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Gender difference in metabolic responses to surface electrical muscle stimulation in type 2 diabetes

Toshiaki Miyamoto [a,*], Kazuhito Fukuda [b], Kohei Watanabe [c], Masami Hidaka [a], Toshio Moritani [d]

[a] Graduate School of Health Science, Hyogo University of Health Sciences, Kobe, Japan
[b] First Department of Internal Medicine, University of Toyama, Toyama, Japan
[c] School of International Liberal Studies, Chukyo University, Aichi, Japan
[d] Graduate School of Human and Environmental Studies, Kyoto University, Kyoto, Japan

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ABSTRACT

Objective: The aim of this study was to examine whether or not there is a gender difference in metabolic responses to surface electrical muscle stimulation (sEMS) in type 2 diabetes (T2DM). Methods: Ten men and eight women with T2DM participated in two sessions; in both sessions the subjects were investigated after a breakfast and that in one occasion they underwent 30-min sEMS while in the other they were followed while resting. Blood and gas exchange data were compared between genders as to the extent of blood glucose and non-esterified fatty acids responses to sEMS. Results: The time course change of blood glucose concentration after sEMS did not statistically differ between genders while sEMS could attenuate postprandial blood glucose level regardless of gender ($p < 0.05$). Women had a lower respiratory quotient and lactate concentration during sEMS when compared with men ($p < 0.05$). Conclusions: This study indicated that sEMS might have resulted in lower anaerobic glycolysis in women as compared to men with T2DM. sEMS is expected to be a new exercise method in T2DM. Determining the possible gender differences and precise mechanisms might further shed some light for the efficacy of sEMS use for clinical practice.

1. Introduction

One of goals of diabetes therapy is to improve postprandial hyperglycemia which is a dominant and independent risk factor for cardiovascular disease and mortality in type 2 diabetes (T2DM) (DECODE study group on behalf of the European Diabetes Epidemiology Group, 1999). Also, postprandial hyperglycemia is associated with significant long-term complications, particularly damage to the kidney, eyes, nerves, heart, and blood vessels (The Diabetes Control and Complications Trial Research Group, 1993; Yki-Jarvinen, 1998). It is well known that exercise has been a cornerstone of diabetes management, along with diet and medication since it may have beneficial effects on metabolic risk factors for the development of diabetic complications (American Diabetes Association, 1997). Actually, there is increasing evidence that a single bout of voluntary exercise following a meal can attenuate postprandial hyperglycemia (Derave et al., 2007; Larsen et al., 1997).

However even though the patients with T2DM are recommended to perform voluntary exercise, many of them are restricted from the recommended exercise (e.g., walking or ergometry exercise), because of excessive obesity, orthopedic diseases, or severe diabetic complications. To solve this problem, recently, it has been shown that surface electrical muscle stimulation (sEMS) with low stimulation frequency could be an effective method to enhance glucose metabolism. We reported that, by means of euglycemic clamp, a single bout of sEMS (20 min) significantly enhanced whole body glucose uptake during and after the cessation of sEMS (Hamada et al., 2003) and that sEMS enhanced whole body glucose uptake significantly greater than voluntary ergometry exercise at the identical oxygen uptake in the presence of significantly higher blood lactate and respiratory quotient (RQ) (Hamada et al., 2004). Furthermore, we provided first evidence that sEMS could successfully attenuate postprandial glucose concentration in middle-aged men with metabolic syndrome (Kimura et al., 2010) and patients with T2DM (Miyamoto et al., 2012). These results lead us to expect that sEMS is a candidate for new exercise method in patients with T2DM and/or excessive obesity who cannot perform adequate voluntary exercise.

* Corresponding author. Address: Department of Rehabilitation, Graduate School of Health Science, Hyogo University of Health Sciences, Kobe, 650-8530, Japan. Tel.: +81 78 304 3073; fax: +81 78 304 2773.
E-mail address: t-miyamoto@huhs.ac.jp (T. Miyamoto).

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On the other hand, it has been suggested that a gender difference exists in the relative utilization of carbohydrates and lipids as fuel sources during endurance exercise (Roepstorff et al., 2002). For given relative submaximal exercise intensities, women oxidize a smaller proportion of carbohydrate relative to lipid than do men, as indicated by lower RQ values (Kendrick et al., 1987; Tarnopolsky, 2000; Tarnopolsky et al., 1995). Furthermore, lower net glycogen utilization and blood lactate concentrations have been observed in women compared with men while both were exercising at similar relative intensities (Tarnopolsky, 2000). It has been speculated that, since men depletes muscle glycogen stores more than women during exercise, this could increase glucose uptake more in men than women during the postexercise period, as lower muscle glycogen levels are associated with increased glucose uptake (Horton et al., 2006). Also, it has been reported that type I /type II muscle fiber area ratios in women was higher than that in men (Moritani et al., 1991). Since sEMS primarily activates glycolytic type II fibers, in which glycogen is substantially utilized (Hamada et al., 2004; Sinacore et al., 1990), we hypothesized that sEMS would induce a lower glucose metabolic response in women than men.

