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Summary

The purpose of this study was to compare the vascular responses in the brachial artery and perceived intensity of two different formulas of topical menthol gels prior to and following a bout of maximum voluntary muscular contractions (MVMCs).

18 adults completed the same protocol on different days using blinded topical menthol gels (Old Formula and New Formula). Heart rate, brachial artery blood flow (ml/min), vessel diameter and reported intensity of sensation were measured at baseline (T1), at 5 min after application of the gel to the upper arm (T2), and immediately following five MVMCs hand grips (T3).

The New Formula exhibited a significant decline in blood flow (−22.6%) between T1 and T2 which was not different than the nonsignificant declines under the Old Formula 1 (−21.8%). Both formulas resulted in a significant increase in perceived intensity of sensation between T1 and T2. Blood flow increased significantly with the New Formula (488%) between T2 and T3 and nonsignificantly with the Old Formula (355%).

Keywords

Menthol; Vascular response; Maximum exercise

Introduction

Topical gels that containing menthol as the active ingredient are commonly employed by Chiropractors, Physical Therapists, Massage Therapists and other practitioners. These gels are indicated for relief of low back pain, central or neuropathic pain and pain associated with osteoarthritis. When combined with chiropractic care, a topical gel containing menthol significantly reduced LBP compared to the chiropractic-only group (Zhang et al., 2008). Wasner et al. (2008) reported that topical menthol had an analgesic effect among patients with peripheral and central neuropathic pain. Kraemer et al. (2005) also reported that a topical menthol gel improved the functional ability of knee arthritis patients. Another study demonstrating the anti-nociceptive effects of menthol studied mice on a hotplate and indicated that the temporary pain relief from menthol was as effective as morphine (Galeotti et al., 2002). In a double blind study McKay et al. (2003) reported that a topically applied gel containing menthol was effective in relieving the pain and stiffness of osteoarthritis patients without adverse effects. In a more recent study, Topp et al. (2013a) reported that a topical gel containing 3.5% menthol resulted in significant decreases in pain (35–37%) among knee osteoarthritis patients while performing functional tasks, particularly when performing tasks which required repetitions over the knee's full range of motion. Thus, it appears that topical menthol is effective at relieving pain in a variety of chronic pain conditions.

The topical application of menthol gels has also been demonstrated to reduce arterial blood flow in the upper and lower extremities adjacent at the application site. Twenty seconds of menthol applied to the oral cavity significantly decreased blood flow in the nose (Kashima and Hayashi, 2013). In a study of decerebrate cats the application of topical menthol gel reduced the exercise blood flow within an

activated muscle without a systemic effect on heart rate (Ragan et al., 2004). These authors and others examining topical menthol gels reported peak mean arterial pressure responses, evoked by static muscle contraction were significantly attenuated after application of the gel (Ragan et al., 2004, Ichiyama et al., 2002) thus, leading to a reduction in overall blood flow to the area. It is thought that the reduction in the pressor response is due to the inhibition of the small-diameter sensory nerve fibers that are known as group III and IV afferents that synapse with the central nervous system (Ragan et al., 2004). These authors concluded that topical menthol may reduce blood flow to the underlying tissues through stimulation of cold receptors of the skin.

