Effect of electrical stimulation on blood glucose level and lipid profile of sedentary type 2 diabetic patients

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**Background:** Physical exercise has emerged as a major tool in the prevention and management of diabetes mellitus, but a large diabetic population is not physically fit for regular exercise programme due to associated complications of diabetes and old age. This unique study is an attempt to explore the use of electrical stimulation as a method of treatment of type 2 diabetic patients. **Aims:** This study was designed to analyze the effects of electrical stimulation on blood glucose level, lipid profile, and physiological parameters of sedentary type 2 diabetic patients. **Settings:** This study was experimental in nature with different subject design. **Materials and Methods:** The experimental group (N = 20) underwent electrical stimulation through surface electrodes placed over motor points of quadriceps femoris muscles for 40 min/day, 3 days/week continued for 2 weeks. Twenty diabetic subjects who received placebo treatment served as the control group. Physiological parameters were measured, and blood samples taken both before and after treatment on the first day and the last day of the intervention in both groups. **Statistical Analysis:** Related and unrelated t-tests were used for statistical analysis. **Results and Conclusion:** The percentage change in blood glucose level scores of the experimental group (12.71%) was much higher as compared to the control group (4.06%) after a single session of treatment. Following 2 weeks of electrical stimulation, the blood glucose level was significantly reduced in experimental group, but there was an insignificant fall in the same for the control group. Our results suggest that electrical stimulation can be used to assist in the control of blood glucose level in type 2 diabetic patients.

**KEY WORDS:** Blood glucose level, carbohydrate oxidation, glucose uptake, lipid profile

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**Introduction**

Physical exercise has emerged as a major tool in the prevention and management of diabetes mellitus. The metabolic effects of a regular exercise programme are well documented and accepted as an important means of achieving blood glucose regulation in type 2 diabetes mellitus. Recent epidemiological studies have provided evidence that a low level of physical activity is associated with an increased incidence of type 2 diabetes,[1,2] Increased physical activity delays the onset of type 2 DM or even prevents the disease in about 50% of susceptible individuals (positive family history of T2DM, body mass index > 25, hypertension, or gestational diabetes),[3] whereas a lack of physical activity is associated with increased insulin resistance in muscles[4] and glucose intolerance despite increased endogenous insulin secretion.[5]

Physical training improves glucose tolerance in individuals with type 2 DM, in persons with type 1 DM it may diminish insulin requirements.[6] The beneficial effect of a regular exercise on glucose control appears to reflect the cumulative effect of the transient improvement in glucose tolerance following each individual bout of exercise.[3] A single bout of exercise results in the translocation of GLUT4 to the plasma membrane in skeletal muscle of an individual and through this mechanism exercise enhances skeletal muscle glucose uptake in individuals with type 2 diabetes.[7]

Tamura et al. found that 2 weeks of diet and exercise therapy decreased intramyocellular lipid content and increased muscle insulin-mediated glucose uptake.[8] Physical activity exerts pronounced effects on substrate utilization and insulin sensitivity, which in turn potentially lower blood glucose and lipid profile. Exercise training also improves many other physiological and metabolic abnormalities that are associated with T2DM such as lowering body fat, reducing blood pressure, and
normalizing dyslipoproteinemia, but a large diabetic population is not physically fit for regular exercise programme due to associated complications of diabetes and old age.

Investigators have cast doubts on the efficacy and feasibility of physical training as a long-term treatment for a majority of type 2 diabetic patients, especially over the age of 55 because of other interfering diseases which may complicate or severely hinder all physical training apart from very low-intensity exercise programmes.

Regular physical exercise helps to control blood glucose level in diabetic patients, but there are individuals who are restricted from voluntary physical activity or are in a bedridden state due to chronic illness, spinal cord injury, or complications of diabetes. More recently, Mikines et al. and Stuart et al. have concluded that physical inactivity caused due to bed rest for as little as 7 days is associated with a substantial reduction in insulin sensitivity primarily in an inactive skeletal muscle with little change in insulin action on the liver. In addition, prolonged physical inactivity has been shown to decrease the oxygen-carrying capacity of skeletal muscle and also results in decrease muscle GLUT-4 content associated with insulin resistance.

