

LEECH THERAPY IN THE MANAGEMENT OF KNEE OSTEOARTHRITIS-A REVIEW

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ABSTRACT

Leech therapy is a frequently used treatment modality in traditional system of medicine including Unani medicine and involves application of medicinally viable leech species either alone or in combination with pharmacological agents. It has been used for the management of various rheumatological disorders including knee Osteoarthritis (OA). Knee OA, a degenerative arthritis of the knee joint, is characterized by joint pain, stiffness, crepitus, varying degrees of functional limitation and reduced quality of life. The objectives of treatment of Knee OA are reduction of pain and stiffness, maintenance of function, retarding the disease progression and improvement in the quality of life. A number of studies have been carried out to evaluate the efficacy of

leeching in the management of knee OA. In this review we systematically present the observations and results of these studies.

KEYWORDS: Rheumatology, Unani, Degenerative, Pain, Enzymes.

INTRODUCTION

Leech therapy involves application of medicinally viable leech species, on any part of human body for therapeutic purposes and has been used either alone or in combination with oral pharmacological agents. Leeches are segmented hermaphrodite, hematophagous, invertebrate animals that belong to phylum *Annelida*. Different species of leech are being used in different parts of world. *Hirudo medicinalis*, is the most common species used in Europe and is being chiefly bred under controlled conditions in leech farms. Other species that have been used are: *H. troctina* in North Africa, *H. nipponia* in Japan, *H. quinquestriata* in Australia,

Poecilobdella granulosa, *Hirudinaria javanica* and *Hirudinaria manillensis* in south-east Asia, *Haementeria officinalis* in Mexico and *Macrobdella decora* in the USA.^[1] In Indian subcontinent *Hirudinaria granulosa* has been effectively used for therapeutic purposes.^[2]

Traditionally Leech therapy has been used as a method of bloodletting that results in the expulsion of vitiated blood from the body in an attempt to restore health.^[3,4,5,6] It has now been observed that in addition to sucking of blood, leading to decongestion, leeches inject an array of biochemically active substances at the site of application resulting in therapeutic effects.^[7] The decongestive effect of leeches is achieved by two conceivable mechanisms. The first mechanism involves the blood sucked by the leech itself and secondly by the passive bleeding at the site of leech application. Leeches temporarily increase the tissue perfusion levels by actively drawing off blood and maintain physiological requirements within the congested tissue. An increased superficial skin perfusion around the leech bite has been demonstrated using Laser Doppler flowmetry. Secondly the leech injects its salivary secretions that contain a number of biochemically active molecules including hirudin, apyrase, collagenase, hyaluronidase etc at the site of bite reducing congestion owing to their anti-coagulant effect.^[8]

Leech therapy is a frequently used treatment modality for the management of various disease including knee OA in traditional systems of medicine including Unani system.^[2] OA is by far the most common form of arthritis and one of the leading causes of pain and disability worldwide. Pain, stiffness, joint deformity and loss of joint mobility have a substantial impact on individuals. OA of the large joints especially knee joint reduces patient mobility and accounts for more trouble with climbing stairs and walking than any other disease.^[9]

The objectives of managing knee OA include reduction of pain, stiffness, maintenance or improvement of function, retarding the disease's progression and improvement of quality of life. We reviewed the clinical trials that were conducted to evaluate the efficacy and safety of Leech therapy in the management of knee OA, the aim being to identify, organize and evaluate various studies and isolating the research gaps.

EFFECTIVENESS OF LEECH THERAPY

A total of five studies are reported in this review (Table 1) with sample size ranging from 40 to 113. In three out of five trials test group received only leech therapy while in two studies test group received polyherbal Unani formulations in addition to leech therapy. The study

with shortest study duration had a treatment protocol of 3 weeks while the longest one had 6 month treatment protocol. Outcome measures used by these studies included WOMAC, KOOS scales for evaluating pain, stiffness and physical function.

Table-1.