Previous studies have demonstrated that a commercially produced topical gel containing 3.5% menthol (Biofreeze®) can have a significant effect on reducing arterial blood flow. Arterial blood flow in all of these studies was measured by having the target vessel imaged longitudinally by pulse-mode ultrasound, using a 12–5 MHz linear array transducer (Doppler). In an early study by Olive et al. (2010) the application of this 3.5% menthol gel significantly reduced blood flow in the brachial artery within 60 s of application, and this effect was maintained for at least 10 min after application. The approximate 19% reduction in blood flow observed in this study resulting from the topical menthol gel was similar to the reduction in blood flow observed in the vessel during the application of cold. In a follow up study the effects of ice and the 3.5% menthol gel were compared on blood flow and muscle functioning. The results of this study indicated that the 3.5% menthol gel had a fast-acting effect on reducing blood flow, within 5 min. This reduction in blood flow was short-lived, and could not be detected 20 following application. While the application of ice appeared to reduce blood flow after a prolonged duration (Topp et al., 2011a). These investigators also reported that muscle strength appeared to be inhibited at 20 min after ice application but not at 20 min following the application of the 3.5% menthol gel. In another study by this same team (Topp et al., 2011b) the 3.5% menthol gel was compared to a 10% menthol wipe on blood flow of the treated and untreated lower extremities following an acute bout maximum voluntary muscular contractions (MVMCs) of the quadriceps and hamstrings. Both menthol dosages resulted in significant decreases in popliteal blood flow in the treated (−19.60 to −8.39%) and untreated sides (−14.72 to −5.4%) while the control condition demonstrated an increase in blood flow bilaterally (+26.40 to +15.19%) within 60 s following the MVMCs. These results indicate that the topical menthol gel has a rapid effect on reducing ipsilateral and possibly contralateral arterial blood flow. In a more recently completed study radial artery blood flow and perceived discomfort were measured prior to and following the application to the forearm of 3.5% menthol gel, crushed ice, 3.5% menthol gel and crushed ice and a no treatment control (Topp et al., 2013b). The results of this study indicated that the ice reduced blood flow 20%–24%, topical menthol reduced blood flow −17% to −24%, ice and menthol reduced blood flow −36% to 39% with no changes in blood flow observed in the control condition (Topp et al., 2013b). The menthol gel alone reduced blood flow similar to the application of crushed ice and combining crushed ice with menthol appeared to have an additive effect on reducing blood flow. These authors concluded that the topical gel containing 3.5% menthol in addition to resulting in temporary analgesia reduces arterial blood flow.

The formula of the 3.5% menthol gel (Biofreeze® or Old formula) examined in these previous studies has been recently discontinued by the manufacture. This Old formula include 3.5% menthol, camphor, carbomer, FD&C Blue#1, FD&C Yellow#5, glycerine, herbal extract, isopropyl alcohol, methylparaben, propylene glycol, silicon dioxide, triethanolamine and water. The New formula of gel or Biofreeze II®contains 4% menthol with no parabens or propylene glycol and a new botanical

blend of ilex, arnica, aloe, boswellia, calendula, green tea, burdock root and lemon balm. Since the formulary of this topical application of menthol has being modified it seems prudent to compare the effects of the new and old formulas. Thus, purpose of this study was to compare the vascular responses in the brachial artery and perceived intensity of two different formulas (Old formula vs New formula) of topical menthol gels prior to and following a bout of maximum voluntary muscular contractions (MVMCs). This purpose was addressed through evaluating the tenability of the following hypotheses:

H1

Vascular responses and perceived intensity will be the same following application of the Old and New formula of topical gels containing menthol treatment to the upper arm.

H2

Vascular responses and perceived intensity will be the same following application of the Old and New formula of topical gels containing menthol treatment to the upper arm following a bout of maximum voluntary muscular contractions (MVMCs) of the arm.

Methods

A repeated measures cross-over design dictated that subjects, were randomly assigned one of the two topical gels during their first data collection visit to the Exercise Science Laboratory. During a second visit to the laboratory separated by more than 5 days, each subject received the topical gel they did not receive during their initial visit. Both the research team and the subjects were blinded to the content of the topical gels by labeling the treatments as “Formula Z” and “Formula L.” During each of these visits to the laboratory the subjects completed the same data collection protocol that involved assessments of the heart rate, brachial blood flow, brachial vessel diameter and self-reported perceived intensity of sensation in upper arm where the gel was applied. Thus, each subject completed the same data collection protocol twice while under the influence of the two different topical gel treatments.

A sample of 18 (9 males and 9 females) healthy adults, 22.44 (SD + 1.95) years of age with an average BMI of 23.97 (SD + 3.88) were recruited through word of mouth and fliers placed on a college campus. These individuals reported not having any chronic or acute health conditions which may affect the blood flow to their forearm (diabetes, peripheral vascular disease, Raynaud's disease, influenza etc.). Individuals who smoked were excluded from the trial. After signing an approved informed consent (HR-2286) and completing a familiarization trial with the data collection protocol subjects were scheduled for two data collection sessions each separated by at least 5 days. At the first data collection session each subject was assigned a random order of the two experimental conditions by selecting a card from a deck of 18 cards. Nine of these cards indicated the subject would receive “Formula Z” during their initial visit and “Formula L” at their second visit. The remaining 9 cards indicated that the subject would receive “Formula L” at their first visit and “Formula Z” at their second visit. The research team was blinded to the content of the treatments by the manufacture of the two topical gels providing the product in two containers labeled “Formula Z” and “Formula L.” Thus, both the research team and the subjects were blinded to the content of the topical gel formulas being evaluated. The blinding of the research team was not broken until the data analysis was completed.

