

Original Article

Cold Therapy in Migraine Patients: Open-label, Non-controlled, Pilot Study

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Some patients with headache report that they have frequently used physical therapies such as application of cold to relieve their headache. There are only a few reported studies related to cold therapies in patients with migraine. In this study, we investigated the effect of cold application on migraine patients. Twenty-eight migraine patients were included. Cold therapy was administered to them by gel cap. Patients used this cap during their two migraine attacks. Before and after the cold therapy, headache severity was recorded by using visual analogue scale (VAS). Patients used this cap for 25 min in each application. They recorded their VAS score just after the therapy and 25 min, 1 h, 2 h and 3 h later. Two patients could not use this therapy due to side effects (one due to cold intolerance and one due to vertigo) in both applications. Therefore, therapeutic efficacy was evaluated in 26 patients. Twenty-five minutes after treatment of the first attack, VAS score was decreased from 7.89 ± 1.93 to 5.54 ± 2.96 ($P < 0.01$). Twenty-five minutes after treatment of the second attack, VAS score was decreased from 7.7 ± 1.8 to 5.4 ± 3.55 ($P < 0.01$). Cold application alone may be effective in some patients suffering from migraine attacks. Its combination with conventional drugs should be investigated in future studies.

Keywords: cold application – cryotherapy – headache – migraine

Introduction

Migraine headache is generally treated by anti-migraine agents, analgesics and anti-emetic agents. Various non-pharmacological methods 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 (1–3). There are some reports which support the efficacy of acupuncture in the treatment of pediatric pain, including migraine (4). Ancient Greek and Egyptian writings show that physicians of that time were concerned about this disease and bloodletting and craniotomy was used in some patients with headache (2,5).

The first cold treatment was done for headache patients in 1849. James Arnott wrote a manuscript on cold therapy in

which he used a mixture of salt and ice in patients to treat headache (6). In another study, the efficacy of extra-cranial pressure in combination with cold to treat headaches was supported. They showed that simultaneous pressure of heat and cold reduced the headache's duration (7). Today, some patients report that they treat their headache using physical therapies, including cold application (5,8–10). Self-administered pain relief manoeuvres have been investigated in primary headache patients. They reported that application of cold was the most-used manoeuvre in migraine without aura (8). In a small study, Friedman *et al.* (11) reported the efficacy of a non-invasive technique, intra-oral chilling, for acute migraine headache pain when compared with oral sumatriptan or placebo. Lance (12) reported the results of a new device, which employs cold, pressure and heat around the head. Fifteen out of twenty migraine patients and six out of seven tension headache patients experienced some reduction in headache severity. In another study, 9% of migraine patients reported that a cold wrap was almost completely effective,

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26.5% moderately effective and 29.0% mildly effective. However, they did not use an objective method to evaluate headache severity (6). As a result, cold therapy is still not used clinically for migraine patients as an alternative or additive modality. In this study, we investigated the utility of cold therapy for migraine attacks.

Materials and Methods

All patients in this study were admitted to the Ministry of Health, Ankara Training and Research Hospital Headache Center. Informed consent was obtained from all patients. We obtained an Ethic Committee approval to conduct the study for patients (between 14 and 60 years) who met the criteria outlined below.

Inclusion Criteria

We proposed that all consecutively admitted patients, who met the following criteria, participate in our study: (i) migraine with aura and migraine without aura; (ii) chronic migraine [migraine headache occurring for 15 or more days per month for more than 3 months in the absence of medication overuse and not attributed to another disorder (other type chronic headache patients excluded)]; and that (iii) diagnosis was made by International Headache Society (IHS) criteria (13). The IHS determined new criteria for headache in 2004 (14), but since our study had started before its publication, we used the criteria reported in 1988 (13).

Exclusion Criteria

We excluded patients who had more than one type of headache (menstrual migraine was also excluded), took prophylactic treatment and patients with analgesic or ergotamine overuse. We reasoned that menstrual migraine may have different clinical characteristics and it can be more resistant than non-menstrual migraine. Patients using prophylactic treatment were deemed to be the possible cause of confusion when evaluating the responses of migraine patients. Twenty-eight migraine patients were included in this study. All patients were evaluated by a neurologist.

