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Effectiveness of electrical muscle stimulation in controlling blood glucose level: A systemic review

Vishwajeet Trivedi

Assistant Professor, School of Medical and Allied Sciences, GD Goenka University, Gurugram

*Corresponding author email: physiovishu87@gmail.com

Divya Goyal

Assistant Professor, School of Medical and Allied Sciences, GD Goenka University, Gurugram

Richa Mahajan

Assistant Professor, School of Medical and Allied Sciences, GD Goenka University, Gurugram

Abstract--The aim is to critically review the relevant evidence on the interrelationships between electrical muscle stimulation and metabolic outcomes. From this review appear that the effects of electrical muscle stimulation resulted in reductions in HbA1c, and other outcome measures of diabetes mellitus type 2. Considering the available evidence, it appears that electrical muscle stimulation could be an effective intervention to help glycemic control, especially considering that the effects of this form of intervention are comparable with what reported with physical exercise. Less studies have investigated regarding electrical muscle stimulation (its duration, type of current, form of impulses, sites to be stimulated etc) offers a synergistic and incremental effect on glycemic control; however, from the available evidences appear that electrical muscle stimulation seems to determine additional change in HbA1c that can be seen significant if compared with other forms of blood sugar control methods.

Keywords---electrical muscle stimulation, type-2 diabetes, glycemic control, HbA1c.

Introduction

Diabetes mellitus (DM) is the most common non-communicable disease worldwide

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and the fourth to fifth leading cause of death in developed countries (Amos et al, 1987). Diabetes mellitus is a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both (Aring et al, 2005). A chronic lack of physical activity is associated with reduced peripheral glucose uptake due to insulin resistance (Lipman et al, 1970). Physical Exercise can directly activate glucose uptake in skeletal muscle by inducing translocation of GLUT-4 glucose transporter to the cell surface via an independent mechanism called contraction stimulated glucose transport (Kennedy et al, 1999). It is proved from various studies that the use of electrical stimulation (ES) causes contraction of muscles, as well as activate glucose uptake in skeletal muscle in strikingly similar way as that of physical exercises (Greemhaff et al, 1993; Kjar et al, 1996). It has been recommended that, for the greatest improvement in glycemic control and insulin sensitivity, exercise intensity needs to be set at 50–80% of maximal aerobic capacity in Type 2 diabetes (ACSM and ADA, 1997), which supports the results drawn by McArdle et al, (2001) who found the long term adaptations of skeletal muscles to chronic electrical stimulation, very similar to that of low intensity aerobic training. Clinically, ES of muscle is useful as a modality of assisting muscle contraction for those who have difficulties in performing voluntary exercise (Lake, 1992). 0

Methods

We searched the English-language medical literature published, using the Medline database of the National Library of Medicine, Cochrane online library, the Educational Resources Information, Center database (ERIC), and the Nursing and Allied Health database (Cinahl). The medical subject headings (MeSH). Our searched were “Electrical stimulation” combined with “type 2 diabetes mellitus,” including all subheadings. We reviewed titles of articles extracted by the search for relevance to the efficacy of ES, and we retrieved the full-text articles for those that were potentially relevant. We manually searched journals related to ES and diabetes mellitus, expected to have the highest relevance in the main library of Punjabi University Patiala. The computer based search strategy included common text words and medical subjects headings related to electrical muscle stimulation and diabetes mellitus type 2.

Study selection

We included the research articles that evaluate the effect of electrical muscle stimulation in patients with type 2 diabetes. Appropriate screened titles and abstracts were selected. We included studies irrespective of duration, publication status, or predefined outcomes. Electrical stimulation has not benefited from as in-depth studies as physical exercises and has been recognized as a useful electrical modality for the reeducation of a paralyzed muscles, in gaining muscular strength as well as in the improvement of insulin action on tissue, leading favorably on control and treatment of type 2 diabetes. The early studies offering preliminary evidence for the benefits of ES with type 2 diabetic patients were published around 12 years ago.

