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Effect of high-voltage pulsed current plus conventional treatment on acute ankle sprain

Efeito da adição da estimulação de alta voltagem ao tratamento convencional do entorse de tornozelo numa etapa aguda

Maria Cristina Sandoval¹, Carolina Ramirez¹, Diana M. Camargo¹, Tania F. Salvini²

Abstract

Background: The effectiveness of high-voltage pulsed current (HVPC) treatments in humans as a means of controlling edema and post-traumatic pain has not yet been established. Objective: To analyze the effects of HVPC plus conventional treatment on lateral ankle sprains. Methods: This was a randomized, controlled, double-blind clinical trial with three intervention groups: CG (control group with conventional treatment); HVPC(-) group (conventional treatment plus negative polarity HVPC); HVPC(+) group (conventional treatment plus positive polarity HVPC). Twenty-eight participants with lateral ankle sprain (2 to 96h post-trauma) were evaluated. Conventional treatment consisted of cryotherapy (20min) plus therapeutic exercises. Additionally, the HVPC(-) and HVPC(+) groups received 30min of electrical stimulation (submotor level; 120 pps). Pain, edema, range of motion (ROM) and gait were assessed before the first treatment session and after the last treatment session. Results: At the final evaluation, there were no significant differences between groups. Nevertheless, the HVPC(-) group had greater values in all assessed parameters. The data analysis showed that the HVPC(-) group had greater reductions in volume and girth, and greater recovery of ROM and gait velocity. This group also reached the end of the treatment (1.7 weeks; range 1.2-2.2) faster than the HVPC(+) group and the CG (2.2 weeks; range 1.8-2.6). Conclusions: There were no differences between the study groups, but the results suggest that HVPC(-) can accelerate the initial phase of recovery from ankle sprain. Article registered in the Clinical Trials.gov under the number NTC 00732017

Key words: electrical stimulation, sprain, inflammation

Resumo

Contextualização: A eficácia da estimulação elétrica de alta voltagem (EEAV) em humanos, como uma forma de tratamento para controlar o edema e a dor pós-traumáticas, ainda não foi estabelecida. Objetivo: Analisar o efeito da adição da EEAV ao tratamento convencional do pós-entorse de tornozelo em humanos. Métodos: Ensai clínico controlado e aleatorizado, duplo cego com três grupos de intervenção: grupo controle (GC) com tratamento convencional; tratamento convencional EEAV(-) e polaridade negativa EEAV (-); tratamento convencional e EEAV polaridade positiva EEAV(+). Vinte e oito portadores de entorse lateral do tornozelo (2 a 96 horas pós-trauma) foram avaliados. O tratamento convencional consistiu em crioterapia (20 minutos) e exercício terapêutico. Adicionalmente, os grupos EEAV(-) e EEAV(+) receberam 30 minutos de estimulação elétrica (nível submotor, 120 pps). As variáveis de dor, edema, amplitude de movimento (ADM) e marcha foram avaliadas antes da primeira sessão de tratamento e após a última sessão de tratamento. Resultados: Na avaliação final, não houve diferenças significativas entre os três grupos. Porém, os indivíduos do grupo EEAV(-) demonstraram valores superiores em todos os parâmetros de avaliação. A análise dos dados mostrou que o EEAV(-) apresentou maior redução do volume e do perímetro, maior recuperação da ADM e da cadência da marcha. Esse grupo também alcançou o término de tratamento mais rápido (1,7 semanas [1,2-2,2]), comparado com o EEAV(+) e o GC (2,2 semanas [1,8-2,6]). Conclusões: Não houve diferença entre os grupos estudados, mas os resultados sugerem que a EEAV(-) pode contribuir para acelerar a recuperação do entorse de tornozelo em sua fase inicial. Artigo registrado no Clinical Trials.gov sob o número NTC 00732017

Palavras-chave: estimulação elétrica; entorse; inflamação

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Introduction

Ankle sprain is a musculoskeletal injury characterized by pain, edema and limitations in range of motion (ROM). It consists of ligament damage, which, based on the symptoms, is classified into three types associated with the severity of the injury\(^1\,^2\). This trauma has a high frequency in the population. In a recent systematic review\(^3\) that assessed 227 epidemiological studies on the prevalence of sports injuries, the authors found that the ankle was the most affected region in 24 of 70 sports and that ankle sprains were the predominant injuries in 33 of 43 sports. Most epidemiological studies\(^3\,^4\) also indicate that lateral ankle sprains account for 95% of injuries to this joint.

