# The Observational Study of Reduction in Inflammatory Markers and Simultaneous Reduction in Joint Inflammation in Patients of Rheumatoid Arthritis Treated by Leech Therapy

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## Abstract

The sense of pain in arthritis carries the highest stigma among the sufferers as well as the treating physicians. It makes the life miserable for the patients along with the disability the disease rheumatoid arthritis causes, which can be correlated to Aamvata in Ayurveda.There are the conventional treatment options which are available in the form of shodhana and shanmana. Besides NSAID.s and corticosteroids in modern medicine rendering many side effects Ayurveda offers drugless healing art in the form of jaloukavacharan also known as leech therapy which is known for the anti-inflammatory and analgesic, anesthetic actions of leech salivary gland secretions. Hence, a protocol was designed for the doctoral research on "Study of inflammatory markers in patients of Rheumatoid Arthritis treated by leech therapy", for the assessment of subjective parameters of pain, swelling, redness, tenderness, loss of function of joints assessed by standard criterion, and objective parameters like CRP and ESR before and after leech therapy for 10 sittings on alternate days. Observations were taken on day 0 and day 21, and follow up taken on day 30 and day 45. Statistical tests were applied which revealed significant results of anti-inflammatory effect of leech therapy on CRP(relative change 23.54%),with p value =0.0001,than ESR(relative change 10.30). Leech therapy was found to be having highly significant effect on pain score (relative change 57.62%), followed by tenderness score(relative change 72%) and followed by significant increase in walking effect (relative change 56.67%). There was statistically significant improvement in other subjective parameters of assessment like swelling on ankle(relative change by 11.73).,knee joint(relative change 10.29),redness(relative change25%),walking effect(relative change 72%),rise in local temperature(relative change 61.90%) withp value,0.0001.with co-relatable clinical improvement.

***Keywords-*** *Leech Therapy, Inflammatory markers, Aamvata, Rheumatoid arthritis, analgesic, anesthetic*

## Introduction

The aim of all Medical Sciences is to provide better health to every human being so as to have a disease free life. With this aim the Indian System of Medicines with respective doctrines are trying their best for one goal i.e. "Conservation of Health by Natural Methods using Nature". World Health organization is also trying it's best to integrate all Medical systems to achieve the goal of "health for all". Ayurveda medical science with its holistic approach has to play a vital role in this direction. "That's the ideal medicine, which relieves from all kinds of miseries," says Charaka.[1] Drug, is not necessarily be given orally. Ayurveda speaks about many modes of healing art, even surgery and para-surgical techniques. Among the para-surgical measures, Raktamokshana enjoys a place of pride since the dawn of medical history. Raktamokshana is a technical term employed to denote the para-surgical procedures to expel out the vitiated blood from selected areas of the body, by specific methods.[2]

The prevalence of RA is between 0.5 and 1% of adults in the developed world with between 5 and 50 per 100,000 people newly developing the condition each year.[3] Of the variety of researches done in arthritis, most of them are done on subjective parameters like pain, swelling, tenderness, etc but not on objective and

specific parameters like Inflammatory markers (CRP and ESR) which carries a point value in ACR/EULAR scale. [4]The ultimate goal of treatment is to reduce pain, decrease inflammation, and improve a person's overall functioning but associated with them are the systemic side effects and prolonged use is not recommended. New classification criteria overruled the "old" ACR criteria of 1987 and are adapted for early RA diagnosis. The "new" classification criteria, jointly published by the American College of Rheumatology (ACR) and the European League against Rheumatism (EULAR) establish a point value between 0 and 10. In these, of the 10 points, 1 point is attributed to elevated ESR (erythrocyte sedimentation rate), and or elevated CRP value (C-reactive protein).[5]

Aetna Journal considers medicinal leech therapy experimental and investigational for treating cancer pain, epidermoid cysts, knee osteoarthritis, inadequate arterial supply or tissue ischemia, priaprism, rheumatoid arthritis and other musculoskeletal diseases, and for all other indications because of insufficient evidence of its effectiveness.[6]

**Research gap analysis**- All the studies done till now are with some Ayurveda pharmacological intervention and Leech therapy and based on subjective parameters like Pain, Swelling etc. less emphasis was given on the objective parameters like Markers of Inflammation (CRP and ESR)

**Research question**-Can the study of inflammatory markers in patients of Rheumatoid Arthritis may be of utility to ascertain efficacy of Leech Therapy with reference to pain, inflammation and swelling?

**Aim-** Assessment of the efficacy of Leech Therapy in the patients of Aamvata (Rheumatoid Arthritis) by evaluation of reduction in Inflammatory Markers(CRP and ESR)

**Objectives-** 1) Pre and Post treatment evaluation of inflammation, CRP and ESR in RA patients.

2) To compare the anti- inflammatory effect(Pain and Swelling) of Leech Therapy Pre and Post treatment in patients of Rheumatoid Arthritis (wsr, Aamvata)

3) To compare the levels of CRP and ESR after leech therapy in RA patients

**Anticipated translator component**
1.A more easily available natural mode of management of RA (Aamvata) in the form of leech Therapy may be introduced in routine practice.

