LOW-FREQUENCY ELECTRICAL STIMULATION OF SKELETAL MUSCLES IN PATIENTS WITH CHRONIC HEART FAILURE

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A b s t r a c t

The aim of this study was to evaluate the effect of low-frequency electrical stimulation of skeletal muscles in patients with chronic heart failure (CHF). Twelve patients with CHF diagnosed by coronarography (NYHA, III-IV; ejection fraction, 19.33 %) were examined before and after five weeks of the low-frequency electrical stimulation of quadriceps and calf muscles (1 h/day, 5 days/week). The patients were on the waiting list for heart transplantation. The medical regimens of all controlled patients were optimised and they were symptomatically stable. The dynamometry testing of quadriceps muscles was performed. The low-frequency stimulation was well tolerated by all subjects. It is concluded that the low-frequency electrical stimulation of quadriceps muscles lasting one week improved the quadriceps muscle strength by 28 %. The results of magnetic resonance imaging analysis of the gastrocnemius muscle showed a significant increase in muscle volume after stimulation. This procedure could be useful in the treatment of patients with severe chronic heart failure.

K e y w o r d s

Chronic heart failure, Low-frequency electrical stimulation, Skeletal muscle, Dynamometry

INTRODUCTION

Chronic heart failure (CHF) is often accompanied by complete hypoperfusion, which affects a great part of the skeletal muscle mass. The intensity of catabolism increases, the reactive oxygen species and a large amount of circulating cytokines stimulate the development of apoptosis. The skeletal muscle oxidative metabolism is depressed, intracellular pH levels decrease, phosphocreatine depletion during exercise increases and phosphocreatine resynthesis decreases (*1*). The increased sympathetic tone and stimulation of the renin-angiotensin-aldosterone system influence the redistribution of regional blood flow and create endothelial dysfunction of all vessels. This leads to an impaired peripheral vascular dilatation in response to vasodilator stimuli and a reduction of blood flow and O_2 supply in skeletal muscles (*2*). Chronic hypoxia strongly damages the structural and metabolic integrity of muscle fibers. The resulting general atrophy decreases the power and fatigue resistance of muscles. Sometimes, this situation progresses to cardiac cachexia.

The beneficial influence of exercise on the aerometabolic capacity and fatigue tolerance in patients with chronic heart failure (CHF) has been repeatedly reported. The commonly used methods of training, however, are based on systemic exercise and are not always tolerated by all CHF patients, especially by those with severe heart failure or with life-threatening arrhythmia. A new approach to cardiac rehabilitation is represented by the method of low-frequency electrical myostimulation (LFMES) of skeletal muscles. In *in vitro* conditions, a LFMES of 10 Hz changes the phenotype of stimulated mammalian skeletal muscle fibers. LFMES transforms the myosin chains of "fast" type to "slow" type ones, which is characterised by a higher resistance to fatigue (*3*, *4*). LFMES also increases capillary density and enhances perfusion in strength muscles of the rat and rabbit (*5*, *6*). The most important is the fact that all these experimental results are also applicable to human conditions. The aim of our study was to evaluate the long-term effects of LFMES on the metabolic performance and structure of skeletal muscles in patients with chronic heart failure.

MATERIALS AND METHODS

Patients

We evaluated a group of 12 patients who had undergone coronarography (class NYHA, II-IV; both sexes; mean age, 56 ± 9 years; ejection fraction, 19.3 ± 3 %). All of them were symptomatically stable and received an optimal pharmacological treatment (ACEI, betablockers, diuretics) that remained unchanged throughout the study.

Protocol of LFMES application

The muscles to be stimulated were quadriceps and calf muscles. Special rectangular electrodes (80x100 mm) were positioned on the thighs and calves. Electrical stimulation was performed for an hour per day, 5 days a week for 5 weeks, using the dual-channel stimulators Elpha 2000 (Danmeter, Odense, Denmark). The stimulators delivered a biphasic current of 10 Hz frequency. The pulse duration was 200 msec with an "on-off" mode of stimulus (20 sec of stimulation followed by 20 sec of pause). The maximal stimulation amplitude was 60 mA.

