

A Pilot Study Using Blood Biomarkers and Physiological Parameters to Assess ThermaCare Heat Wraps for Efficacy and Timing of Application to Reduce Delayed Onset Muscle Soreness from Exercise

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ABSTRACT

Muscle soreness is a problem after exercise and controversy exists on when is the best time to apply heat. A pilot study was performed on 20 young healthy subjects to determine whether no heat (C) or the addition of therapeutic heat (8 hrs ThermaCare heat wrap) applied either immediately (I), after 24 hrs (24), or both times (I24) is most effective for decreasing muscle soreness and the associated muscle inflammatory biomarkers after a biceps' exhausting exercise. Soreness was least in group I24 and greatest in group C. I was second best for reducing soreness and the application 24 group, while less effective, was still better than group C. Comparing data at rest and at 72 hours post-

exercise, all subjects showed approximately a 10% reduction in plasma volume, as measured by Hct. For all groups of subjects, there was an increase in skin temperature 24 hrs after the exercise. But group I and group I24 had more than five times the increase in skin temperature at 24 hrs post-exercise, showing a large carry over effect of heat applied after exercise when muscles are sore. The analysis of the biomarker analytes (HSP 27, Myoglobin, CK, and LDH) plus data showing lower granulocyte count appears to support a hypothesis of more rapid and faster healing in muscle when heat was used after exercise. Ultrasound data showed swelling in the fascia above the muscle in group C and much less in the other groups. In conclusion, although this pilot feasibility study was conducted on a limited group of subjects it provides suggestive evidence that

when heat is applied immediately to the area of the body above the muscles exercised, there is a reduction in muscle soreness and an apparent acceleration in the healing process compared to no heat application.

INTRODUCTION

Delayed onset muscle soreness (DOMS) is a common phenomenon to anyone who rarely exercises or suddenly exercises extensively.¹ It can even occur in athletes who increase their activity above that which they normally engage.² DOMS generally presents as initial soreness that starts within 24 hours of heavy exercise, and whose symptoms can range from slight muscle tenderness to muscle stiffness or severe debilitating pain.³⁻⁵ The severity of the symptoms depends on several factors including the fitness of the individual, age, genetics, training, and intensity of the activity.⁶ The associated with muscle soreness, which can start 3 hours post-exercise, is an elevation in blood biomarkers such as HSP- 27, HSP -70, IL-6, muscle myoglobin, CK, LDH, and IL-10.⁷⁻¹¹ All of these biomarkers, which are measured in blood serum or plasma, are indicators of muscle damage. Depending on the age of the individual and the exercise, the peak discomfort from muscle damage ranges between 24-72 hours post-exercise, but the symptoms may continue as much as 7 days post- exercise.¹²

While DOMS has been poorly studied in people with diabetes, the effects of aging on muscle soreness has been investigated.¹³ DOMS is greater in older than younger individuals, as is the muscle damage associated with even a single bout of exercise.¹³⁻¹⁶ Evidence is that there is reduced proteolytic activity and an elevated production in free radicals in older individuals.^{13,16} This elevated muscle damage prolongs healing time after excessive exercise.¹³ With metabolic impairment and higher levels of free radicals in people with diabetes,¹⁷ DOMS should be even more severe in this population.

Many different types of therapies have been used to reduce delayed onset of muscle soreness. The most common of these is heat.^{4,18}

Heat has been used for thousands of years to relieve the pain from muscle soreness. While pain relief is often cited with heat therapy, increases in tissue healing rates have been poorly quantified. Heating the skin or even the deep tissue relieves the symptoms of muscle soreness.¹⁹ This is due to the effect of heat on voltage-gated calcium channels called Transient Receptor Potential Vanilloid (TRPV1 and TRPV4) channels.^{20,21} These channels are present throughout the skin sensory nerves and vascular endothelial cells.²¹ In response to heat, these channels increase calcium influx into the tissue that they are in.^{22,23} This intracellular increase in calcium inactivates P2X2 purine pain receptors so that heat is associated with a reduction in pain in damaged tissue.^{24,25} The actual pain response associated with tissue damage, especially in deep tissue, is mediated by release of bradykinin and histamines.^{26,27} This then activates P2X2 pain receptors in free nerve endings.