Effect of EMS on various outcome measures of type 2 DM

Hamada et al (2003) reported that low- frequency electrical stimulation (ES) of quadriceps muscles alone significantly enhanced glucose disposal rate (GDR) during euglycemic clamp. 20 minute of stimulation by low-frequency surface Electrical stimulation of quadriceps femoris muscles in this study acutely increased the whole body glucose uptake. In response to ES the stimulatory effect of ES on whole body glucose uptake persisted not only during, but also for at least 90 min after cessation of stimulation stimulation. They suggested that low-frequency ES may become a useful therapeutic approach to activate energy and glucose metabolism in humans. In the subsequent study they compared the acute metabolic effects of ES to lower extremities with voluntary cycle exercise at identical intensity (Hamada, 2004) and observed that whole body glucose uptake demonstrated a significant increase during and after the cessation of ES for at least 90 min. The post-ES effect was significantly greater than that of the post-VE period. These results on healthy adult suggested that ES can substantially enhance energy consumption, carbohydrate oxidation, and whole body glucose uptake at low intensity of exercise and percutaneous ES may become a therapeutic utility to enhance glucose metabolism in humans.

Poole et al (2005) examined whether use of an electrical muscle stimulator mimics exercise in neurologically intact individuals and has metabolic benefits in patients with type 2 diabetes. Acute changes in glucose uptake were measured in five subjects with type 2 diabetes. Body composition, features of the metabolic syndrome and measures of insulin sensitivity were measured before and after 12 weeks of daily use of the stimulator in four subjects with type 2 diabetes. They reported that even though the muscle stimulator acutely increased pulse, blood pressure, energy expenditure and glucose uptake and improved insulin stimulated non-esterified fatty acid suppression, the magnitude of these changes was too small to produce clinical benefit. They concluded that electrical muscle stimulation has limited clinical benefits in patients with type II DM.

Griffin et al (2009) conducted an analysis of metabolic, body composition, and neurological factors before and after 10 weeks of functional electrical stimulation (FES) cycling in persons with SCI as they are at a heightened risk of developing type II diabetes and cardiovascular disease. Eighteen individuals with SCI received FES cycling 2-3 times per week for 10 weeks. An oral glucose tolerance (OGTT) and insulin-response test was performed to assess blood glucose control. They observed that after 10 weeks of training Blood glucose and insulin levels were lower following the OGT and the lean muscle mass increased.

Sharma et al (2010) analyze the effect of electrical stimulation (40 minutes per day, 3 days /week for 2 weeks) on blood glucose level, lipid profile and other physiological parameters of sedentary type 2 diabetic patients. They also found that the ES has significant results on blood glucose control and on these findings they concluded that electrical stimulation can be used as a helpful modality to control the blood glucose level in sedentary type 2 diabetic patients. They also concluded that 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.

Kawaguchi et al (2011) investigated the effects of hybrid training utilizing combined voluntary and electrical muscle contractions, on glucose metabolism and serum IL-6 levels on 7 elderly subjects. Both quadriceps and hamstrings were contracted voluntarily or electrically at the same time for 19 min twice a week. The effects on glucose metabolism and serum IL-6 levels were evaluated after 12 weeks of hybrid training. All of the subjects completed the study, and no severe adverse events developed during the study period. They reported that fasting blood glucose levels and serum IL-6 levels were significantly decreased after hybrid training though no significant differences in body mass index, serum insulin levels, homeostasis model assessment for insulin resistance values, or hemoglobin A1c values were observed after 12 weeks of hybrid training.

Crowe and Caulfield (2012) conducted a pilot study on the effect of unsupervised aerobic neuromuscular electrical stimulation (biphasic, symmetrical with an interphase delay of 100 ms) over 8 type II DM subjects and determined that stimulating the quadriceps, hamstrings, gluteus, and calf muscles by using large hydrogel electrodes for 45 minutes to 1 hour for 8 weeks may have a beneficial effect on hemoglobin A1c with those who will not or cannot do adequate amounts of voluntary exercises. They found Haemoglobin A1c levels improved by $0.8 \pm 0.7\%$ from $7.4 \pm 1.3\%$ (mean \pm SD) to $6.66 \pm 1.0\%$ ($p=0.01$).

