ORIGINAL ARTICLE

Comparative efficacy trial of cupping and serkangabin versus conventional therapy of migraine headaches: A randomized, open-label, comparative efficacy trial

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Background: Migraine headaches are the most common acute and recurrent headaches. Current treatment of a migraine headache consists of multiple medications for control and prevention of recurrent attacks. Global emergence of alternative medicine led us to examine the efficacy of cupping therapy plus serkangabin syrup in the treatment of migraine headaches. **Materials and Methods:** This study was a randomized, controlled, open-label, comparative efficacy trial. We randomly assigned patients with migraine into cupping therapy plus serkangabin group (30 patients) and conventional treatment group (30 patients). An investigator assessed the severity of headache, frequency of attacks in a week and duration of attacks per hour in 5 visits (at the end of 2 weeks, 1, 3 and 6 months). Generalized estimating equations approach was used to analyze repeated measures data to compare outcomes in both groups. **Results:** Average age for cupping therapy group and conventional treatment group were 31.7 (±7.6) and 32.6 (±12.7) years, respectively (P = 0.45). After treatment for 2 weeks; and 1, 3 and 6 months, severity of headache (P = 0.80), frequency of migraine attacks (P = 0.63) and duration of attacks per hours (P = 0.48) were similar in conventional and cupping groups but these symptoms were decreased in each group during the study (P < 0.001). **Conclusion:** There was no significant difference between cupping plus serkangabin therapy and conventional treatment in the treatment and prophylaxis of migraine. The alternative therapy may be used in cases of drug intolerance, no medication response, and in primary care.

Key words: Cupping therapy, migraine, prophylaxis, serkangabin, treatment

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INTRODUCTION

Millions of people worldwide suffer from migraine. Migraine is one of the top 20 causes of disability in the world.[1,2] Migraine causes morbidity and bed rest in more than half of affected people. It causes a decrease in the quality of life, increased absenteeism and reduced productivity at work. It also increases healthcare costs.[2] Migraine attack is usually managed by nonsteroidal antiinflammatory drugs, acetaminophen, $5HT_1$ agonists including ergots and triptans, dopamine antagonists and sometimes opioid analgesics.[3-7] Different medications such as β-blockers, flunarizine, valproic acid, topiramate, amitriptyline, venlafaxine, gabapentin, naproxen, butterbur root, Vitamin B_2 and magnesium are recommended for migraine prophylaxis; however, efficacy and adverse effects are still controversial.[8]

Many diseases especially chronic ones are neither curable nor well palliated. Existing treatments can impose serious adverse reactions and provision of care is fragmented and impersonal.[9] Complementary alternative medicine (CAM) approach is frequently used today. More than 30% of Americans use CAM.[10] Over the past few decades, thousands of studies have been performed via various CAM approaches. Migraine patients seek and explore both conventional and CAM approaches.[11]

Wet cupping is an ancient medical technique used in several contemporary societies in East Asia and the Middle East[12] and it is frequently used for controlling pain.[13] Types of cupping include retained cupping, flash cupping, moving cupping, wet cupping, medicinal cupping, and needling cupping.[14] Wet cupping is a common method. In order to perform this procedure,

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a glass cup is placed on the skin and a vacuum is created inside it. After a few minutes, a superficial incision is placed in the area to suck the blood into the cup. This is repeated several times.[15]

It is being used in the management of hypertension, diabetes mellitus, headaches, renal, and biliary stones and for maintaining health. Little experimental studies have been devoted to test its efficacy to treat migraine headache. Some studies stated that wet cupping have clinical benefits on pain conditions.[12,15,16] Some studies have assessed the pain killing effect of wet cup and have found some advantages;[16-19] nevertheless, there are few studies about the effects of cupping on migraine.[12]

Serkangabin is a traditional drink which is frequently used for headache in Iran. In traditional Iranian medicine (TIM) it is believed that serkangabin has therapeutic effects in many diseases such as diabetes mellitus, hypertension, hyperlipidemia, ischemic heart disease, migraine and cerebrovascular diseases. According to the Iranian traditional literature, serkangabin can cause blood dilution and is easier to make compared with cupping procedure.[20]

Serkangabin from the words (serke, "vinegar") and (angobin, "honey") is a drink which is traditionally produced in Iran. We did not find any studies on the effect of serkangabin in the literature. The mixture of these two methods (wet cupping plus serkangabin) may lead to therapeutic synergy. Therefore, this study evaluated therapeutic and prophylactic effects of cupping and serkangabin and compares it with conventional migraine therapy.