However, blocking pain through heat and other modalities such as Capsaicin²⁸ or menthol²⁹ relieves pain but may or may not promote healing. Blocking pain is a different mechanism than increasing healing rates in tissues.

When muscles are damaged, enzymes and proteins that are normally in muscle and not in the blood such as CK, skeletal muscle LDH, myoglobin, and HSP- 27, HSP -70, IL-6, and IL-10, are found in dose response related levels in the blood.^{7,10,19} Studies that have co-related delayed onset of muscle soreness to these biological markers show a strong correlation between the time course and the intensity of the discomfort and the elevation of these biomarkers in the blood.^{7,8} However, almost no studies have co-related the use of heat, especially thermo-care products, to the onset and magnitude of these biomarkers. The advantage of using blood biomarkers is that unlike subjective pain measurements, which can be altered by heat and menthol and other analgesics, they actually provide very useful information relative to the "time course of the healing process."

Table 1: Control group

	Age(years)	Height (cm)	Weight(kg)	% bf	BMI
Mean	16.51	111.83	48.27	19.58	16.89
SD	13.32	91.33	23.34	9.16	9.65

Table 2: Subjects with heat applied after 24 hours only

	Age(years)	Height (cm)	Weight(kg)	% BF	BMI
Mean	25.40	168.30	71.33	29.60	24.99
SD	2.30	11.67	14.85	7.02	3.12

Table 3: Subjects with heat applied immediately and 24 hours later

	Age(years)	Height (cm)	Weight(kg)	% BF	BMI
Mean	23.40	167.42	64.66	29.18	23.08
SD	0.55	4.24	6.43	6.35	2.30

Table 4: Subjects with heat applied immediately only

	Age(years)	Height (cm)	Weight(kg)	% BF	BMI
Mean	25.80	165.36	74.52	34.26	27.29
SD	3.11	7.85	6.89	7.69	2.29

In the present proposal, we used ThermoCare heat wraps in three different paradigms: one, in which the heat wrap is placed on immediately after the exercise; two, when the heat wrap is placed 24 hrs after the exercise; and three, when ThermoCare heat products are used immediately after and 24 hours post-exercise. The outcome measures were blood CK, LDH, myoglobin, HSP-27, and ultrasound (US) pictures of the muscle assessing the changes in muscle edema and muscle damage.

SUBJECTS

The subjects for this study were 20 healthy individuals between the ages of 20 and 40 years of age. All of the subjects had at least 6 weeks of physical inactivity in the upper body, and their BMI was less than 40. Subjects had no cardiovascular disease, hepatic diseases, were not diagnosed with Rhabdomyolysis, had any recent upper limb injuries, upper limb neuropathy, blood pressure over 140/90 mmHg, or lower than 90/60 mmHg, were not on high doses of alpha or beta agonist/antagonists, or took

any types of NSAID's, Cox 2 inhibitors, calcium channel blockers, pregabalin (ie, Lyrica), or pain reducers. The demographics of each group of subjects are listed on Table 1-4. All methods and procedures were approved by the institutional review board, and all subjects signed a statement of informed consent. The general characteristics of the subjects are listed below.

METHODS

Blood Sampling

Approximately 10 ml peripheral blood was collected from an antecubital vein using a disposable needle and vacutainer for serum or plasma EDTA. Peripheral venous blood was drawn before (Pre), immediately after (Post), and 3 hrs, 24 hrs (1 d), 48 hrs (2 days), and 72 hr (3 days) after each exercise bout. The blood was placed in a refrigerated centrifuge and spun down at 3,000 rpm for 10 min to separate serum or plasma from the cells. The samples were stored at -80°C until analyses of CK, LDH, Mb, and HSP-27 (tissue stress/shock proteins) could be assessed.