Wall et al (2012) investigates the capacity of neuromuscular electrical stimulation (NMES) to increase in vivo skeletal muscle protein synthesis rates in a sample of six elderly type 2 diabetic men (70 ± 2 yr). Type 2 diabetes patients subjected to 60 min of one-legged NMES and showed that NMES directly stimulates skeletal muscle protein synthesis rates in humans. They opined that NMES may represent an effective interventional strategy to attenuate muscle loss in elderly individuals during bed rest and /or in other disuse states.

Miyamoto et al (2012) evaluated whether percutaneous electrical muscle stimulation (EMS) attenuates postprandial hyperglycemia in type 2 diabetes. Eleven patients with type 2 diabetes participated in two experimental sessions; one was a 30-min EMS after a breakfast (EMS trial) and the other was a complete rest after a breakfast (Control trial). In each trial, blood was sampled before and at 30, 60, 90, and 120 min after the meal. They reported that postprandial glucose level was significantly attenuated in EMS trial at 60, 90, and 120 min after a meal ($p < 0.05$).

Khan (2012) found incidentally that the transcutaneous electrical stimulation (TENS) has an effect on blood glucose. He applied TENS once in every 24 hours on the back and the buttocks of an 80 years old patient, to make patient get rid of pain. As the pain symptoms got improved the frequency of TENS was increased to thrice in every 24 hours which results in hypoglycemia (blood sugar level < 4 mmol/L). Discontinuation of TENS resulted in raised blood sugar level. When TENS was restarted, the same hypoglycaemic response was noted. The insulin dosage was adjusted to half of the patient's routine daily requirement with continued application of TENS. He concluded that the episodes of hypoglycemia persists following TENS application, which may be due to effective pain control,

decreased sympathetic stimulation, enhanced insulin sensitivity or altered muscle metabolism due to electrical stimulation.

Summary and Conclusions

Role of ES in contracting the skeletal muscles in similar way as that of voluntary muscle contraction highlighted the role of ES in the control of blood glucose in patients with type 2 diabetes. The studies included in the review have focused on people with impaired glucose tolerance because they are high risk of developing type 2 diabetes. Electrical stimulation has been shown to be beneficial with type 2 diabetic patients in a number of studies. The available evidences are tabulated and presented in table 1. Considering the available evidence, it appears that ES could be an effective intervention to help glycemic control. However, from this review, it is clear that no known RCT, review, meta-analysis have been conducted to address the efficacy of ES over the long term on a large group of patients with type 2 diabetes, since the longest study duration was 6 months. Moreover, no research has yet been undertaken on the efficacy of a Russian current which is most commonly used in weight loss managements in different centers, in order to see the effect on metabolic outcomes in type 2 DM.

Table 1
Summary of the significant studies

S.no.	Author/year	Objectives / Aims	Sample	Outcome measures	Intervention	Results	Conclusion
1.	Hamada et al. / 2003	To examine whether involuntary muscle contraction induced by percutaneous muscle stimulation causes acute enhancement of glucose uptake in human subjects	14 male subjects without any metabolic, cardiovascular or neuromuscular disorders	blood plasma glucose monitoring, Respiratory gas measurement	Low-frequency ES through surface electrodes placed over motor points of both quadriceps Femoris muscles for 20 minutes in supine position. Subjects were required a maximum of four visits to the laboratory. separated by at least 1 wk.	Mean oxygen uptake during ES was significantly higher than that of the pre stimulation period (3.2 ± 0.1 vs. 5.7 ± 0.1 ml/kg/min, $P < 0.01$) The respiratory gas exchange ratio and blood lactate concentration gradually decreased	The stimulatory effect of ES on whole body glucose uptake persisted not only during, but also after, stimulation.