The data collection protocol was the same at both data collection sessions except for the different treatment condition applied to the subject's upper right arm. Each subject was told to refrain from caffeine intake or heavy physical exertion for 4 h prior to the data collection sessions. At each data collection session the subject arrived at the environmentally controlled Exercise Physiology Laboratory and reclined in a supine position on a padded table quietly for 5 min following arrival. Following this 5 min rest each subject's heart rate and blood pressure were recorded in their left arm. Following these assessments, the subject's baseline brachial artery blood flow (ml/min) brachial artery diameter (cm) were measured on the right side using a General Electric 3 Ultrasound Doppler. The subject's perceived intensity of sensation was also measured on the right side at the time the brachial artery flow and diameter were assessed using a 0–10 analog scale anchored at 0 with “No sensation” to 10 “Highest intensity imaginable.” Immediately following collection of baseline data during each data collection session one of the two randomly assigned treatment conditions were applied to the subject's right upper arm. These treatments (Formula L or Formula Z) were be applied at 2.5 mL per 500 cm2 to entire upper arm (approximately 4 ml) by a gloved technician over a duration of less than 5 s. The application area included around the entire circumference of the right upper arm from the humeral head to the humeral medial epicondyle. At 5 min following application of the treatment to the subject's right arm their right side brachial artery blood flow, artery diameter and intensity of sensation were again measured. Immediately following this second data collection, the subject was asked to grip a hand grip dynamometer (Lafayette Instrument, Lafayette, IN) as hard as possible 5 times for 5 s each with 5 s of rest between each maximum voluntary muscle contraction (MVMC). Brachial artery blood flow, artery diameter and intensity of sensation were again measured immediately following completion of the five maximum hand grip exercises. Thus, brachial blood flow, brachial diameter and intensity of sensation were collected at rest prior to any treatment (T1), 5 min following application of one of the topical menthol gel treatments (T2) and immediately following five maximum hand grip exercises on the right side (T3).

Repeated measures analysis (R-ANOVA) were be employed using the IBM SPSS 17.0 package to address the study hypotheses. This statistic was employed to assess for differences in vascular responses and perceived intensity as a result of applying the two topical menthol gels (Hypothesis 1) and as a result of the topical gels immediately following five hand grip MVMCs with the treated arm (Hypothesis 2). These analyses determined the effect of the different treatments or time or the interaction of treatment by time on the outcome variables. Significant main or interaction effects ($p < .05$) were further evaluated using Tukey's least significant difference (LSD) post hoc comparisons with $p < .05$ considered the minimal level of statistical significance.

Results

Table 1 displays the vascular responses and perceived intensity at baseline (T1) prior to any intervention and 5 min following the application (T2) of the New and Old formula of the topical menthol gels. These analyses indicate that neither the application of the New or Old formula had any significant effect on heart rate or vessel diameter. These analyses also indicated a significant decrease in blood flow (22%) in the brachial artery 5 min following the application of the New formula. Although similar the 21% decrease in brachial blood flow following application of the Old formula did not achieve statistical significance. Measures of blood flow were not different between the treatments at baseline (T1) or 5 min following application of the topical menthol gels (T2). The subject's perceived intensity of

sensation increased significantly following application of both the Old and New formulas and were not distinguishable from one another at baseline or 5 min following baseline.

Table 1. Comparing vascular responses at baseline (T1) with 5 min following the application of the Old and New formula of menthol gel (T2).