Measurements of CBC and Hct and

Plasma Biomarkers

A three part CBC differential and Hct were measured on the Mindray (Mindray North America, Mahwah, NJ) automated blood cell analyzer. Plasma CK and LDH activity were measured spectrophotometrically using test kits on the Mindray BS-120 discrete and random access Clinical Chemistry Analyzer (Mindray North America, Mahwah, NJ). For the measurement of plasma Mb, and HSP-27, commercially available enzyme-linked immunosorbent assay (ELISA) kits were used according to the manufacturers' instructions. Plasma Mb was determined by an ELISA assay on a 96 well plate format from CalBiotech (CalBiotech, Spring Valley, CA). HSP-27 plasma levels were determined by ELISA assays on a 96 well plate format from Ray Biotech (Ray Biotech, Norcross, GA). For all ELISA assays, the absorbance will be measured spectrophotometrically with an ELISA microplate reader (MTX Lab Systems, Multiscan MCC 340, McLean, Virginia) and the concentration of each plasma analyte/substance, with an optimal standard curve "fit", was dose interpolated from the derived calculated dose response curve established within the same assay performance time interval. The Elisa kits were

HSP 27: RayBiotech #ELH-HSP27-001

Myoglobin: CalBiotech #MG017C

And for CK, LDH on the Mindray BS 120 machine the reagents, were from Pointe Scientific, Inc

CK #12-C7522-100

LDH #12-L7572-100

Measurement of Skin Temperature

Skin temperature was measured by a Flir 650 thermal imager (Flir Systems, Boston, MA). The temperatures were measured from four locations on the skin above the biceps muscle.

Body Fat Determination

Body fat was determined by electrical impedance with an RJL Systems Quantum X Bioelectric Impedance Analyzer (Minneapolis, MN). The unit measures resistance

and reactance with 0.1 ohms of resolution. Four electrodes are placed on the body, two source electrodes on the hand and foot and two recording electrodes on the hand and foot. The system places, through the source electrodes, a current of approximately 0.1 milliamps at 100,000 cycles per second frequency with a sine wave. The recording electrodes then record the signal transmitted through the body and use this to calculate body fat content to software provided by RJL Systems. The Quantum x, with the multiplexed BIA cable allow multi-zone and segmental measurements to be taken quickly and easily in 26 segments to calculate body water and body fat.

Determination of Fat Thickness

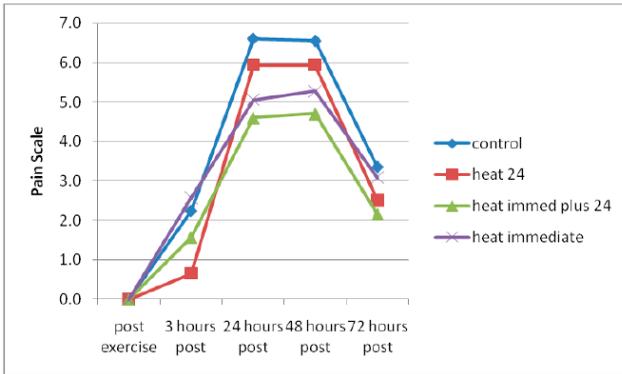
Subcutaneously

Subcutaneous fat thickness was determined with a 2D-3D high resolution ultrasound (Mindray M7, Duluth, GA). The ultrasound head uses a L34 head with a 1 cm standoff. By using the unit at a frequency of 10 MHz through the 1 cm standoff, the thickness of the skin and subcutaneous fat layer can be measured. One investigator did all measurements on all subjects.

Muscle Strength

Muscle strength was determined with a strain gauge transducer. The strain gauge transducer involved four strain gauges placed on opposite sides of a steel bar. When the bar was bent, the strain gauges, arranged as a Wheatstone bridge, were deformed and an electrical output was provided. The power source of the Wheatstone bridge was provided by a BioPac (BioPac Systems, Goleta, CA) system DAC100 bioelectric amplifier module. The signal, amplified 5,000 times, was then digitized through a BioPac MP150 analog to digital converter at a resolution of 24 bits and a frequency of 1,000 samples per second and stored digitally for later analysis. Data analysis and storage was accomplished on Acknowledge 9.1 software from BioPac (BioPac Systems, Goleta, CA). Strength was determined on three occasions with each contraction being 3 seconds in duration

Figure 1: Average soreness in the 4 groups of subjects over the 3 day period.



and at least 1 minute separating the contractions. The average of the three measurements was the maximum strength.

