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Research Article

Post-auricular leech therapy reduced headache & migraine days in chronic migraine

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ABSTRACT

Background: Migraine is an exceedingly common disorder that causes substantial pain, disability and societal burden. Unfortunately, conventional treatments are insufficient, inadequate, or associated with significant risks, such as overuse, abuse or addiction. The Unani system of Medicine has been treating migraine since centuries. Leech therapy (*Irsale Alaqa*) has been employed successfully in severe persistent headache, mania and insomnia since decades.

Aim: The purpose of our study was to evaluate the impact of post auricular leech therapy in migraine and to collect data to warrant further clinical trials.

Methods: We conducted a case series on 7 patients who had failed conventional oral treatments for the migraine. After informed consent, post auricular leech therapy was done. Patients were asked to keep detailed headache calendars, documenting the number of headache days, migraine days, the intensity of headaches/ migraines and analgesic usage. We compared these parameters before and after 2 months of therapy.

Results: We observed a reduction in the number of headache & migraine days and amount of painkillers used without any adverse effects. ($P \leq 0.01$) Improvement in quality of life was also observed.

Discussion: We reviewed the literature related to the medicinal leeches (*Hirudo medicinalis*), used for the treatment in these cases. Leech saliva contains certain potent anesthetic, anti-inflammatory and vasodilator substances, suggesting plausible mechanisms of action in these cases.

Conclusion: The preliminary findings indicate the safe and potential therapeutic role of leech therapy. So further trials should be carried out to explore the therapeutic potential of this therapy in chronic migraine.

Keywords: Chronic Migraine, leech therapy, *hirudo medicinalis*, headache, Unani Medicine, complementary Medicine.

Article Info: Received 15 Dec 2018; Review Completed 28 Jan 2019; Accepted 29 Jan 2019; Available online 15 Feb 2019



Cite this article as:

Ansari S, Fasihuzzaman, Jabeen A, Sultana A, Khan QA, Post-auricular leech therapy reduced headache & migraine days in chronic migraine, Journal of Drug Delivery and Therapeutics. 2019; 9(1-s):75-80
<http://dx.doi.org/10.22270/jddt.v9i1-s.2345>



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INTRODUCTION

Chronic migraine is a distinct and relatively recently defined sub-type of Chronic Daily Headache (CDH). Chronic Migraine (CM) is defined by the International Headache Society (IHS-2R) as "a debilitating condition where patients suffer headaches for 15 days or more per month, with migraine on at least 8 of those days,¹ occurring in a patient with a lifetime history of at least five prior migraine attacks not attributed to another causative disorder and no medication overuse.² In real terms, this means that a person who is affected by CM has a headache or migraine for more than half the days in the month. Episodic migraine (EM) is the other sub-type of CDH, which is defined as less than 15 headache days per month.

Migraine is part of most disabling of neurological disorders. The World Health Organization (WHO) has identified migraine among the world's top 19th leading causes of disability.³ Estimates of migraine prevalence vary, due to non-uniform study methodology. There are no population-based studies from India. Based on large epidemiologic studies worldwide, the prevalence of migraine was about 18% of women and 6% of men. Migraine imposes an enormous health burden on individual headache sufferers and on society. It is a recurrent and often a lifelong illness characterized by attacks include features such as headache of moderate or severe intensity, nausea (the most characteristic), one-sided and/or pulsating quality, aggravated by routine physical activity with a duration of

hours to 2-3 days. Its prevalence peaks during the most productive years, between the ages of 25 and 55 years which leads to work loss and reduced productivity.^{1, 4} CM population also had higher rates of cardiovascular and respiratory comorbidities, such as hypertension, high cholesterol, stroke, emphysema or chronic obstructive pulmonary disease, and asthma.⁵ Therefore, WHO classified CM as more disabling than blindness, paraplegia, angina or rheumatoid arthritis.

