Different frequencies of transcutaneous electrical nerve stimulation on sympatho-vagal balance

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ABSTRACT. This study aims to evaluate the effects of TENS at different frequencies on autonomic balance in healthy volunteers. It is a case-control study, and was composed of fourteen healthy volunteers (5 women) with 28 (3.9) years old who underwent low (10 Hz 200ms⁻¹) and high (100 Hz 200ms⁻¹) frequency TENS. The interventions were randomized and applied for 30 minutes in the trajectory brachial nerve plexus from non-dominant member. Intensities were adjusted every 5 minutes and maintained below motor threshold. The autonomic balance was assessed before and after interventions by heart rate variability (HRV). TENS 10 Hz increased 10% sympathetic activity and decreased 10% parasympathetic activity; however, TENS 100 Hz showed opposite effects (p < 0.05). The sympatho-vagal balance increased with low frequency TENS and decreased with high frequency (p < 0.05). It can be concluded that different frequencies of TENS applied in the trajectory brachial nerve plexus modify cardiovascular autonomic responses. High frequency TENS reduces sympathetic activity and increases the parasympathetic, which favors beneficial effects on autonomic balance in healthy volunteers.

Keywords: electric stimulation, autonomic nervous system, heart rate.

Diferentes frequências da estimulação elétrica nervosa transcutânea no balanço simpato-vagal

RESUMO. Este estudo objetiva avaliar os efeitos de diferentes frequências da TENS sobre o balanço autônomo em voluntários saudáveis. Estudo caso-controle composto de quatorze voluntários saudáveis (5 mulheres), com 28 (3,9) anos de idade que foram submetidos a baixa (10 Hz 200 ms⁻¹) e a alta (100 Hz 200 ms⁻¹) frequências da TENS. As intervenções foram randomizadas e aplicadas por 30 minutos sobre a trajetória do plexo nervoso braquial do membro não dominante. As intensidades foram ajustadas a cada 5 minutos e mantidas abaixo do limiar motor. O balanço autônomo foi avaliado antes e após as intervenções pela variabilidade da frequência cardíaca (VFC). TENS a 10 Hz aumentou 10% da atividade simpática e diminuiu 10% a atividade parassimpática, mas a TENS a 100 Hz apresentou efeitos opostos (p < 0.05). O balanço simpático-vagal aumentou com a TENS de baixa frequência e diminuiu com a alta frequência (p < 0.05). Conclui-se que as diferentes frequências da TENS aplicadas sobre a trajetória do plexo nervoso braquial modificam as respostas autônomas cardiovasculares. A alta frequência da TENS reduz a atividade simpática e aumenta a parassimpática, o que favorece aos efeitos benéficos sobre o balanço autônomo em voluntários saudáveis.

Palavras-chave: estimulação elétrica, sistema nervoso autônomo, frequência cardíaca.

Introduction

Transcutaneous electrical nerve stimulation (TENS) is a therapeutic modality used primarily in the management of acute and chronic pain (Chesterton, Foster, Wright, Baxter, & Barlas, 2003; Sbruzzi et al., 2012; Vance, Dailey, Rakel, & Sluka, 2014; Bi et al., 2015). The application of this resource comprises the interaction of different parameters, such as intensity, frequency, pulse duration, application time, and positioning of the electrodes (Chesterton et al., 2003). The frequency TENS is one of the most studied parameters, being classified in high frequency (> 50 Hz), which acts more in the sensory threshold activating the gate modulator of pain in the cord spinal level; and low frequency (< 50 Hz), which acts over the threshold engine and promotes the release of endogenous opioids (Chesterton et al., 2003). This form of electroanalgesia also interacts with the cardiovascular system, particularly through of
autonomic nervous system (ANS) (Stein, Dal Lago, Ferreira, Casali, & Plentz, 2011; Vieira et al., 2012; Franco et al., 2014). Sympatho-vagal imbalance, especially the hyperexcitation is associated to the development of hypertension, cardiac arrhythmias and sudden death (Marmar & Shivkumar, 2008; Rizas et al., 2014). Therapeutic techniques that correct this imbalance are associated with reduced cardiovascular mortality (European Society of Cardiology [ESC], 1996). TENS is presented as a potential non-pharmacological resource that can be applied in the management of some cardiovascular diseases, such as hypertension (Chauhan et al., 1994; Cramp, Gilsenan, Lowe, & Walsh, 2000; Raimundo et al., 2009; Stein et al., 2011). Previous studies have demonstrated that TENS application reduced the systemic blood pressure of healthy volunteers (Sherry, Oehrlein, Hegge, & Morgan, 2001; Nitz, 2003; Vieira et al., 2012) and hypertensive patients (Kaada, Flatheim, & Woie, 1991; Jacobsson, Himmelmann, Bergrant, Svensson, & Mannheimer, 2000). However, these results have not been confirmed by other studies (Lazarou & Athanasios, 2009), thus its application is still questionable in this clinical condition.