Analog Visual Scale

A 10 cm visual analog scale was used. It is a horizontal line across a piece of paper 10 cm long. One end was marked “pain free” and the other “very sore.” The subject was asked to place a vertical slash across the line where appropriate.

The Exercise

The subjects participated in the same exercise to induce the DOMS. The targeted muscle for this study was the biceps brachii (the elbow flexors). To provoke DOMS in this muscle, the subjects carried out four sets of 25 biceps curls against resistance until failure (fatigue). The resistance used was different for each subject. This was determined by testing each participant for their maximum strength (RM). To do this, we used a strain gauge device, to measure muscle strength as outlined above. The dynamometer was fixed to a bench at a 45° angle, so that the subject could not recruit any muscle other than the biceps. They determined their RM for the biceps muscle of the chosen arm, and to get a moderate intensity exercise out of each subject we made them sustain the intended session of exercise with 35% of their RM calculated as the average of the three strength recordings.

PROCEDURES

Four groups of subjects participated. One

group exercised but did not have heat applied after exercise. A second group exercised and had heat applied immediately for 8 hours with ThermaCare heat wraps. A third group did not have heat applied until 24 hours and then for 8 hours. A fourth group had heat applied immediately and at 24 hours. Exercise was conducted as described under methods and the blood drawn up to 3 days and analyzed for muscle damage biomarkers specified under methods. At the same

time, the subjects were asked to show on a scale how sore they were and, if heat was applied, the scale was repeated after the heat was removed.

DATA ANALYSIS

Statistical analysis involved the calculation of means, standard deviations, related and unrelated t tests, and analysis of variance. The level of significance was $p \leq 0.05$.

Blood analytes were measured and corrected for changes in serum volume. This was accomplished by first correcting the hematocrit from venous blood to the true whole body hematocrit by multiplying the venous hematocrit by 0.873.30 The change in plasma volume after the first day was then calculated to correct for any shifts in plasma volume impacting the concentration of analytes in subsequent measures.30 The formula was

$$Ca = (Hct2 (100 - Hct1)) / Hct1 (100 - Hct2)Cb$$

Where

Ca = Final analyte concentration
HCT1= hematocrit on the control day

HCT2= hematocrit on the test day

Cb = analyte test concentration

RESULTS

Strength

The average strength of the subjects was 11.8+/-3.3 Kg. There was no statistical difference in the strength between the FOUR

groups of subjects ($P>0.05$). When accomplishing the exercise bouts, there was variability in how many lifts the subjects could accomplish before they were fatigued, even though they all exercised at the same percent of their maximum strength. For the four groups, the average number of lifts that could be accomplished was 77.2 ± 21.9 , giving a coefficient of variation of 28.3% among the group. The number of repetitions decreased with each bout. For example, the first bout averaged 24.5 ± 1.1 out of 25 possible reps, but by the third bout, the average number of repetitions was 16.9 ± 7.1 out of 25 possible repetitions.

Soreness

After 3 hours, the average soreness for the group was small, averaging 1.76 ± 1.0 out of 10 points where 10 is very sore. After 24 hours, the average soreness was 5.6 ± 0.9 out of 10 for all of the subjects. After 48 hours, it averaged 5.6 ± 2.1 on a 10 point scale for the group. At 72 hours, it was 2.8 ± 1.3 on a 10-point scale. Of the three groups using heat, the least soreness was in the group that used heat immediately and at 24 hours. The average soreness for each group is shown in Figure 1. Soreness was

greatest in the control, (no heat group), and least in the group where heat was applied immediately and heat after 24 hours group. Heat applied immediately after exercise was second best for reducing soreness and heat at 24 hours, while less in effect, and was still better than control no heat data.

Skin Temperature

Skin temperature was assessed at four locations with the Flir IR imager. From these measurements, the individual regions were analyzed as to the average temperature for each region and, by averaging the four regions, the temperature for the entire palmer surface of the upper arm.