						toward the end of ES. The mean increase in GDR above prestimulation was 2.5 mg/kg/m in during stimulation ($P < 0.01$)	
2.	Hamada et al. / 2004	To examine the acute metabolic effects of ES to lower extremities compared with voluntary cycle exercise (VE) at identical intensity	8 men with age 24.8 ± 0.6 year	Respiratory gas measurement, Glucose uptake measurement	(1) In the supine position, both lower leg (tibialis anterior and triceps surae) and thigh (quadriceps and hamstrings) muscles were sequentially stimulated for 20 minutes. (2) Voluntary supine exercise for 20 min using a cycle ergometer.	The blood lactate concentration 3.2 ± 0.3 mmol/l ($P < 0.01$), whole body carbohydrate oxidation ($P < 0.01$), Whole body glucose uptake ($P < 0.01$) were significantly increased post experiment in electrical stimulation group than the group with voluntary exercise.	ES can substantially enhance energy consumption, carbohydrate oxidation, and whole body glucose uptake at low intensity of exercise. Percutaneous ES may become a therapeutic utility to enhance glucose metabolism in humans.
3.	Poole et al / 2005	To determine whether use of an electrical muscle stimulator mimics exercise in neurologically intact individuals	Eight patients, age 46–61, with type 2 Diabetes.	Waist circumference, Weight, Body mass index, % body fat,	Quadriceps and abdominal muscles stimulated for 8 sec alternately. A current of 30mA was used	The muscle stimulator acutely increased pulse, blood	Although the muscle stimulator acutely mimics exercise, limitations

		and has metabolic benefits in patients with type 2 diabetes.		Total cholesterol, High-density lipoprotein, cholesterol, Triglycerides, Fasting glucose, Fasting insulin, Haemoglobin A1c, blood pressure, Calculated 10 years cardiac risk, OGTT, Hyperinsulin aemic clamp.	for 30 min and then increased to 40mA for a further 30 min. for 12 weeks	pressure, energy expenditure and glucose uptake. Daily use over 12 weeks improved insulin stimulated nonesterified fatty acid suppression but did not result in changes in body composition or clinical parameters.	in the size of the stimulating current mean that the magnitude of these changes is too small to produce clinical benefit.
4.	Griffin et al. / 2009	To conduct a comprehensive analysis of metabolic, body composition, and neurological profiles before and after 10 weeks of FES cycling in individuals with paralysis from SCI.	Eighteen individuals with SCI	Body composition, ASIA neurological classification of SCI, oral glucose tolerance and insulin response test, plasma cholesterol (total-C, HDLC, LDL-C), triglyceride, and inflammatory markers (IL-6, TNF-a, and CRP).	FES cycling over quadriceps, gluteal and hamstring muscles for 2-3 times per week for 10 weeks.	Total FES cycling power, work done, Lean muscle mass increased, whereas, bone and adipose mass did not change. The ASIA motor and sensory scores for the lower extremity significantly increased with training. Blood glucose	Significant improvements in blood glucose control and inflammatory markers occurred with an increase in lean muscle mass and motor and sensory ability. It is expected that continuous use would be required to maintain the observed health benefits across the life span.