The migraine has been documented & described nearly in all classical text of Unani medicine as a disease entity "Shaqeqa." *Shaqeqa* is an Arabic word, derived from the word "Shaq" which means a part or a side, as the headache is usually one sided. Hippocrates (460-375 BC) was the first to describe such constellation of symptoms that included aura, pain and vomiting as part of a singular disorder.^{7, 8, 9} *Jalinoos/ Galen* (131-201 AD) mentioned the disease "hemicrania" meaning "half of the head" to describe such headaches. Hemicrania translated from Greek to Latin became "hemicranium" and was transformed to "megrim" in old English and "migrain" in French.⁸

Leech therapy (*Irsale Alaq*) is one of a regimen under the regimenal therapy (*Ilaj bit tadbeer*) in Unani medicine.¹⁰ Medicinal leeches (*Hirudo medicinalis*) have been used in various clinical studies to provide relief in chronic pain conditions such as osteoarthritis¹¹⁻¹⁶, chronic pain syndrome¹⁷, severe cancer pain¹⁸ etc. including migraine.¹⁹ So we performed the present case series to assess the impact of post-auricular leech therapy in CM cases.

MATERIAL & METHODS

Informed consent was drawn from the patients in their known languages. Study was approved by institutional ethics committee. Human data included in this case series was obtained in compliance with the Declaration of Helsinki as revised in 1983.

Intervention

Before leech therapy, patients were investigated with set of laboratory tests such as complete blood count, random blood sugar, clotting time (CT), bleeding time (BT), international normalized ration (INR) and detection test for HIV I & II, HBsAg and HCV to rule out any blood borne infectious disease, coagulation disorder, anemia, diabetes etc. which forbid leech application. After the fulfilling criteria, single medicinal leech (*Hirudo medicinalis*), was applied at post auricular region bilaterally every fifteen days for 2 months (at baseline, 15th day, 30th day and 45th day of enrollment).

Procedure: Under hygienic condition, patient was allowed to lie down at prone position in the minor operation theatre. Post auricular region was cleaned with fresh water and draped. A small prick was given with a sterile needle at post auricular region at the level of auricular tubercle. Let the small amount of blood to ooze out so that the leech could get attached easily. 1 medicinal leech was applied.

After 30 min, when the leech has sucked an average of 5-10ml of blood, leech was detached by pouring a drop of betadine in leech bite area. Sometime leech also got detached itself. We allowed the blood to flow for a few minutes after detachment. Later on, leech bite area was cleaned with betadine solution and antiseptic compression bandaging was done. Next day, dressing was opened to check for fresh bleeding and patient was thereafter discharged. (Figure 1)

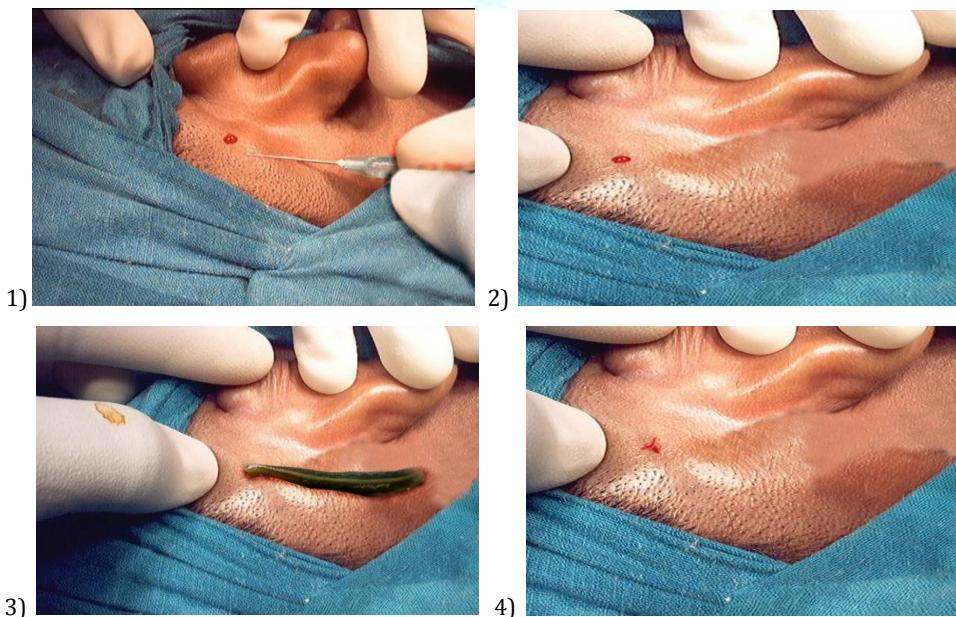


Figure 1: Procedure of leech application

Case presentation

Case 1: A 35-years-old Indian female of low socio-economic status, admitted from Medicine OPD of Majeedia Unani Hospital (MUH), presented with a 10-years history of debilitating migraine headaches 25-26 days and 15-16 migraine days with classic aura per month, satisfying the International Classification of Headache Disorders-2 (ICHD-2) criteria. She described them as the worst feeling of her