Initially, the ankle sprain shows the typical signs of an inflammatory process. One of them is edema, which is characterized by an excessive amount of fluid accumulated in the interstitial spaces of tissues\(^1\). Edema causes pain and can slow or impede the exchange of nutrients between cells and capillaries, slowing the healing process. The accumulation of fluid due to stasis worsens the inflammatory process, which can result in the death of cells with consequent tissue necrosis. It can also generate a longer period of immobility, fibrosis, adhesions, and finally, joint stiffness\(^5\).

Although high-voltage pulsed current (HVPC) is one of the therapeutic modalities used in the treatment of edema and post-traumatic pain\(^6\), its effectiveness in humans is not yet proven. This type of current is characterized by a twin-spike, monophasic waveform, generating a voltage greater than 150V and a low total current (1.5 mA), with very short duration (5-100\(\mu\)s) and greater interpulse intervals. These characteristics allow HVPC to generate little or no electrochemical reactions between the skin and the stimulation electrodes, causing a comfortable sensation. This type of electrical stimulation has also been used in wound healing, and due to its short pulse duration, it is not recommended for denervated muscles\(^6\).

Most studies that investigated the effects of HVPC on edema were conducted in animals, and only one in humans\(^5\). In this clinical study\(^5\), the effects of three therapeutic interventions were compared (HVPC[−]; HVPC placebo; intermittent pneumatic compression) in the treatment of chronic post-traumatic edema of the hand. No statistical differences were found between HVPC(−) and compression, but there was an increased reduction in edema in the group treated with HVPC(−) compared to the placebo group.

In animal studies, the results of Bettany, Fish, and Mendel\(^7\) and Taylor et al.\(^8\) indicated a reduction in edema in traumatized frog limbs treated with HVPC (75\(\mu\)s, 120 pps, submotor level intensity, and negative polarity). Mohr, Akers, and Landry\(^9\) also studied edema in traumatized hind limbs of rats, applying frequencies of 80pps and pulse durations of 35\(\mu\)s, and observed a greater reduction in edema. However, there were no differences in relation to the traumatized, but untreated control group.

Dolan et al.\(^10,^11\) conducted some studies on the effects of HVPC on acute post-traumatic edema. In one of the studies\(^10\), the effects of ibuprofen were compared with the effects of HVPC(−) on post-traumatic edema in the hind limbs of rats. The current was applied for three continuous hours at 90% of the motor threshold and 120pps. The results showed reduced edema in all groups (ibuprofen; HVPC[−]; ibuprofen plus HVPC[−]) after the interventions, when compared to the untreated group. However, there were no statistical differences between treatments. Similar results were found in a study that compared the effects of HVPC(−) and cryotherapy on the treatment of post-traumatic edema\(^11\).

It can be observed in previous studies that some parameters, such as current type, polarity, time of application and level of stimulation, are important and should be considered during treatments in order to make HVPC effective in reducing edema. In the literature, several studies showed negative results with alternating current\(^12\) or low voltage current\(^13\), positive polarity\(^14\), and motor stimulation levels\(^15,^16\). These discrepancies in results may be due to the different parameters used in HVPC, a fact that also made it difficult to compare these studies.

The reviewed studies showed some of the advantages of using HVPC to control edema, but there were no conclusive results of the effects of these interventions on humans. The hypothesis of the present study is that HVPC(−) accelerates the recovery of the inflammatory process in the initial phase post-ankle sprain. Thus, the aim of this study was to analyze the effects of HVPC on post-ankle sprain in humans.

Methods

A double-blind, controlled clinical trial with three intervention groups was conducted according to the standards of the Declaration of Helsinki, with prior approval (no. 5612/2003) from the Ethics Committee of Universidad Industrial de Santander (UIS), Colombia. The participants signed an informed consent form to take part in the study.