Dynamometry

The dynamometry of quadriceps muscles was performed every week, using the dynamometer PC-2 SDT (Czech Republic).

Magnetic resonance spectroscopy

To evaluate the muscle metabolic patterns, the phosphorus-31 nuclear magnetic resonance spectroscopy (^{31}P MRS) of gastrocnemius muscle was performed. The exercise protocol for ^{31}P MRS was based on repeated plantar flexions of equal amplitudes at a frequency of 0.5 Hz against a calibrated load. The initial workload was 1W and increased by 0.25 W every 3 minutes. Spectra were collected every minute; the protocol was discontinued when fatigue appeared. The recovery period was monitored for 10 min and the spectrum was evaluated every 30 seconds. The relative concentrations of inorganic phosphates (Pi) and phosphocreatine (PCr) were calculated by integration and corrected for different saturations. Changes in PCr concentration were expressed as the PCr/PCr+Pi ratio. The PCr recovery rate was calculated and expressed, using the time constant (1/k), according to the standard protocol described by *Hanada et al.* (*7*).

MAGNETIC RESONANCE IMAGING

The volumes of soleus and gastrocnemius muscles were determined by the method of magnetic resonance imaging (MRI), using a FLASH 2D (gradient echo) sequence in the axial plane with a pulse repetition time of 600 msec, an echo time of 10 msec, a slice of 10 mm with a 5-mm interslice gap and a total number of slices equal to 26. Finally, a planimetric estimation of the muscle cross-sectional area was performed and the total muscle volume was calculated.

All nuclear magnetic resonance measurements (^{31}P MRS and MRI) were obtained using a Siemens 1.5 T Magneton imaging system (Erlangen, Germany). The experimental protocol completed with the Declaration of Helsinki was approved by the local Ethics Committee. A written informed consent was obtained from each subject prior to their participation.

STATISTICAL EVALUATION

The Wilcoxon paired test was used for statistical analysis. The statistical significance was defined as $P < 0.05$.

RESULTS

The low-frequency electrical stimulation resulted in improved quadriceps muscle strength (F_{max}) by 28% as early as at one week and persisted until the end of stimulation at 5 weeks. The baseline values of systolic (SBP) and diastolic blood pressure (DBP) and heart rate (HR) remained unchanged during the measurement (*Table 1*).

The analysis of muscle metabolic parameters, using ^{31}P magnetic resonance spectroscopy of gastrocnemius muscles, did not show any essential changes. There was only a slight tendency to a diminution of the time constant (1/k) of PCr post-exercise resynthesis after 5 weeks of LFMES, but this was without statistical significance (*Table 2*).

In contrast to the results obtained by MRS, the analysis of muscle volumes by MRI showed a significant increase in muscle mass in gastrocnemius muscles after 5 weeks of LFMES (*Table 3*).

DISCUSSION

The use of chronic low-frequency stimulation in experimental models has helped to study muscle plasticity. It seems that LFMES involves qualitative and quantitative changes in different elements of the strength muscle fibers. Both structural and functional alterations may probably be caused by transformations of fast protein isoforms to their slow counterparts, which is followed by an increased activity of oxidative enzymes, improved oxygen consumption and growth of the terminal microvascular bed. These changes provide a basis for the general improvement of muscle metabolic patterns, including the diminution and

Table 1
Results before and after the low-frequency electrical stimulation of skeletal muscles (mean ± SD)

LFMES	SBP (mmHg)	DBP (mmHg)	HR (bpm)	F_{max} (N)
Before stimulation	101 ± 6	67 ± 7	69 ± 3	230 ± 57
After 1 week	105 ± 5	70 ± 3	67 ± 7	*295 ± 64
After 5 weeks	104 ± 5	71 ± 3	68 ± 6	* 292 ± 61