life, with a pain scale rating of 10 out of 10 on the VAS scale. The MRI showed no obvious abnormality. The total MSQ (migraine specific quality of life questionnaire) score in the first visit was 20 which showed severity in headache and extremely deranged quality of life in this case. Patient was taking Voveran (Dichlofenac sodium 75mg) injection and Combiflam tablet (Ibuprofen, 400mg and Paracetamol, 325mg) around 6-8 tablets to control her symptoms. She

also was also taking Triptan and other NSAIDs but since 2 years was getting no relief.

Case 2: 29-years-old Indian female came to OPD of MUH female with complains of migraine, hair loss and gastritis from 3 years, satisfying the ICHD-2 criteria for CM. She typically had more than 20 days per month of headaches. She experienced migraine without aura, around 10 per month. The total MSQ score in the first visit was 30. Patient was taking Voveran injection and Dichlovene (Dichlofenac, 50mg & Paracetamol, 500mg), around 2 tablets during migraine and one tablet daily to ease her headache.

Case 3: 50 years old female Indian patient admitted with a long history of migraines, and headaches from 10 years. She had severe headaches of more than 15 days and migraine without aura for more than 12 days per month, diagnosed as CM. She occasionally required parenteral analgetic injectables by a local practitioner at home. She was taking Dichlovene (Dichlofenac, 50mg & Paracetamol, 500mg), around 2 tablets daily to relieve such headaches. Total MSQ score in the first visit was 30.

Case 4: 38 years Indian male came to the outpatient department of MUH with history of migraine and polyarthralgia, complying with the ICHD-2 criteria for CM. He typically experienced more than 8 migraines per month without classic aura, as well as mild to moderate frequent episodic daily headache. Patient was taking Voveran injection during migraine and Dichlofenac 100mg SR during daily headaches. Total MSQ score in the first visit was 42.

Case 5: Another 35-years-old Indian female, admitted in MUH, presented with a 12-years history of migraine headaches 25-26 days with hair fall and insomnia. She typically experienced around 16-17 migraine days with classic aura per month, complying with the International Classification of Headache Disorders-2 (ICHD-2) criteria. Imaging of the brain showed no obvious abnormality. Total MSQ score in the initial visit was 20 which showed severity in headache and extremely deranged quality of life in this case. Patient was taking Voveran (Dichlofenac sodium 75mg) injection and Combiflam tablet (Ibuprofen, 400mg and Paracetamol, 325mg) around 3 tablets but was getting no relief.

Case 6: 25 years old Indian female admitted in MUH, satisfying the ICHD-2 criteria for CM. She typically had more

than 15 days per month of headaches. She experienced migraine without aura, around 8 per month. Total MSQ score in the first visit was 44. Patient was taking Voveran injection and Dichlovene (Dichlofenac, 50mg & Paracetamol, 500mg), around 2 tablets during migraine to alleviate her symptoms.

Case 7: 55 years Indian male, admitted in MUH, satisfying the ICHD-2 criteria for CM. He typically experienced more than 18 days headache and more than 10 days migraine without aura per month. Patient was taking Ibuprofen 600mg around 2 tablets with parenteral analgesia to alleviate his symptoms. Total MSQ score in the first visit was 20.

Outcome Measures

Patients were requested to keep the detailed headache calendar. Results were evaluated based on reduction in the number of migraine days, number of daily migraine headache days and amount of analgesic use. Improvement in quality of life was assessed with migraine specific quality of life questionnaire (MSQ score) version 2.1. MSQ comprises of 14 questions which addresses three dimensions (role function restrictive, preventive, and emotional function. Each of the three MSQ dimensions was scored independently. For each dimension, a higher score indicates a better health status.