	Baseline (T1)	**5 mins post-application (T2)**	**Raw change (% change)**
HR beats/min			
New	64.64 ± 3.57	63.17 ± 3.67	−1.47 (−2.27%)
Old	63.34 ± 3.57	65.40 ± 3.67	2.40 (1.67%)
Blood flow			
New	63.13 ± 8.32	48.86 ± 6.80*	−14.27 (−22.60%)
Old	50.23 ± 8.32	39.56 ± 6.80	−10.67 (−21.24%)
Vessel diameter			
New	0.349 ± 0.011	0.345 ± 0.015	-0.004 (−1.15%)
Old	0.346 ± 0.011	0.348 ± 0.015	0.002 (0.58%)
Intensity of sensation			
New	0.00 ± 0.00	4.00 ± 0.49*	4.00 (4000%)
Old	0.17 ± 0.12	4.44 ± 0.53*	4.29 (2511%)

*Significant ($p < .05$) change within group over time.

Table 2 presents the vascular responses and perceived intensity at 5 min following the application of the New and Old formula of the topical menthol gels (T2) and immediately following a bout of maximum voluntary muscular contractions (MVMCs) with the treated arm (T3). The analysis of these data indicate no significant differences in heart rate, vessel diameter or perceived intensity of sensation within the treatment conditions over time or when comparing the treatment condition at T2 and T3. Immediately following the bout MVMCs, blood flow in the brachial artery significantly increased following application of the Old formula (488%). The increases in blood flow observed following application of the New formula and the bout of MVMCs appeared dampened and did not achieve a statistical significance (355%).

Table 2. Comparing vascular responses at 5 min post-application (T2) and immediately following exercise (T3) with the Old and New formula of menthol gel.

	5 mins post-application (T2)	**Immediate following exercise (T3)**	**Raw change (% change)**
HR beats/min			
New	63.17 ± 3.67	71.82 ± 11.47	(13.69%)
Old	65.40 ± 3.67	86.34 ± 11.47	(32.02%)
Blood flow			
New	48.86 ± 6.80	219.67 ± 27.54	(355.73%)
Old	39.26 ± 6.80	231.12 ± 6.80*	(488.70%)
Vessel diameter			
New	0.345 ± 0.015	0.353 ± 0.014	(2.32%)
Old	0.348 ± 0.015	0.360 ± 0.014	(3.45%)
Intensity of sensation			
New	4.00 ± 0.49	4.56 ± 0.37	0.56 (1.40%)
Old	4.44 ± 0.53*	4.72 ± 0.52	0.28 (6.31%)

*Significant ($p < .05$) change within group over time.

Discussion

These results provide some support for the hypotheses that both the Old and New formulas of the topically applied menthol gels produce similar vascular responses and perceptions of intensity prior to and following a bout of MVMCs. The finding that heart rate and vessel diameter appeared to be unaffected by either of the formulas of topical menthol gel are consistent with studies examining the effect of topical menthol on these outcomes (Topp et al., 2011a). The findings that the New formula of topical menthol gel reduced blood flow through the brachial artery is also consistent with previous studies who reported that blood flow was reduced by a similar percentage at 5 min following the application of a topical menthol gel (Olive et al., 2010, Topp et al., 2011b, Topp et al., 2013b). Although not statistically significant the changes in blood flow through the brachial artery following application of the Old formula (21%) appeared clinically indistinguishable from the New formula (22%). Thus, the New formula resulted in statistically significant reduction in arterial blood flow. Although not statistically significant, the Old Formula of the topical menthol gel appeared to have a similar effect on reducing blood flow. These findings that topical menthol reduces blood by approximately 20% are consistent with previous investigators studying the effects of topical menthol on arterial blood flow.

Supporting this observed similar effect of the two formulas is the similar increases in perceived intensity of sensation reported by the subjects when either topical menthol gel were applied. Although comparisons in pain relief between the two topical menthol formulas was beyond the scope of this study, the similar increase in intensity of perceptions following the application of both of the topical menthol gels supports the contention that the formulas have a similar effect on perception. This similar effect of both of the topical menthol gels on perceptions may indicate that both formulas have a similar analgesic effect although this hypotheses needs to be empirically confirmed. Topical menthol gels are classified as ‘topical analgesics’ with a mechanism of action defined as a “counter-irritant,” based on the Gate Control Theory (Melzack and Wall, 1965). Topical menthol gels are thought to produce a cooling sensation by inhibiting calcium currents of neuronal membrane (Gaudioso et al., 2012). Menthol is noted for eliciting perceptions of cold through its effects on the transient receptor potential family of ion channels or (TRP's). Haeseler et al. (2002), has postulated that the stimulating effect of menthol on cold receptors may have an anti-nociceptive effect causing an inactivation of sodium channels of the alpha subunit resulting in hyperpolarization or blocking the signal of pain transduction &/or impulses from pain receptors.