Clinically, electrical stimulation is used as a modality of assisting muscle contraction for those who have difficulties in performing voluntary exercise. A number of studies have focused on the effect of electrical stimulation in disabled or physical inactive individuals. Chilibeck et al. concluded that electrical stimulation-assisted training is effective for increasing glucose transporters and improving insulin sensitivity in patients with spinal cord injury. According to Mohr et al., individuals with spinal cord injury have an increased prevalence of insulin resistance and type 2 diabetes mellitus. In able-bodied individuals, training with large muscle group increases insulin sensitivity and may prevent type 2 diabetes. However, individuals with spinal cord injury cannot voluntary recruit major muscle groups, but by functional electrical stimulation they can perform ergometer bicycle training. Mohr et al. concluded that electrically induced bicycle training performed three times per week increases insulin sensitivity and GLUT-4 content in skeletal muscle in subjects with spinal cord injury. According to Hamada et al., low frequency electrical stimulation may become a useful therapeutic approach to activate energy and glucose metabolism in humans. The study provided evidence for the enhancement of whole body glucose uptake during and after human skeletal muscle low frequency electrical stimulation.

These studies are limited to subjects not clinically diagnosed with diabetes mellitus; similar studies in the diabetic population have not yet been conducted. This study is an attempt to explore the use of electrical stimulation as a new method for type 2 diabetic patients who are unable to participate in a regular exercise programme. To serve the purpose, relevant biochemical parameters, i.e. blood glucose, blood cholesterol, triglycerides, high density lipoprotein, and physiological parameters, i.e. heart rate, respiratory rate, and blood pressure, were measured for changes after intervention in the study.

To our knowledge, this is the first report demonstrating the effect of electrical stimulation on the blood glucose level and lipid profile of patients with type 2 diabetes mellitus.

Materials and Methods

Design
The study was experimental in nature with a different subject design.

Participants
Twenty patients with type 2 diabetes mellitus above the age of 55 years having a sedentary lifestyle and BMI > 27 were included in the study.

Experimental Protocol
The subjects attended a pre-participation screening phase 3 days prior to the start of experiment to rule out the associated complications of diabetes, recent injuries, cardiopulmonary problems, and disorders other than diabetes. Following this screening phase, a medical examination and clearance from a physician were taken for participation in the study. They were informed of the nature, purpose, and parameters of the study before taking voluntary consent to participate in the study, and they continued their medication, diet, and other activities of daily living as before. With the suggestion of a diabetologist, a carbohydrate snack including two pieces of bread and a cup of tea was added 3 to 4 h before the start of experiment to reduce the risk of hypoglycemia after an overnight fasting in diabetic patients. This study was approved by ethical committee in Guru Nanak Dev University, Amritsar.
The subjects were randomly divided into two equal groups; each group having 10 diabetic patients; one was the experimental group and other was the control group. The experiment group was made to undergo 40 min electrical stimulation of quadriceps with 20 min each; with intensity up to tolerable limits of the subject since this was the standard procedure.\cite{17-20}

The faradic current was of sufficient intensity and produced a good amount of contraction. The current was surged so that contraction gradually increased and decreased in strength, in a manner similar to a voluntary contraction. On the other hand, the control group was made to undergo placebo treatment for the same time period, i.e. 40 min; this also involved electrical stimulation of quadriceps muscle but intensity only up to sensory level. A mild pricking sensation was experienced by the patient, but the faradic current was of insufficient intensity to produce muscle contraction.

