EFFECTS OF A TOPICALLY APPLIED COUNTERIRRITANT (EUCALYPTAMINT) ON CUTANEOUS BLOOD FLOW AND ON SKIN AND MUSCLE TEMPERATURES

A Placebo-Controlled Study[1]

Chang-Zern Hong,[2] MD and Frank G. Shellock, PhD

This study was designed to investigate the effects of a new product of counterirritant, Eucalyptamint, on the cutaneous circulation and on skin and muscle temperatures. Ten normal subjects (six males and four females, with an average age of 34±6 yr) were involved in this study. Eucalyptamint was applied to the anterior forearm skin of one side, and placebo was applied to the contralateral forearm. The subjective feelings, cutaneous blood flow, and skin temperature were measured before and periodically (5-min intervals) after the application of the compound. Muscle temperature was measured before and 30 min after the application of the Eucalyptamint. There was no significant effect on the subjective sensation. However, there were statistically significant ($P < 0.05$) increases in cutaneous blood flow (up to 4 times base-line) and skin temperatures (up to 0.8°C higher than base-line) after the application of Eucalyptamint with the effects lasting up to 45 min after the application. The muscle temperature was also increased (0.4°C) significantly ($P < 0.05$) 30 min after application of the Eucalyptamint. There were no significant changes in the placebo application. The results of this study suggested that the new product of counterirritant, Eucalyptamint, produced significant physiologic responses that may be beneficial for pain relief and/or useful to athletes as a passive form of warm-up.

KEY WORDS: Counterirritants, Cutaneous Circulation, Skin Temperature, Muscle Temperature

Counterirritants are agents used locally to irritate the intact skin for the purpose of relieving pain originating in the muscles, viscera or remote area. The mechanism for such pain relief is probably related to localized vasodilatation and subsequent increase in local circulation and tissue temperature.[1]

There are numerous over-the-counter topical counterirritants currently available. These products are frequently used by athletes or patients with various types of pain syndromes. They usually contain menthol and/or camphor. A new product, Eucalyptamint, containing natural eucalyptus oil has been recently available on the market. It also contains natural menthol and anhydrous lanolin. Menthol is a commonly used counterirritant.[2] Lanolin is an emollient and protective cream.[3] Eucalyptus oil is also a counterirritant, and is more often applied to the mucosa of the respiratory tract as an expectorant.[4]

It has been suggested that an increase of body temperature may improve physical performance[5–13] and reduce the incidence of injury[11–13] in athletes. Some of these mechanisms may be related to the associated increase in blood flow.[6,8] For therapeutic purposes, increase of local temperature and local blood flow may reduce the pain and the inflammatory process.[14] Apparently, the physiologic effects of a topical counterirritant/analgesic are based on the increase of local circulation and local temperature.

This study was designed to assess the increase of cutaneous blood flow and skin and muscle temperatures due to the effect of this new product of counterirritant, Eucalyptamint, compared to a placebo.

MATERIALS AND METHODS

Subjects

A total of 10 healthy adult volunteers (six males and four females) with an average age of 34±6 yr (range = 23–43) were studied. Exclusion criteria included the following: (1) pregnancy; (2) the pres-

0894-9115/91/7001-0029$03.00/0
AMERICAN JOURNAL OF PHYSICAL MEDICINE & REHABILITATION

[1] From the Department of Physical Medicine and Rehabilitation, University of California Irvine Medical Center, Orange, California (C.-Z.H.), and the Department of Medicine and Diagnostic Radiology, University of California Los Angeles and Cedars-Sinai Medical Center, Los Angeles, California (F.G.S.).

[2] To whom all correspondence and requests for reprints should be addressed at: PM&R, Route 81, UCI Medical Center, P.O. Box 14091, Orange, CA 92613-4091.

ence of any health problem including a history of cardiovascular, pulmonary, gastrointestinal, hematologic or neurologic disorders; (3) known sensitivity to menthol, alcohol, camphor or acetone; and (4) concomitant treatment with any form of medication. They all signed the consent form.

Eucalyptamint

Eucalyptamint is a natural product with the contents consisting of eucalyptus oil and lanolin, and 15% natural menthol. It is a new product of counterirritant manufactured by Naturopathic Laboratories, Inc., 3110-A 44th Avenue North, St. Petersburg, FL 33714, and marketed by CIBA-GEIGY.

Standardization of Dosage and Application

Since it is possible that the simple act of massage that is used to apply topical preparations may increase local circulation and/or temperature, the counterirritant was compared to a placebo (aqueous ultrasound gel).

