The Effects of BIOFREEZE® on Cutaneous Blood Flow in Normal Subjects as Measured by Doppler Ultrasound

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Abstract

Objective: To compare blood flow in cutaneous and subcutaneous tissue superficial to the deltoid muscle after an application of BioFreeze®.

Materials and Methods: Repeated-measures design in which blood-flow data was collected from subjects immediately before and at intervals following the application of BioFreeze®. 10 healthy adults with no impediment to the blood flow in their left deltoid, recruited through word of mouth and class-room announcements. A controlled quantity of BioFreeze® spray, 5 full pumps, was applied at a standardized distance of 6 inches from the skin of the participant. The area was then interrogated by power Doppler ultrasound imaging. Data was collected immediately before application, immediately after application, and at 1, 3, 5, and 10 minutes following the application of BioFreeze®.

Results: The BioFreeze® spray did not increase the amount of detectable blood flow within the cutaneous and subcutaneous layer as measured with power Doppler ultrasound to a statistically significant level relative to the baseline measures.

Conclusion: Cutaneous and subcutaneous blood flow is not altered by the topical application of BioFreeze® spray in the short-term.

Keywords: *cryotherapy, cutaneous blood flow*

Introduction

Soft tissue injuries and pain syndromes are commonly accompanied by inflammation. Various topical therapies have been employed in an attempt to minimize pain and enhance muscular strength and function following soft-tissue injury. These therapies, including the application of topical gels and sprays, have been employed by athletic trainers, physical therapists, chiropractors, and other health care providers in an attempt to minimize the injury and return the individual to full function as soon as possible.

BIOFREEZE® is currently classified as a "counter irritant," which is believed to reduce the sensation of pain via the Gate Control Theory by Melzak and Wall. Menthol, one of the primary active ingredient in *BIOFREEZE*®, has been found to control pain through the stimulation of cold receptors that are believed to control pain through the opioid or glutamate system[(1)]. Recent research has also indicated the blockade of sodium channels contributes to the efficacy of menthol as a topical analgesic[(2)]. Menthol has also been found to reduce blood flow and produce vasoconstriction similar to ice[(3)]. Ice, however, has been shown to inhibit strength, while menthol does not[(4)]. In contrast to the action of menthol, the isopropyl alcohol found in *BIOFREEZE*® acts as a vasodilator[(5)]. *BIOFREEZE*® also contains glycerin, which is most commonly known for its application in the treatment of myocardial infarction. Glycerin has also been shown to act as a vasodilator when applied topically[(6)]. Due to the conflicting nature of these substances the final effect of *BIOFREEZE*® on cutaneous blood flow is, at present, unknown.

Materials and Methods

The design of the study used repeated measures in which blood flow data was collected from subjects at 6 points. The data collection protocol was the same for the intervention applied to each patient. Before any data collection, subjects read and signed an informed consent and exclusion criteria form that were approved by the Logan College of Chiropractic institutional review board. After we obtained consent all subjects were informed of the nature of the intervention and data-collection protocol.

Ten healthy adults (3 men and 7 women) were recruited to participate in the study through word of mouth and classroom announcements. Subjects reported no health conditions that may have altered the blood flow in their left deltoid. Participants were excluded on the basis of the following criteria: any scars, rashes, or other skin lesions of the area of inspection; any diagnoses vascular disorder, skin disease, or systemic disease; allergy to latex; any allergy or previous negative reaction to menthol, glycerin, or isopropyl alcohol; or pregnancy. Participants were also required to be between the ages of 20 and 45 years.

Subjects reported to the radiology laboratory and were placed in a seated position with their left deltoid bared. The subjects received application of 5 full sprays of BioFreeze® (Hygenic Corporation, Akron, OH) spray from a distance of 6 inches from the patient's skin surface overlying the deltoid. Cutaneous blood flow was assessed by power Doppler ultrasound with GE Logiq e (GE Healthcare, Milwaukee, WI) ultrasound machine immediately before the application of BioFreeze® and again immediately afterwards. Further data-collection was performed at 1, 3, 5, and 10 minute intervals following the application of BioFreeze®. A still frame file of the ultrasound was collected at the specified data-collection intervals and was analyzed. The number of vascular foci was counted per image and was recorded as the measure of vascular activity.