Sample

Twenty-eight participants (18 men, 10 women), between 18 and 26 years of age (21±2.5 years) were assessed and underwent physical therapy treatment at the Physical Therapy clinic of the University. Inclusion criteria were: post-traumatic edema caused by ankle sprains classified as mild (minimal pain and functional limitations, without hematoma, normal gait) or...
Effect of electrical stimulation on sprain

moderate (limping gait, localized edema, moderate functional loss) within the first 96 hours after injury and with positive anterior drawer signs or lateral tilt in the ankle joint. Participants were excluded if they had severe sprains (severe edema and hematoma, inability to support weight and total function loss) or diseases that could interfere with the edema and pain (skin lesions, systemic diseases or prior trauma), and if they were making regular use of anti-inflammatory drugs or had been subjected to treatment, such as traction, massage, immobilization or manual therapy.

The treatment groups were distributed as follows:
- CG: control group that received conventional treatment;
- HVPC(+): group that received conventional treatment and HVPC, using active electrodes with positive polarity;
- HVPC(-): group that received conventional treatment and HVPC, using active electrodes with negative polarity.

Block allocation was used to avoid possible selection bias in the allocation of treatments and to ensure that the three groups were balanced in their baseline characteristics. The block allocation sequence was generated by means of a random number table and, after that, the allocation of treatments to patients was performed. Assessments and interventions were made, respectively, by two trained physical therapists with no access to the identification of the treatment groups or the type of polarity used in the HVPC.

Procedures

The variables of gender, age and dominant limb were analyzed. Regarding the clinical history of sprain, the following aspects were identified: the affected limb, the post-trauma period (hours), the type of sprain (mild or moderate) and the causes. We also identified the possible intake of analgesics and the history of previous ankle injuries.

The following dependent variables were considered: pain, ROM, edema and some gait parameters. Pain was assessed at rest, on palpation and in all four movements of the ankle (dorsal flexion, plantar flexion, inversion and eversion), using a horizontal visual analog scale (VAS) ranging from 0 to 10 cm, where 0 represented no pain and 10 represented the worst pain experienced by the participant. The participants were also asked to indicate the degree of pain on the VAS, and the distance to the location marked was then measured and recorded in cm.

The edema was measured by means of girth measurement and water displacement volumetry. The first was measured with a tape measure in two places: around the ankle on the distal end of the lateral malleolus and around the foot, on the highest part of the longitudinal internal arch. The mean was taken between the two measurements for each limb, and the differences between right and left limbs were recorded.

Water displacement volumetry was chosen because some authors consider it as the gold standard for measuring edema. A volumetric tank with an output for excess water into a graduated cylinder of 500 ml was used. The participant was instructed to sit on a chair and slowly introduced the affected limb into water with the knee at 90° of flexion and the ankle in neutral position, until it was fully supported by the surface of the foot at the bottom of the tank. The volume of the displaced water was then measured in the graded cylinder. Finally, the same procedures were performed with the contralateral limb.

The ROMs of dorsal and plantar flexion, inversion and eversion of both ankles were measured with a standard goniometer, following the protocol of Norkin and White. All movements started with the ankle at an angle of 90° between the leg and foot. For data analysis, the differences between the ankles were used. Finally, the following descriptive gait variables were evaluated: step length, stride length and gait velocity. For these measurements, the participant was instructed to walk on a black carpet where the footprints were recorded and the step and stride length were measured. Gait velocity was evaluated by recording the number of steps per minute.

The participants received physical therapy treatment once a day, with five sessions per week, on consecutive days until the participants reached the end of the treatment or until they completed the eight weeks of treatment. There were two assessments: an initial assessment before starting treatment and a final assessment when the participant completed the physical therapy treatment.

End of treatment

To determine the end of treatment, measures from the VAS were used. The end of treatment was defined as the time elapsed, in weeks, to reach a value ≤ 1 cm in the assessment of pain with movement. This variable was chosen to determine the end of treatment because pain is considered a multidimensional process, associated with tissue damage that affects the functional capacity of the participant.