MATERIALS AND METHODS

Study design and participants

Researchers of the CAM Research Center of Birjand University of Medical Sciences (BUMS) designed and conducted this randomized, controlled, open-label, comparative efficacy trial of cupping therapy and serkangabin versus conventional therapy in 2012. This study was approved by medical ethics committee of BUMS, and it was registered at ClinicalTrials.gov by number of NCT01476930.

Population of study included patients aged 15-50 years, with a current history of migraine with or without aura and according to international headache society criteria, 2004.[17] Patients with following criteria were not included:

1. Uncontrolled hypertension.
2. Ischemic heart disease.
3. Cardiac arrhythmia or symptomatic Wolff-Parkinson-White syndrome.
4. Previous stroke or transient ischemic attack.
5. Severe liver or renal impairment.
6. Any other severe or disabling medical condition.
7. History of alcohol or analgesic or psychotropic drug abuse.
8. Contraindication to or known hypersensitivity to drugs.
9. Current use or use in the previous 2 weeks of monoamine oxidase-inhibitors and other migraine related medication.
10. A pain disorder other than migraine as the primary presenting problem.
11. Current psychological treatment, psychiatric disorder needing immediate or priority treatment.
12. For women, current or planned breastfeeding or pregnancy or unwillingness to use an established contraceptive method.

Written informed consent was obtained from all patients before their inclusion into the study.

A pilot study was done for gathering some assumptions for calculating the study sample size. Sample size was calculated 29 patients in each groups according these assumptions: Alpha error of 5%, power of 85%, mean of headache severity after 2 weeks treatment in the conventional methods equal to 5.1 (±1.1) and in the serkangabin group 4.2 (±1.4). Then 391 headache patients were examined, and 76 confirmed migraine cases were divided into two study groups by simple randomization using random number table. Totally, 16 cases were excluded, and finally 60 cases were included in the study (41 were women and 19 men).

Then the study group completed a 6 months study program. 30 patients were treated with cupping and serkangabin and 30 patients with conventional migraine treatment protocols.

Instruments and drugs

All patients examined by a neurologist to confirm the diagnosis of a migraine headache. The study involved 5 visits (at the end of 2 weeks, 1, 3 and 6 months after treatment). The patients provided either conventional medical treatment or cupping therapy plus serkangabin. History and physical examination were done by one physician. A researcher assessed severity of headache by visual analog scale (0 = no pain to 10 = very severe pain) and frequency of attacks in a weak and duration of attacks per hour. The history was taken from patients by one medical doctor investigator. In conventional treatment group, standard treatment conducted by a neurologist that lasted for 6 months including migraine attack control and prophylactic medications. Medications used for a migraine attack were as follows:

1. Ergotamine tartrate USP (Tolidarou Pharmaceutical Co., Tehran, Iran) 2 mg tablet (DAROU PAKHSH PHARMA.

CHEM. Co) in the beginning of attack and every 30-min if necessary for control of pain with a maximum dose of 6 mg.
2. In case of no medication response or ergotamine intolerance the drug was replaced by sumatriptan succinate USP (Hakim Pharmaceutical Company) 50 mg tablet early in the attack and repeated every 2 h if necessary, with a maximum dose of 200 mg. The prophylactic treatments were nortriptyline or propranolol.

We tried to maximize the efficacy and tolerability of β-blocker and tricyclic antidepressant treatment by using a flexible target dose. Treatment was started with one 10 mg tablet of propranolol hydrochloride USP (Tolidarou Pharmaceutical Co., Tehran, Iran) 3 times daily which increased as tolerated to 40 mg 3 times daily at week 4. Participants, who did not tolerate 3 times daily dose of 20 mg and were unimproved according to the neurologist view, were switched to nortriptyline hydrochloride USP (Loghman Pharmaceutical and Hygienic Co.) 25 mg nightly, which increased to 50 mg nightly at week 2. Then medical treatment continued for the rest of the 6 months of study.

In cupping therapy group, cupping and serkangabin therapy was conducted by TIM specialist who had 10 years of experience in TIM. Wet cupping (hijama with bloodletting) was done monthly for 3 times, beginning 2 weeks after the first appearance according to "Aam" protocol Figure 1 (Midline interscapular area at the level of third to fifth thoracic vertebrae, T3-T5) with single use only, 100 ml plastic cups [Figure 2a and b].