A standardized amount (i.e., 2.5 cm in length and 5 mm in diameter with a total volume of $5^2 \times 2.5$ cm^3) of Eucalyptamint and placebo was determined with an applicator. These compounds were applied to a predetermined circle of 5 cm in diameter drawn on the flexor aspect of the upper forearm since this area is usually hairless and is convenient for the measurement of temperature and blood flow. The Eucalyptamint and the placebo were applied simultaneously on both forearms for 2 min continuously with circular massage of symmetrical pressure and constant speed by one of the researchers who was not involved in the measurement of temperature and blood flow and who randomly decided the side of forearm for application of Eucalyptamint or placebo. The researchers measuring the temperature and blood flow, and the subject were blind to the side on which the active agent was applied.

Experimental Protocol

All subjects were studied in an environmentally controlled room that had a constantly maintained and consistent room temperature (20–24°C), relative humidity (40–50%) and air speed (<0.1 M/s). The subjects were quietly resting in a seated position and exposed to the ambient conditions for a period of at least 15 min before commencement of any of the protocols. The study was performed at least 2 h after the ingestion of food or liquids.

Before the application of the Eucalyptamint and placebo (aqueous gel), the base-line cutaneous blood flow and skin and muscle temperatures were measured. The Eucalyptamint was then applied to the anterior upper forearm skin on one side, and the placebo was applied on the similar area of the other forearm as previously described. The cutaneous blood flow and skin temperature were measured at 5-min intervals for a period of 60 min after the application of these compounds. Muscle temperature was measured again 30 min after the application. The subject was also asked to describe his/her subjective feelings during the study period at 5-min intervals.

Subjective Perceptions

An assessment of sensory perceptions of temperature was conducted using a standardized scaling system as follows: 1 = cold; 2 = cool; 3 = slightly cool; 4 = no change; 5 = slightly warm; 6 = warm; 7 = hot.[15]

Measurement of Cutaneous Blood Flow

Cutaneous blood flow was measured by the state-of-the-art, laser-Doppler velocimetry method.[16] The noninvasive technique utilizes laser light that is delivered to and detected from the area of interest (i.e., skin surface) by flexible, graded index, fiber optic light wires (TSI Blood Perfusion Monitor, TSI Incorporated, St. Paul, MN). The Doppler-broadening of laser light scattered by moving red blood cells within the tissue is analyzed in real-time by an analog processor that provides a continuous output of instantaneous blood volume and the effective blood flow. A circular probe, 1.5 cm in diameter, was attached to the skin surface with a two-sided adhesive perforated disc to measure cutaneous blood flow on each forearm skin area of the subject. The unit of measurement is millimeters per minute per 100 g of tissue. It is a sensitive and reliable tool with a correlation coefficient of 0.88 as compared to xenon flow measurement.[16] It offers immediate measurement of flow in the steady state.

Measurement of Skin Temperature

Skin temperature was measured with a noncontact infrared thermometer (Meditherm, Everest Interscience, Tustin, CA). This device had an accuracy and resolution of 0.1°C and a response time of less than 0.5 s.[17] In this study, it usually took 1 to 2 s to obtain a steady reading for each measurement.

Measurement of Muscle Temperature

A specially constructed 25-G thermistor needle was used to measure muscle temperature. The design of this device was based on previous description and in consideration of the subject's safety and comfort.[18] The sterilized thermistor needle was inserted perpendicularly into the flexor digitorum superficialis muscle for a predetermined distance (10 mm). Particular caution was exercised to avoid punctures of the surface blood vessels. Resolution of the thermistor was ±0.004°C whereas accuracy was ±0.01°C.[19] In this study, the measurement was performed with needle inserted in muscles for 2 s.

Data Analysis

The numerical data of subjective perception, cutaneous blood flow and skin and muscle temperatures were averaged from all 10 subjects to obtain the mean and SD. Two-side analysis of variance (ANOVA) was applied to determine if there were any significant changes in subjective perception, cutaneous blood flow and skin temperature. Paired *t* test was used to test the significance of difference between the muscle blood flow at 30 min after Eucalyptamint application and the base-line data. A *P* value of less than 0.05 was considered as statistically significant.

RESULTS

Subjective Perceptions

The overall average of quantitative changes in subjective perception to temperature was not statistically significant based on ANOVA (Table 1). Five subjects (three male, two female) felt warm throughout the whole course of study; three subjects (all female) felt cool throughout the whole study; and two subjects (2 male) had either warm or cool feelings at different times of the study.