Cap Administration

All patients kept a diary for two migraine attacks (before and after the treatment). The diary included the time patients used the gel cap, visual analogue scale (VAS) of patients (before the treatment and 25 min, 1 h, 2 h, 3 h post-treatment), associated symptoms (i.e. nausea and vomiting) and side effects.

Cold therapy was administered to the patients by gel cap (Fig. 1) during both migraine attacks. The cap was stored in a freezer. At the onset of the migraine attacks, patients wore the cap and used it for 25 min. We choose 25 min as the time for application of the gel cap based on the results of two published studies (1,6). Headache severity was measured by VAS (0: no pain to 10: severe pain) and pain relief was measured on a



Figure 1. The picture of cap used in the study.

similar scale. They recorded their headache severity before the cap was placed and then 25 min, 1 h, 2 h and 3 h after the cap therapy. Analgesic treatment was not taken within 25 min after the onset of cold therapy. If patients did not experience adequate relief from the headache, we allowed them to use analgesics 25 min after the onset of cold therapy.

In this study, we did not evaluate the patients beyond 3 h. This is a pilot study to determine the short-term effect of the treatment.

Response Evaluation

An objective response was defined as a 50% or greater reduction in pretreatment headache severity as measured by VAS. Patients with VAS score (0) were evaluated as having a complete response. A clinical benefit was defined as a reduction in VAS by >25% in pretreatment headache severity. We thought that a 25% decrease in VAS score is an important level of clinical benefit. Therefore, we mentioned a 25% reduction in VAS as a clinical benefit. A patient whose VAS showed increase, no change or <25% decrease was defined as no response.

Statistical Analysis

Bonferroni corrected Mann–Whitney *U*-test and Paired Samples *t*-test were used for statistical analysis. *P*-values <0.05 were accepted as significant.

Results

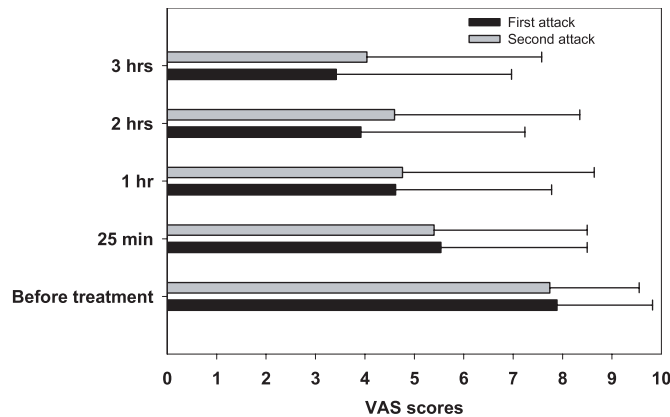
All patients were female and the median age was 29.25 ± 7.92 years (range: minimum 14; maximum 48). Twenty-six patients had migraine without aura and two patients had migraine with aura. The patients' mean number of attacks per month was 3.11 ± 1.2 (minimum 1; maximum 5). Characteristics of patients are shown in Table 1. Two patients could not use this therapy due to side effects (one due to cold intolerance and one due to vertigo) in both applications, leaving 26 patients to evaluate.

Table 1. Characteristics of patients

Patients	n	Gender		Mean age (SD)	Frequency of attacks	Disease duration (year)	Attack duration* (hour)	Initial VAS scores
		Female (%)	Male (%)					
Response (+)*	13	13 (100)	0(0)	28.0 ± 7.8	3.30 ± 1.37	4.38 ± 4.42	21.23 ± 6.75	8.00 ± 2.04
Response (-)*	13	13 (100)	0(0)	31.0 ± 8.9	3.07 ± 1.03	5.46 ± 5.66	19.00 ± 7.95	7.69 ± 2.01
Total	28	28 (100)	0(0)	29.25 ± 7.9	3.11 ± 1.24	78 ± 4.84	20.39 ± 7.11	8.89 ± 0.91

$P > 0.05$.

*Response among 26 patients in 25 min of the first attack (two patients excluded from the response evaluation because of side effects).