The application of BioFreeze® was from a standard 4 oz. spray pump bottle. Prior to applying the intervention to each participant BioFreeze® was applied to one 8.5 in. X 11 in. sheet of standard ($75 g/m^2$) Universal Copy Paper via the same 4 oz. fluid spray pump bottle. 5 full pumps were applied to the paper from a distance of 6 inches. Pre- and pos- spray weight of the paper was measured by a Denver Instrument XP-300 scale (Denver Instruments, Bohemia, NY) to measure the amount of BioFreeze® applied via this method. The average amount of menthol gel applied via the spray pump bottle was 0.01025 oz with a range of 0.0045-0.012 oz.

Pre-spray paper weight (oz)	Post-spray paper weight (oz)	Difference (amount of BioFreeze®) (oz)
0.1650	0.1735	0.0085
0.1665	0.1780	0.0115
0.1680	0.1790	0.011
0.1655	0.1700	0.0045
0.1620	0.1745	0.0125
0.1660	0.1780	0.012
0.1670	0.1780	0.011
0.1635	0.1720	0.0085
0.1680	0.1800	0.012
0.1695	0.1805	0.011

Means and standard deviations of the pixel-bsed Doppler measurements at baseline, immediately after application, and at the 1, 3, 5, and 10 minute intervals were calculated. A Kolmogorov-Smirnov test was performed to assess the normality of the data. The distribution being normal, a Wilcoxan signed-rank test was used to assess the differences of the means of the pre-(baseline) and post-intervention (immediate, 1, 3, 5, and 10 minutes post application) measurements.

Results

A Kolmogorv-Smirnov test revealed the data to be normally distributed. The mean number of vascular foci measured before the application of BioFreeze® was 2.6 foci per image (SD 1.3, range 0-4). Immediately post-application the mean was 2.2 (SD 1.8, range 0-4). At 1-, 3-, 5-, and 10-minute intervals, the mean number of vascular foci was 2.4 (SD 1.1, range 1-5), 2.5 (SD 1.4, range 1-5), 2.8 (SD 1-5, range 1-6), and 2.1 (SD 1.3, range 1-5), respectively. Statistical analysis using a paired t-test comparing the baseline data with the immediately post-application data, 1 minute post-application, 3 minute post-application, 5 minute post-application and 10 minute post-application revealed p-values of 0.48, 0.59, 0.61, 0.64, and 0.24, respectively. There was no statistically significant difference between the baseline data and any subsequent timepoint.

Discussion

The results of this study stand in contrast to previous studies that have found menthol to act as a vasoconstriction agent[(3)], as well as the vasodilatory action demonstrated by isopropyl alcohol[(5)] and glycerine[(6)]. Our study indicates that the conflicting vaso-active nature of these active ingredients rescind the effects of one another when applied in combination.

The lack of constrictive effect of as BioFreeze® on blood vessels may contribute to an acute inflammatory process. Inflammation is a natural part of the healing process. When left uncontrolled, however, the inflammatory process can contribute to increased pain, delayed healing, and future disability. It is, therefore, recommended that the application of BioFreeze® be used with caution when considering acute injuries and syndromes accompanied by inflammation.

Ice has long been used to reduce the inflammatory component of soft-tissue injuries and pain syndromes, as well as reduce the pain associated with such injuries. While our study shows that the application of as BioFreeze® will not effectively address inflammation, recent studies have demonstrated that menthol-based analgesic's, such as BioFreeze®, decreased perceived discomfort to a greater extent than ice. Additionally, the constrictive effect of ice restricts the tetanic forces a muscle is able to produce, a quandary not produced by topical analgesic[(7)]. This, in combination with the offsetting vasoactive properties of the active ingredients of BioFreeze® make it ideal for application to soft-tissue injuries when continued performance is still possible or necessary. BioFreeze® would also be beneficial in sub-acute and chronic conditions where the goals of treatment transitions from reducing inflammation and promoting anatomical rest to that of restoring function and reducing painful intolerances.

It is recommended that future investigation focus on the ability of BioFreeze® to act as an aid in the restoration functional movement, circumvention of fear avoidance patterns, and reduction in pain perception.

Conclusion

Cutaneous and subcutaneous blood flow is not altered by the topical application of BioFreeze® spray in the short-term.

References

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