Cutaneous Blood Flow

As shown in Table 1, within 5 min after application of Eucalyptamint, the cutaneous blood flow had increased an average of about 4 times the baseline, and then decreased gradually until 45 min later and became statistically insignificant (based on ANOVA). There was a tendency of increases in cutaneous blood flow when the placebo was applied, but not statistically significant (based on ANOVA). For the individual subject, the peak increase in cutaneous flow in the experimental forearm ranged from 1.6 to 6.9 times above the baseline.

Skin Temperature

The average skin temperature was significantly increased as soon as 5 min after application of Eucalyptamint, and lasted until 45 min after application, based on ANOVA (Table 1). The average peak change in skin temperature was about 0.8°C higher than the base-line temperature 15 min after Eucalyptamint application. The peak change for the individual subject ranged from 0.1 to 1.9°C. The changes in placebo application were not significant.

Muscle Temperature

The muscle temperature was significantly higher 30 min after application of Eucalyptamint as compared to the base-line (paired *t* test; Table 1). The range of increases were from 0.1 to 1.1°C for the individual subject.

DISCUSSION

The results of this study demonstrated that local application of Eucalyptamint significantly increased cutaneous blood flow and skin and muscle temperatures over the area of application. Thus, Eucalyptamint may be used as an effective local counterirritant.

Massage itself may cause an increase in peripheral circulation and temperature of the skin.[20,21] From our study, it was found that there were minimal changes of skin blood flow from placebo application that were not statistically significant as compared to the application of Eucalyptamint (based on ANOVA). Therefore, all the changes observed in this study were related to Eucalyptamint itself rather

TABLE 1

Effects of Eucalyptamint on cutaneous sensation, cutaneous blood flow and skin and muscle temperatures

	Cutaneous Sensation		Skin Temperature (°C)		Muscle Temperature (°C)	Skin Blood Flow (ml/min/100 g)	
Time	Control	Eucalyptamint	Control	Eucalyptamint	Eucalyptamint	Control	Eucalyptamint
Baseline	4.0 ± 0.0	4.0 ± 0.0	31.3 ± 0.8	31.5 ± 0.7	34.99 ± 0.64	1.51 ± 0.68	1.64 ± 0.76
5 min	3.8 ± 0.0	4.3 ± 1.6	31.1 ± 0.9	32.2 ± 0.8*		2.27 ± 2.27	6.40 ± 4.56*
10 min	4.1 ± 0.6	3.6 ± 1.7	31.3 ± 0.9	32.2 ± 0.9*		2.42 ± 2.25	5.38 ± 3.27*
15 min	4.1 ± 0.3	4.2 ± 1.9	31.3 ± 0.8	32.5 ± 1.0*		2.01 ± 1.32	4.88 ± 4.04*
20 min	4.0 ± 0.3	4.1 ± 1.9	31.3 ± 0.9	32.2 ± 1.0*		1.98 ± 1.27	4.53 ± 2.77*
25 min	4.0 ± 0.0	4.2 ± 1.9	31.3 ± 0.9	32.2 ± 1.0*		2.03 ± 1.33	4.45 ± 2.46*
30 min	4.0 ± 0.0	4.3 ± 2.0	32.2 ± 0.9	32.1 ± 0.9*	35.39 ± 0.65*	1.78 ± 1.16	4.14 ± 1.93*
35 min	4.1 ± 0.0	4.2 ± 1.9	31.2 ± 0.8	32.1 ± 0.8*		1.69 ± 1.06	4.23 ± 1.67*
40 min	4.1 ± 0.3	3.8 ± 1.7	31.2 ± 0.8	32.0 ± 0.8*		1.58 ± 1.03	3.77 ± 1.77*
45 min	4.1 ± 0.3	3.8 ± 1.7	31.2 ± 0.8	32.0 ± 0.7*		1.60 ± 1.15	3.52 ± 1.33*
50 min	4.1 ± 0.3	3.7 ± 1.6	31.2 ± 0.8	31.9 ± 0.7		1.60 ± 1.10	3.36 ± 1.36
55 min	4.1 ± 0.3	3.6 ± 1.8	31.0 ± 0.8	31.7 ± 0.8		1.72 ± 0.99	3.34 ± 1.14
60 min	4.0 ± 0.0	3.6 ± 1.8	31.0 ± 0.7	31.6 ± 0.9		1.54 ± 0.84	3.41 ± 1.25

* $P < 0.05$, statistically significant compared to placebo or baseline (values are mean ± 1 SD).

than the effect of massage. This is consistent with a previous study on other types of counterirritant containing menthols and methylsalicylate.[17]

Due to the increase of cutaneous circulation from the effect of counterirritant, there is always a feeling of warmth in the area of application.[1] However, we were unable to find statistically significant quantitative changes in subjective feelings. It is likely that the cooling effect of menthol,[2] and/or the evaporation of the substances applied[22] may dilute the effect of the warming sensation.