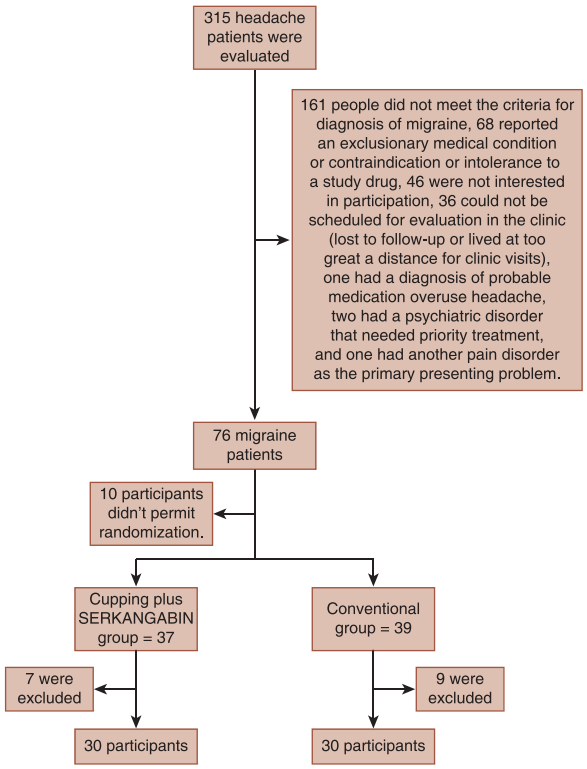

Figure 1: Design and profile of participants at baseline. Several participants were excluded from the study because of not showing up on time despite several reminder calls

In order to produce serkangabin, some honey should be boiled in a large pot of water for 2-3 min. Then the content of Pan is mixed with vinegar. Then it is cooled at room's temperature and the peppermint water (Peppermint Water) is added to the mixture. In order to make serkangabin-drink, a cup of this syrup is mixed with 4-5 cups of water. A full glass of syrup serkangabin (200 ml) will be taken every night for 60 days from the first appearance. Each 200 ml of serkangabin syrup consists of 15 ml of multifloral honey, 15 ml of distilled peppermint water (distillate of peppermint leaf-mentha piperita-soaked in purified water) and 7 ml of grape (Vitis vinefera) vinegar, made from fermented grape.

Data analysis

Study outcomes were (1) frequency of attacks in a week, (2) duration of attacks and (3) severity of headache. The outcome trends were compared between the cupping therapy and conventional treatment groups during the 6 months period.

Data analysis was done by SAS software version 9.1 (SAS Institute, Cary, NC, USA). Chi-square and Fisher exact test were used to compare categorical variable between the two groups. The quantitative variable was compared between the two groups by independent *t*-test. Repeated Measurement by generalized estimation equation method was used to assess the main effect and interactions between time and treatment groups. Also, adjustment for age and sex was considered in the models.

Figure 2: Superficial incisions are made on the skin using 15-22 gauge surgical blade in Midline interscapular area at the level of third to fifth thoracic vertebrae, T3-T5 (a) then sucking with single use 100 ml plastic cups (b) until it is filled with blood. The cup is removed, and the process is repeated 3 times

RESULTS

Mean and standard deviation of age for cupping therapy group and conventional treatment group were 31.7 ± 7.6 and 32.6 ± 12.7 years, respectively (P = 0.45). There were no statistically significant difference between two groups in relation to sex, marital status, oral contraceptive (OCP) consumption, residence, family history of headache and age [Table 1]. Treatment was accompanied by no relevant changes in vital signs, electrocardiogram or results of cardiovascular examination.

Figure 3 shows that the severity of headaches 2 weeks; and 1, 3 and 6 months after treatment were not different between conventional and cupping groups (P = 0.80). According to Table 2, frequency of attacks in a week, after 2 weeks; and 1, 3 and 6 months of treatment were indistinguishable as well (P = 0.63). Also duration of the attacks per hours after 2 weeks, 1, 3 and 6 months after the treatment were not different in conventional and cupping groups which is presented in the Figures 4, 5 and Table 2 (P = 0.48). According to the result, both treatments were effective in reducing the severity, frequency and duration of headache during the different period of follow-up [Table 2].

DISCUSSION

To our knowledge, this is the first controlled trial that compared serkangabin syrup and cupping in patients with migraine. In this trial, treatment of migraine with either cupping plus serkangabin or conventional treatment resulted in similar outcomes. Severity of headaches, duration and frequency of attacks were similar in two treatment groups during 6 months of study. The results of our study showed that an alternative therapy by cupping plus serkangabin was an effective approach to headache treatment and prophylaxis in patients with migraine.