Statistical Analysis

Statistical significance was calculated by means of a Wilcoxon signed rank test, using Graphpad Instat 3.10 32 for windows [Graphpad softwares Inc, San Diego, California, USA] created July 10, 2009.

ns - Non significant, * $P < 0.05$ significant, ** $P < 0.01$ very significant, *** $P < 0.001$ extremely significant.

RESULTS

After 2 months (4 sittings) of leech therapy extremely significant relief in condition of the patients was observed. Improvements in the following parameters were observed after treatment.

Effect on number of migraine headache days: Before treatment, mean headache days in these patients were around 19.14 days/ month, which significantly reduced to around 5/ month days after treatment ($P \leq 0.01$) [Table 1]

Table 1: Effect of leech therapy in migraine headache days in chronic migraine

Case No.	Pre-Treatment	Post- Treatment
Case 1	25.5	10
Case 2	20	7
Case 3	15	3
Case 4	15	0
Case 5	25.5	10
Case 6	15	0
Case 7	18	5

Effect on number of migraine days: Before treatment, mean migraine days in these patients were 11.42 days/ month, which significantly reduced to 2.71 days/ month after treatment. ($P \leq 0.01$) [Table 2]

Table 2: Effect of leech therapy migraine days in chronic migraine

Case No.	Pre-Treatment	Post- Treatment
Case 1	15.5	4.5
Case 2	10	4
Case 3	12	4
Case 4	8	0
Case 5	16.5	5.5
Case 6	8	0
Case 7	10	1

Effect on total MSQ (migraine specific quality of life questionnaire) score: Before treatment, mean MSQ score in role function restrictive, preventive and emotional function dimension in these 7 patients were 14.71, 9, & 8 respectively which after treatment upgraded to 32, 19.85, & 16.25 respectively. ($P \leq 0.01$) [Table 3]

Table 3: Effect of leech therapy in MSQ Score in Chronic Migraine

Case No.	Role function restrictive		Role function preventive		Emotional function	
	Pre-Treatment	Post-Treatment	Pre-Treatment	Post-Treatment	Pre-Treatment	Post-Treatment
Case 1	9	28	6	16	5	12
Case 2	14	31	8	18	8	16
Case 3	12	36	9	18	9	16
Case 4	21	33	12	22	9	17
Case 5	9	28	6	20	5	18
Case 6	23	34	12	23	10	17
Case 7	15	34	10	22	10	18

Case 3, 4, 6 and 7 (57.14%), stopped taking NSAID's while in the other participants, dose was significantly tapered. Patients (100%) met their normal sleep pattern. No adverse events were observed during and after leech therapy.

DISCUSSION

Migraine has been documented in Unani system of Medicine as entity "shaqeqa" with clinical manifestation of episodes of recurrent severe headaches, typically unilateral and throbbing, which may be associated with nausea, vomiting, photophobia or phonophobia. Approximately one-third of patients with migraine also experience 'aura' - transient neurological symptoms which are most frequently visual, but may involve speech and/or other senses.²⁰ Migraine with or without aura, both are three times more common in females than males.²¹

India is the richest source of medicinal leeches. Hence, leeches have been applied for various therapeutic purposes since decades. Secretion of the salivary glands of medicinal leeches contains more than 100 bioactive substances. These secretions include vasodilators, bacteriostatic, analgesic, anti-inflammatory and anticoagulants, anti-edematous, which eliminate microcirculatory disorders, restore the damaged vascular permeability of tissues and organs, eliminate hypoxia, reduce blood pressure, increase immune

system activity, resolving the cause of pain and improve the bioenergetic status of the organism.²² More than 20 identified bioactive substances such as antistasin, eglins, guamerin, hirudin, saratin, bdellins, complement, and carboxypeptidase inhibitors have been identified. They have analgesic, anti-inflammatory, platelet inhibitory, anticoagulant, and thrombin regulatory functions, as well as extracellular matrix degradative and antimicrobial effects.²³ U.S. Food and Drug Administration (USA-FDA) has allowed the sale of leeches in this country for plastic surgery, the general purpose and microsurgery in 2004.²²

The present case series was performed with five females and two male patients of CM who were satisfying the ICHD-2R criteria. After 4 sittings of leech therapy at bilateral post-auricular region, highly significant reduction in mean migraine headache days and migraine days per month was observed (Wilcoxon signed rank $P \leq 0.01$) [Figure 2].