Therapeutic interventions

Conventional treatment

The three groups underwent a physical therapy treatment often recommended for ankle sprain:
- Initial phase: cryotherapy (bag of crushed ice for 20 minutes), around the entire ankle joint, combined with elevation of...
the affected limb, isometric and unresisted active exercises in all degrees of freedom of the ankle joint, until the limits of pain without weight bearing;

- Intermediate phase: introduced when the unresisted active movements were performed without pain. Cryotherapy maintained during this period. Introduction of exercises with progressive loading, progressive weight bearing during gait and proprioceptive exercises on stable surfaces;


HVPC parameters

A high-voltage stimulator (Intelect 500, Chattanooga Corp, Chattanooga, TN, USA) was used, with a direct monophasic pulsed current and twin spikes of 5 and 8ms separated by an interpulse interval of 75µs. Monopolar stimulation was used with a dispersive electrode placed on the lumbar region and two active electrodes applied to the internal and external malleolus of the ankle. The current intensity was at submotor level, i.e., too weak to elicit a visible motor response. The intensities were chosen based upon animal studies that reported positive results7,8,10,11,25. Because the participants were in the acute phase of injury, this intensity would avoid the risks of generating muscle contractions and increase the trauma. The choice of polarity depended on the group allocation, and the frequency used was 120 pps. HVPC was applied once a day for 30 minutes. The equipment was calibrated prior to the intervention, using an oscilloscope (Tektronix TDS 1002) to verify the selected parameters.

Statistical analysis

The comparisons between the study groups, before and after the interventions, for girth, volume, ROM, step length, and stride length were based on the differences between the affected and unaffected lower limbs. For pain and gait velocity, the values obtained at the initial and final assessments were analyzed. Additionally, the percentage of recovery for volume and girth were calculated with the following formula: initial difference between affected and unaffected limbs - final difference between affected and unaffected limbs x 100 / initial difference between affected and unaffected limbs. For this analysis, one-way ANOVA was used. To determine the mean time to reach the end of treatment, a survival analysis was applied, in which the functions per intervention group were compared using the Wilcoxon test.

The comparison between the CG and the HVPC(-) and HVPC(+) groups was made with multivariate analysis, applying the Cox proportional hazards model to determine the hazard ratios (HRs). Each HR establishes the probability of reaching the end of treatment over a certain period of time. This model allowed the adjustment of the effects of HVPC(-) and HVPC(+) by the variables that could potentially affect the results, such as gender and age, and by the variables recorded in the clinical history of sprains. This model was submitted to diagnostic testing, adjusting with the analysis of proportional hazards and the link test (p=0.89), to determine the final adjustment for the regression analysis26. In all analyses, the significance level was α=0.05, and STATA 9.0 software was used.

Results

The baseline characteristics, such as gender, age, dominant limb and clinical history, were homogeneous. In 27 participants (96.4%), the right limb was the dominant limb, although only 10 of them had suffered the injury to that limb. The mean post-sprain period for the three groups was 31.4±17.6 hours and no difference was observed between them. Overall, trauma caused by forced inversion was the most common cause of sprains (n=22). This was the first episode of sprain for the majority of the assessed participants (n=17; Table 1).

The analysis of the initial assessments found no statistical differences between groups, except for plantar flexion ROM (p=0.03; Table 2). In the final assessment, there were no significant differences between groups, although clinical improvements were observed for all parameters, particularly in the HVPC(-) group. There was a higher percentage of reduction in volume and girth for this group, which also showed increased recovery of plantar flexion, dorsal flexion and eversion, as well as gait velocity, when compared to the other groups (Table 2).

