

Received: 2017.05.07
Accepted: 2017.07.04
Published: 2017.12.29

Changing Efficacy of Wet Cupping Therapy in Migraine with Lunar Phase: A Self-Controlled Interventional Study

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Source of support: Departmental sources

Background: The aim of this study was to evaluate the effect of blood-letting with wet cupping therapy (WCT) in migraine treatment and to determine whether there was any difference according to the phase of the moon when the treatment was applied.

Material/Methods: This self-controlled study was conducted in Karabuk between 2014 and 2016. Patients who were diagnosed with migraine were enrolled in the study. Migraine disability assessment questionnaire (MIDAS), demographic characteristics, migraine attack frequency and duration, and family history was used to assess the severity of headache. WCT was applied in 3 sessions and the questionnaire was administered before and 3 months after the final WCT session. Wilcoxon signed-rank test was used in pre-and posttreatment measurements, and the Chi-square test was used to check independence in two-way categorical tables.

Results: A total of 85 patients were included. The reduction in MIDAS scores and number of migraine attacks was significantly greater in the WCT applications made in the first half of the month compared to those in the second half of the month. Although the reduction in visual analog scale (VAS) scores was greater in the second half of the month, it was also significant in the applications made in the first half of the month.

Conclusions: WCT was found to be an effective treatment of migraine. The effect on MIDAS, VAS, and the number of attacks was significantly better when the application was made in the second half of the month compared to those made in the first half.

MeSH Keywords: **Medicine, East Asian Traditional • Migraine Disorders • Moon**

Full-text PDF: <https://www.medscimonit.com/abstract/index/idArt/905199>

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Background

Migraine is characterized by frequent attacks of moderate to severe intensity. It is associated with autonomic symptoms and also limits daily activities, impairs professional and educational performance, and affects activities in the family and society [1]. Many pharmacological agents (e.g., 5-HT₃ antagonists, nonsteroidal antiinflammatory drugs, beta blockers, serotonin re-uptake inhibitors, and topiramate) are used as medication to control migraine headache and to reduce the intervals of migraine attacks [2]. In addition to drugs, complementary and alternative medicine (CAM) methods are widely used throughout the world because of the side-effects of pharmacological treatments and the fact that frequent use of medications can lead to medication-overuse headaches [3]. In a study by Lee et al. in the USA, the most common CAM methods used by migraine patients were avoidance of light, hot/cold therapy, diet, vitamin supplements, acupuncture, chiropractic methods, and relaxation/meditation [4], but cupping therapy was reported to have been used by only 1 of 2477 patients. A study of cupping therapy as migraine treatment reported it was effective in the treatment of headache and migraine, with mean headache severity decreased by 66% following WCT [5].

Wet cupping therapy (WCT) is a method currently widely used in Asia, Africa, and the Far East, and in recent years it has started to become known as an application within alternative medicine in Europe. The Prophet Mohammed had blood-letting applied both as preventive medicine and as a treatment method, and there are many Islamic traditions related to the recommendations of the Muslim community. The correct time for the application of blood-letting under normal conditions has traditionally been reported to be the days after the second week of the lunar month. In narratives on this subject, the 17th, 19th, 21st, and 23rd days of the lunar month are recommended. Interpretations of the related traditions have established a relationship between these times and the phases of the moon, stating that blood flow in the human body is affected by this [6].

The aim of this study was to evaluate the effect of WCT in migraine treatment and to determine whether there was any difference in WCT efficacy according to the phase of the moon when the treatment was applied.

Material and Methods

Study design

This self-controlled study was conducted in Karabuk University Training and Research Hospital from 2014 to 2016. The study included patients selected from the Neurology Department,

who were followed up for 2 years for migraine. All types of migraine headache were considered for eligibility. Patients were separated into 3 groups by the neurologist according to the migraine type: aura, without aura, and others. Patients were given extensive information about WCT and written consent was obtained.

Patient selection

Patients who were diagnosed with migraine and met the International Classification of Headache Disorders: 2nd edition (ICHD-II) diagnostic criteria for migraine were enrolled in the study [7]. Eligibility criteria included age 18–55 years and an average of at least 2 headaches per month. Patients were excluded for any of the following: other types of headache (e.g., cervical disc hernia, or tension headache), isochronous of psychiatric disorders, cranial trauma or operation, onset of headache disorder less than 2 years previously, pregnancy, malignancy, cluster headache, psychiatric disorders, suspicion that the headache disorder had a specific etiology, cranial neuralgia, WCT treatment within the previous 12 months, and lack of consent or cooperation with the research procedures.

Assessment Tools

A questionnaire was applied, which included demographic characteristics: migraine attack frequency and duration, and family history. Drugs in current use were recorded and were not changed during the study.