Following the MVMCs, heart rate, vessel diameter and perceptions of intensity were unchanged between T2 and T3 with either formula of topical menthol. This lack of effect of menthol and MVMCs on heart rate, vessel diameter and perceptions of intensity are similar to the findings of Topp et al. (2011b) who compared topical menthol applications with a control condition following MVMCs. When comparing brachial artery blood flow following the MVMCs the statistically significant increases in blood flow following application of the Old formula (488%) also appeared clinically different than the non-statistically significant changes in blood flow the New formula (355%). This difference may be attributable to a higher dose of menthol &/or the different ingredients in the New formula (4%) attenuating the hyperemic effect of the MVMCs compared to the Old formula (3.5%). The current findings that blood flow statistically increased following MVMCs under the Old formula is in contrast to the previous study that indicated that the 3.5% topical menthol gel reduced blood flow following

MVMCs (−19%) in the popliteal arteries (Topp et al., 2011b). There are a number of possible explanations for these conflicting findings. First, different muscle groups (hand grip vs knee extension/flexion) and different types of MVMC exercises (isometric vs isokinetic) were employed to stimulate exercise induced hyperemia in these two studies. A second justification for these different findings is that the duration of time between the MVMCs and completing the assessment of blood flow were different in the two studies. The current protocol assessed blood flow immediately following the MVMCs while the previous study protocol involved a delay of approximately 60 between MVMCs and vascular assessments that resulted from transferring the subject between the isokinetic dynamometer and the Doppler apparatus.

In addition to the differences in methods when comparing the current results with previous studies the results must be interpreted cautiously due to a number of methodological limitations. The small sample size likely yielded underpowered statistics that did not unequivocally support the hypotheses of the study. Using the effect sizes described in this and other study studies, investigators will be able to conduct future studies that are adequately powered examining the vascular effects of topical menthol gels. A second limitation in the study design was the lack of a true control. This flaw is only partially addressed through the repeated measures nature of the design in which all subjects were exposed to all treatments. The addition of a true control consisting of a topical gel absent of menthol may differentiate the effect of the menthol from a placebo or expectation effect. The challenge to future investigators is to identify a suitable placebo with a similar odor and skin sensation as the menthol gel treatment in order to maintain the double blind nature of the design.

Conclusion

The New formula of topical menthol gel resulted in statistically significant reductions in blood flow (−22.60%) 5 min following application similar to that reported by previous investigators. This reduction in blood flow was clinically similar to the nonstatistically significant changes in blood flow observed 5 min following application the Old formula of menthol gel (−21.24%). As well, both formulas resulted in indistinguishable statistically significant increases in perceived intensity of sensation 5 min following application and following MVMCs. Following the MVMCs blood flow significantly increased (488.70%) when the Old formula had been applied while the increases in blood flow following the MVMCs and the New formula (355.73%) did not achieve statistical significance. These findings appear to indicate that the New formula of topical menthol may inhibit blood flow similarly or to a greater extent when compared to the Old formula. These results must be interpreted cautiously due to the low statistical power resulting from a small heterogeneous sample.