The findings of our study is congruent with those of other studies and indicate that cupping therapy is a promising CAM treatment method for migraine headache and other painful conditions such as carpal tunnel syndrome (CTS), low back pain, and fibromyalgia.[12,16,18-23] Ahmadi, *et al.* in their study on cupping therapy in chronic headaches compared headache severity, frequency of headache days in month and medication consumption before and 3 months

Table 1: Demographic and clinical data of the cases

Variables	Conventional (%)	Cupping plus serkangabin (%)	*P*
Sex			
Male	7 (23.3)	12 (40)	0.165
Female	23 (76.7)	18 (60)	
Marital status			
Single	8 (26.7)	7 (23.3)	0.766
Married	22 (73.3)	23 (76.7)	
OCP consumption			
Yes	2 (6.7)	0	0.492†
No	28 (93.3)	30 (100)	
Residence			
Urban	27 (90)	29 (96.7)	0.612†
Rural	3 (10)	1 (3.3)	
Family history of headache			
Yes	17 (56.7)	15 (50)	0.605
No	13 (43.3)	15 (50)	
Smoking			
Yes	2 (6.7)	0	0.492†
No	28 (93.3)	30 (100)	
Age (mean)	32.6 (±12.7)	31.7 (±7.6)	0.459††

There were no statistically differences between two groups according to sex, marital status, OCP consumption, residence, family history of headache and age; †Analyzed by Fisher exact test; ††Analyzed by independent *t*-test; OCP = Oral contraceptive

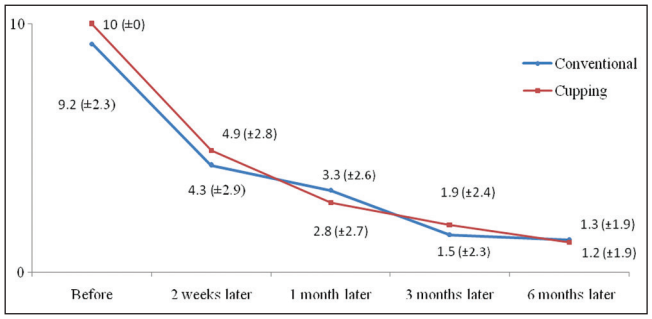

Figure 3: Comparison of severity of headaches between study groups during the study

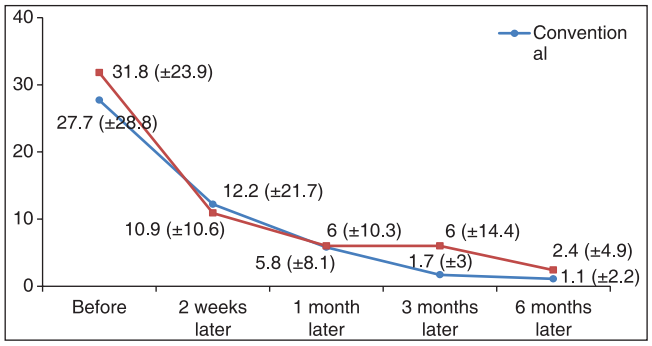

Figure 4: Comparison of duration of attacks per hours between first and next presentations and the end of the study in two study groups

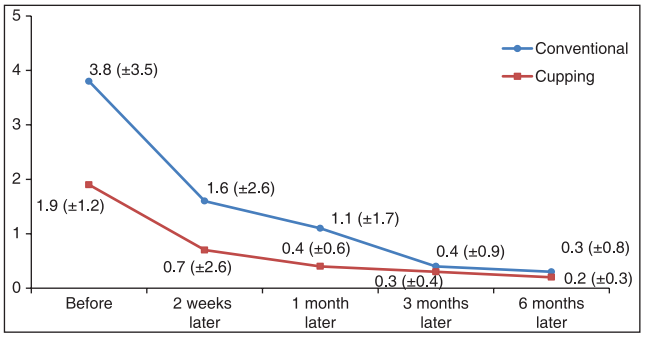

Figure 5: Comparison of frequency of attacks in a week between first and next presentations and the end of study in two study groups

Table 2: Comparison of severity, frequency and duration of headache between study groups during the study following sex and age control