The Turkish version of the migraine disability assessment questionnaire (MIDAS) developed and tested by Stewart and Lipton was used to assess the severity of headache-related disability [2,8]. This simple, self-administered, 7-item questionnaire focuses on disability in 3 areas (school or work life; everyday household tasks; and family, social, or leisure activities) in the first 5 items. The 6th item questions the number of days with headache in the last 3 months and the last item is a visual analog scale (VAS) to evaluate the pain level. The questionnaire was administered before and 3 months after the final WCT session.

Wet Cupping Technique

All patients underwent 3 staged WCTs consecutively, at 1-month intervals (0 days, 30 days, and 60 days). WCT was performed using disposable vacuum cups on 5 acupuncture point locations: DU 14 (Dazhui) point on the posterior median line, in the depression below the processus spinosus of the 7th cervical vertebra; UB 42 (Pohu) points bilaterally on the back, 3.0 cun lateral to the lower border of the spinous process of the 3rd thoracic vertebra interscapular region; and UB 46 (Geguan) points bilaterally on the back, 3.0 cun lateral to the



Figure 1. Application and areas of WCT.

lower border of the spinous process of the 7th thoracic vertebra (Figure 1). Each WCT procedure took about 20 min and was conducted in 5 phases:

1. Sterilization: The selected regions is disinfected with povidone iodine before the procedure.
2. Primary sucking: The cup is placed on the selected sites and the air is withdrawn from inside the cup by manual suction. The cups are located on the skin and left for a period of 3 to 5 minutes.
3. Scarification: Superficial incisions, 2–3 mm in depth and 3–5 mm in length, are made on the skin using a number 15 sterile surgical blade.
4. Blood-letting by secondary sucking: The cups are located on the skin again, in the same manner as described above, and left until filled with blood from the capillary.
5. Disconnection and dressing: The cups filled with blood are removed and destroyed as medical waste. A dressing with sterile sponge is applied.

Statistical analysis

Data analysis was conducted in 2 steps. First, descriptive statistics were obtained. Second, the Wilcoxon signed-rank test was applied to pre-and posttreatment measurements. The chi-square test was used to check independence in two-way categorical tables. The results of data showing normal distribution are stated as mean ± standard deviation, (SD) and those that did not show normal distribution are given as median values. A value of $p < 0.05$ was considered statistically significant. All analyses were applied using R software (version 3.2.2).

Approval for the study was granted by the Ethics Committee of Turgut Özal University (no: 99950669/236, dated 30.06.2014).

Results

A total of 85 patients of 128 who met the study criteria were accepted to participate to the study. Patients were classified according to the type of migraine as Group I (n=41) with aura, Group II (n=26) without aura, and Group III (n=18) other types of migraine (mixed). The distributions of the groups according to age, gender, number and duration of attacks, and family history of migraine are shown in Table 1. No difference was determined between the groups in respect to age and gender. The number of attacks was determined as being greater in Group I and the duration of the headache was shorter in Group II.

MIDAS, VAS scores and number of attacks pre-and post-WCT were compared and an 83.25% improvement was observed in the whole study group in the MIDAS scores, a 68.24% improvement in the number of attacks, and 76.47% improvement in the VAS scores.

The parameters were compared according to whether the WCT was applied in the first or the last 14 days of the month. The reduction in the MIDAS scores and number of migraine attacks was statistically significantly greater in the WCT performed during the first half of the month compared to those in the second half of the month. Although the reduction in

Table 1. Comparisons of the groups according to mean age, gender, family history, attack frequencies and duration of headache.

Migraine type	n	Mean age (years)	Gender		Family history		Number of attacks last 90 days	Duration of headache (hours)
			F (n)	M (n)	Present	Absent		
With aura	41	40.34±9.03	23	18	32 (78.04%)	9 (21.96%)	30.14±23.22	21.04±17.57
Without aura	26	38.85±9.32	12	14	10 (38.46%)	16 (61.54%)	21.69±20.33	14.26±8.35
Mixed	18	43.67±7.03	10	8	10 (55.55%)	8 (44.45%)	48.41±26.04	32.94±14.36
P value		0.121	0.707				0.000	0.000

Table 2. Comparisons of the MIDAS scores, number of attacks and VAS scores according to the WCT performed at the first or second half of the month.

	WCT performed at the first 14 days of lunar phase (n=29)			WCT performed at the last 14 days of lunar phase (n=54)		
	Before WCT median (min-max)	After WCT median (min-max)	P value	Before WCT median (min-max)	After WCT median (min-max)	P value
Reduction in MIDAS score	55 (15-160)	47 (12-140)	0.93	41 (9-234)	27.5 (3-132)	0.000
Reduction in number of attacks	20 (6-100)	20 (6-100)	0.18	20 (5-90)	13.5 (3-90)	0.000
Reduction in VAS value	7 (4-10)	7 (4-9)	0.03	8 (5-10)	5 (2-8)	0.000

Table 3. Comparisons of the effect of WCT performed at the first and second half of the lunar phases according to migraine type.