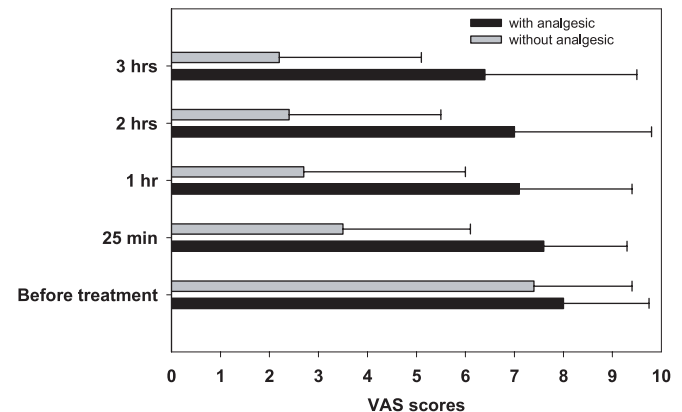
**Figure 2.** VAS scores before and after the treatment of two attacks.

Half of the Patients Reported a Clinical Benefit

In the first application, 13 patients (50%) reported a clinical benefit 25 min after the cold therapy. Objective response was observed in 10 (38.4%) patients including three (11.5%) patients who had a complete response. However, the other half did not respond and needed to use analgesics 25 min after cold therapy. Mean VAS scores of patients decreased from 7.89 ± 1.93 to 5.54 ± 2.96 in 25 min, 4.62 ± 3.16 in 1 h, 3.92 ± 3.32 in 2 h and 3.42 ± 3.55 in 3 h after cold therapy in first attack. VAS scores at the twenty-fifth minute, first hour, second hour and third hour of treatment were found to be significantly lower compared to VAS scores before treatment ($P < 0.01$) (Fig. 2). In patients with a clinical benefit, the mean number of attacks was 3.30 ± 1.37 , the mean pretherapy VAS score was 8.00 ± 2.04 and the duration of migraine attack was 21.23 ± 6.75 h. In patients who did not have any clinical benefit, mean attack number was 3.07 ± 1.03 , mean VAS score before the therapy was 7.69 ± 2.01 and duration of migraine attack was 19.00 ± 7.95 h. These were not significantly different between patients with or without clinical benefit ($P > 0.05$).

Benefit Increased with Second Application

In the second application, 15 (57.6%) patients reported a clinical benefit 25 min after the cold therapy. Objective response was observed in 9 (34.6%) patients including 2 (7.7%) patients who had a complete response, but 11 (42.4%) did not respond and used analgesics. Mean VAS scores decreased from 7.74 ± 1.81 to 5.40 ± 3.10 in 25 min,

**Figure 3.** VAS scores before and after the treatment in patients with and without analgesic use.

4.76 ± 3.88 in 1 h, 4.60 ± 3.75 in 2 h and 4.04 ± 3.54 in 3 h. VAS scores at the twenty-fifth minute, first hour, second hour and third hour of treatment were found to be significantly lower compared to VAS scores before the treatment ($P < 0.01$) (Fig. 2).

Among 13 patients who responded to cold therapy in the first attack, 10 of them (76.9%) also responded during their second attack. Similarly, among 15 patients who did not respond in the first attack, 9 (60%) did not have any response in the second attack.

Median Analgesic Intake Time Increased with the Second Application

Median analgesic intake time after onset of cold therapy was 45.0 ± 35.7 min (range: 25–120 min) in the first application and 81.36 ± 118.4 (range: 25–420 min) min in the second. Figure 3 shows the changes in VAS scores before and after the treatment in patients with and without analgesic use. Three patients reported a side effect during the two applications. Two patients had cold intolerance and one had vertigo. One patient with cold intolerance and another with vertigo did not continue the therapy.

Discussion

Migraine is a chronic disease characterized by frequent attacks, high levels of pain and disability during attacks,

causing reduced quality of life between attacks (15–18). It is a widespread disorder in the world, affecting ~10–15% of general population (19). There are four types of therapeutic choice for migraine patients as follows: general measures, abortive therapy, pain relief measures and prophylactic therapy (20). Abortive therapy is commonly employed to eliminate head pain and other symptoms associated with acute migraine headache (1). 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. It is well known that evidence-based complementary and alternative medical therapies have shown remarkable success in healing acute as well as chronic diseases (21,22). Therefore, non-pharmacological methods are worthy of investigation.

