Brief Research Report
Efficacy of a 0.1% Capsaicin Hydrogel Patch for Myofascial Neck Pain: A Double-Blinded Randomized Trial

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Author contributions: Jae-Heung Cho developed treatment protocol and preparation of manuscript; Eun-Joo Kim, Yu-Jeong Cho, and Koh-Woon Kim participated in experimental data collections and writing of the manuscript; Jia-You Fang contributed to the design of the study and participated in data experimental collection and writing of the manuscript; and Mi-Yeon Song contributed to the design of the study, provided treatment protocols, and was responsible for acquisition of funding for the study.

Abstract

Objective. The objective of this study was to evaluate the efficacy of a hydrogel patch containing capsaicin 0.1% compared with a placebo hydrogel patch without capsaicin to treat chronic myofascial neck pain.

Design. The study was designed as a double-blinded randomized controlled trial.

Setting. The study was set at Kyung-hee University Hospital at Gangdong, Korea.

Subjects. Sixty-one participants between 18 and 65 years with at least 3 months duration of neck pain and a clinical presentation of myofascial pain syndrome were enrolled in the study from September 1 to November 20, 2010.

Interventions. Participants received capsaicin 0.1% hydrogel patches or control hydrogel patches without capsaicin according to the randomization scheme. All participants were instructed to apply one patch to each side of the neck and shoulder girdle overlying the point of maximal pain for 12 hours daily during the duration of the 4-week study.

Outcome Measures. Each participant completed five surveys at baseline, at 2 weeks after the start of treatments, and at the conclusion of the 4-week study. The primary outcome measure was visual analog scale (VAS). Other outcome measures included the Neck Disability Index (NDI), Beck’s Depression inventory (BDI), Short Form 36 Korean version, and Euroqol 5-D.

Results. Fifty-seven patients completed the study. The mean VAS, NDI, and BDI scores were significantly decreased at 2 and 4 weeks after the start of the intervention in both groups. There was no significant difference between the two groups in any of the outcome measures.

Conclusions. Future research may help to discern specific effects of capsaicin, trigger point stimulation by application of the patch, and the placebo effect.

Key Words. Capsaicin; Myofascial; Trigger Point Injections

Introduction

Myofascial trigger points are a common source of musculoskeletal neck pain. Trigger points are defined as localized, hyperirritable nodules residing within a palpable taut band of muscle with characteristic referral patterns [1].

The pathogenesis of trigger points and myofascial pain is not fully understood. However, capsaicin has been shown
to induce pain and hyperalgesia in human tendon tissues and to increase trigger point sensitivity in humans [2,3].

Capsaicin activates transient receptor vanilloid 1 (TRPV1) receptors in afferent C peripheral nerve fibers. TRPV1 ligand-gated cation channels cause a depolarization, action potential initiation and transmission of pain neurotransmitters, such as Substance P, to the spinal cord. Agonists of TRPV1 receptors, with repeated use, cause desensitization of TRPV1 channels that inhibits the initiation of nerve transmission and may alleviate pain [4]. Because peripheral nociceptors that express TRPV1 receptors have been found to induce pain and hyperalgesia in tendon tissue and trigger points, targeting TRPV1 in the skin overlying trigger points or in the tendon may be potentially useful for pain management for myofascial neck pain.

A previous open-label study demonstrated that topically applied capsaicin may decrease subjective neck pain [5]. A systematic review of topical capsaicin for chronic pain suggested that topically applied capsaicin has moderate to poor efficacy in the treatment of chronic musculoskeletal or neuropathic pain alone, though may have a role as an adjuvant treatment [6]. The present study set out to evaluate of the efficacy of a hydrogel patch containing capsaicin 0.1% compared with a placebo hydrogel patch without capsaicin to treat chronic myofascial neck pain.

Methods

Participants

Participants between 18 and 65 years with greater than a 3-month duration of neck pain and a clinical presentation of myofascial pain syndrome were enrolled in this double-blinded randomized controlled study after providing written informed consent from September 1 to November 20, 2010. Myofascial pain was diagnosed by a history of injury or excessive strain on the cervical and thoracic muscle groups and a physical exam finding of trigger points demonstrated by an area of tenderness overlying the trapezius muscle and associated with local or regional pain. Patients who had used capsaicin in the last 4 months and patients with allergy to capsaicin, rash or skin infection overlying the neck and girdle area, radiculopathy or structural abnormalities in the area being treated, or unstable underlying disease such as cardiovascular, hepatic, renal, and central nervous system disorders were excluded from the study. Pregnant and breast-feeding women were not allowed to participate in the study.

A total of 61 participants were recruited for the study, and four participants dropped out during the study; one for pregnancy, two lost to follow-up and one for personal reason. Fifty-seven participants completed this study. This study was approved by the Institutional Review Board of Kyung-hee University Hospital at Gangdong. Recruitment was done through newspapers, advertisements, and hospital websites.

