Topical Menthol Gel Versus a Placebo Gel on Postmanipulation Pain and Range of Motion in Patients With Mechanical Neck Pain

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Purpose: The purpose of this study is to determine whether patients with mechanical neck pain who received topical menthol gel application to their neck before cervical manipulation experienced a reduction in pain and an increase in neck range of motion following cervical manipulation.

Methods: Patients (mean age, 35 years) with nonradicular mechanical neck pain were randomly assigned to a control (n = 31) or a treatment (n = 29) group. Five minutes before cervical manipulation, controls received topical placebo gel application to their neck, whereas the treatment received topical application of a menthol-containing gel (Biofreeze®). Participants rated their neck pain on a 10-point scale before application of the gel (Pre) and at 1 min (T1), 10 min (T2), 20 min (T3), and 30 min (T4) after cervical manipulation. Six measures of neck range of motion were assessed before the topical applications of gel and at T1 and T4. Repeated-measures ANCOVA was performed to compare the pain and neck range of motion following manipulation while controlling for premeasures.

Results: There were no significant differences between the groups’ pain or range of motion assessed at Pre. The treatment group reported significantly (P < .05) reduced pain at T2, T3, T4 compared to T1, while the control group did not experience significant change in their pain compared to T1. Neither study group rated a change in neck range of motion during the study.

Conclusion: Topical menthol application before manipulation may reduce neck pain, but it has no measurable effect on neck range of motion following cervical manipulation among patients with mechanical neck pain.

Keywords: Neck pain; manipulation; topical menthol

Key Points After cervical manipulation, topical menthol (Biofreeze) applied to the neck reduced post-manipulation soreness in patients with mechanical neck pain, but it did not change the cervical range of motion.

INTRODUCTION

Neck pain is the fourth leading cause of disability, with an annual prevalence rate exceeding 30%. Most episodes of acute neck pain will resolve with or without treatment, but ~50% of individuals will continue to experience some degree of pain or frequent occurrences.1,2 Almost 50% of the individuals who complain of neck pain experience incomplete resolution of their symptoms.3 Neck pain is also the second most common complaint patients present with in chiropractic treatment facilities.4

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Mechanical neck pain has been defined by Cleland\(^5\) as “non-specific (pain) in the area of the cervicothoracic junction that is exacerbated by neck movements.” This definition does not include the cause of mechanical neck pain because there are a variety of combinations of underlying biomechanical and physiologic disorders, trauma, and psychological factors that result in mechanical neck pain. To evaluate and treat mechanical neck pain, health practitioners take a detailed history, perform a physical examination, and when medically necessary visualize the structures of the area through X-rays, computed tomography scans, and magnetic resonance imaging scans. The development of mechanical neck pain is commonly accompanied by reduced neck range of motion with or without a clear initiating event or structural deformity.\(^6\) Conservative treatment of this condition involves interventions to reduce pain and improve intersegmental mobility while the provider provides treatment or information to guide the patient on how to increase neck range of motion, muscular coordination, endurance, and strength.\(^7\)

One effective treatment option to treat patients with mechanical neck pain is cervical manipulation.\(^8\) However, cervical manipulation has been reported to result in adverse effects in 30%–61% of all patients including increased neck pain, stiffness, headache (or head pain), and radiating pain.\(^9\) A majority of these adverse effects begin on the day of therapy, last <24 h, and are reported to range from mild to moderate by patients.\(^10\) Investigators have also reported that cervical manipulation can result in acute muscle soreness that may last up to 6 h post manipulation.\(^11\) Current evidence suggests that although there are mild-to-moderate increases in neck pain immediately after neck manipulation, the long-term benefits of neck manipulation include increased neck range of motion and decreased pain levels among patients with neck pain.\(^12\)

The immediate post-manipulation neck pain experienced by some patients is offset by the long-term benefits of neck manipulation.\(^13\) While pain immediately following cervical manipulation does not typically last >24 h, this temporary increase in pain may deter patients from maintaining compliance with other prescribed therapies.\(^14\) For example, increased pain following cervical manipulation may contribute to a lack of compliance with prescribed rehabilitation therapies, which is essential for managing pain symptoms.\(^15\)

Topical application of menthol has long been considered to be an effective treatment for mild-to-moderate pain.\(^16\) Investigators have confirmed the pain-relieving effects of topical application of menthol on a variety of conditions including neuropathic pain,\(^17\) knee osteoarthritis,\(^18\) and carpal tunnel syndrome.\(^19\) A more recent study indicated that topical application of menthol was effective in reducing pain among patients with nonradicular, acute neck pain.\(^11\) Topically applied menthol relieves mild-to-moderate pain and no previous clinical trials have reported any adverse events resulting from the use of the topical menthol. This evidence appears to indicate that topical application of menthol may be effective in mitigating pain immediately post cervical manipulation and is accompanied by a low risk of adverse effects.