As shown in Tables 5 and 6, there was a disparity in the skin temperature by each region. For the whole limb (Table 5), temperature actually decreased at 24 and 48 hours while it increased at 3 hours in all groups of subjects. However, when looking at the region just over the belly of the biceps, (Region 3, Table 6), the muscle temperature increased at 3 and 24 hours and reduced at 48 hours for all subjects.

Interestingly, the greatest increase in skin temperature was for the groups that had heat applied immediately after the exercise.

Table 5: The change in skin temperature compared to the resting data at 3, 24 and, 48 hours post exercise in the four groups of subjects. Each point is the mean of five subjects for all regions.

	3 hours	24 hours	48 hours
control	0.01	0.23	-0.12
heat at 24	1.23	0.51	0.83
heat immediate plus 24	0.96	1.26	-0.49
Heat immediately	1.57	0.84	-0.66

Table 6: The change in skin temperature compared to the resting data at 3, 2,4 and 48 hours post exercise in the four groups of subjects. Each point is the mean of five subjects for region 3.

	3 hours	24 hours	48 hours
control	0.20	0.38	-0.26
heat at 24	1.48	1.44	0.92
heat immediate plus 24	-0.60	3.54	-0.96
Heat immediately	1.32	2.92	-0.98

Figure 2: Average skin temperatures in region 4 for each group of 5 subjects.

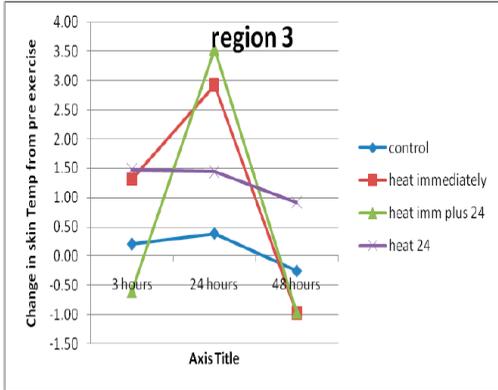
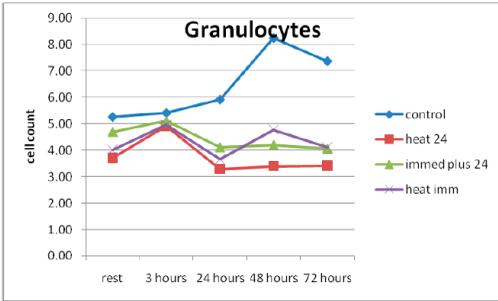


Figure 4: The granulocyte cell count in the venous blood at rest, 3 hours after exercise, 24, 48 and, 72 hours post exercise in each of the groups of subjects as a mean response of the group.



Here the average skin temperature 24 hours after the exercise was over 30 centigrade compared to the average of the other two groups of about 10 centigrade compared to the pre-exercise resting skin temperature. This is shown graphically in Figure 2 for region 3 as an average for all subjects in each group.

Comparison of soreness to increase in skin temperature

Although the groups were small, when pooled, for example, at 24 hours, there was no correlation between soreness and skin temperature in region 3. However, since all four groups had different heat protocols, this pooling negates the changes. The correlation between soreness and skin temperature at 24 hours post-exercise in group 1 and 2

Figure 3: Corrected plasma volume in the subjects showing the average for all four groups for 72 hours post exercise.

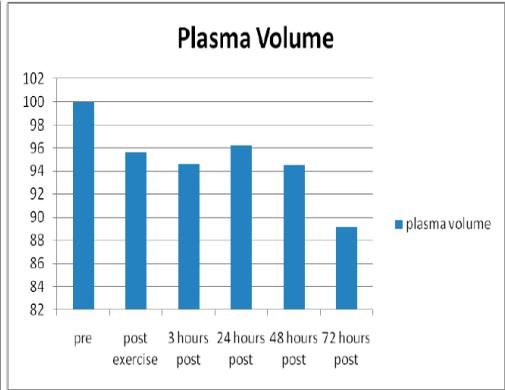
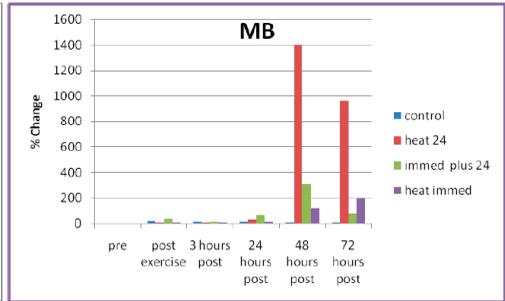


