increased affinity to oxygen (ten times higher than that of normal hemoglobin), diabetic patients experience a chronic hypoxia which leads to a compensational polycythemia.

The present study indicated that glycosylated hemoglobin showed an insignificant decrease compared to $V_{O_{2max}}$. Of course, previous studies have signposted that glycosylated hemoglobin cannot be solely articulated as the reason for increased $V_{O_{2max}}$. Nonetheless, other physiological factors such as those in muscle tissue (increased capillary density, oxidative enzymes, etc.) are required to elevate essential $V_{O_{2max}}$.

The present study faced with some limitations such as incomplete control over nutrition of the subjects, daily lifestyle, and repetitious blood samplings. However, the present study can be complimented due to its in-vivo performance. Uniqueness of the present study is in comparing the effects of AE and WBV on glycemic factors of diabetic patients for the first time. However, more studies should be performed to elucidate the effects of the methods.

CONCLUSION

Generally, insignificant results of the present study can be attributed to the small number of samples and improper time and intensity of exercise. It can be concluded that effect of whole body vibration on glycaemia control is similar to that of aerobic exercise. However, whole body vibration can be considered as a better way to exercise in a shorter time for majority of diabetic patients who suffer from obesity and unwillingness to join active physical activities.

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REFERENCES

1. Carpenter Charles CJ, Griggs R, Benjamin JJ. Endocrine & Metabolic Disease. In: Andreoli T and et al. *Cecil Essentials of Medicine*. 7th Ed. Philadelphia: W.B. Saunders; 2007.
2. Snowling NJ, Hopkins WG. Effects of different modes of exercise training on glucose control and risk factors for complications in type 2 diabetic patients. *Diabetes Care* 2006;29:2518-27.
3. Praet SFE, Van Loon LJC. Optimizing the therapeutic benefits of exercise in type 2 diabetes. *J Appl Physiol* 2007;103:1113-20.
4. Baum K, Votteler T, Schiab J. Efficiency of vibration exercise for glycemic control in type 2 diabetes patients. *Int J Med Sci* 2007;4:159-63.
5. Cardinal M, Rittweger J. Vibration exercise makes your muscles and bones stronger: fact or fiction? Review. *J Brit Menopause Society* 2006;12:43-9.
6. Bosco C, Iacovelli M, Tsarpela O, et al. Hormonal responses to whole body vibration in men. *Eur J Appl Physiol* 2000;81:449-54.
7. Cardinale M, Bosco C. The use of vibration as an exercise intervention. *Exerc Sport Sci Rev* 2003;31:3-7.
8. Kern MJ, Wells A, Stephens JM, et al. Insulin responsiveness in skeletal muscle determined by glucose transporter (GLUT4) protein level. *Biochem J* 1990;270:397-400.
9. Kline GM, Porcari JP, Hintermeister R, et al. Estimating of Vo₂max from a one-mile track walk, gender, age, and body weight. *Med Sci Sports Exerc* 1987;19:253-9.
10. Siri WE. Body composition from fluid space and density. In J. Brozek & A. Hanschel (Eds). *Techniques for measuring body composition*. Washington, DC: Natinal Academy of Sciences.1961; PP: 223-244.
11. Tso TK, Huang WN, Huang HY, Chang CK. Elevation of plasma interleukin-18 concentration is associated with insulin resistance levels in patients with systemic lupus erythematosus. *Lupus* 2006;15:207-12.
12. Robergs RA, Roberts SO. 9th chapter. *Fundamental Principles of Exercise Physiology: for Fitness, Performance and health*. Boston: McGraw-Hill. 2000; Pp: 492-3.
13. Baum K, Votteler T, Schiab J. Efficiency of vibration exercise for glycemic control in type 2 diabetes patients. *Int J Med Sci* 2007;4:159-63.
14. Fauci A, Longo DL, Kasper DL, et al (eds). *Endocrine, Metabolism and Nutrition Diseases*. Harrison's Principle of Internal Medicine. 17th ed. New York : McGraw-Hill Companies, Inc. 2008; P:267.
15. Bonen N. Benefits of exercise for type 2 diabetics. *Can J Appl Physiol* 1995;20:261-79.
16. Poierer P, Trambly A, Broderick T. Impact of moderate aerobic exercise men treated with oral hypoglycemic agents. Is insulin sensitivity enhanced only in nonobese subjects? *Med Sci Monit* 2002;8:CR59-65.

17. Di Loreto C, Ran Chelli A, Lucidi P, et al. Effects of whole body vibration exercise on the endocrine system of healthy men. *J Endocrinol Invest* 2004;27:323-7.
18. Dela F, Handberg A, Mikines KJ, et al. GLUT4 and insulin receptor binding and kinase activity in trained human muscle. *J Physiol (lond)* 1993;469:615-24.
19. Dela F, Plog T, Handberg A, et al. Physical training increases muscle GLUT4 protein and mRNA in patients with NIDDM. *Diabetes* 1994;43:862-5.
20. Ebeling P, Bourey R, Koranyi L, et al. Mechanism of enhanced insulin sensitivity in athletes: increased blood flow, muscle glucose transport (GLUT4) concentration, and glycogen synthase activity. *J Clin Invest* 1993;92:1623-31.
21. Ivy JI, Zderic TW, Fogt DL. Prevention and treatment of non-insulin dependent diabetes mellitus. *Exerc Sport Sci Rev.* 1992; 27:1-35.
22. Fritz T, Wandell P, Aberg H, Engfeldt P. Walking for exercise – dose three times per week influence risk factor in type 2 diabetes? *Diabetes Res Clin Pract* 2006;71:21-7.
23. Vancea DMM, Vancea JN, Fernandes Pires IF, et al. Effect of frequency of physical exercise on glycemic control and body composition in type 2 diabetic patients. *Arq Bras Cardiol* 2009;92:22-8.
24. Tseng CL, Brimacombe M, Xie M, et al. Seasonal patterns in monthly hemoglobin A1c values. *Am J Epidemiol* 2005;161: 565-74.
25. Chait A, Bierman EL. Pathogenesis of macrovascular disease in diabetes. In: Kahn CR, Weir G (eds). *Joslin's Diabetes Mellitus*. 13th ed. Philadelphia: Lea and Febiger. 1994; Pp:648-64.
26. Niemcyrk SJ, Speers MA, Travis LB, Gary HE. Psychosocial correlates of hemoglobin A1c in young adult with type 1 diabetes. *J Psychosomatic Res* 1990;34:617-27.