Before the experiment, the subject was made to rest for 10 min in supine lying. The subject was made to wear the polar short-range telemetry strap on the chest and monitoring watch on his/her wrist. The physiological parameters such as heart rate, respiratory rate, and blood pressure were measured at the end of this period with the patient in supine lying, blood sample was taken from antecubital vein at the cubital fossa by a lab technician using a 21 gauge needle and 10 mL syringe for biochemical analysis. All these values were noted as the baseline values of first session, i.e., R1—for the experimental group and R1′—for the control group.

The stimulator used for experiment was biomed muscle stimulator, a commonly used stimulator in the rehabilitation department. A frequency of 50 Hz was used, and it has been the most common protocol for human studies.\cite{21}

Surface electrical stimulation at a frequency of 50 Hz or more on human quadriceps produces forces up to 60% of maximum voluntary isometric contraction.\cite{22} Surface rubber electrodes were used to deliver the current, one of which was placed over the femoral triangle and the other positioned over the distal portion of quadriceps femoris, unilaterally. The face of the electrodes which was to be applied to the skin was coated with aquasonic gel to reduce the impedance. The electrodes were then strapped to the thigh by means of micropore tapes to maintain good contact.

After 20 min of electrical stimulation in the experimental group or placebo treatment in the control group, the electrodes from one quadriceps femoris were fixed to other side quadriceps femoris for the next 20 min. At the end of a total of 40 min of electrical stimulation, the subjects underwent measurement of all the physiological parameters and again blood samples were taken for biochemical analysis. The values obtained were recorded as changes at the end of first session; R2—for the experimental group and R2′—for the control group. With this, the first session of experiment was completed. Following the similar procedure, patients were made to undergo total six sessions of electrical stimulation/placebo treatment within 2 weeks, 3 days/week. On the last day of treatment, i.e., sixth session, subject again underwent measurement of all physiological parameters and blood samples were taken for biochemical analysis before and after the treatment. These values were recorded as R3, R4 for the experimental group and R3', R4' for the control group.

Statistical Analysis

Related $t$-test was used to determine the changes in pre-post readings of various parameters after application of electrical stimulation. The inter-group comparison, i.e., in between experimental group and control group, was done with unrelated $t$-test.

Results

The results obtained from this study showed a significant decrease in blood glucose level following the application of electrical stimulation, but the changes in other parameters of the study, i.e., lipid profile (blood cholesterol, triglycerides, and high density lipoproteins) and physiological parameters (heart rate, respiratory rate, and arterial blood pressure), showed a statistically insignificant change following the application of electrical stimulation [Figure 1].

![Figure 1: Effect of electrical stimulation on blood glucose level (mg/dL) of patients with type 2 diabetes mellitus.](http://www.ijddc.com)
After a single session of electrical stimulation, there was significant decrease in post-treatment scores of blood glucose level than the pre-treatment scores both in experimental group (t = 8.27, P = 0.000) and control group (t = 12.13, P = 0.000), but the percentage decrease in pre–post scores of experimental group (10.35%) was much higher as compared to control group (4.06%). The blood glucose level score in the sixth session of electrical stimulation showed a significant difference (decrease) in the experimental group (t = 5.026, P = 0.001), but an insignificant difference (t = 0.534, P = 0.607) in control group.

The intergroup comparison showed that there is no significant difference between the pre-treatment scores of experimental group and control group in the first session, but there is significant difference (t = 2.30, P < 0.05) between pretreatment scores of experimental group and control group in the sixth session.

Table 1 shows that post-treatment blood glucose level (176.88 ± 43.74) mg/dL was significantly (t = 8.272; P = 0.000) different from pre-treatment blood glucose level (197.30 ± 47.027) mg/dL after a single session of electrical stimulation, in experimental group. There was also a significant (t = 12.136; P = 0.000) difference in blood glucose from (204.50 ± 53.86) mg/dL to (196.20 ± 52.47) mg/dL after placebo treatment in control group. However, the percentage decrease of blood glucose level in the experimental group (10.35%) was much higher as compared to control group (4.06%).