Controversy exists as to whether medication applied locally to the skin has any effect on the deeper tissues. The intact skin has generally been considered to be impermeable to the passage of therapeutic substances from outside the body to the systemic circulation. However, under certain circumstances, the skin can be semipermeable to certain substances.[22–25] Recent studies on transdermal administration of analgesics[26,27] and topical application of local anesthetics[28] for pain relief are good examples to indicate skin absorption of externally applied drugs.

There are several explanations for the physiological action of counterirritant in pain relief. The first mechanism is that the stimulation of sensory nerve endings elicits a localized vasodilatation of the skin owing to axon reflexes,[1] or a vasodilatation in a remote area because of reflexes acting through the cerebrospinal axis.[1] Second, counterirritants may induce a summation of pain stimuli from the skin and reduce the pain generated in the remote area (such as muscle pain) either via the gate control theory,[29] or via the opioid-mediated analgesic system.[30]

The associated increase in tissue temperature as demonstrated in our study may play an important role in pain relief mechanism. In the therapeutic aspects, the relief of pain and inflammation may be effectively achieved through a local rise of temperature and increase in local blood flow as in the case of heat therapy.[14] The rate of firing of the group I-A afferents (large fibers) was increased by warming, but the majority of the secondary endings (smaller fibers) showed cessation of firing when heated.[31] Therefore, thermal stimulus may affect the pain sensation as explained by the gate theory of Melzack and Wall.[29]

Investigations of individuals performing exercise at various body temperatures have indicated that the ability to do physical work tends to be improved at elevated temperatures.[5,6,8–10] For this reason, most athletes incorporate some form of a "warm-up" procedure before engaging in more strenuous physical activity. Most of the physiological mechanisms of "warm-up" are temperature-dependent phenomena.[6,11–13,32] There are various types of warm-up techniques that can be used to increase local muscle and/or total body temperature in preparation for more strenuous activity. Active warm-up involved physical activity as opposed to passive warm-up which raises the body temperature by some external means such as diathermy, heating pads, steam baths and hot showers. A possible advantage of passive warm-up over active warm-up is that there is less of a possibility of impairing the subsequent exercise performance due to depletion of energy substrates because little or no physical activity is involved. The findings from our study suggest that local application of Eucalyptamint may be used as an alternative method for passive warm-up.

It was very difficult to obtain an absolutely blind study in this study as the subject might feel the temperature changes and might smell the eucalyptus oil from evaporation. The relative paucity of muscle temperature measurements on a single superficial site was another limitation in this study. These factors might limit the accuracy of our subjective measurement, but might not affect too much the objective measurements on temperature and blood flow.

In conclusion, local application of this new product, Eucalyptamint, on the forearm skin significantly increased the cutaneous blood flow and the skin and muscle temperatures, lasting for approximately 45 min. Based on these findings, it is suggested that Eucalyptamint may be beneficial for pain relief and/or useful to athletes as a passive form of warm-up. However, further study will be required to confirm its clinical applications.

ACKNOWLEDGMENTS

We wish to thank Dennis Hong for his involvement in the measurement of temperature in this study, and Phyllis Wood for her help in the preparation of the manuscript.

REFERENCES

1. Aviado DM: Dermatologic pharmacology, in: *Pharmacological Principles of Medical Practice.* Baltimore, Williams & Wilkins, 1972, pp 875–898.

2. Polano MK: Noncorticosteroid specific drugs, in: *Topical Skin Therapeutics.* New York, Churchill Livingstone, 1984, pp 50–100.

3. Polano MK: Basic materials for topical application, in: *Topical Skin Therapeutics.* New York, Churchill Livingstone, 1984, pp 12–23.

4. Collins PW: Antitussives, in Burger A (ed): *Medical Chemistry,* 3rd ed, volume II. New York, Wiley-Interscience, 1970, pp 1351–1384.

5. Asmussen E, Boje O: Body temperature and capacity for work. *Acta Physiol Scand* 1945;10:1–22.

6. Bergh U: Human power at subnormal body temperatures. *Acta Physiol Scand Suppl* 1980;478:1–39.

7. Malareki I: Investigation on physiological justification of so-called "warming-up." *Acta Physiol Pol* 1954;5:533–546.