Various non-pharmacological methods have been investigated in the past to control the pain of acute migraine attacks. Application of an ice pack is a frequently used procedure (1,5,8,20,23). However, there are only a few reported studies in the literature regarding this non-pharmacological therapy (1–3,5–7). Since the potential benefits of cold application in headache patients have not yet been clearly understood, we decided to investigate the benefits of cold application on migraine patients.

Lance (12) reported the results of a new device which employs cold, pressure and heat around the head. They showed that headache severity was reduced in 15 out of 20 migraine patients, and in 6 out of 7 tension headache patients. Diamond and Freitag (5) found that a cold pack was effective in 71% of headache patients, 80% of which were migraine headaches. In a study reported by Robbins (6), 9% of migraine patients reported the cold wrap as almost completely effective, 26.5% as moderately effective and 29.0% as mildly effective. However, they did not use an objective method to evaluate headache severity. As a result, these are small studies and the methods used are not practical for routine practice. New studies are still needed to show the exact role of cold therapy for migraine attacks.

In our study, migraine attacks were treated in ~50% of the patients by cold therapy alone, with significantly decreased VAS scores after the therapy. In addition, we found that the benefit of cold therapy continued progressively over time. VAS scores gradually decreased after the therapy. This shows that the benefits of cold therapy continued after the onset of therapy. Moreover, there was consistency in the cold applications. Seventy-six percent of patients who had a response in their first attack benefited from the cold therapy in the second attack. Similarly, 60% of the patients who did not respond in the first attack had no response in the second attack, either.

This study is not a randomized study and there is no control group comparing usual therapeutic approaches such as anti-migraine agents and anti-emetics. Therefore, we cannot conclude that cold therapy is definitely effective in migraine attack and we cannot suggest an evidence-based use of cold

therapy in migraine patients. We can say, however, that cold therapy alone warrants investigation in future randomized control studies.

In pharmacological trials on migraine drugs, rescue medications are usually allowed after 2 h. In our study, we allowed our patients to take analgesics 25 min after the therapy onset. However, median analgesics intake time after onset of cold therapy was 45.0 min in the first and 81.36 min in the second attack of patients who did not respond to gel cap therapy.

In the present study, 13 patients in first application and 11 in second application used analgesic drugs due to inefficacy of cold therapy alone. As seen in Fig. 3, the patients who did not respond adequately to analgesic therapy also had lower VAS scores. Therefore, we think that this patient group is a refractory subgroup. However, we do not know whether earlier treatment of these patients with analgesic therapy would cause better responses.

The placebo effect in the pharmacological treatment of migraine attacks may influence evaluation of the studies. In a meta-analysis of 31 trials involving acute migraine patients, it has been reported that the mean proportion of subjects who experienced a treatment response to placebo was 28% (24). In our study, the response rate was 50% in the first attack and 57% in the second attack. Moreover, placebo effect may vary in each patient and each attack. Therefore, our results cannot be completely attributed to placebo effect of gel therapy. However, we cannot ignore its possible effect on our results.

If we accept the cold treatment as an effective modality in migraine patients, there is still one more question to be resolved: How does cold affect the migraine headache? Local anesthesia is important in the use of cryotherapy. Lowering pain stimuli may be caused by a decrease in contraction. The gate theory suggests that the cold sensations overwhelm and block transmission of the pain stimuli into the cerebral cortex. Ice reduces the release of some substances including histamines, vasoactive substances and enzymes that stimulate nerve endings (6). However, the exact mechanism of cryotherapy is still unclear.

In Vijayan's (1) study, two patients could not apply adequate pressure in cold therapy because of tenderness. In our study three patients showed side effects in both applications. Two patients had cold intolerance and one had vertigo. Two of them discontinued the therapy. The use of gel packs is a safe method of applying cold in adjunct treatment of acute headache.

Conclusion

Cold application alone may be effective in some patients suffering from migraine attacks. This study is not a randomized study and there is no control group comparing usual therapeutic approaches such as anti-migraine agents and anti-emetics. However, randomized studies are needed to clarify the efficacy of cold therapy alone in these patients. Its use in combination with well-known therapeutic tools such as anti-migraine agents, analgesics and anti-emetic agents should be investigated in further studies.

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