Hemodynamic changes of TENS are linked to its effects on autonomic balance. Stein et al. (2011) have demonstrated that the TENS low frequency (10 Hz) applied on paravertebral ganglionar region decreased sympathetic activity, and high frequency (100 Hz) increased this activity in healthy youngs (Stein et al., 2011). The TENS low frequency (2 Hz) applied to acupuncture point (BL 13 Feishu located lateral to the lower border of the T3 vertebra) also reduces the sympathetic activity (Ngai & Jones, 2013). However, Vieira et al. (2012) have showed that TENS at high frequency (80 Hz) applied to the dorsal region (C7 and T4) decreased the sympathetic activity of healthy young and older people (Vieira et al., 2012). These results are reinforced by the assessment of sensitivity of α1-adrenergic receptors in healthy volunteers, where the TENS low frequency (10 Hz) applied in the trajectory of the brachial nerve plexus increased the sensitivity of these receptors, and high frequency (100 Hz) presented opposites results (Franco et al., 2014).

These contradictory results stimulated us to investigate the effects of different frequencies of TENS applied in the trajectory of the brachial nerve plexus on ANS, since this form of application is usually used in the non-pharmacological management of cervicobrachial pain (Basson, Stewart, & Mudzi, 2014; Moreno-Martín & Santana-Pineda, 2014). The hypothesis is that this therapeutic applied in the trajectory of the brachial nerve plexus (Franco et al., 2014) resource modifies the autonomic balance, with the high frequency being responsible for the decrease of the sympathetic activity, demonstrating that this application site presents opposite results to previous studies (Stein et al., 2011; Vieira et al., 2012; Ngai & Jones, 2013). The aim of this study was to evaluate the effects of TENS at low (10 Hz) and high (100 Hz) frequencies on autonomic balance in healthy subjects.

Material and methods

Setting and participants

This case-control study was approved by the Health Research Ethics Committee of Universidade Federal do Rio Grande, Brazil (CEPAS-FURG, No. 022/2013). The evaluations were carried out from January 2013 to July 2014 at Dr. Miguel Riet Corrêa Jr. University Hospital, Universidade Federal do Rio Grande (Rio Grande, Rio Grande do Sul State, Brazil). Subjects were informed about the study protocol and gave their informed written consent before their participation.

The subjects who joined the study were between 20 and 35 years old; presenting a body mass index lower than 30 kg m⁻²; nonsmokers; with no symptoms of skeletal muscle disorders; with no previous diagnosis of rheumatic, cardiovascular, metabolic, neurological, oncological, immune, or hematological diseases; with no evidence of psychiatric and/or cognitive disorders; and were not using any type of medication. Volunteers presenting inflammatory response (C-reactive protein < 3 mg dL⁻¹, fibrinogen 200 or 400 mg dL⁻¹), leukocytosis (>11.00 x 10³ mm⁻³), or who had consumed alcoholic beverages up to 24hours (h) before the test were excluded.