2. If the hypothesis is proven and Leech therapy is found to be effective in the reduction of levels of CRP and ESR ,a non-pharmacological method which is used as Biotherapy may be introduced in reducing the markers of inflammation in patients of RA.

3. Similarly. leech therapy is a known para-surgical tool in the treatment of some peculiar features of arthritis like joint pain and restricted movement ,hence, it can be validated in this study on RA , for re-establishment.

**Research Design:**

Nature of study: Experimental Study.

Study type: Open label single group experimental study

Commensurate Sample Size: Total 61 patients were selected, allocated into a single group by convenience sampling method.

**Variables** –CRP (evaluated by quantitative method),ESR (evaluated by quantitative method,Pain (VAS scale),Swelling (Metric method),Redness (present /Absent),Tenderness (Dr. Frank Painter's scale),Rise in local temperature (Present/absent) were the variables and criteria of assessment in the patients of RA.

**Review of literature**- Amavata is one of the crippling diseases, claiming the maximum loss of human power. It is not only a disorder of locomotor system but is a systemic disease and is named after its chief pathogenic constituents i.e. Ama and Vata. Sandhishoola, Sandhishotha, Stabdhata and Sparshasahyata are salient features of the disease. The disease Amavata run a chronic course and Jadya, Sankocha, Anga vaikalya etc. are responsible for crippling of the patients in the long run.[7]

This disease can be correlated to Rheumatoid Arthritis that stands parallel to Amavata in its clinical features. RA is a chronic inflammatory arthropathy, which most commonly affects middle aged women. Despite intensive research, the aetiology of Rheumatoid Arthritis remains unknown. In spite of available

treatment options, it cripples the patient for the rest of his life. Moreover, it affects the younger and middle aged people, substantially hampering the economy and affecting the productivity of the society and subsequently of the Nation. Thus, the disease has great challenge to the Clinicians and Researchers.[8]

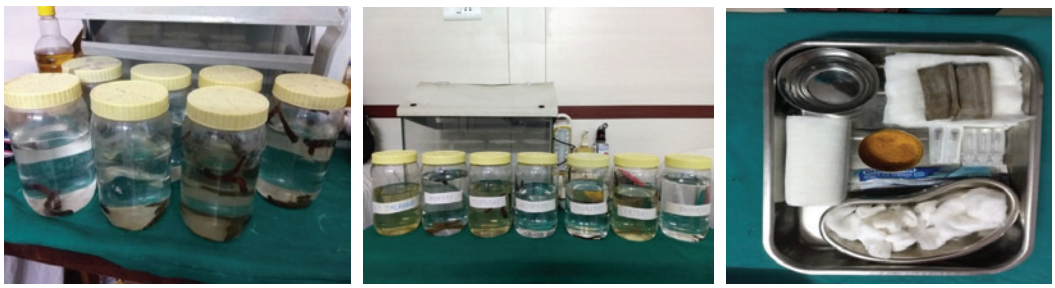
According to the symptomatology Amavata is very similar to rheumatoid arthritis, a disease of unknown aetiology. So many hypotheses have been put forward to explain its aetiology but still the research is going on. Nowadays theories of autoimmune mechanism, genetic susceptibility and free radicals are most commonly incriminated role in etiopathology of Rheumatoid Arthritis. The diagnosis is made mostly on the basis of a person's signs and symptoms. X-rays and laboratory testing may support a diagnosis or exclude other diseases with similar symptoms.[9]

**Inflammatoory markers**-The Erythrocyte sedimentation Rate (ESR) and C-reactive Protein (CRP) are blood tests that are Markers to detect Inflammation. These are certain useful blood tests to help diagnose and monitor the inflammatory activity and response to treatment in diseases like Rheumatoid Arthritis, diabetes, Alzheimer's disease, Osteo Arthritis, Cellulitis, SLE, etc.The "new" classification criteria, jointly published by the American College of Rheumatology (ACR) and the European League against Rheumatism (EULAR) in 2012 and 2019 establish a point value scale between 0 and 10 to diagnose RA based on the levels of ESR and CRP.In these, 1 point is attributed to elevated ESR (erythrocyte sedimentation rate)and or elevated CRP value (C-reactive protein).[10]