The HVPC(-) group also showed shorter recovery times (median survival time: 1.7 weeks; range 1.2-2.2), compared to the HVPC(+) group and the CG (median survival time: 2.2 weeks; range 1.8-2.6), however, there were no statistical differences between groups. The same results were confirmed by the Wilcoxon-Breslow test (1.75, p=0.42). The Cox regression model showed that the HVPC(-) group had a significant increase in the probability of completing the treatment; with a HR of 2.5 (95% CI, 1.02-6.4), when compared to the other groups (Figure 1). The only variable that significantly reduced the probability of completing the treatment was type 2 sprain, with a HR of 0.36 (95% CI, 0.15-0.87).
Table 1. Medical history according to study group.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Intervention Group</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Conventional</td>
<td></td>
</tr>
<tr>
<td></td>
<td>treatment</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CG</td>
<td>n:10</td>
</tr>
<tr>
<td>Age (years)*</td>
<td>21.3±2.7</td>
<td></td>
</tr>
<tr>
<td>Right dominant limb</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Injured dominant limb</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Time elapsed since trauma (hours)*</td>
<td>29±16.6</td>
<td>33.8±21.7</td>
</tr>
<tr>
<td>Cause of injury</td>
<td>Forced inversion</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>3</td>
</tr>
<tr>
<td>Previous sprains</td>
<td>First time</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Second time</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>More than twice</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3</td>
</tr>
</tbody>
</table>

* (Mean±SD); CG: Control Group; HVPC(-): High-Voltage Pulsed Current with negative polarity; HVPC(+): High-Voltage Pulsed Current with positive polarity.

Table 2. Initial and last evaluation by study group.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Intervention group</th>
<th></th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Conventional</td>
<td></td>
</tr>
<tr>
<td></td>
<td>treatment</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CG</td>
<td>n:10</td>
</tr>
<tr>
<td>Pain Intensity- VAS (cm)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>1.0±1.6</td>
<td>0.03±0.09</td>
</tr>
<tr>
<td>Palpation</td>
<td>5.8±2.9</td>
<td>0.7±0.84</td>
</tr>
<tr>
<td>Movement</td>
<td>3.7±2.2</td>
<td>0.6±0.05</td>
</tr>
<tr>
<td>Girth (cm)</td>
<td>Injured limb</td>
<td>27.6</td>
</tr>
<tr>
<td></td>
<td>Healthy limb</td>
<td>26</td>
</tr>
<tr>
<td>Difference between limbs*</td>
<td></td>
<td>26.1</td>
</tr>
<tr>
<td>Recovery percentage</td>
<td>62.4</td>
<td>60.3</td>
</tr>
<tr>
<td>Volume (ml)</td>
<td>Injured limb</td>
<td>1630.6</td>
</tr>
<tr>
<td></td>
<td>Healthy limb</td>
<td>1515.2</td>
</tr>
<tr>
<td>Difference between limbs*</td>
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<td>41.8±52.4</td>
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<tr>
<td>Recovery percentage</td>
<td>66.5</td>
<td>70.0</td>
</tr>
<tr>
<td>ROM (grades)*</td>
<td>Plantar flexion</td>
<td>-13±8.2</td>
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<td></td>
<td>Dorsal flexion</td>
<td>-6±5.7</td>
</tr>
<tr>
<td></td>
<td>Inversion</td>
<td>-10±10.7</td>
</tr>
<tr>
<td></td>
<td>Eversion</td>
<td>-10±7.0</td>
</tr>
<tr>
<td>Gait*</td>
<td>Step length (cm)</td>
<td>9.1±7.7</td>
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<tr>
<td></td>
<td>Stride length (cm)</td>
<td>12.7±13.2</td>
</tr>
<tr>
<td></td>
<td>Gait speed (steps/min)</td>
<td>94±22.6</td>
</tr>
</tbody>
</table>

* (Mean±SD); † Recovery percentage: initial difference between limbs - final difference between limbs X 100 / initial difference between limbs; Girth, volume, ROM, step length, and stride length are recorded as the difference between the injured limb and the healthy limb; CG: Control Group; HVPC(-): High-Voltage Pulsed Current with negative polarity; HVPC(+): High-Voltage Pulsed Current with positive polarity.
Discussion

In the present study, there were no statistically significant differences between groups. However, the results indicated changes that could be relevant from a clinical perspective. The regression model showed that the groups that received additional stimulation reached the end of treatment, but the participants of the HVPC(-) group had a shorter recovery time. The number of participants (n=28) may have been a limiting factor for the identification of statistical differences. These preliminary results suggested that HVPC(-) improved the process of inflammation and tissue repair, characterized by reduced edema, increased ROM, and better gait parameters, leading to faster recovery of functionality.