Study design

The sample was composed of fourteen volunteers (according to the sample calculation), randomized by a computer program (www.random.org). The information was sealed in a brown envelope, and the different interventions (TENS 10 Hz and TENS 100 Hz) were randomly assigned on the assessment day being the blind volunteers the interventions. Different interventions (crossover) were performed on two consecutive days. A flowchart of the volunteers is presented in Figure 1.
Interventions

During the application of the protocol, the volunteers were lying comfortably in a supine position, with a head elevation of 30°, resting their knees and elbows on the bed. The spots where the electrodes were placed were previously cleaned with 70% alcohol. TENS equipment (Quark, model Nemesys 941, Brazil), wave form biphasic symmetric, was applied in the trajectory of the brachial nerve plexus from the superior member. Auto adhesive electrodes (5 x 5cm area) were used and placed distally in the dorsal region of the wrist and in the proximal region of the cervicothoracic region (between C4 and T1) on the upper limb no dominant, as shown in Figure 2. TENS was applied for 30 minutes (min.) at a low (TENS, 10 Hz 200 ms⁻¹) or high (TENS, 100 Hz 200 ms⁻¹) frequency (Franco et al., 2014). The intensity of the current was adjusted, initially and after every 5 min., under the motor threshold. The equipment was standardized before and after data collection.

Measurements

The volunteers were evaluated before to after the intervention on two consecutive days, with fasting of 12h. The autonomic balance was assessed by heart rate variability (HRV) and the heart rate signal was acquired through a pulse frequency meter mark Polar model 810i (Gamelin, Berthoin, & Bosquet, 2006). The acquisition of ECG signal (sample rate–1 kHz) of the time series of RR was acquired in continuous intervals (10 min.) before and immediately after the intervention. Data were transferred to a computer and RR intervals were processed to calculate HRV parameter using the HRV analysis software KUBIOS (Kuopio, Finland). HRV was analyzed in the time and frequency domain, using the area of greatest stability in RR intervals corresponding to 5 min of recordings (containing at least 256 consecutive beats) during controlled breathing.

Physical and biochemical parameters

Anthropometric variables, blood samples and systemic blood pressure were collected in the fasted state of 12h in the first day of evaluations. Blood tests were automatically processed (ABX kits, Horiba Diagnóstica, Curitiba, Brazil) and analyzed by microscopy. Glucose levels were measured by
Triglycerides (mg dL\(^{-1}\)) 83.6 (26.6) 
HDLc (mg dL\(^{-1}\)) 47.6 (15.9) 
Urea (mg dL\(^{-1}\)) 28.7 (9.8) 
GOT (U L\(^{-1}\)) 27.4 (7.5) 
GPT (U L\(^{-1}\)) 29.2 (10.8) 
C-reactive protein (mg dL\(^{-1}\)) 1.5 (1.1) 
Fibrinogen (mg dL\(^{-1}\)) 304.5 (60.3) 

Data are presented as mean (standard deviation); HDLc: high density lipoprotein; LDLc: low density lipoprotein; GOT: glutamic-oxaloacetic transaminase; GPT: glutamic-pyruvic transaminase.

HRV data in response to different frequencies of TENS are shown in Table 2. The resting heart rate was within the normal limits and did not change across the low (10 Hz) and high (100 Hz) frequency TENS. The standard deviation of all normal to normal RR (NN) intervals (SDNN) and the percentage of intervals differing more than 50ms different from preceding interval (pNN50) did not modify in response to different interventions. The square root of the mean of the normal to normal RR (NN) intervals (SDNN) showed a reduction in low frequency and an increase in high frequency TENS (Interaction: \(p < 0.001\)).