Figure 5: Average blood myoglobin in the 4 groups of 5 subjects up to 72 hours normalized as a percent change from the resting values.



was not significant. In the 2 groups that received heat immediately, there was a significant correlation for either the heat immediately group ($r=-0.62$), immediately plus 24 group ($r=-0.77$) or the combined 10 subjects examined together ($r=-0.74$). Thus with heat use immediately after the exercise, the greater the increase in skin temperature at 24 hours post exercise, the less the soreness. This carry over effect of sustained skin temperature after 24 hours seems to be a good thing since the greater the skin temperature, the less the muscle soreness.

Hematocrit and plasma volume

Hematocrit was corrected to true body hematocrit, and from this measure, the plasma volume was calculated to correct the concentration of the analytes. All four groups

showed a reduction in hematocrit over the 3 days after the exercise. This reduction was significant ($p < 0.01$). From the change in hematocrit, the change in plasma volume after exercise was calculated and is shown in Figure 3.

White Cells

The white cell count at rest and post exercise in a 3-part differential was done. White cells respond to tissue damage as an aid to tissue repair by increasing in concentration with cellular damage.³¹ The highest white cell count was in the control subjects for total white cells. Here white cells increased throughout the test period, showing muscle signaling of damage. Total white cells actually dropped or stayed constant in the heat groups.

Mid-range white cells, monocytes, eosinophils, and basophils, were not different between the heat groups but increased dramatically in the control, non-heat group.

Granulocytes were not different in the heat groups or the control group at 24 hours, but then increased to almost double the value of the other three groups in the control group as shown in Figure 4.

Blood Biomarkers

Myoglobin

The normal range of myoglobin is between 0 and 85 nanograms per milliliter of blood. It shows damage to heart or skeletal muscle.³² The average myoglobin at rest was 28.8 ± 6.9 nanograms per milliliter for these subjects (all 20), well within reference range. There was no difference in the groups until 48 hours post-injury. Here, myoglobin jumped to 516 ± 422 nanograms per milliliter in the group that only had heat at 24 hours, whereas there was a smaller increase in the heat 24 and heat immediate group but still an increase above baseline values. The smallest increase was in the heat immediate group of the three heat groups. Myoglobin was falling back toward normal at 72 hours post-exercise. Figure 5 shows the myoglobin for the four groups normalized to the baseline value. As seen from the normalized values, the heat at 24 hours group had the

largest increase in myoglobin.

LDH (Lactic Acid Dehydrogenase) is an enzyme found in all tissues in the body. A high level in the blood can result from a number of different diseases.³³ Also, slightly elevated levels are associated with damage to skeletal muscle.³⁴ For example, when someone has a heart attack, blood levels of total LDH will raise within 24 to 48 hours, peak in 2 to 3 days, and return to normal in 10 to 14 days. Normal blood values are up to 200 mg per liter of blood. Here, all subjects started in the normal reference range. The resting value for the group of 20 subjects was 140.5 ± 26.7 mg per liter. The only clinically significant increase was in the heat at the 24-hour group where it increased at 72 hours to 233 ± 48 mg per liter. There was also an increase at 72 hours in the heat immediate plus 24 hour group at 72 hours but the value was still in the normal clinical reference range. The control group showed no increase in LDH over the 72 hour period as did the heat immediate group. These data are normalized and shown in Figure 6 as a percent of the resting values.

Creatine Phosphokinase (CK)

Blood levels of CK rise when heart cells are injured. It reaches its highest level in 18 to 24 hours and returns to normal within 2 to 3 days.³⁵ The amount of CK in blood also rises when skeletal muscles are damaged. People who have greater muscle mass have higher CK levels than those who don't, and African-Americans may have higher CK levels than other ethnic groups. Very heavy exercise (such as in weight lifting, contact sports, or long exercise sessions) can also increase CK. The normal range is 21-220 nanograms per milliliter. Thus, at rest, the 20 subjects average 120.2 ± 28.2 and well within normal range. CK stayed fairly constant in the control group peaking at 183 at 3 hours and then slowly coming back to normal. In the heat immediate group, CK increased at 48 and 72 hours. The greatest increase was in the heat at 24 hour group with the heat immediate plus 24 hour group falling in the middle. For the heat 24 hours

group, CK increased to 3280 nanograms per at 72 hours. These data are shown normalized in Figure 7.