The purpose of this study is to determine whether patients with mechanical neck pain who received topical menthol gel application to their neck before cervical manipulation experienced a reduction in pain and an increase in neck range of motion following cervical manipulation. This purpose was addressed by testing two hypotheses:

\(H1\): Patients with mechanical neck pain who receive a topical menthol gel application to their neck before cervical manipulation will report a significant reduction in pain post manipulation compared with those who receive a placebo gel application before cervical manipulation.

\(H2\): Patients with mechanical neck pain who receive topical menthol gel application to their neck before cervical manipulation will experience significantly increased neck range of motion post manipulation compared with those who receive a placebo gel application before cervical manipulation.

**METHODS**

A randomized, double-blind clinical trial was conducted to determine whether the application of a topical menthol gel (Biofreeze\(^6\)) to the neck before cervical manipulation among patients with mechanical neck pain decreased pain and increased the neck range of motion post manipulation. Prior to any participants being enrolled in the study, the protocol was reviewed and approved by Marquette University Institutional Review Board (HR-2355). Patients with nonradicular mechanical neck pain who presented to a single outpatient chiropractic clinic and were prescribed cervical manipulation by the clinic staff were provided with a recruitment flier describing the study. The flier explained the study and directed interested individuals to contact a member of the research staff to discuss the project. Interested participants were told that their decision to or not to participate in the research study would have no impact on their current or future relationship with the clinic where the research project was being conducted. During this initial meeting, a member of the research team explained the project in detail, evaluated the individual for inclusion and exclusion criteria, and obtained written informed consent from the participants. Once the participant provided informed consent, they were scheduled to participate in the trial at their next scheduled cervical
manipulation appointment in the clinic. During their next visit one of two topical gels were randomly applied to the participant’s neck 5 minutes before undergoing cervical manipulation. One of these gels was Biofreeze which contains 3.5% menthol as the active ingredient. The other was a placebo gel with no menthol. The Biofreeze and placebo gels had identical packaging, similar color, texture, and “menthol-like” scent. Each container of gel was labeled with a different code as “Brand X” or “Brand Y”. The contents of these topical gels were unknown to the research staff, the clinic staff, and the participant. The participant was asked to rate their neck pain immediately before application of the gel to their neck and again at 1, 10, 20, and 30 min following completion of their cervical manipulation therapy. Six measures of neck range of motion were also assessed before the application of any gel at 1 and 30 min following completion of their cervical manipulation therapy. Once the data collection and analysis were completed, the contents of the two gels were disclosed by the manufacturer who provided the Biofreeze and the placebo gels.

Participants were recruited at an outpatient chiropractic clinic that specializes in sport and spine rehabilitation between January and May of 2013. A convenience sample of patients attending this clinic was recruited until 60 participants completed the trial. The sample size of 30 participants per group was anticipated to yield adequate statistical power (\( \eta = .80 \)) to detect a moderate effect (\( d = .4 \) to .6) of the intervention on the outcome variable of neck pain. Individuals were included in the study if they were between the ages of 18–65 years, presented to their initial clinic visit with nonradicular mechanical neck pain \( \geq 3 \) on a 1–10 pain scale associated with hypomobility, and it was determined by the licensed clinical staff that manipulation was indicated for the patient condition. Exclusion criteria included patients not receiving a cervical manipulation; patients with radicular signs and/ or symptoms or neck pain associated with hypermobility; and patients who did not consent to be in the study.

Data collection was conducted during a single clinic visit. Background characteristics were collected from participants’ clinical chart. Variables extracted from the chart included gender, age, duration since onset of symptoms, height, weight, body mass index and consumption of pain medications in the previous 24 h. Neck pain was measured immediately before application of the gel to participants’ neck (Pre) and again at 1 (T1), 10 (T2), 20 (T3) and 30 (T4) min following completion of their cervical manipulation therapy. The type of cervical manipulation performed was the chiropractic diversified technique. Although there are some individual styles, in general, this technique is a high-velocity, low-amplitude lateral thrust with minimal rotation of the cervical spine/facet joints performed in the supine position with the hands. The technique performed was most often performed to the affected region(s) of the spine, i.e. upper cervical, mid-cervical or lower cervical, on one or both sides of the neck. Occasionally, the treatment would vary slightly based on clinical presentation/indications on an individualized basis. At each of these 5 intervals, the participant rated their pain using a 1–10 visual analog pain scale (VAS) in response to the question, “On a scale of 1 to 10 how much neck pain are you having at this moment, with 1 being ‘no pain’ and 10 being the ‘worst pain imaginable’. This measure of pain has long been used in clinical practice to identify the severity of pain.\(^{20}\)

Between T1 and T4, patients sat upright quietly in the treatment room where their cervical manipulation therapy was conducted.