Table 1 also shows that blood glucose level after six sessions electrical stimulation (148.11 ± 18.53) was significantly decreased (t = 5.026, P = 0.001) in the experimental group as compared to the control group (207.22 ± 58.16) with reference to the pre-treatment scores.

The intergroup comparison showed that there is no significant difference between the pre-treatment scores of experimental group (197.30 ± 47.027) mg/dL and the pre-treatment scores of control group (204.50 ± 53.86) mg/dL in the first session, but there is a significant (t = 2.30, P < 0.05) difference between the pre-treatment scores of experimental group (169.67 ± 23.94) mg/dL and pre-treatment scores of control group (215.40 ± 58.13) mg/dL in the sixth session.

The first session post-treatment scores of experimental group (176.88 ± 43.74) mg/dL and control group (196.20 ± 52.47) mg/dL showed insignificant difference, but the post-treatment scores of sixth session showed significant (39.92%, P < 0.05) difference between experimental group (148.10 ± 18.53) mg/dL and control group (207.22 ± 58.16) mg/dL.

The line graph clearly represents the decreased blood glucose level in the experimental group which followed six session of electrical stimulation as compared to the control group which received placebo treatment for the same time period.

There was no significant difference between the pre- and post-treatment scores of blood cholesterol level in the experimental group as well as the control group. Though the six sessions of electrical stimulation did not produce a statistical significant change in blood cholesterol level, the mean value fall from 167.80 mg/dL (±40.58) to 162.10 mg/dL (±26.05) was noteworthy. Changes with prolonged use of electrical stimulation may yield statistically significant results. No such change (fall) was observed in control group.

There was no significant difference between the pre- and post-treatment scores of triglycerides level of experimental group as well as control group. Though the six sessions of electrical stimulation did not produce a statistical significant change in triglycerides, a mean

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<th>Group</th>
<th>First session</th>
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<td>176.88 ± 43.74</td>
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<td>204.50 ± 26.86</td>
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<td>0.898 NS</td>
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<td>R1R2</td>
<td>8.272***</td>
<td>12.136***</td>
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*Significant at P < 0.05, **significant at P < 0.01, and ***significant at P < 0.001. NS, non significant.
value fall from 126.00 mg/dL (±57.31) to 115.70 mg/dL (±49.18) was observed. No such change (fall) was observed in control group.

There was no significant difference between the pre- and post-treatment scores of high density lipoproteins of experimental group as well as control group. The mean value fall was also negligible.

Discussion

Diabetes is a major public health problem and is emerging as a pandemic. Several efficacious and economically acceptable treatment strategies are currently available to reduce the burden of diabetes complications. Regular physical exercise is widely perceived to be beneficial for type 2 diabetic patients as it influences several aspects including blood glucose concentration, insulin action, and cardiovascular risk factors. However, a large diabetic population is restricted from voluntary physical activity due to associated complications of the syndrome.

With this study, we tried to develop a new treatment strategy for these sedentary type 2 diabetic patients. The study analyzed the metabolic effects of electrical stimulation and the results of our study favored the hypothesis that electrical stimulation of group muscles has a significant effect on the blood glucose level of sedentary type 2 diabetic patients. The comparison between the blood glucose pre-treatment scores of experimental group and the pre-treatment scores of control group on the last session of study showed a significant difference between the two groups. Although with a single session treatment results were statistically significant in both the experimental group and the control group, after the 2-week treatment period results remained significant only in the experimental group. The control group showed an insignificant fall in blood glucose level.