The reduction in mean migraine headache days and migraine days per month after treatment with leech therapy ($P \leq 0.01$), observed in our study might be much greater than those

reported in the treatment with botulinum toxin infiltrations ($P = 0.250$) (Bergmans et al, 2014)²⁴ and stromal vascular fraction (Bright et al, 2014)²⁵. Both of these case series have included CM cases similar to our cases. However, case series performed with botulinum toxin infiltration did not report any significant reduction in analgesic use.²⁴ While in our study, four cases (case 3, 4, 6 & 7) have completely discontinued their analgesic drugs. Moreover, in two phase 3 Research Evaluating Migraine Prophylaxis Therapy (PREEMPT) trials which have recruited 1384 patients of CM and treated them with botulinum toxin for 12 weeks. Results of this large clinical trial reported that 70% of these patients had less than half of the number of headaches they had originally experienced. In our study, cases treated leech therapy reported nearly 1/4th of the headaches they originally had. Further, botulinum infiltration therapy is costly and the commonest side effects are neck pain, muscular weakness, and drooping of the eyelid.²⁶

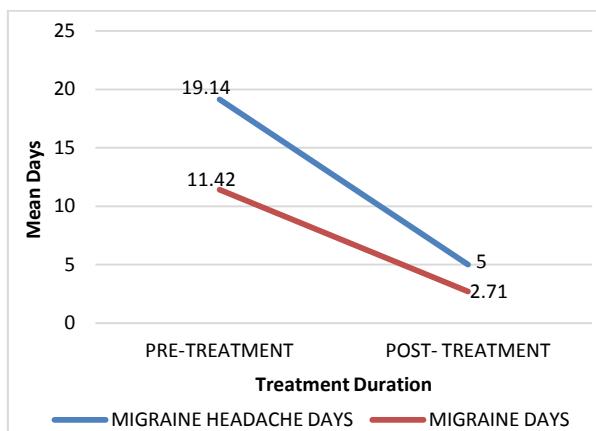


Figure 2: Effect of leech therapy on migraine headache and migraine days

This is the second reported study to our knowledge, to examine the effect of post auricular leech therapy in chronic migraine. Previously, Bakhshi et al have conducted a quasi-experimental pilot study to evaluate leech therapy in migraine headache but they have used 1 to 3 leeches in a single session unilaterally as well as they have not evaluated effect of leech therapy on migraine days and quality of life. They reported that single course of leech therapy offers benefits equal to propranolol 80 mg/day and amitriptyline 50 mg/day ($P=0.00$) in reducing pain in women with migraine headaches and its benefits persist at least for three months.¹⁹

The neurovascular theory of migraine states that excessive cortical excitability occurs due to hyperexcitability of neurons via. cutaneous allodynia in CM.^{27, 28} Due to this hyper-excitability, propagation of cortical spreading depression (CSD) occur in cortical cells.^{4, 28, 29} CSD leads to hypoperfusion of cortical cells owing to vaso-constriction of cortical vascular bed which starts migraine and headache attacks evident by observations of Olsen et al and PET scan during migraine attacks.⁴ Headache may end when compensatory hyper-perfusion occurs which activate trigeminal vascular system (TVS) to stimulate the release of CGRP (calcitonin G related peptide) from peripheral neuronal terminals. The latter is the key neuropeptide in the mechanism of migraine and levels correlate with the degree of headache pain. CGRP plays an important role in the transmission of meningeal input to the brain^{4, 26} and cause neurogenic inflammation of the dura matter.³⁰