Study	Design	'N'	Duration	Treatment with leeches	Dose/ Device	Control
A. Michalsen (2003) ^[10]	Randomized controlled	51	13 weeks	Single trial	4-6 leeches	Topical Diclofenac-sodium 10mg-1 g gel
Stange R (2012) ^[11]	Randomized controlled crossover	52	3 weeks	Single trial	8 leeches	Transcutaneous electric nerve stimulation (TENS)
Stefan Andereya (2008) ^[12]	Randomized controlled	113	6 months	Group 1 single trial Group 2 Double trial	4 leeches	Placebo with artificial leech.
SM Abaas Zaidi (2009) ^[2]	Randomized controlled	40	6 weeks	4 sittings 14 day interval	3 leeches	Unani polyherbal formulation (<i>Safoof Mafasil Khas</i>) and topical herbal oil (<i>Suranjan Oil</i>)
Shiffa M (2013) ^[13]	Randomized controlled	60	8 Weeks	5 sittings along with Unani formulation on days 0,7,14,21 and 28	2 leeches	<i>Qurs-e-Mafasil Jadeed 5mg twice daily for 28 days</i>

A treatment regimen with 4 leeches in knee OA was studied by A. Michalsen et al., on 51 subjects and observations suggested significant improvement in pain as compared to baseline in the leech group after one week. The mean WOMAC pain score (\pm SD) reduced from 53.5 ± 13.7 (n =24) to 19.3 ± 12.2 (n =24) at 7 days in the leech therapy group and from 51.5 ± 16.8 (n = 27) to 42.4 ± 19.7 (n \pm 26) in the diclofenac group. The estimated group difference for pain relief was highly significant on day seven (-23.9 [CI, -32.8 to -15.1]; ($P < 0.001$) in favour of leech therapy although the difference was most pronounced on day 3 (-29.5 [CI, -36.3 to -22.6]; $P < 0.001$). The group difference diminished over time and was insignificant at day 28 ($P = 0.061$) and day 91 ($P=0.084$).The study reported an improvement in joint function and stiffness in the leech group and the group difference sustained till 91 days in contrast to pain. Quality of life was improved only in leech group on day 28 with a group difference of 0.49 [CI, 0.07 to 0.91]; $P = 0.023$), however, at day 91, the group difference was no longer detectable 0.13 [CI, -0.31 to 0.56]; $P -0.2$). The study concluded that leech therapy seems to be an effective symptomatic treatment for knee OA and suggested that re-treatments with

leech will be necessary for the therapy to become clinically viable for long-term management of knee OA.^[10]

Stange R et al. conducted a randomized controlled trial with a cross over at week 6 on 52 knee OA patients. While one group was started with leeching the other received Transcutaneous Electrical Nerve Stimulation (TENS) with a crossover at 6 weeks after first treatment and further observation for 3 more weeks. Total study duration was 9 weeks. In the leech group, treated with single therapy of eight leeches, highly significant improvements were observed in Lequesne's index (L.I) and Visual Analogue Scale (VAS) between days 0 and 21. However in the control group there was no significant improvement over the same period using transcutaneous electric nerve stimulation. In leech group the L.I reduced from a mean of 12.07 ± 4.24 to 9.37 ± 5.10 on day 21 while in control group at same point of time the change was not pronounced (11.66 ± 3.42 to 11.63 ± 3.05) and the difference in effect between the groups was significant in favour of the leech group. Similar effects were observed in VAS with a mean reduction of 1.7cm in leech group and the difference was significant as compared to TENS group where the difference was just 0.02 cm. In the second phase of the study after the crossover L.I dropped by similar amounts when leeching was done as second procedure and the reduction remained unchanged till the end of study (63 days). Similar results were observed for overall assessment of VAS after the crossover. The study concluded that a single session of leech therapy showed significant, relevant and sustained effects, comparable to other trials with leeches.^[11]

Evaluating single and double application of leeches (*Hirudo medicinalis*) application in Knee Osteoarthritis, Stefan A et al. conducted a trial on 113 patients using KOOS, WOMAC, VAS and intake of pain medication as outcome measures. Leech therapy either once or twice showed significant improvement compared to base line values in both the KOSS and WOMAC cumulative scores at all follow-up examinations except for the stiffness. Significant improvement was observed in KOOS score at all follow-up occasions in the control population while the cumulative WOMAC score improved significantly over time except at the 1 week and 6-month follow-up. Subjective pain intensity (VAS) became significantly reduced during the whole observation period of 6 months in all the groups. Consumption of pain medication showed a significant reduction in the patients that underwent leech application either one or twice as compared to placebo control group. Comparison of single leech group and double leech group with control revealed that second leeching after an

interval of 4 weeks led to better improvement in knee related outcome measures and the single leech therapy did not produce similar results during the study period. The study concluded that leech therapy could have a place as an additional symptomatic treatment modality for OA and might be adapted in case of failure of the conventional non-operative and surgical treatment modes.^[12]