Six measures of neck range of motion were assessed in the sagittal, frontal, and horizontal planes using the Acumar DataCapture handheld dual inclinometer. This device has demonstrated a high degree of reliability (.87 to .92) without requiring calibration.\(^{21}\) These assessments included neck movements of flexion, extension, right-side bending, left-side bending, left rotation, and right rotation. These measures of neck range of motion were obtained before gel application to the participant’s neck (Pre) and again at 1 (T1) and 30 (T4) min following completion of cervical manipulation. These data collection intervals were selected to minimize the effect of repeated neck range of motion assessments affecting neck pain and contributing to neck range of motion following manipulation. The participant was instructed to perform the neck motion five times to their maximum range of motion, without causing an increase in pain. The greatest range of motion in degrees achieved over the 5 trials was considered the individual’s maximum range of motion for the specific neck motion. Each trial of these neck motions was measured from the anatomical position by the same research staff at each data collection point.

Participants were randomly assigned by coin flip to receive 1 of 2 topical gel formulas applied to their neck. Both formulas were prepared by the manufacturer and were delivered to the research staff in de-identified dispensers labeled as “Brand X” and “Brand Y.” Following data collection and analysis, the manufacturer disclosed the contents of the 2 topical gel formulas as Brand X containing Biofreeze and Brand Y containing a control gel with a similar packaging, texture, and scent as Brand X but without the active ingredient of menthol. The estimated surface area of the average adult’s neck is 350 cm and the standard dose of Biofreeze to achieve a clinically significant effect has
been cited to be 1 mL/200 cm² of skin surface area.\textsuperscript{22} Using these data, \textsim 1.75 mL of the assigned gel was applied to each participant’s neck (posterior, anterior, left lateral, and right lateral) by the same member of the research team, 5 min before an independent practitioner performing cervical manipulation on the participant. The 5-min duration between gel application and performing the patient’s cervical manipulation was chosen on the basis of a previous study which demonstrated that BioFreeze had a measurable effect within 5 min of application.\textsuperscript{22}

Data were transcribed from data collection sheets or original data sources into IBM SPSS Statistics V.22 spreadsheets. These spreadsheets were double-checked for data entry and transcription accuracy. Descriptive statistics confirmed the appropriateness of using parametric statistics to evaluate the hypotheses. The first step in the analysis was to compare the 2 groups to determine the effectiveness of randomization to produce similar groups with regard to all of the variables collected at Pre. To address \textit{H1}, a repeated-measure ANCOVA was calculated to determine if the study groups changed their pain rating during any of the 4 data collection points following manipulation while controlling for pain ratings collected at baseline (Pre) before manipulation. Significant main effects of the ANCOVA (time, group, interaction) were further addressed by calculating Tukey least-significant difference post hoc comparisons. This statistical model was selected to moderate the differences in participants’ initial levels of pain before beginning any treatments. A similar statistical model was used when addressing \textit{H2}. Separate repeated-measures ANCOVAs were calculated to determine if the study groups changed their neck range of motion during any of the 2 data collection points following manipulation while controlling for the measure of neck range of motion collected at baseline (Pre) before manipulation.

RESULTS

Table 1 presents comparisons of background characteristics, pain ratings, and the six measures of neck range of motion before the application of any intervention at Pre. This table indicates that there were no statistically significant differences (\textit{P} < .05) between the 2 study groups on any of the background characteristics or measures of pain or neck range of motion. The sample included individuals of \textsim 35 years of age, suffering for >100 days with neck pain, completed close to 9 previous clinic visits for their neck pain, and reported a moderate amount of neck pain before the application of any interventions. Of particular note is the observation that a majority of the participants did not consume any pain medication within the previous 24 h. At Pre, the participants in both the treatment and control groups reported a moderate degree of neck pain at 5.10 and 4.29 out of 10, respectively. This nonsignificant 20% difference in neck pain between the study groups assessed at the Pre data collection point supported the decision to use the ANCOVA statistic which controlled for this difference in the analysis to address the hypothesis based on the participant’s Pre measures.