HSP 27

The results of the HSP27 measurements are shown in Figure 8. As shown in the Figure, HSP27 peaked at 24 hours for all groups of subjects. It was higher in the heat groups but not to a large extent. By 72 hours, it was back to normal. It did seem to be an excellent index of delayed onset muscle soreness. The people who were the sorest at 24 hours had the smallest HSP27 (correlation -0.4). It would seem that HSP27 shows faster healing and less soreness. This would explain why it is higher in the three heat groups since, a high level seems to imply protein transcription and healing.

ULTRASOUND IMAGING

The results of the use of ultrasound imaging to assess changes in muscle structure post-exercise are typified in Figures 9 and 10. Ultrasound imaging at a frequency of 10 million cycles per second on the Mindray M5 ultrasound showed a distinctive difference between the control and the groups where heat was applied. In the control exercise group, as shown in Figures 9 and 10, comparing pre-exercise to post exercise at 48 hours, a thickened band appeared in the fascia subcutaneously and just above the muscle (see orange arrow in the picture). This is consistent with edema and damage to the facial layers. In contrast in subjects who had heat applied on the skin above the biceps muscle 24 hours after exercise there was little swelling. Facial damage is often related to over exertion and a cause of muscle pain.

In the groups of subjects that had heat applied immediately or immediately and 24 hours post- exercise, no swelling at all was seen.

DISCUSSION

The standard treatment suggested by athletic trainers after heavy exercise is the application of cold for 24 hours followed by heat.^{4,9,36} Heat is then used later to reduce

Figure 6: Average blood myoglobin in the 4 groups of 5 subjects up to 72 hours normalized as a percent change from the resting values.

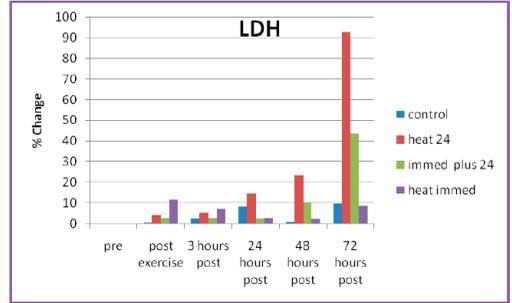


Figure 7 Average blood CK in the 4 groups of 5 subjects up to 72 hours normalized to the resting values.

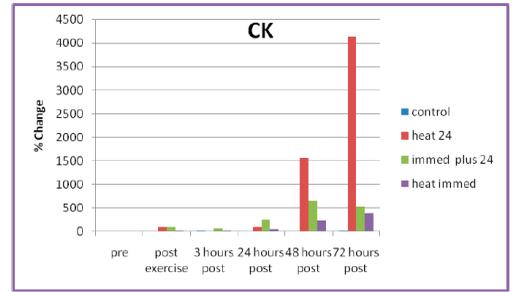
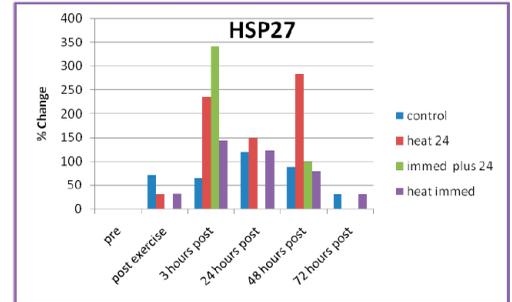