						and insulin levels were lower following the OGTT, levels of IL-6, TNF- α , and CRP were all significantly reduced.	
5.	Sharma, et al. / 2010	To analyze the effect of electrical muscle stimulation on blood glucose level, lipid profile, and physiological parameters (HR, BP, RR) of sedentary type 2 individuals.	10 patients in each experimental and control group of age >55 years	Blood glucose level, Lipid profile, BP, RR, HR.	Electrical stimulation over both quadriceps femoris muscle for 20 minutes each, 3 days / week for 2 weeks.	Blood glucose level in experimental group was reduced significantly (t=5.026, p=0.001)	Electrical muscle stimulator can be used to assist in the control of blood glucose level in type 2 diabetic patients.
6.	Crowe & Caulfield / 2010	(1) if NMES was an acceptable training modality for men with type 2 diabetes mellitus and (2) to assess effects on haemoglobin A1c levels	8 men with type 2 DM of age 53 \pm 8 years	Primary outcome measures were changes in haemoglobin A1c and the responses in a questionnaire on participants' perceptions of the system. Body mass and composition were also measured before and after the NMES intervention period.	NMES system for 1 h, 6 times weekly for 8 weeks, unsupervised, at home over the bilateral quadriceps, gluteal, hamstring and calves	Haemoglobin A1c levels improved by 0.8 \pm 0.7% from 7.4 \pm 1.3% (Mean \pm SD) to 6.6 \pm 1.0% (p=0.01). All participants recommend it and would continue to use it twice a week 'to maintain improvements.	NMES may be acceptable and have a beneficial effect on haemoglobin A1c.
7.	Kawaguchi et al / 2011	Investigate the effects of hybrid training on glucose metabolism and	7 elderly subjects	body mass index, serum insulin levels,	Both quadriceps and hamstrings were contracted voluntarily or	fasting blood glucose levels	Hybrid training decreased fasting

		serum IL-6 levels in elderly people		homeostasis model assessment for insulin resistance values, or hemoglobin A1c values, fasting blood glucose level	electrically at the same time for 19 min twice a week for 12 weeks.	were significantly decreased (114 ± 13 vs. 103 ± 9 mg·dL ⁻¹); $p = 0.0340$) serum IL-6 levels was statistically significantly different (44.0 ± 35.6 vs. 14.6 ± 10.5 pg·mL ⁻¹); $p = 0.0180$), and significantly different Correlation found between serum IL-6 levels and fasting blood glucose levels ($\rho = 0.883$; $p = 0.0306$)	blood glucose and serum IL-6 levels in elderly people.
7.	Miyamoto et al. / 2012	To examine whether percutaneous electrical muscle stimulation (EMS) attenuates postprandial hyperglycemia in type 2 diabetes.	Eleven patients with type 2 diabetes, age 57.0 ± 2.7 years.	blood lactate concentration, HbA1c, Total cholesterol, HDL-cholesterol, LDL-cholesterol, triglyceride, glucose, insulin, C-peptide, non-esterified fatty acids (NEFA), and Creatine phosphokina	Each subject participated in 30-min EMS after breakfast (EMS trial) and the other involved a complete rest after breakfast (Control trial), electrodes applied over quadriceps, biceps femoris, and gluteus maximus muscles with a	Postprandial glucose level was significantly attenuated in EMS trial at 60, 90, and 120 min after a meal ($p < 0.05$). The C-peptide concentration was	The present results provide first evidence indicating that EMS is a new exercise method for treating postprandial hyperglycemia in individuals with type 2 diabetes, especially

				se (CPK) concentrations	gap of 1 wk between the consecutive sessions.	also significantly lowered in EMS trial ($p < 0.01$)	who cannot perform adequate voluntary exercise because of excessive obesity, orthopedic diseases, or severe diabetic complications.
8.	Wall et al. / 2012	To investigate the capacity of neuromuscular electrical stimulation (NMES) to increase in vivo skeletal muscle protein synthesis rates in older type 2 diabetes patients.	Six elderly type 2 diabetic men of age 70 ± 2 years divided into 2 groups: STIM & CON.	Blood plasma level, muscle biopsy.	60 min of one-legged NMES over the quadriceps muscle of one side.	blood glucose concentrations decreased significantly throughout the experiment to 6.6 ± 0.5 mmol/l ($P < 0.01$). The overall increase in muscle protein-bound phenylalanine enrichment over the 4 hours poststimulation period was 30% greater in the STIM compared with the CON leg ($P < 0.01$). Muscle protein synthesis rates were greater in	NMES likely represents an effective interventional strategy to attenuate muscle loss in elderly individuals during bed rest and/or in other disuse states.

						the STIM compared with the CON leg during recovery from NMES (0.057 ±0.008 vs. 0.045± 0.008%/h , respectively, $P < 0.01$)	
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