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ORIGINAL ARTICLE

Comparing the effect of heat and cold therapy on the intensity of nitrate-induced migraine type headache in cardiac inpatients: A randomized controlled trial

Kalp hastalarında ısı ve soğuk terapinin nitrogliserine bağlı migren tip baş ağrısı şiddeti üzerine etkilerinin karşılaştırılması: Randomize kontrollü bir çalışma

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Summary

Objectives: This study aimed to compare the effect of heat and cold therapy on the intensity of nitroglycerine-induced migraine type headache in cardiac inpatients.

Methods: This randomized controlled trial was conducted on a total of 75 cardiac inpatients in three groups design (heat or cold therapy and control group) as pre-test and post-test. Patients in the intervention group received heat or cold therapy for 25 min, 2 times (at 1 h interval), patients in the control group did not receive any heat or cold therapy. Headache intensity was measured by the numeric rating scale for pain, in three groups of study for 3 times (just before the study, at the end of applying the first therapy, and at the end of applying the second therapy).

Results: No baseline differences existed among the three groups for the mean pain scale score (p=0.781) just before the study; but the difference between three groups after applying heat and cold therapy was statistically significant (p=0.000).

Conclusion: This study demonstrated that applying heat and cold therapy may reduce the intensity of nitrate-induced migraine type headache in cardiac inpatients. Considering this fact that approximately 10% of patients cannot tolerate nitrate therapies due to unbearable headache, applying heat or cold therapy in patients with nitrate-induced migraine type headache is recommended to improve patient's adherence to treatment.

Keywords: Cardiac patient; cold; heat; migraine, nitrate.

Öz

Amaç: Bu çalışmanın amacı kardiyak hastalarda ısı ve soğuk terapi uygulamasının nitrogliserine bağlı migren tipi baş ağrısı şiddeti üzerine etkilerini karşılaştırmaktı.

Gereç ve Yöntem: Bu randomize kontrollü çalışma, ön test ve son test olarak üç grup tasarımında (ısı veya soğuk terapi ve kontrol grubu) toplam 75 kardiyak hasta üzerinde gerçekleştirilmiştir. Müdahale grubundaki hastalar 25 dakika boyunca, iki kez (1 saatlik aralıklarla) ısı veya soğuk terapi aldı, kontrol grubundaki hastalar herhangi bir terapi almadı. Baş ağrısı şiddeti, ağrı için sayısal derecelendirme ölçeği ile, üç çalışma grubunda 3 kez (çalışmadan hemen önce, ilk terapinin uygulanmasının sonunda ve ikinci terapinin uygulanmasının sonunda) ölçülmüştür.

Bulgular: Çalışmadan hemen önce üç grup arasında ortalama ağrı skalası skoru (p=0,781) için bazal fark yoktu; ancak ısı ve soğuk terapi uygulandıktan sonra üç grup arasındaki fark istatistiksel olarak anlamlı idi (p=0,000).

Sonuç: Bu çalışma, ısı ve soğuk terapi uygulanmasının kardiyak hastalarda nitrata bağlı migren tipi baş ağrısının şiddetini azaltabildiğini göstermiştir. Hastaların yaklaşık %10'unun dayanılmaz baş ağrısından dolayı nitrat tedavilerine tahammül edemediği gerçeği göz önüne alarak, nitrata bağlı migren tipi baş ağrısı olan hastalarda ısı veya soğuk terapi uygulaması, hastanın tedaviye uyumunu artırmak için önerilmektedir.

Anahtar sözcükler: Kardiyak hasta; soğuk; ısı; migren; nitrat.

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Introduction

Organic nitrates are potent vasodilators and are the most widely used antianginal agents during acute events. They selectively dilate epicardial coronaries and also enhance collateral flow; they also inhibit platelet aggregation. However, headache and tolerance being the major deterrents.[1] Nitroglycerine (NTG)-induced headache is the most prominent side effect of nitrate therapy in patients with chest pain and has a detrimental effect on the quality of life.[2–4] Headache caused by the vasodilatation of cerebral veins is the commonest side effect of nitrates; headache is more common with glyceryl trinitrate, both sublingual and transdermal preparations.[1] Nitrate-induced headaches typically manifest in one of two ways: "Immediate" headaches with mild to medium severity developing within an hour of medication ingestion and "delayed" headaches occurring 3–6 h after nitrate intake that are much more severe, with migraine-like symptoms. Delayed migraines appear to be dose dependent and are more likely to occur in individuals with a family history of migraines.[5]