The analysis to address \textit{H1} indicated a significant time effect (\textit{P} < .05), although the nonsignificant group and interaction effects showed that the groups were not different at any data collection point over the duration of the study. Post hoc comparisons based on the time effect did reveal that the treatment group reported a significant decrease in pain at T2, T3, and T4 compared with their measures at T1, while the control group did not report a significant change in their pain levels over the duration of the study (Table 2). Table 2 also presents the comparisons within and between groups on the six measures of neck range of motion. This table indicates that the study groups exhibited similar levels of neck range of motion over all data collection points. Further, neither of the study groups showed a significant change in their neck range of motion at 1 (T1) or at 30 (T4) min following cervical manipulation. These measures of the sample’s neck range of motion were less than the anatomical norms cited previously.\textsuperscript{23}

DISCUSSION

The descriptive analysis of the sample supports the external validity of the study findings. This analysis indicated that participants in both groups at Pre reported a moderate level of neck pain (4–5/10), with neck range of motion measures being less than the previously established anatomical norms. In addition to this observation, the individuals who volunteered for this study were, on average, middle-aged, female, with a BMI of 27 and suffering with neck pain longer than 100 days.

The statistical analysis partially supported the study hypotheses. Although, the participants in the 2 study groups reported similar neck pain over the 30 min following cervical manipulation, participants who received the gel containing menthol reported a significant reduction in pain following this procedure. Examination of the adjusted mean pain values in the study groups indicated that the treatment group reported a 40% decline in their neck pain between T1 and T4, whereas the control group reported a 23% decline in their pain over the same duration. This reduction in neck pain resulting from topically applied menthol is consistent with previous authors who reported that topical menthol reduces neck pain.\textsuperscript{11} These findings are also consistent with findings of other investigators who reported the pain-reducing effects of topical menthol among individuals suffering...
from acute ankle sprains, chronic lower back pain, and delayed muscle soreness. The pain-mitigating mechanism of the action of topical menthol application has been hypothesized by Wasner et al. The authors propose that as menthol stimulates TRPM8 receptors in the skin, the activation threshold for vasoactive C nociceptors and cold-specific A delta fibers is lowered. When activated, these fibers "block the gate" for pain sensations. Thus, the pain-reducing effect of topical menthol reported in this study is consistent with other clinical trials and with the hypothesized mechanism of action that topical menthol activates cold receptors that block pain impulses.

The findings did not support H2. Neither the treatment nor the control group exhibited a significant change in any of the 6 measures of neck range of motion over the duration of the study. There are a number of explanations for this finding. First, although the literature indicates that neck pain and neck range of motion are inversely related, the application of topical menthol in this study did not appear to impact the range of motion. Thus, the decreases in pain following cervical manipulation that appear to be potentiated with topical menthol do not seem to affect the neck range of motion during the 30 min following the manipulation. A second explanation is that cervical range of motion may also be affected by a number of other variables such as thoracic spine hypomobility, fear-avoidance, internal motivation, personal effort, pliability of the soft tissues of the neck, and uncovertebral joints of the cervical spine. The compliance of tissues of the neck may not be amenable to a one-time application of topical menthol.

**RECOMMENDATIONS**

The findings support the efficacy of applying a menthol gel to the neck of patients with mechanical pain.
neck pain 5 min before cervical manipulation. The application of topical menthol before neck manipulation appears to reduce neck pain during the 30 min following the manipulation. Practitioners may wish to apply topical menthol before neck manipulation to reduce post-manipulation pain. Post-manipulation pain has been demonstrated to be inversely related to treatment satisfaction, and greater treatment satisfaction results in greater compliance with treatment recommendations. Future studies may wish to examine if reductions in post-cervical manipulation pain, attributable to topical menthol, last longer than 30 min. Finally, future researchers need to determine if these reductions in pain following cervical manipulation attributable to topical menthol facilitate greater compliance with treatment recommendations.

**LIMITATIONS**

Although promising, the results of this study need to be considered in light of a number of limitations to the internal and external validity. First, the volunteers for this study may not represent all patients who suffer from neck pain. A majority of the current sample indicated they were in pain for a long period of time and had undergone a number of therapy sessions. These factors may have contributed to an expectation or Hawthorne effect of the therapy, although this threat may have been mitigated by the double-blind design. Second, the documentation of a participant’s consumption of pain medications was for the previous 24 h instead of the 3–4 h before the cervical manipulation when most oral pain medications are effective. Further there was no attempt to document the participant’s use of any other pain-relieving interventions. Both of these contaminating factors may have influenced the participant’s use of any other pain-relieving interventions. Both of these contaminating factors may have influenced the participant’s pain ratings and need to be considered in future trials, although randomization of the sample may have minimized these threats. Finally, the sample was homogenous and recruited from a single clinic. Thus, the findings may not be applicable to a more diverse group of patients with mechanical neck pain.

**REFERENCES**


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