The frequency-domain analyzes demonstrated that the variance of RR intervals over the temporal segment (Total power ms\(^2\)) and power in low frequency range (LF between 0.04-0.15 Hz) remained unchanged throughout the study. However, the power in high frequency range (HF, between 0.15-0.4 Hz) decreased in the low frequency and increased in the high frequency (Interaction: \(p < 0.001\)) (Table 2). After the normalization of the data, TENS 10 Hz increased 10% of sympathetic activity (LF n.u.) and decreased 10% of parasympathetic activity (HF n.u.) (Figure 3A).

On the other hand, TENS 100 Hz presented opposite effects, observing a reduction of the sympathetic activity (LF n.u.) and an increase of the parasympathetic (HF n.u.) by approximately 10% (Figure 3B). The sympathetic and parasympathetic activities presented a mean difference between of the interventions (10 Hz vs 100 Hz) of 20% (95% CI = 9 to 32). The sympathetic-vagal balance, expressed by the LF/HF index, increased after the application of low frequency TENS and decreased after the use of high frequency TENS (Figure 3C). The LF/HF index presented a mean difference between of the interventions (10 Hz vs 100 Hz) of -0.97 (95% CI = -0.3 to -1.6).

### Results

The sample was composed of fourteen volunteers (5 women), with 28 (3.9) years old, body mass index 24.4(2.9) kg m\(^{-2}\), relation Waist/Hip 0.84(0.06), systolic blood pressure 114.3(7.5) mmHg and diastolic blood pressure 77.6(3.8) mmHg. The biochemical characteristics are shown in TABLE 1 and were within the normality range.
Table 2. Summary of heart rate variability data.

<table>
<thead>
<tr>
<th>Variable</th>
<th>TENS 10 Hz</th>
<th>TENS 100 Hz</th>
<th>Group</th>
<th>Conditions</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
<td>Before</td>
<td>After</td>
<td></td>
</tr>
<tr>
<td>Mean HR (bpm min.(^{-1}))</td>
<td>61.40 (6.84)</td>
<td>61.23 (6.06)</td>
<td>63.32 (5.87)</td>
<td>61.37 (6.90)</td>
<td>0.661 0.138 0.209</td>
</tr>
<tr>
<td>SDNN (ms)</td>
<td>81.59 (36.62)</td>
<td>95.02 (34.58)</td>
<td>83.37 (26.92)</td>
<td>106.26 (40.90)</td>
<td>0.479 0.063 0.601</td>
</tr>
<tr>
<td>rMSSD (ms)</td>
<td>75.93 (38.47)</td>
<td>68.10 (33.21)</td>
<td>71.08 (39.61)</td>
<td>97.52 (47.07)</td>
<td>0.378 0.149 &lt; 0.001</td>
</tr>
<tr>
<td>PNN50(%)</td>
<td>34.69 (19.96)</td>
<td>33.06 (18.58)</td>
<td>38.10 (17.36)</td>
<td>43.96 (16.81)</td>
<td>0.465 0.264 0.199</td>
</tr>
<tr>
<td>Triangular index</td>
<td>14308 (3510)</td>
<td>15770 (3898)</td>
<td>16893 (4630)</td>
<td>17915 (4201)</td>
<td>0.149 0.080 0.794</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>TENS 10 Hz</th>
<th>TENS 100 Hz</th>
<th>Group</th>
<th>Conditions</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
<td>Before</td>
<td>After</td>
<td></td>
</tr>
<tr>
<td>TP (ms(^2))</td>
<td>7513 (6436)</td>
<td>9679 (6903)</td>
<td>7535 (5193)</td>
<td>1011 (5857)</td>
<td>0.907 0.068 0.869</td>
</tr>
<tr>
<td>LF (ms(^2))</td>
<td>2498 (1934)</td>
<td>2879 (2397)</td>
<td>2536 (2574)</td>
<td>2713 (1789)</td>
<td>0.927 0.535 0.820</td>
</tr>
<tr>
<td>HF (ms(^2))</td>
<td>3033 (3085)</td>
<td>2006 (1768)</td>
<td>2474 (2902)</td>
<td>4543 (3143)</td>
<td>0.406 0.230 0.019</td>
</tr>
<tr>
<td>LF (n.u.)</td>
<td>50.33 (14.59)</td>
<td>60.12 (10.92)*</td>
<td>50.84 (12.20)</td>
<td>39.80 (13.70)</td>
<td>0.803 0.027 &lt; 0.001</td>
</tr>
<tr>
<td>HF (n.u.)</td>
<td>49.66 (14.59)</td>
<td>39.87 (10.92)*</td>
<td>49.15 (12.20)</td>
<td>60.19 (13.70)</td>
<td>0.803 0.027 &lt; 0.001</td>
</tr>
<tr>
<td>LF/HF</td>
<td>1.23 (0.76)</td>
<td>1.71 (0.82)*</td>
<td>1.180 (0.66)</td>
<td>0.74 (0.42)**</td>
<td>0.826 0.034 &lt; 0.001</td>
</tr>
</tbody>
</table>