Various types of headache remedies have been tried by headache sufferers for thousands of years and some of these methods are still in use.[6] A variety of drugs are known to be effective in the treatment of migraine. Their side effects, however, may restrict their use in some patients and the medications used in these patients may worsen the present headache or even create a new kind of headache known as a drug abuse headache. Therefore, non-pharmacological methods are worthy of investigation.[7] Complementary and alternative medicine includes systems and practices that are not presently a part of conventional medicine.[8] Various complementary and alternative medicines including massage, trigger point therapy, reflexology, spinal manipulation, therapeutic heat or cold, and exercise therapy have also been investigated in the past for migraine patients.[7–11] Mechanical techniques to alleviate migraine symptoms have been used for many years, cooling and compression being the most frequently applied. Application of cold/cryotherapy is the most common non-pharmacological self-administered pain-relieving method currently used by migraine sufferers.[12] Application of heat to the head during headache also has a historical background.[6]

Hence, this randomized controlled trial designed to compare the effect of heat and cold therapy on the intensity of NTG-induced migraine type headache in cardiac inpatients. We hypothesized that cool or heat therapy would decrease the mean of headache intensity in the both of experimental groups of study.

Material and Methods

Approval and study population

The study protocol was approved by the Ethics Committee of Urmia University of Medical Sciences (Ethical code of this study is IR.UMSU.REC.1398.326). The study was conducted in accordance with the principles of the Declaration of Helsinki. A written informed consent was obtained from each participant. This single-center, randomized controlled study, with a pre-posttest design included a total of 75 patients. Inclusion criteria were as follows: Male or female aged ≥40 years and ≤70 years; previously diagnosed with cardiovascular disorder, willingness to participate in this study, and giving a written informed consent. Exclusion criteria were as follows: Patients who had headache just before TNG infusion (menstrual migraine was also excluded), took prophylactic treatment and patients with analgesic or ergotamine overuse, pregnancy, and participation in another interventional study during this research.

Details of power calculations and sample size

Since there was not any study on the impact of applying heat and cold therapy in cardiac inpatients population, the appropriate information was not available to calculate sample size for this study. Based on the study of Mohamed and Mohamed,[13] which is related to our study, the sample size was calculated n=19 by the following formula:

$$n = \frac{(s_1^2 + s_2^2)^2 (z_{\frac{\alpha}{2}} + z_\beta)^2}{(\bar{x}_1 - \bar{x}_2)^2}$$

Finally, we concluded recruitment of 25 patients for each group could give us 90% power to detect a difference in the mean amount of headache intensity at α level of 0.05. Hence, we registered 75 patients (25 for each group).

Data collection and measures

Data were obtained from the demographic information form and numeric rating scale (NRS) pain.

The NRS is a measure of pain intensity in adults. Although various iterations exist, the most commonly used is the 11-item NRS. It is a segmented numeric version of the visual analog scale in which a respondent selects a whole number (0–10) that best reflects the intensity of his/her pain. It is anchored by terms describing pain severity. NRS pain is a single 11-point numeric scale, with 0 representing no pain and 10 representing severe pain ("as bad as you can imagine" and "worst pain imaginable").[8] For randomization in this study, an independent investigator made random allocation cards using computer-generated random numbers. The allocator kept the original random allocation sequences in an inaccessible third place and worked with a copy. She used the codes H, C, and N (H for the experimental group with heat therapy, C for the experimental group with cold therapy, and N for the control group). Then, she continued randomization until 25 samples were allocated to each of the experimental groups and 25 to the control group.

Participants in all of three groups of study were asked to complete the patient information questionnaire before the intervention. Headache intensity was measured by the NRS pain, in three groups of study for 3 times (just before the study, at the end of applying the first therapy, and at the end of applying the second therapy). In addition, associated symptoms (i.e., nausea and vomiting) and side effects were documented.

Interventions for control group

The control group had their routine/traditional care and received their treatment as usual. They did not receive any (heat or cold) therapy.

Interventions for experimental groups

A master student at the Division of Medical Surgical Nursing applied heat or cold therapy for the experimental groups.