There are no data, at least to our knowledge, concerning gender differences in metabolic response to sEMS. Determining gender differences in the effects of sEMS on glucose metabolism, therefore, is an important step in the delineation of biological factors that may impact the physiological benefits of sEMS. Accordingly, the purpose of this study was to investigate gender based differences in during and post-sEMS metabolism.

2. Methods

2.1. Participants and informed consent

Ten men and eight age-matched postmenopausal women with T2DM volunteered to participate in this study (Table 1). All of them had been diagnosed as T2DM according to the criteria of the World Health Organization for classification of diabetes. Patients were controlled by diet and/or oral hypoglycemic agents (Table 2). In addition, all subjects had normal cardiovascular, renal, hepatic, gastrointestinal, and neurological functions as assessed by clinical screenings and patients with concurrent medical conditions preventing exercise were excluded. Informed consent, approved by the Ethical Committee of Japan Post Kyoto Teishin Hospital (#21-3), was obtained from all patients before enrollment.

2.2. Experimental design

In this study, we used the same experimental protocol as in our previous study (Miyamoto et al., 2012). A schematic diagram of the experimental protocols is shown in Fig. 1. Each subject participated in 2 experimental sessions; i.e., one involved a 30-min sEMS after breakfast (sEMS trial) and the other involved a complete rest after the same breakfast (Control trial). The testing protocol was not different between the trials except that the subjects underwent 30-min sEMS after the test meal in the sEMS trial. The two trials were performed in random order, with an interval of at least 1 week. In each trial, subjects took a 20-min rest on the bed from 08:10 am after height and body mass were measured. Then, in a supine position, respiratory gas exchange and electrocardiogram (ECG) were measured for 10 min after confirming stable respiration, as a baseline (pre-prandial) measurement. After the gas exchange and ECG measurement, blood lactate concentration was measured by the lactate oxidase method with an automated analyzer (Lactate Pro, Arklay, Kyoto, Japan). At the same time, blood was sampled from the antecubital vein for determinations of HbA_{1c}, Total-Cholesterol, HDL-Cholesterol, LDL-Cholesterol, triglyceride, glucose, insulin, C-peptide, non-esterified fatty acids (NEFA) concentrations. After these pre-prandial measurements were finished, the breakfast meals were served. It contained 612 kcal (61% carbohydrate, 21% fat, and 18% protein). Intake of breakfast was completed within 20 min and patients took their usual medications. After the breakfast, the subject in each trial kept rest on the bed, and then, 30 min after the breakfast, the subject underwent either 30-min sEMS or 30-min rest on the bed. Again, the respiratory gas exchange and ECG were measured between 40 and 50 min after the meal (i.e., from 10 to 20 min into the 30-min sEMS treatment in sEMS trial and during complete rest in Control trial) and blood lactate concentration was determined 60 min after the meal. In addition, postprandial venous blood was sampled at 30, 60, 90 and 120 min after the meal in each trial. The room temperature was maintained at 24–26 °C.

2.3. sEMS procedure

Five silicon-rubber stimulation electrodes (Homer Ion, Tokyo, Japan) were applied over quadriceps, hamstrings and gluteus muscle groups on each leg (area per leg 288 cm^2) and attached with covers made of polyethylene. The 3-ch separate output circuit and three pairs of electrodes were located per leg (i.e., the stimulation was bipolar) (Fig. 2). We moistened electrodes before applying sEMS in order to lower the impedance of the electrode–skin contact. A stimulator (KH-3, Homer Ion, Tokyo, Japan) delivered monophasic square-wave pulses of 0.2-ms duration at a frequency of 4 Hz. All of the muscles were simultaneously contracted for 30 min. The stimulation intensity was gradually increased for 5 min and set to about 6.0 ml/kg/min oxygen consumption at

Table 1
Subject characteristics.

	men (n = 10)	women (n = 8)	
Age (year)	56.3 ± 9.2	63.9 ± 11.9	NS
Height (cm)	169.9 ± 6.1	156.4 ± 9.0	$p < 0.05$
Weight (kg)	70.2 ± 13.0	51.6 ± 9.8	$p < 0.05$
Body mass index (kg/m^2)	24.2 ± 3.6	20.9 ± 2.7	$p < 0.05$
Body fat (%)	23.8 ± 5.2	29.8 ± 7.7	NS
HbA_{1c} (%)	6.9 ± 0.6	7.3 ± 1.1	NS
Fasting glucose (mmol/l)	6.58 ± 1.35	6.49 ± 0.74	NS
HOMA-IR	1.67 ± 0.99	1.54 ± 1.14	NS
Cholesterol (mmol/l)	4.71 ± 0.49	4.89 ± 0.29	NS
Triglyceride (mmol/l)	1.29 ± 0.51	1.14 ± 0.53	NS
LDL-cholesterol (mmol/l)	2.93 ± 0.41	2.85 ± 0.61	NS
HDL-cholesterol (mmol/l)	1.17 ± 0.20	1.46 ± 0.42	NS
Duration of recognized diabetes (year)	5.9 ± 1.8	10.9 ± 6.5	NS

Values are means ± SD. BP, Blood Pressure; HOMA-IR, Homeostasis model assessment-insulin resistance.
$p < 0.05$, Significant difference between genders; NS, No Significance.