8. Martin BJ, Robinson S, Wiegman DL, Aulick LH: Effect of warming up on metabolic responses to strenuous exercise. *Med Sci Sports Exerc* 1975;7:146–149.

9. Muido L: The influence of body temperature on performances in swimming. *Acta Physiol Scand* 1946;12:102–109.

10. Richards DK: A two-factor theory of the warm-up effect in jumping performance. *Research Quarterly* 1968;39:668–673.

11. Shellock FG: Physiological benefits of warm-up. *The Physician and Sportsmedicine* 1983;11:134–142.

12. Shellock FG: Physiological, psychological, and injury prevention aspects of warm-up. *Natl Strength Conditioning Assoc J* 1986;8:24–27.

13. Shellock FG, Prentice W: Warming-up and stretching for

improvement of physical performance and prevention of sports-related injuries. *Sports Medicine* 1985;2:267.

14. Lehmann JF, de Lateur BJ: Therapeutic heat, in Lehmann JF (ed): *Therapeutic Heat and Cold*, 3rd ed. Baltimore, Williams & Wilkins, 1982, pp 404–562.

15. Gagge AP, Stolwijk JAJ, Hardy JD: Comfortable and thermal sensations and associated physiological responses at various ambient temperature. *Environ Res* 1967;1:1–20.

16. Stern MD, Lappe DL, Bowen PD, Chimosky JE, Holloway GA, Kaiser HR, Bowman RL: Continuous measurement of tissue blood flow by laser-Doppler velocimetry. *Am J Physiol* 1977;232:H441–H446.

17. Shellock FG: Effect of a topically applied counterirritant/analgesic on skin blood flow. *Med Sci Sports Exerc* 1987;19:549.

18. Shellock FG, Swan JHC, Rubin SA: Muscle and femoral vein temperatures during short-term maximal exercise in heart failure. *J Appl Physiol* 1985;58:400–408.

19. Shellock FG, Rubin SA: Simplified and highly accurate core temperature measurements. *Med Prog Technol* 1982;8:187–188.

20. Skull CW: Massage—physiologic basis. *Arch Phys Med* 1945;261:159.

21. Wakim KG: Physiologic effects of massage, in Rogoff JB (ed): *Manipulation, Traction and Massage*, 2nd ed. Baltimore, Williams & Wilkins, 1980, pp 45–50.

22. Post BS: Effect of percutaneous medication on muscle tissue: an electromyographic study. *Arch Phys Med Rehabil* 1961;42:791–798.

23. Franz TJ: Percutaneous absorption on the relevance of in vitro data. *J Invest Dermatol* 1975;64:190–195.

24. Marks J, Rawlins MD: Skin diseases, in Speight TM (ed): *Avery's Drug Treatment: Principles and Practice of Clinical Pharmacology and Therapeutics*, 3rd ed. Baltimore, Williams & Wilkins, 1987, pp 439–479.

25. Polano MK: Model trials for the evaluation of topical drugs, in: *Topical Skin Therapeutics*. New York, Churchill Livingstone, 1984, pp 145–160.

26. Gourlay GK, Kowalski SR, Plummer JL, Cherry DA, Gaukroger P, Cousins MJ: The transdermal administration of fentanyl in the treatment of postoperative pain: pharmacokinetics and pharmacodynamic effects. *Pain* 1989;37:193–202.

27. Plezia PM, Linford J, Kramer TH, Iacono RP, Hameroff SR: Transdermal therapeutic system (Fentanyl) for postoperative pain: an efficacy, toxicity, and pharmacokinetic trial. *Anesthesiology* 1986;66:A210.

28. Hallen B, Carlsson P, Uppfeldt A: Clinical study of a lignocaine-prilocaine cream to relieve the pain of venepuncture. *Br J Anaesth* 1985;57:326–328.

29. Melsack R, Wall PD: Pain mechanisms: a new theory. *Science* 1965;150:971–979.

30. Fields HL, Basbaum AI: Endogenous pain control mechanism, in Wall PD, Melzack R (eds): *Textbook of Pain*, 2nd ed. New York, Churchill Livingstone, 1989, pp 206–217.

31. Mense S: Effects of temperature on the discharges of muscle spindles and tendon organs. *Plfugers Arch* 1978;374:159–166.

32. Bennett AF: Thermal dependence of muscle function. *Am J Physiol* 1984;247:R217–R229.