Procedures

Participants were randomized to two groups by using computer-generated random assignment (Figure 1). Study researchers and the clinicians involved in the treatment of the patients were blinded to the randomization process.

Eligible participants received capsaicin 0.1% hydrogel patches (Caleb Pharmaceuticals Inc., Taoyuan, Taiwan) or control hydrogel patches without capsaicin (Caleb Pharmaceuticals Inc.) according to the randomization scheme.

Skin with the size of 2.5 cm in diameter was chosen because the presence of trigger points range from 0.5 cm to 2 cm [1]. Myofascial trigger points in the neck and shoulder girdle happen to overlap with fibromyalgia tender points as well as Korean medicine acupoint GB21 [7].

Each group underwent a 4-week treatment protocol. All participants were instructed to apply one patch to each side of the neck and shoulder girdle overlying the point of maximal pain for 12 hours daily during the duration of the study. Placebo hydrogel patches were 2.5 cm in diameter with a breathable cloth backing. The experimental patches were identical to placebo patches except contained capsaicin 0.1% (500 μg).

Subjects were assessed at a clinic visit at baseline. Before any treatment, all participants underwent dermal allergy skin testing to check for hypersensitivity to the capsaicin patch. The subjects were seen at 2 weeks after initiation of treatment and at the end of the 4-week treatment period to assess for adverse effects.

Measures and Data Analysis

Efficacy

Each participant completed five surveys at baseline, at 2 weeks after the start of treatments, and at the conclusion of the 4-week study. The primary outcome measure was visual analog scale (VAS) [8,9]. Other outcome measures included the Neck Disability Index (NDI) [10,11], Beck’s Depression inventory (BDI) [12], Short Form 36 (SF-36) Korean version [13,14], and Euroqol 5-D (EQ-5D).

To compare baseline characteristics between the control and experimental groups, t-tests for continuous data and the Chi-squared test for dichotomous data were performed. Paired t-tests were used to evaluate for statistically significant changes between VAS for maximal pain intensity for each group over the previous 24 hours. Repeated measure two-factor analysis was used to analyze the differences among VAS at baseline, 2 weeks, and 4 weeks VAS, NDI, BDI, SF-36, and EQ-5D. Change between groups, interaction between groups, and observed time were analyzed. A P-value less than 0.05 was considered statistically significant. For all statistical analysis, the Statistical Package for the Social Sciences
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(SPSS) 14.0 program for Windows (SPSS Inc., Chicago, IL, USA) was used.

Safety

Safety was assessed by continuous monitoring of adverse events and periodic assessments of vital signs. Participants were asked to record adverse events during treatment.

Results

Patients

Fifty-seven patients completed the study. Baseline characteristics of the participants allocated into the two groups were similar (Table 1). There were no significant differences between the two groups in baseline demographics.

Efficacy

The mean VAS, NDI, and BDI scores were significantly decreased at 2 weeks and 4 weeks after the start of the intervention in both groups. However, there was no significant difference in the VAS score between the two groups (Table 2, Figure 2) nor in any of the other outcome measures (Table 3).

Safety

Seven mild adverse events were reported, 3 in the treatment group and 4 in the control group (Table 4). The

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Subject demographics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td>Treatment Group (N = 30)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2</td>
</tr>
<tr>
<td>Female</td>
<td>28</td>
</tr>
<tr>
<td>Age</td>
<td>40.33 ± 14.15</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>56.38 ± 7.22</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>159.36 ± 7.60</td>
</tr>
<tr>
<td>Body mass</td>
<td>22.24 ± 2.70</td>
</tr>
</tbody>
</table>

Values represent the mean ± standard deviation.
majority of them were symptoms related with the capsaicin hydrogel patch or control hydrogel patch, and disappeared in a few days. No serious adverse events were reported.

**Discussion**

In this study, patients with myofascial neck pain who applied a hydrogel patch containing capsaicin 0.1% and

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**Table 2** Changes of VAS scores for experimental and treatment groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Baseline</th>
<th>2 Weeks</th>
<th>4 Weeks</th>
<th>Group</th>
<th>Time</th>
<th>Group × Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS</td>
<td>Treatment</td>
<td>4.98 ± 1.77</td>
<td>3.86 ± 1.64**</td>
<td>2.89 ± 1.71**</td>
<td>2.287 (0.136)</td>
<td>34.10† (0.000)</td>
<td>0.387 (0.680)</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>5.56 ± 1.56</td>
<td>4.34 ± 2.17**</td>
<td>3.77 ± 2.52**</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VAS = visual analog scale.
Values represent the mean ± standard deviation.
P-values from paired t-test between baseline and 2, 4 weeks, * P < 0.05; ** P < 0.001.
P-values from repeated measure two-factor analysis of variance, † P < 0.05; ‡ P < 0.001.