Groups		WCT performed at the first 14 days			WCT performed at the last 14 days		
		Before WCT median (min-max)	After WCT median (min-max)	P value	Before WCT median (min-max)	After WCT median (min-max)	P value
With aura	MIDAS	51 (31-90)	42 (26-82)	0.68	55 (19-234)	30 (3-132)	0.000
	No of attacks	15 (6-60)	12 (6-100)	0.62	28 (6-90)	15 (3-75)	0.000
	VAS	7 (5-10)	7 (4-8)	0.17	8 (5-10)	5 (2-8)	0.000
Without aura	MIDAS	35 (15-160)	36 (12-110)	0.44	34 (9-90)	19 (8-60)	0.000
	No of attacks	12.5 (6-100)	12 (6-100)	0.46	15 (6-45)	11 (3-24)	0.000
	VAS	6 (4-9)	5 (4-6)	0.20	7 (6-9)	5 (3-6)	0.000
Mixed	MIDAS	95 (54-158)	96 (65-140)	0.47	100 (13-155)	65 (6-132)	0.022
	No of attacks	50 (20-90)	55 (30-90)	0.04	45 (5-90)	20 (3-90)	0.057
	VAS	9 (6-9)	9 (4-9)	0.59	9 (7-10)	7 (6-8)	0.034

the VAS scores was greater in the second half of the month, it was also significant in the applications made in the first half of the month (Table 2).

When the effect of WCT performed at the first or second half of the month was evaluated according to the type of migraine, we found that the reductions in the median MIDAS scores, median number of attacks, and median VAS scores were greater in the applications made in the second half of the month compared to those in the first half. The reductions in the median MIDAS scores and median VAS scores in the Mixed type group were found to be statistically significant. Although a reduction was seen in the median number of attacks, it was not statistically significant. The median number of attacks in the Mixed type group was significantly increased in the WCT performed during the first half of the month (Table 3).

Discussion

In this study, the efficacy of WCT on migraine was evaluated and we investigated whether there was any change in this effect according to the phase of the moon when the application was made. The results of the study demonstrated that WCT was effective in the treatment of migraine and was significantly better when the application was made in the second half of the month compared to those made in the first half.

There are studies in the literature that have reported that WCT is effective in many different diseases, primarily pain-related diseases such as low back pain, skelalgia, fibromyalgia, generalized pain, infection pain (herpes zoster), neuralgia pain (headache and sciatica), and cough or asthma, acne, common cold, and urticaria [9]. However, there are few studies on the use of WCT in migraine treatment. In a study by

Duo, a combination of cupping and acupuncture was used and a positive response to treatment was reported in 94% of patients [10]. The method of that study differed from the current study in that acupuncture was applied and dry cupping to the same areas of the back. In a study by Ahmadi et al. of patients with migraine and tension-type headaches, WCT was reported to be equally effective in all age groups, in both males and females, and in both migraine and tension-type headache [5]. However, no evaluation according to the phase of the moon was made in those studies.

WCT is one of the oldest documented medical techniques, with the earliest documented evidence traced to ancient Macedonia, circa 3300 BC [2]. Despite the long history of cupping in many cultures around the world, the mechanisms through which cupping might prove efficacious as a treatment are unknown. Many theories have been suggested to explain the mechanism of cupping therapy. According to the Taibah theory proposed by El Sayed related to the scientific mechanism of WCT (known as Al-hijamah in Islam), WCT seems to be related in principle to the scientific principles governing excretory functions of the kidney. WCT causes increased capillary filtration, local collection of filtered fluids, lymph, and interstitial fluids, and their retention inside the lifted skin. This dilutes chemical substances, inflammatory mediators, and nociceptive substances, bathes nerve endings in collected fluids, and breaks tissue adhesions, resulting in decreased pain [11]. The neuropeptides involved in the pathogenesis of headache include substance P, vasoactive intestinal polypeptide (VIP), and calcitonin gene-related peptide (CGRP), which are important mediators in the pathogenesis of migraine and other primary headaches [12]. Recently, serum interleukin (IL)-6 levels have been reported to be high in migraine patients [13]. In light of the Taibah theory, migraine and headache can be treated by WCT and this may be due to the WCT-induced plasma clearance effect through the removal of excess fluids, chemical mediators, IL-6, vasoactive substances, and neuropeptides that cause headaches [11]. Furthermore, the skin is punctured during WCT and this injury to the skin leads to the release of β -endorphin and adrenocortical hormones into the circulation. Endothelin-1, a pain mediator synthesized by normal skin keratinocytes upon skin injury, can also produce analgesia via releasing of β -endorphin from keratinocytes [14,15].