Data are presented as mean (standard deviation); HR – Heart Rate (bpm min.\(^{-1}\)); SDNN = standard deviation of all normal to normal R-R (NN) interval; Rmssd = Square root of the mean of the squares of successive R-R interval differences; pNN50 = percentage of intervals differing more than 50 ms different from preceding interval; Total power (TP ms\(^2\)) = The variance fo RR intervals over the temporal segmente; LF (ms\(^2\)) = Power in low frequency range (0.04-0.15 Hz); HF (ms\(^2\)) = Power in high frequency range (0.15-0.4 Hz); LF (n.u.) = LF power in normalized units; HF (n.u.) = HF power in normalized units; LF/HF = Ratio LF (ms\(^2\))/HF (ms\(^2\)); *p < 0.05 vs Before; †p < 0.05 vs 10 Hz.

Discussion

The different frequencies of TENS applied in the brachial nerve plexus interfered in the ANS modifying the sympathetic-vagal balance, as demonstrated in this study. The interference of this therapeutic resource on heart rate variability (HRV) has been previously demonstrated in young (Stein et al., 2011; Ngai & Jones, 2013) and older (Vieira et al., 2012) people; however, these studies differ in results and application parameters when compared to the current study. The increased sympathetic activity is related to the risk of life (Marmar & Shivkumar, 2008), and interventions that decrease this activity reduce mortality from cardiovascular disease (ESC, 1996). In this context, TENS is presented as a potential therapeutic resource able to interact in different clinical conditions, such as hypertension, in addition to its analgesic effects widely described in literature (Chesterton et al., 2002; Sbruzzi et al., 2012; Vance et al., 2014; Bi et al., 2015). This interaction of TENS with the cardiovascular system is demonstrated by vasodilation (Cramp et al., 2000; Miller, Gruben, & Morgan, 2000; Sherry et al., 2001; Vieira et al., 2012), increased blood in peripheral and coronary blood flow (Chauhan et al., 1994; Jessurun et al., 1998; Cramp et al., 2000; Miller et al., 2000; Sandberg, Sandberg, & Dahl, 2007), decreased peripheral vascular resistance (Mannheimer, Emanuelsson, & Waagstein, 1990; Sherry et al., 2001), and heart rate (Nitz, 2003). The combination of these mechanisms reduces the blood pressure demonstrated in healthy volunteers (Sherry et al., 2001; Nitz, 2003; Vieira et al., 2012) and in hypertensive patients (Kaada et al., 1991; Jacobsson et al., 2000). Previous studies have demonstrated the therapeutic potential of TENS (70 Hz) in patients
with severe coronary artery disease, in which the application on the chest region showed decreased angina pectoris crisis, reduced circulating levels of epinephrine and norepinephrine (Mannheimer et al., 1990; Chauhan et al., 1994), attenuation of ST segment depression (Mannheimer et al., 1985), reduced systolic blood pressure (Mannheimer et al., 1990) and nitroglycerin consumption (Mannheimer et al., 1985).