Cold or heat therapy was administered to the patients by compress bag during migraine attacks (Fig. 1). The cold compress bags (15–18°C) were stored in a refrigerator, and the heat compress bags (40.5°C) were stored in a warmer. At the onset of the migraine attacks, the compress bags were applied on patients' neck and they used it for 25 min. We choose 25 min as the time for application of the compress bag based on the results of three published studies.[7,9,14] Headache intensity was measured by the NRS pain and pain relief was measured on a similar scale. They recorded their headache intensity before the compress bag was placed and then after the first and the second heat or cold therapy. Analgesic treatment was not taken within 120 min after the onset of first cold or heat therapy. If patients did not experience adequate relief from the headache without taking analgesic (within this 120 min), they were taken analgesics, but we excluded them from this study.

Figure 1. Cold or heat therapy was administered to the patients by compress bag during migraine attacks.

Statistical analysis

Statistical Package for the Social Sciences software version 22 was used for statistical analysis. Numbers were shown as a percentage, mean, and standard deviation for identifying characteristics of participants. Results were accepted at the confidence level of 95% and the statistical significance level of $p<0.05$. The Chi-square, one-way ANOVA, and repeated measurement tests were used for evaluating the statistical significance in the sociodemographic data, medical characteristics, and headache intensity in the three groups before the study and 2 times after the intervention.

Results

Demographic characteristics of participants at the baseline

Participants included in the study compared to each other regarding variables such as gender, educational level, employment status, comorbidity (diabetes mellitus), smoking history, and age that might affect the results of the research. No baseline differences existed between the three groups of study regarding

Table 1. Socio-demographic and medical characteristics of the groups (n=75)

Characteristics	Control (n=30)		Heat (n=30)		Cold (n=30)		Test results
	n	%	n	%	n	%	
Age (mean±SD)	60.53±10.35		57.23±12.21		55.03±13.72		F=1.551 df1=2 df2=87 p=0.218
Gender							Chi^2=1.170
Male	15	50.0	11	36.7	14	46.7	df=2
Female	15	50.0	19	63.3	16	53.3	p=0.557
Educational level							Chi^2=1.709
Illiterate	8	26.7	11	36.7	9	30.0	df=4
High school	4	13.3	6	20.0	5	16.7	p=0.789
University	18	60.0	13	43.3	16	53.3	
Employment status							Chi^2=1.970
Employee	12	40.0	7	23.3	9	30.0	df=2
Workless	18	60.0	23	76.7	21	70.0	p=0.373
Diabetes mellitus							Chi^2=1.156
Yes	14	46.7	17	56.7	13	43.3	df=2
No	16	53.3	13	43.3	17	56.7	p=0.561
Smoking history							Chi^2=3.271
Yes	11	36.7	5	16.7	7	23.3	df=2
No	19	63.3	25	83.3	23	76.7	p=0.195

SD: Standard deviation; F: F test in the analysis of variance (ANOVA); d.f: Degree of freedom; X^2=Chi-square test.

Table 2. Comparison of mean and standard deviation of headache intensity in each of the studied groups just before the intervention (after intravenous NTG injection)

Headache intensity	Control (n=30) Mean±SD	Heat (n=30) Mean±SD	Cold (n=30) Mean±SD	Test results
Just before the intervention	4.90±0.80	5.03±0.88	4.90±0.84	F=0.248 df1=2 df2=87 p=0.781

SD: Standard deviation; F: F test in the analysis of variance (ANOVA); d.f: Degree of freedom.

these demographic characteristics, and groups were similar each other (Table 1).

Headache intensity

Headache intensity was statistically similar (p=0.781) between the three groups just before the intervention (after receiving intravenous NTG) (Table 2), but the differences were statistically significant after the intervention (p=0.000) (Table 3). The results showed reduced intensity of headache in the cold and heat therapy groups compared with control group after the intervention (Table 3, 4).

In Table 3 (on the intensity of headache), three effects have been tested:

Interaction between time and intervention

The statistical test indicated that the interaction between time and intervention from the first to second intervention was significant on the mean of

Table 3. Analysis of measured headache intensity

Headache intensity	Total squared error	Degree of freedom	Average squared error	F	P	Partial eta squared
Main effect of time	85.422	1	85.422	50.045	0.000	0.365
Interaction of time with intervention	33.078	2	16.539	9.689	0.000	0.182
Component of time effect error	148.500	87	1.707			
Main effect of intervention	33.156	2	16.578	3.981	0.022	0.084
Component of intervention effect error	362.311	87	4.164			

F test in the analysis of variance (ANOVA).