Conventional NSAID's, and other anesthetic and anti-inflammatory drugs benefits on the basis that they downstream propagation of CSD³⁰ as well as reduced the

plasma protein extravasation in the dura matter and nociceptors in peripheral arm of TVS and meninges.^{32, 33} The observed anti-migraine effect with leech therapy could be due to presence of anesthetic and anti-inflammatory substances in leech saliva such as antistasin, hirustasin, ghilantens, eglin C, LDTI, complement C1 inhibitor, guamerin and piguamerin, carboxypeptidase inhibitor, bdellins and bdellastasin²³ which when enters the circulation might have prevented the propagation of CSD viz a viz prevented the hypoperfusion of cortical cells which is the culprit of beginning of migraine attacks.²² Hypoperfusion and later on compensatory hyper-perfusion is associated with inflammation of the cortical cells, TVS and neural sheaths of neurons which lead to migraine headache.³¹ Leech saliva contains above mentioned anti-inflammatory and antiedematous substances which might have reduced the inflammation of cortical areas, peripheral arm of TVS as well as neural sheath, could be the plausible mechanism of reduction of migraine headaches in our patients.²²

Conventional medicine such as Beta adrenergic blockers (propranolol, atenolol etc.) seems to exert therapeutic effects in migraine via actions at sites in the central nervous system (CNS) intimately involved with nociception (locus coeruleus, thalamus). Propranolol has a high affinity for 5-HT binding sites in the CNS and antagonizes serotonin (5-HT1A and 5-HT2B receptors), thus reducing neuronal hyperexcitability viz prevention of propagation of CSD.^{34, 35} In addition, they relax smooth muscles of blood vessels by blocking B-adrenergic receptors.³⁵ It is well known that leech saliva contain substances such as acetylcholine.²³ Acetylcholine acts as an antagonist to the 1-tryptophan, facilitating the catabolism of serotonin. It is equally a relaxant of endothelial smooth muscle.³⁶ Thus, acetylcholine in leech saliva might have antagonize serotonin and reduced the hyperexcitability in neurons as well as acted as well as relaxed smooth muscles of blood vessel, similar B-blockers.

Bakhshi et al. have proposed that the anti-inflammatory and analgesic substances in the leech saliva might have the property to reduce the release of CGRP from neurovascular terminals through inhibition of TVS and thus induced the analgesic action. Also, physical effects of leech therapy in reducing pain might be due to the excretion or dilution of numerous inflammatory mediators such as cytokines.¹⁹

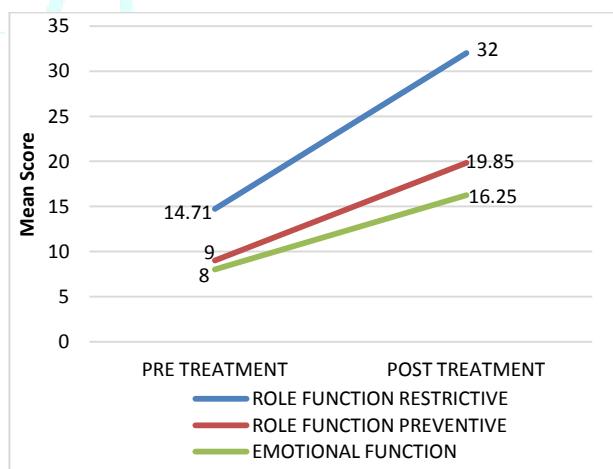


Figure 3: Effect of leech therapy on dimensions of MSQ score

Similarly in our study, our cases have experienced improved quality of life after leech application. Mean scores of MSQ dimensions (role function restrictive, preventive and emotional function) was upgraded. [Figure 3] For each dimension, a higher score indicates a better health status. So significant improvement in quality of life of patients was

observed in our study, possibly due to reduction in migraine & tension states, return toward normal sleep pattern, reduction in amount of analgesic drugs and associated symptoms of NSAID induced gastritis.

CONCLUSION

In our experience, post auricular leech therapy can significantly control migraine headache and migraine days without any adverse events. The therapy can improve the quality of life in chronic migraine cases. So further clinical trials should be conducted to substantiate absolute efficacy and mechanism of action of medicinal leeches by measuring CGRP (calcitonin G related peptide) levels in chronic migraine.

Acknowledgements: We appreciate the co-operation of our study patients. We are thankful to the medical doctors and staff of center for Ilaj bit tadbeer, School of Unani medical education and research, Jamia Hamdard, New Delhi.

Conflicts of interest: Authors declared none

Financial support and sponsorship: Nil

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