LFMES, low-frequency electrical stimulation; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate, Fmax, maximal strength; *, $P < 0.05$

Table 2
Results of ^{31}P magnetic resonance spectrum analysis of the gastrocnemius muscle before and after five weeks of low-frequency electrical stimulation

Muscle metabolic pattern	Values before LFMES (mean ± SD)	Values after LFMES (mean ± SD)	*P* value (Wilcoxon paired test)
PCr/PCr+Pi at rest	0.88 ± 0.27	0.89 ± 0.35	NS
Maximal workload	1.69 ± 0.53	1.92 ± 0.1	NS
PCr/PCr+Pi at maximal workload	0.51 ± 0.1	0.52 ± 0.1	NS
PCr resynthesis time constant	81.1 ± 79.1	53.2 ± 28.2	NS

LFMES, low-frequency electrical stimulation; PCr, phosphocreatine; Pi, inorganic phosphates; NS, not significant

Table 3
Results of magnetic resonance imaging analysis of muscle mass volumes of the soleus and gastrocnemius muscles before and after five weeks of low-frequency electrical stimulation

Stimulated muscle	Muscle mass volume (cm^3)	
	Before LFMES	After LFMES
Soleus muscle	315.2 ± 65	331.5 ± 44
Gastrocnemius muscle	254.3 ± 47	* 278.6 ± 38

LFMES, low-frequency electrical stimulation; *, $P < 0.05$

prevention of atrophy and increased resistance to fatigue. Such events could play a very important role in the situation of chronic heart failure that is typically characterised by impaired oxidative capacity.

The data presented above indicate that the long-term low-frequency electrical stimulation of skeletal muscles can improve some metabolic and circulatory parameters in CHF patients. The previously published results showed a significant improvement of exercise capacity parameters (VO_{2peak}, VO_{2AT}) in patients with CHF after 5 weeks of LFMES (*9*).

In our study, LFMES was well tolerated. Both after 1 and 5 weeks of stimulation, quadriceps muscle strength was improved by 28%. Very similar results were also obtained by MRI. The significantly increased muscle volume mass seems to contribute to the structural and functional (and very probably also metabolic) improvement of both calf and quadriceps muscles.

We can conclude that LFMES is a safe and well-tolerated method without any dangerous side-effects. In a relatively short time, it can induce a significant improvement of skeletal muscle conditions, including an increase in muscle strength and mass, in CHF patients. In some cardiac patients, LFMES may be used as an alternative to the conventional exercise training and thus provide an opportunity to improve the quality of their lives.

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NÍZKOFREKVENČNÍ ELEKTRICKÁ STIMULACE KOSTERNÍCH SVALŮ U PACIENTŮ S CHRONICKÝM SRDEČNÍM SELHÁNÍM

S o u h r n

Cílem této studie bylo posouzení vlivu nízkofrekvenční elektrické stimulace kosterních svalů u pacientů s chronickým srdečním selháním (CHF). Dvanáct pacientů s CHF (koronarografie, NYHA III-IV, EF=19,33) bylo vyšetřeno před pětitýdenní nízkofrekvenční elektrickou stimulací čtyřhlavých a lýtkových svalů a po ní (jedna hodina denně, 5 dnů týdně). Pacienti byli na seznamu pro transplantaci srdce. Lékařské režimy všech kontrolovaných pacientů byly optimalizovány a pacienti byli symptomaticky stabilní. Byla provedena dynamometrie čtyřhlavých svalů. Nízkofrekvenční stimulace byla dobře snášena. Dospěli jsme k závěru, že nízkofrekvenční elektrická stimulace čtyřhlavých svalů trvající jeden a pět týdnů zlepšila sílu čtyřhlavého svalu o 28 %. Výsledky analýzy MRI m.gastrocnemius ukázaly signifikantní zvýšení svalového objemu po stimulaci. Tento postup by mohl být užitečný při léčení pacientů se závažným chronickým srdečním selháním.

A c k n o w l e d g e m e n t s

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