Outcome	Parameter	Estimate	SE	95% CI		P
				Lower limit	Upper limit	
Severity of headache	Time	−0.5729	0.1656	−0.8975	−0.2484	0.0005
	Group	−0.1296	0.1453	−0.4144	0.1553	0.3725
	Time*group	0.0275	0.1089	−0.1860	0.2409	0.8009
	Age	−0.0042	0.0025	−0.0091	0.0007	0.0926
	Sex	0.0036	0.552	−0.1047	0.1118	0.9483
Frequency of headache	Time	−0.7310	0.1902	−1.1037	−0.3583	0.0001
	Group	0.2546	0.2357	−0.2073	0.7166	0.2800
	Time*group	0.0646	0.1344	−0.1978	0.3280	0.6306
	Age	0.0089	0.0048	−0.0006	0.0184	0.0657
	Sex	−0.2063	0.1675	−0.5346	0.1220	0.2182
Duration of headache	Time	1.1479	0.2901	0.5793	1.7165	<0.001
	Group	0.9359	0.5696	−0.1805	2.0523	0.1004
	Time*group	−0.1299	0.1841	−0.4908	0.2309	0.4804
	Age	−0.0179	0.0203	−0.0577	0.0219	0.3791
	Sex	−0.2400	0.4130	−1.0495	0.5695	0.5612

SE = Standard error; CI = Confidence interval

after cupping. It revealed statistically significant decrease (86%) in the frequency of days with headache, medication consumption (80%) and severity of headache (66%). In 93% of patients, it had positive therapeutic effects.[12] Lauche *et al*. in their study of cupping in neck pain concluded that cupping appeared to be effective in relieving chronic nonspecific pain which had an influence on pain processing.[19] Cao, *et al*. showed reduction in fibromyalgia pain and number of tender points in their study of cupping therapy.[22] Lee, *et al*. in their assessment of systematic reviews of cupping effectiveness, stated that it was effective in reducing pain.[15] Cao, *et al*. in their systematic review stated that the majority of studies on cupping show potential benefit on pain conditions.[16] Michalsen, *et al*. in a randomized clinical trial on effects of cupping in CTS concluded that it may be effective in relieving pain and other symptoms related to CTS.[23] Farhadi *et al*. in their randomized controlled study on wet cupping for nonspecific low back pain concluded that it was safe and acceptable to patients and more effective than usual care.[21]

There are very few studies in the literature that might provide clues about mechanism of wet-cupping.[21] It has been suggested that wet-cupping analgesia is similar to the effect of acupuncture and occurs via segmental, extra-segmental and central regulatory action.[24]

Cupping and serkangabin can adjust some neurotransmitter like serotonin, dopamine, endorphin, calcitonin-gene related peptide and acetylcholine which are connected to headaches. In addition, they can adjust hematocrit and immune system through bleeding and local inflammation. Local inflammation activates complementary immune system and increases the level of immune products.[12] However, the mechanism is still unknown[18] and needs further studies.

Serkangabin is made from honey, peppermint water, and vinegar. Therefore, some pain relief effects of this drink may be originated from the therapeutic effects of these herbal drugs.

Limitations in our study include: For the reason that it was a new treatment protocol, there were no similar studies to assist us with the study sample size. The study had longer follow-ups and includes other factors like cost, side effects, patient's preference and compliance. However, relapse after treatment may suggest revised approaches. Moreover, in our study the advantages are due to both wet cupping plus serkangabin and further studies are required to distinguish the effects. The other limitation was the open-labeled design of our study. There might be a supposed psychological effects related to cupping that is effective in reducing pain by itself. This effect, in case of being accurate, could be considered as an advantage of cupping procedure. Consequently, authors recommend re-evaluation of periodic wet cupping biannually in prevention of migraine relapse after prophylactic treatment.

CONCLUSION

Our study suggests that cupping plus serkangabin therapy is effective parallel to that of conventional therapy in management and prophylaxis of migraine headaches. However, this may be used in cases of medication intolerance, nonresponsive medication, and primary care.

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AUTHOR'S CONTRIBUTIONS

MN, MDF and JH were responsible for the study concept and design. Literature search done by MN,MDF and MKhR.MN and MDF obtained funding from BUMS. Cupping done by MN and JH. Neurologic evaluation and confirming migraine diagnosis and conventional treatment, performed by MDF. NS, JH and MDF were involved in acquisition of data. GhSh analyzed and interpreted the data and did the statistical analysis. MKhR and MN drafted the manuscript, and all authors critically revised it for important intellectual content. MN, MDF, JH and MKhR provided administrative, technical, or material support. MN and MDF supervised the study.

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