**Table 3** Changes of survey instrument scores for experimental and treatment groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Baseline</th>
<th>2 Weeks</th>
<th>4 Weeks</th>
<th>Group</th>
<th>Time</th>
<th>Group × Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDI</td>
<td>Treatment</td>
<td>22.60 ± 11.65</td>
<td>17.47 ± 9.31**</td>
<td>14.17 ± 8.37**</td>
<td>0.733 (0.396)</td>
<td>24.89† (0.000)</td>
<td>0.236 (0.790)</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>24.04 ± 11.83</td>
<td>20.04 ± 13.17**</td>
<td>17.04 ± 12.36**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BDI</td>
<td>Treatment</td>
<td>31.00 ± 6.14</td>
<td>28.27 ± 4.88**</td>
<td>27.40 ± 6.05**</td>
<td>0.740 (0.405)</td>
<td>54.00† (0.000)</td>
<td>54.00 (0.811)</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>32.22 ± 8.95</td>
<td>30.00 ± 7.31</td>
<td>28.52 ± 6.90**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SF-36</td>
<td>Treatment</td>
<td>68.93 ± 7.16</td>
<td>71.14 ± 9.25</td>
<td>72.13 ± 9.46</td>
<td>0.034 (0.853)</td>
<td>2.592 (0.079)</td>
<td>0.565 (0.570)</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>69.79 ± 7.37</td>
<td>70.20 ± 8.57</td>
<td>71.11 ± 9.43</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>EQ-5D</td>
<td>Treatment</td>
<td>7.03 ± 1.61</td>
<td>6.80 ± 1.58</td>
<td>6.63 ± 1.69</td>
<td>1.191 (0.280)</td>
<td>5.570† (0.005)</td>
<td>0.873 (0.420)</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>7.70 ± 1.84</td>
<td>7.04 ± 2.05*</td>
<td>7.11 ± 1.72</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NDI = Neck Disability Index; BDI = Beck Depression Inventory; SF-36 = Short Form 36; EQ-5D = Euroqol 5-D
Values represent the mean ± standard deviation.
P-values from paired t-test between baseline and 2, 4 weeks, * P < 0.05; ** P < 0.001.
P-values from repeated measure two-factor analysis of variance, † P < 0.05; ‡ P < 0.001.
the placebo hydrogel patch without capsaicin for a 4-week period both had statistically significant decrease in VAS, NDI, and BDI. No statistically significant difference was found between the two groups.

Relatively low-concentration capsaicin patches of 0.1% were used in this study to minimize local burning sensation and side effects as opposed to 8% capsaicin patches that were studied for the treatment of post-herpetic neuralgia [15].

In published studies on the safety of capsaicin patches, a pharmacokinetic testing of 8% capsaicin patches demonstrated no significant systemic absorption [16]. In addition, epidermal nerve fiber density largely recovered 24 weeks after the application of the 8% patch, and no statistically significant changes in heat or cold sensation thresholds were observed [17]. So, the 0.1% patch is presumably safe from the standpoint of local skin irritation, systemic absorption, and epidermal nerve fiber degeneration.

Although the potential of a burning sensation with capsaicin is well known, treatment with the capsaicin 0.1% patch was well tolerated. Nearly all patients completed the full treatment duration.

The study had limitations that should be considered. The placebo patch was placed on a tender area of the shoulder girdle. The patient was instructed to press on the trapezius muscle to identify the proper location to place the patch. The possibility of a therapeutic effect by pressing the trigger point area, similar to massage or acupressure, cannot be excluded and may have led to an underestimation of the efficacy of the patch relative to the placebo patch.

Another potential limitation is the improper placement of the patches by the study subjects. As a trigger point has been reported to cover an area of 0.5–2 cm, study subjects may have not covered the trigger point with the patches. This would also have led to an underestimation of the efficacy of the capsaicin patch.

Future research is needed to determine specific effects of the capsaicin patch and trigger point stimulation. Therefore, additional investigation may be warranted to include a control group that receives no patch as well as more experimental groups to isolate each of the variables that may have contributed to findings of the improved VAS in both groups in the study. Further studies may also benefit from a higher-potency capsaicin patch or from using the capsaicin patch as an adjunct to treatment of myofascial neck pain with other self-care, medication, and office-based approaches. In addition, monitoring for longer periods of time may help determine the overall effect of the capsaicin patch as well as determine when a subject may return to baseline from the prior treatment.

Acknowledgments

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References


Table 4

<table>
<thead>
<tr>
<th></th>
<th>Treatment Group (N = 30)</th>
<th>Control Group (N = 27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Itching</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Burning</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Erythema</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Sum</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

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