In this study, the application of TENS at high frequency (100 Hz) decreased the sympathetic activity and increased the parasympathetic, resulting in an improvement of sympatho-vagal balance, while the low frequency TENS (10 Hz) showed opposite results. The reduction of the sympathetic activity assessed through HRV by high frequency (80 Hz) TENS has been demonstrated in healthy young and older people (Vieira et al., 2012). These results are reinforced by alterations in the sensibility of α1-adrenergic receptors in healthy volunteers, in which the high frequency (100 Hz) TENS decreased and low frequency (10 Hz) increased the sensibility of these receptors (Franco et al., 2014). In opposition to these studies, the sympathetic activity was increased by high frequency (100 Hz) TENS and decreased by the low frequency (2 Hz and 10 Hz) in healthy young (Stein et al., 2011; Ngai & Jones, 2013). This divergence between the results of the studies may be explained, at least in part, by the different parameters used.

Among the parameters of TENS use, the application site of the electrodes is particularly important in the autonomic balance changes. The positioning of the electrodes varies considerably. They might be fixed on the injury, on dermatomes and near the site of injury (Sluka & Walsh, 2003). In this study, electrodes were placed along the brachial nerve plexus, which is normally used in cervicobrachial pain (Basson et al., 2014; Moreno-Martín & Santana-Pineda, 2014). This was described in a recent study (Franco et al., 2014) that used the same parameters of TENS as the present study.

Previous studies that evaluated the effects of TENS on HRV stimulated ganglion paravertebral region (Stein et al., 2011), lateral to the lower border of the T3 (acupuncture point BL 13 Feishu) (Ngai & Jones, 2013) or dorsal region between the C7 and T4 vertebrae (Vieira et al., 2012), which, apparently, excited only pre or post-ganglionic neurons. In this present study, pre and post-ganglionic neurons of the ANS were successively stimulated, suggesting that a higher pulse frequency TENS is sufficient to reduce the sympathetic activity. It was previously demonstrated that high frequency TENS in the precordial region decreased circulating catecholamines in heart disease patients (Mannheimer et al., 1990; Chauhan et al., 1994), and when applied along the brachial nerve plexus a reduction on the sensitivity of α1-adrenergic receptors in healthy volunteers was observed (Franco et al., 2014). In these studies, the stimuli were applied to the postganglionic neurons. On the other hand, the low frequency TENS, which acts more on the motor threshold (Chesterton et al., 2003) and when applied to the portion of a distal segment (postganglionic neuron) improved muscle contraction and increased peripheral vascular resistance (Miller et al., 2000; Sandberg et al., 2007), resulting in an increase of the cardiac sympathetic activity immediately after application, as demonstrated in this present study. However, this low frequency stimulation when applied to the preganglionic region reduces cardiac sympathetic activity (Sherry et al., 2001), since it does not generate contraction of the muscle of the distal segments and consequent increase of peripheral vascular resistance. Thus, low frequency stimulation applied in preganglionic neurons is likely to have the same effects as the high frequency applied to the postganglionic neurons.

Clinically, this form of TENS application at high frequency reduces the sensitivity of these receptors and increases venous compliance, which favors the reduction of systemic arterial pressure, the perception of a potential non pharmacological therapy, especially for patients presenting refractory hypertension and/or hypertensive crisis. However, the low frequency may have opposite results. The absence of plasma catecholamine measures and the absence of evaluation of blood pressure during and after the application of TENS are the limitations of the present study.

Conclusion

Different frequencies of TENS applied along the brachial plexus interfere in ANS and modify the sympathetic-vagal balance. TENS at low frequency (10 Hz) increased sympathetic activity and decreased parasympathetic activity. On the other hand, TENS at high frequency (100 Hz) decreased sympathetic activity and increased parasympathetic, which reinforces the hypothesis of its beneficial effects on autonomic balance in healthy volunteers.

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