Table 4. Comparison of mean and standard deviation of headache intensity in each of the studied groups in the first, second, and third measurements

Group	Mean and standard deviation of headache intensity		
	First measurement (before the intervention)	Second measurement (after the first intervention)	Third measurement (after the second intervention)
Control	4.90±.80	4.40±1.63	4.56±1.85
Heat	5.03±.88	3.70±1.51	2.60±1.67
Cold	4.90±.84	3.76±1.67	3.53±1.88

headache intensity (p=0.000), and pain intensity decreased with time.

Main effect of time

There was a statistically significant difference in the mean of headache intensity at different times (p=0.000).

Main effect of intervention

The main purpose of this research was to investigate this effect. ANOVA results showed that the mean headache intensity in the first to second intervention significantly differed between the heat therapy, cold therapy, and control groups (p=0.022), indicating that heat and cold therapy, both were effective in reducing headache intensity.

Discussion

This randomized controlled study was designed to compare the effect of heat and cold therapy on the intensity of NTG-induced migraine type headache in cardiac inpatients.

Our study findings support our hypothesis that applying heat and cold therapy would decrease the mean of headache intensity in the experimental groups of study. Paired samples t-test showed a statistically significant difference in the mean amount of headache intensity between experimental groups and control group of study, after the intervention (p<0.05), suggested that applying heat and cold therapy may reduce the amount of nitrate induced migraine type headache intensity in cardiac inpatients.

Nitrates play a prominent role in the management of angina pectoris in coronary artery disease. The nitrates provide an antianginal effect with vasodilation in veins, and systemic and coronary arteries. In addition, nitrates lead to vasodilation in intracranial arteries in humans. As a consequence of vasodilation of the intracranial arteries, cerebral blood flow increases and vascular type headache is triggered.[15] Our study is consistent with the study by Ucler et al.[7] who conducted cold therapy in migraine patients using a form of capillary gel for temperature reduction and reported that migraine pain was reduced in some patients.

Similar to our research, the results of Dehghan and Farahbod's study entitled: The efficacy of thermotherapy and cryotherapy on pain relief in patients with acute low back pain indicated that the application of thermotherapy and cryotherapy accompanied with a pharmacologic treatment could relieve pain in the patients with acute low back pain.[16]

Furthermore, our study is in line with the study of Emani et al.[8] entitled: "The effect of applying reflexology massage on NTG-induced migraine type headache" that concluded: Reflexology massage can reduce the intensity of nitrate-induced headache.

The findings of our research are consistent with the study of Garra et al.[17] entitled: "Heat or cold packs for neck and back strain" demonstrated that: The addition of a 30 min topical application of a heating pad or cold pack to ibuprofen therapy for the treatment of acute neck or back strain results in a mild yet similar improvement in the pain severity.

In addition, our study was consistent with the study by Foralosso et al.[18] entitled: "Cryotherapy in Tension Headache: Analysis of the frequency of symptoms," their findings indicated a decrease in the frequency of pain, especially pressure pain throughout the period, with the use of cryotherapy in the cervical region.

Another randomized controlled trial that used cryotherapy as a treatment for migraine conducted by was Sprouse-Blum et al.[19] with the purpose of producing cooling in intracranial vessels, reported that there was reduction of pain for such patients.[19]

In addition, the study of Mohamed and Mohamed indicated that local heat applications in patients with moderately knee osteoarthritis every other day decreased pain, stiffness, and physical functional disability.

Limitations

Limitations of the present study included: (a) The relatively moderate patient population and (b) the participants in our study were recruited only from one hospital. Therefore, we recommend multicenter study containing a large number of participants to confirm our findings.

Conclusion

This study demonstrated applying heat or cold therapy may reduce the intensity of nitrate-induced migraine type headache in cardiac inpatients. Considering this fact that approximately 10% of patients cannot tolerate nitrate therapies due to unbearable headache, applying heat or cold therapy in patients with nitrate-induced migraine type headache is recommended to improve patient's adherence to treatment.

Ethical Approval: The study protocol was approved by the Ethics Committee of Urmia University of. Medical Sciences (Ethical code of this study is IR.UMSU. REC.1398.326).

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