In the religion of Islam, it is said that the Prophet Mohammed had blood-letting applied both as preventive medicine and as a treatment method and there are many Islamic traditions related to the recommendations of the Muslim community. The correct time for the application of blood-letting under normal conditions has traditionally been reported to be the days after the second week of the lunar month. Interpretations of the related traditions have established a relationship between these times and the phases of the moon, stating that blood flow in the human body is affected by this [6].

The seasonal and circadian rhythms of human and animal physiology and behavior have been fairly well described, but little is known about the effects of the lunar cycle. There are studies which have reported that at the time of a full moon, there is an increase in sudden unexpected deaths in epilepsy, violent and acute behavioral disturbance, non-affective psychotic disorders, depression, gastrointestinal hemorrhage, and acute myocardial infarctions. The occurrence of spontaneous abortion and attacks of atrial fibrillation may also be related to lunar phases [16]. Chakraborty and Ghos suggested that the gravitational pull of the moon may affect the cardiovascular functions of the human body and that the physical efficiency of humans is increased at the time of a new moon and full moon due to these altered cardiovascular regulations [17]. Many people have been shown to be magnetosensitive, with elevated arterial blood pressure correlated with increased geomagnetic activity [18].

The proposed geoelectric and geomagnetic biological effects show an increase in cerebral and central nervous system effects, cardiovascular events, circadian rhythm changes, epilepsy, headaches, inflammation, and psychiatric admissions. Increased alpha and beta brain waves, biogenic magnetite, calcium flux, cryptochrome response, DNA-breaks ferroelectric effects, gene expression, ion channel effects, serum C-reactive protein, and decreased melatonin production was shown [16]. Takemura et al. suggested that moonlight intensity also has a direct influence on the serum level of melatonin produced by the pineal glands [19]. Earth's magnetic fields affect Ca^{2+} ions in pinealocytes involved in the regulation of cAMP synthesis, which mediates the conversion of serotonin into melatonin, and their leakage suppresses melatonin production. The circadian rhythm of melatonin secretion controls the overall activity of the human body, from eating to sleep and metabolism [20]. Melatonin is affected by the pineal gland, which is sensitive to the Earth's magnetic fields and its production has been shown to be influenced by the lunar cycle in fish and also in humans [21,22]. It has also been suggested that melatonin plays a role in the etiology of migraine and that melatonin levels are low in migraine patients. There are studies which have shown that in some cases, the administration of melatonin to migraine patients has resulted in pain relief and decreased headache recurrence [23].

The pineal gland is considered to be a photoneuroendocrine transducer that translates environmental information into neuroendocrine molecules. Melatonin is synthesized from serotonin via the enzyme N-acetyltransferase, which is emitted in a circadian cycle from the suprachiasmatic nucleus, which receives photic stimuli via the retinohypothalamic tract [24]. In 1952, Jacobsen identified a relationship between migraine and an oculocephalic sympathetic abnormality in the neural pathway, which regulates the secretion of melatonin by the pineal gland [25]. In a small study by Claustrat et al., the nocturnal

plasma melatonin profile and melatonin kinetics during melatonin infusion in migraine patients were assessed and results were obtained supporting the hypothesis that melatonin helps in the resynchronization of biological rhythms. The authors stated that such symptomatic improvement could be due to any number of the biochemical actions of melatonin, such as resetting the biological rhythm, inhibiting prostaglandin synthesis, inhibiting nitric oxide synthesis, and depressing calcium uptake, or from the direct effect on cerebral blood vessels via receptor sites [26].

Conclusions

The results of the present study, conducted to evaluate the effect of WCT in migraine treatment, show that WCT is effective in the treatment of migraine, and the effect on MIDAS, VAS, and the number of attacks was significantly better when the application was made in the second half of the month compared to those made in the first half. WCT applied in the second half of the month was more effective on migraine, which

could be related to the melatonin level. The above information shows that the reduction in melatonin levels could be caused by both the low level of melatonin in migraine patients and by the geomagnetic biological effect. There is a need for further studies on this subject.

Limitations

The likelihood of inherent bias in the studies was assessed based on the description of randomization, blinding, withdrawals, and allocation concealment. Even though blinding patients might be difficult in studies of cupping, specifically wet cupping, assessor blinding can be achieved. Although Myeong et al. reported that sham cupping made by applying less and ineffective pressure could be used in studies, this is only valid for dry cupping, as such a sham application cannot be made in wet cupping [27].

Acknowledgement

Neurologist Dr. Omer Hakan Yavasoglu for patient selection.

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