Figure 8: Average blood HSP27 in the 4 groups of 5 subjects up to 72 hours



soreness and increase healing.^{4,37,38} However, several recent studies have examined this concept and found that, in large clinical trials, unless a joint such as the shoulder joint was involved, there was no evidence that there was any advantage using cold after exercise to prevent or reduce delayed onset muscle soreness.^{4,37,38} In these studies, cold appears to have no positive effect on soreness at all. However, these same studies do show that heat, at the end of the exercise,

seems to increase range of motion and reduce soreness.^{4,37,38}

In the present investigation, heat applied immediately after the exercise in 10 subjects reduced muscle soreness at 24, 48, and 72 hours. Further, when heat was used just after exercise, there was a carryover such that at 24 hours, the skin temperature was elevated by 30 centigrade even 24 hours later, 16 hours after the heat packs were removed. Thus it appears that the heat packs still had an effect a full 24 hours after application, if the muscles were initially sore. Further, the warmer the skin temperature was at 24 hours, the less there was of soreness. Heat reduced facial edema in the heat groups compared to the control subjects. Certainly, it is not the skin that caused the heat to be elevated 24 hours post-exercise in the subjects where heat was applied just after exercise. Skin is a shell tissue and its temperature is usually about 6 degrees less than that of the core.³⁴⁻⁴³ The skin must be kept cooler than the core so

Figure 9: Ultrasound image of the biceps muscle before exercise in a control subject



that heat can move from the core to the skin and be removed by radiation, convection, conduction, and evaporation.³⁹⁻⁴³ This allows core temperature to be maintained at a regulated level.⁴⁴⁻⁴⁹

When individuals exercise, their muscles generate heat and, as a result, the overlying skin is warmed by the conductive heat exchange. This is predicted by the Pennes model.⁴⁸⁻⁵¹ Heat moves from the muscle both into the blood perfusing muscle and is dissipated throughout the body and also

flows to the cooler skin area.^{40,48,50,51} Muscle, like skin, is a shell tissue and, while it is warmer than the skin, it is still usually 3-40 centigrade less than core temperature.^{42,43,48,49}

Therefore, if muscle blood flow remained elevated post-exercise, the warmer core blood would keep the muscle warm and hence the overlying skin would stay warm. Even tumors under the skin have this effect and therefore form the basis for thermal imaging of breast tumors.⁵²

Figure 10: Ultrasound image of the biceps muscle 48 hours after exercise in a control subject



The elevated skin temperature 24 hours post-exercise in all subjects is probably due to higher blood flows in muscle due to inflammation from the exercise and repair of tissue damage. But if heat was applied just after exercise, the skin temperature was substantially higher than that seen without heat application when assessed at 24 hours. There seemed to be a large carryover increase in muscle circulation that lasted over 16 hours after the heat pack was removed. The fact that areas of the skin not above the muscle had no carryover effect also supports the idea that the heat is generated in the muscle. If it was the skin, all four areas would be warmer 24 hours post-heat application. The effect of the carryover seems to be that increased heat and circulation allowed the muscle to heal faster. The evidence for this is that first, the greater circulation would wash metabolites from muscle, and second, increased circulation should promote faster healing. Data collected here shows a greater washout of CK, LDH and myoglobin from muscle with heat. This is also seen in the white cell count. Elevated white cells in the control subjects point to prolonged tissue damage, the tissue recruiting granulocytes to mediate the damage. This was not seen in the heat groups where granulocyte counts remained low. Blocking inflammation and pain alone with ibuprofen reduces the cytokine response but does not increase healing³¹. Here, healing appeared to improve. The ultrasound images also show less damage and edema with heat compared to the controls.

These preliminary data suggests that there is more expedient healing and less pain with heat application immediately after exercise. However, limitations must be noted with this pilot feasibility study:

- 1) The study cohorts were five subjects per group and as such that there needs to be a larger N per group so as to enhance statistical power to appropriately support these preliminary findings and further substantiate the hypothetical claims.

- 2) This is evident in the cytokines data where there is wide variability between subjects. A larger N per group would reduce this variance to more a more normally distributed data set, thus allowing for more appropriate use and acceptance of statistical parametric analysis.

- 3) Although convenient for a pilot feasibility study, the single muscle group used was very small. A more significant enhanced response would be obtained with exercise that involves a larger body muscle mass such as both biceps or large muscle groups in the legs or lower back. This would be more realistic and representative of everyday true life exercise experience.

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