The present results indicated that treatment with HVPC(-) plus conventional treatment provided a clinical advantage when compared to conventional treatment alone (cryotherapy and exercise) in the recovery of post-ankle sprain participants. These results agree with previous animal studies\textsuperscript{7,10,11,25,28} that showed the effectiveness of HVPC(-) in the treatment of post-traumatic edema. Electrical stimulation treatments with different characteristics have not been reported to have positive results in reducing edema in animals, as demonstrated by Karnes, Mendel, and Fish\textsuperscript{13}, using low-voltage pulsed current. Cosgrove et al.\textsuperscript{12} compared the monophasic pulsed currents to symmetrical biphasic currents and found that the latter showed less reduction in edema compared to the CG. Taylor et al.\textsuperscript{28} found that only HVPC(-), but not the alternating current, caused reductions in the output of macromolecules from microvessels of capillaries of hamsters with post-traumatic edema. Man, Morrissey, and Cywinski\textsuperscript{29}, in a recent study, used low voltage currents to treat ankle edema in humans, but also reported no significant differences compared to the CG.

The submotor level of stimulation was selected in the present study to prevent muscle contraction and possible mechanical stress to the area, which could expand the tissue injury. The reduction in edema using this intensity has been shown in several animal studies\textsuperscript{7,10,11,25,27,28}. Another study used a current at motor threshold in the treatment of ankle sprain (acute phase) in humans and found no difference between the treatment group and the CG\textsuperscript{26}. It is difficult to compare the results of these studies because, in addition to using different levels of stimulation, they were also performed with different species (animals and humans).

In the present study, a 30min period of application of HVPC was used. This period was chosen to mimic what is usually done in clinical settings. However, a longer period of stimulation may have been more effective in reducing edema, as demonstrated by Bettany, Fish, and Mendel\textsuperscript{17} in animals. Taylor et al.\textsuperscript{8} also suggest that the treatment applied to humans is not as effective in reducing edema. In their work with frogs, they found that HVPC(-) only maintained its effect for 4 to 7.5 hours post-treatment. Dolan and Mendel\textsuperscript{30} and Mendel and Fish\textsuperscript{30} also suggest that the application time of HVPC(-) should be increased during the acute post-trauma phase to obtain better results. Another important aspect is the need to begin the post-trauma treatment with HVPC(-) plus conventional treatment as soon as possible to avoid increased edema because once it is established, its reduction becomes more difficult. This factor may have influenced the results obtained in the present study, as the participants only initiated therapy several hours (2-96hrs) post-sprain.

The polarity was shown to be a parameter that influences the reduction in edema. Negative polarity was more effective in most analyzed studies\textsuperscript{7,10,11,25,27,28}, unlike a study that selected the anode as the active electrode\textsuperscript{14}. This effect was also observed in the present study, in which the HVPC(-) group showed a higher percentage of reduction in edema and also a greater probability of reaching the end of treatment sooner.

The physiological mechanism by which the negative polarity affects the edema is still unknown. One hypothesis was proposed by Cosgrove et al.\textsuperscript{12}, who suggested that the conduction of electrical current with negative polarity through tissues shifts or repels the negatively charged plasma proteins, located in the interstitial areas of trauma, a phenomenon known as cataphoresis. This proposal is controversial and was rejected by Mendel and Fish\textsuperscript{30}, who believe that the phenomenon of electric or polar field does not occur with HVPC(-) due to the short pulse durations.

In the present study, the comparisons of the effects of each of the assessed parameters in the treatment groups failed to show significant differences, perhaps due to the sample size, which could be considered a limitation of the study. In this respect, the sample size was influenced by the strict inclusion criteria established with the purpose of homogenizing participant characteristics. Another aspect that may have influenced the results was the previous application of ice, which might have reduced the conduction velocity, not allowing optimal electrical stimulations. Although the present study may be considered a preliminary study, the results indicated that further research would be useful to obtain more information about the effects of HVPC post-trauma. Thus, future studies should be conducted with greater samples, longer periods of application, and variations in HVPC intensity.

Conclusions

The results showed no significant differences between groups. However, they suggest a possible contribution of HVPC(-) to the acceleration of recovery during the initial healing phase of ankle sprain in humans.
References