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References

Galeotti et al., 2002 N. Galeotti, L. Di Cesare Mannelli, G. Mazzanti, A. Bartolini, C. Ghelardini. **Menthol: a natural analgesic compound.** Neurosci. Lett., 322 (3) (2002), pp. 145-148. http://dx.doi.org/10.1016/S0304-3940(01)02527-7

Gaudioso et al., 2012 C. Gaudioso, J. Hao, M.-F. Martin-Eauclaire, M. Gabriac, P.Delmas. **Menthol pain relief through cumulative inactivation of voltage-gated sodium channels.** PAIN, 153 (2) (2012), pp. 473-484. http://dx.doi.org/10.1016/j.pain.2011.11.014

Haeseler et al., 2002.
G. Haeseler, D. Maue, J. Grosskreutz, J. Bufler, B. Nentwig, S.Piepenbrock, M. Leuwer. **Voltage-dependent block of neuronal and skeletal muscle sodium channels by thymol and menthol.** Eur. J. Anaesthesiol., 19 (8) (2002), pp. 571-579

Ichiyama et al., 2002 R.M. Ichiyama, B.G. Ragan, G.W. Bell, G.A. Iwamoto. **Effects of topical analgesics on the pressor response evoked by muscle afferents.** Med. Sci. Sports Exerc., 34 (9) (2002), pp. 1440-1445

Kashima and Hayashi, 2013 H. Kashima, N. Hayashi. **Facial skin blood flow responses to irritant stimuli in the oral cavity.** Auton. Neurosci. Basic Clin., 174 (1–2) (2013), pp. 61-65

Kraemer et al., 2005
W.J. Kraemer, N.A. Ratamess, C.M. Maresh, J.A. Anderson, J.S. Volek, D.P. Tiberio, R.L. Hesslink, J r.. **A cetylated fatty acid topical cream with menthol reduces pain and improves functional performance in individuals with arthritis.** J. Stren. Condition. Res., 19 (2) (2005), pp. 475-480

McKay et al., 2003 L. McKay, H. Gemmell, B. Jacobson, B. Hayes. **Effect of a topical herbal cream on the pain and stiffness of osteoarthritis: a randomized double-blind, placebo-controlled clinical trial.** J. Clin. Rheumatol., 9 (3) (2003), pp. 164-169

Melzack and Wall, 1965 R. Melzack, P.D. Wall. **Pain mechanisms: a new theory.**
Science, 150 (3699) (1965), pp. 971-979

Olive et al., 2010 J.L. Olive, B. Hollis, E. Mattson, R. Topp. **Vascular conductance is reduced after menthol or cold application.** Clin. J. Sport Med., 20 (5) (2010), pp. 372-376

Ragan et al., 2004 B.G. Ragan, A.J. Nelson, J.H. Foreman, G.W. Bell, G.A. Iwamoto. **Effects of a menthol-based analgesic balm on pressor responses evoked from muscle afferents in cats.** Am. J. Vet. Res., 65 (9) (2004), pp. 1204-1210

Topp et al., 2013a R. Topp, J.A. Brosky Jr., D. Pieschel. **The effect of either topical menthol or a placebo on functioning and knee pain among patients with knee OA.** (Research Support, Non-U S Gov't). J. Geriatr. Physcial Ther., 36 (2) (2013), pp. 92-99

Topp et al., 2013b R. Topp, E.R. Ledford, D.E. Jacks. **Topical menthol, ice, peripheral blood flow, and perceived discomfort.** J. Athletic Train., 48 (2) (2013), pp. 220-225

Topp et al., 2011a R. Topp, L. Winchester, A.M. Mink, J.S. Kaufman, D.E. Jacks. **Comparison of the effects of ice and 3.5% menthol gel on blood flow and muscle strength of the lower arm.** J. Sport Rehabil., 20 (3) (2011), pp. 355-366

Topp et al., 2011b R. Topp, L.J. Winchester, J. Schilero, D. Jacks. **Effect of topical menthol on ipsilateral and contralateral superficial blood flow following a bout of maximum voluntary muscle contraction.** Int. J. Sports Phys. Ther., 6 (2) (2011), pp. 83-91

Wasner et al., 2008 G. Wasner, D. Naleschinski, A. Binder, J. Schattschneider, E.M. McLachlan, R. Baron. **The effect of menthol on cold allodynia in patients with neuropathic pain.** Pain Med., 9 (3) (2008), pp. 354-358

Zhang et al., 2008 J. Zhang, D. Enix, B. Snyder, K. Giggey, R. Tepe. **Effects of biofreeze and chiropractic adjustments on acute low back pain: a pilot study.** J. Chiropractic Med., 7 (2) (2008), pp. 59-65