Applying three leeches on the tender points of the affected knee in knee osteoarthritis patients, Zaidi et al., conducted a randomized controlled trial on 40 knee OA patients. Leeches were applied at an interval of 14 days up to 6 weeks along with oral administration of a poly herbal Unani formulation and a local application while in control group only polyherbal formulation and local application was used. It was observed that in the Leech therapy group WOMAC pain score and stiffness decreased significantly while functional ability also increased significantly over the course of 6 weeks of treatment in leech group. Over the study period of 6 weeks the WOMAC index for pain decreased by 29.02% [95% C.I= 27.08, 30.96; P<0.001], stiffness by 58.87 % [95% CI=27.08, 30.96 P<0.001] and functional ability increased by 40.56% [95% CI=39.50, 41.62; P=0.001] in the leeching group. In the control group improvement in pain, morning stiffness and physical function was also statistically significant at all points of time, however between the group difference was statistically significant in favour of leech group. Active range of motion improved in the leeching group only while the improvement observed in control group was insignificant.^[2]

In a similar kind of study Shiffa et al. applied two leeches in the affected knee joint at days 0,7,12, 21 and 28 along with a polyherbal Unani formulation in the test group of 30 patients while the 30 patients in the control group were given polyherbal formulation only. The leech group demonstrated highly significant improvements in all outcome measures at week 4 and 8 when compared with baseline values. However, in the control group the improvement was only statistically significant on 4th week while the improvement was insignificant on 8th week. The study observed that the effect of Leech therapy on pain, physical function and other symptoms persisted for four weeks even after the last application of leeches on day 28.^[13]

In all the studies there were no reports of any serious adverse effects following application of leeches except for mild itching and irritation at the site of application. There was no report of any infection in any of the studies. Michalsen A et al. reported itching at the site of bite lasting for a mean of 4 days in 17 patients out of the total 24 patients receiving leech therapy.

Other minor adverse effects included local skin reaction in 1 patient, dizziness in one patient prolonged oozing of blood from the site of bite in 1 patient and local burning sensation in 2 patients. There were no reports of infection following application of leech.^[10] No serious adverse effects were reported by Stange *et al.* from a randomized controlled trial applying leeches in knee osteoarthritis.^[11]

Stefan A reported no adverse effects or local complications in 34 patients out of total 73 patients who received leeches either once or repeatedly at 4 week interval. However 39 patients developed a local irritation at the site of application, with moderate itching which receded in 4 weeks in all cases. Bleeding from site of application was seen in 2 patients which was easily managed by compressive dressing. The study did not report any other complication or infection.^[12] A common minor side effect of mild itching at the site of leech bite lasting for a mean of 4 days was recorded by Zaidi *et al.* They reported a slight but clinically non-relevant decrease in hemoglobin levels after leeching.^[2] Shiffa *et al.* did not report any adverse side effects in any of the 30 patients of test group.^[13]

DISCUSSION

Leech therapy is currently being used for the management of various diseases both in conventional and traditional systems of medicine ranging from micro and reconstructive surgery to alopecia areata. In traditional medicine Leech therapy finds its role in the management of almost all the joint disorders and OA being the most prevalent is frequently managed by application of leeches. Although only a few clinical studies have been carried out for evaluation efficacy of Leech therapy in the management of knee OA all of them have reported results favoring their use. There has been marked decrease in the pain after application of leeches, joint stiffness also decreased with increased joint mobility levels. No effect was recorded on joint crepitus or on the reduced joint space. Disease progression was not studied in any of the studies. Most of the studies have suggested reapplication of leeches to achieve a better long term effect.^[2,10,12]

Although Leech therapy can be used in the symptomatic management of knee osteoarthritis a number of queries are still to be investigated and answered. The optimal number of leeches to be applied, maximum or minimum time of application, site of application and frequency of application is still not well defined and needs further studies. In spite of the fact that no cases of infection with leech gut symbionts has been reported in any of the studies larger observational trials should be planned so that role of antibiotic prophylaxis is investigated.

Pre-application sterilization of leeches using disinfecting agents is a debatable subject and should be taken care of in the future trials. As of now the mechanism of action of Leech therapy in OA remains obscure and except for few postulated theories there is no established mode of action. It needs to be established whether the effect of Leech therapy remains local or the enzymes released by leech at the site of application have systemic effects as well.

CONCLUSION

We conclude that Leech therapy is effective in the management of knee OA with only mild adverse effects and can be effectively adapted for alleviation of pain and other symptoms associated with it. Its effect is prolonged and lasts for as long as 4 weeks and can therefore markedly reduce the intake of oral analgesics having number of adverse effects. Further blinded randomized studies should be designed having larger sample sizes.

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