Exercise can increase the rate of glucose uptake via two distinct mechanisms, i.e., an insulin independent one (contraction-stimulated glucose uptake) and an insulin-dependent one (post-exercise increase in insulin sensitivity). Wallberg-Henrikson et al. have shown in isolated rat skeletal muscle that the activity of insulin-independent glucose uptake to maximally enhanced immediately after exercise and then gradually wears off, but in 34% of the initial activity in situ present at 180 min. In contrast, increased insulin sensitivity is undetectable in the early phase of the post-exercise period and becomes prominent at 180 min after exercise.[19] In line with these findings, Price et al. have shown in human muscles that post-exercise glycogen repletion occurs in an insulin-independent manner for ~ 1 h after exercise and thereafter insulin-dependent glycogen repletion becomes significant.[23]

In our study insulin-independent mechanism, i.e. contraction stimulated glucose uptake is proposed to be responsible for the decrease in blood glucose level in a single session. Our application of electrical stimulation directly activates the glucose uptake in quadriceps muscle by inducing trans location of GLUT-4 glucose transporters to the cell surface via this insulin-independent mechanism. However, the decrease in blood glucose level after 2 weeks of electrical stimulation found in this study is likely to be due to the accumulation of insulin-dependent effect of increase in insulin sensitivity. This insulin-dependent effect may come into play during the post-stimulation period, i.e. in between the various sessions of electrical stimulation and this gives more positive results in the final session of the study. The stimulation of AMP-activated protein kinase (AMPK) in response to contraction induced by electrical stimulation may be associated with increased glucose uptake in quadriceps muscle. AMPK is stimulated by various glycogen depleting stimuli, such as contraction, hypoxia, and hyperosmolarity and have positive effects on glucose uptake and fatty acid oxidation in skeletal muscles.

Hultman and Spriet studied the muscle metabolism in response to the electrical stimulation and demonstrated that the use of electrical stimulation for 45 min at 20 H frequency causes a 44% decrease in glycogen concentration in quadriceps muscle.[24] and Kim et al. have also found a significant decrease in glycogen content using ES for 60 min at 50 Hz.[25] Henning et al. revealed that with external ES, motor units for type II fibers are more active due to larger axonal diameter, thus ES results in preferential activation of type II fibers that have a larger capacity for glycogen utilization in humans.[26,27] In addition, rates of glycoegenolysis during ES are twofold higher in type II fibers than type I fibers.[28] These findings and earlier observations seem to suggest that there occurs a large activation of glycolytic type II fibers by ES resulting in a significant decrease in blood glucose level and thereby possibly improving insulin sensitivity in the long run.

Lehmann and Spinas evaluated the effects of a 3-month physical training programme on the lipid profile of type
2 diabetic patients and found a significant improvement of plasma lipids with a 20% decrease in triglycerides, unchanged total cholesterol, and 23% increase in high density lipoproteins, respectively.[19] Baldwin et al. and Carlson et al. reported that during prolonged exercise, energy for muscle contraction is derived from both plasma free fatty acids and intramuscular triglycerides.[20,21] Although the effects of a regular exercise programme on the lipid profile of type 2 diabetic patients is well documented, the influence of electrical stimulation on the lipid profile of diabetic patients is not well documented in the literature.

In this study, the effect of ES on all the parameters of lipid profile was insignificant and this may be attributed to the shorter duration and lesser intensity of the contractile activity of the muscles. With the electrical stimulation of quadriceps muscles, the intensity of muscle contraction was not critical enough to produce significant changes in the lipid profile of patients with type 2 diabetes mellitus.

In our study, the changes in heart rate, respiratory rate, and arterial blood pressure were not statistically significant. These findings are in agreement with Davis et al.[22]

All subjects who participated in this study were sedentary type 2 diabetic patients without associated complications of syndrome; therefore, it is not clear whether similar metabolic effects would be shown in the bedridden diabetic patients with chronic illness. In addition, the muscle mass involved in contraction is expected to affect the magnitude of decrease in blood glucose level. A greater decrease in blood glucose level may be achieved if more muscles are employed by using more stimulation electrodes.

From this study, it was concluded that electrical stimulation can be used as a helpful modality to control the blood glucose level in type 2 diabetic patients, but the intensity of muscle contraction with the application of electrical stimulation was not critical enough to produce significant changes in lipid profile and other physiological parameters.

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