**Leech Therapy** can be defined as the use of leeches in medical treatment. This therapy helps in letting out impure or deoxygenated blood from given area with the help of leech bite. The Leech sucks blood from the site as well as transmits some enzymes in its saliva having anesthetic, anti-inflammatory, anticoagulant, vasodilatation effect etc.thereby giving prolonged oozing effect from the site of bite.Studies suggest that leech SGS(Salivary gland secretions) contains more than 150 bioactive substances and has anti-edematous, bacteriostatic, analgesic, resolving actions. It eliminates microcirculation disorders, restores damaged vascular permeability of tissues and organs, eliminates hypoxia, reduces blood pressure, increases immune system activity, detoxifies the tissue, releases it from the threatening complications, such as infarct, stroke, improves bio-energetic status of the organism through rejuvenationHence Leech Therapy has been established as one of the most efficacious therapies in Ayurveda but due to lack of relevant evidence not in vogue.[11]

**Materials**-Leeches and Leech Lab and other procurements as per the SOPs of Jaloukavacharana[12]and tablets of Paracetamol

**Leeches and leech lab**



**Pic no-1,2,3 Leech lab, labeled containers for patients and Required material for Leech therapy**

**Photos of patients with RA on knee joints**

**Pics no 4,5,6,7**

**Photos of patients with RA on ankle joints**

**Pics no 8,9,10,11**

**Inclusion Criteria-**Patients in the age group 20 to 70 yrs. with special features of RA were selected for study like two or more swollen jointsand with elevated erythrocyte sedimentation rate (ESR), and or elevated CRP value (C-reactive protein) were selected for the research protocol.

**Exclusion Criteria-**All infective types of Arthritis, pregnant ladies, lactating mothers,HIV and Hbsag positive patients,patients on treatment of IHD,patients with bleeding disorders.

**Methods-**The patients suffering from Aamvata (RA) in whom knee joints were involved is the target population.

Patients of Aamvata, whether sero positive or sero negative,in whom CRP and ESR were raised were chosen for leech therapy. Painful Knee joint and ankle joint (were preferred for Leech therapy).Leech Therapy was done on alternate day Such 10 sessions were done. On every instance, 2 or 3 leeches (small to moderate size were applied which were found to suck 5 to 15 ml of blood as average.

This is a single group interventional Study in which pre and post treatment assessment was done on certain objective parameters like markers of inflammation ie CRP and ESR and subjective parameters like pain, swelling, redness, tenderness, rise in local temperature, restricted movements of joints. Blood investigations like CBC, CRP, ESR, RA factor, Bleeding time and Clotting time, HIV and Hbsag were performed prior to leech therapy. CRP, ESR, BT and CT were repeated after leech therapy.

The observations were taken on day 0 and day 21 of leech therapy. Leech Therapy was performed on alternate day on affected joint according to the standard operating procedures of Raktamokshana by Jalouka, on preferably the knee and ankle. The observations were compared before and after therapy and statistical data drawn quantitatively

## Results and Discussion

In the doctoral research "Study of inflammatory markers in patients of rheumatoid Arthritis treated by leech therapy". the sample size was 61 calculated as a convenience sampling with simple randomization.The distribution of patients according to various parameters was done.Statistical tests were applied and data is drwn which is diescribed in tables.

**Table no 1- Distribution of patients according to gender-**

| Category | No.of patients | Percantage |
|---|---|---|
| Male | 28 | 45.9%= |
| Female | 33 | 54.1% |

Table no. 1 reveals that, of the 61 patients, 28 were male and 33 were female

**Table no 2- Distribution according to Chronicity of Symptoms**

| Duration (months) | Number | Percent |
|---|---|---|
| 0 to 6 | 16 | 26.23 |
| 7 to 24 | 28 | 45.9 |
| More than 24 | 17 | 27.87 |

Table no 2, reveals that, when 3 groups were formed to classify the chronicity like 0 to 6 months, 7 to 24 months and more than 24 months, maximum no of patients ie 28 were found in 7 to 24 months group.

**Table no 3-Distribution of subjects according to Type of Pain**

| **Table : Distribution of subjects according to type of pain** | | |
|---|---|---|
| **Type of pain** | **Number** | **Percent** |
| Bheda(Throbbing) | 13 | 21.31 |
| Daha(Burning) | 13 | 21.31 |
| Kartanvata(cutting) | 11 | 18.03 |
| Toda(pricking) | 13 | 21.31 |
| Vruschik danshvata | 11 | 18.03 |

According to the distribution of type of pain, Table no 3, the type of pain on highest frequency was toda, Bheda and daha ie13 patients each were found to suffer from pricking, throbbing and burning type of pain.

These were the demograohic criterion ilustratrd in n-61.

**Table no 4 -Summary table showing effect of leech therapy on important parameters**

| **Outcome** | **Before** | **After** | **Effect size** | | |
|---|---|---|---|---|---|
| Measure (% or Mean) | (at Day 1) | (at day 21) | Absolute Change (After-Before) | Relative (%) change from baseline* | Significance (P value) |
| Pain (%) (moderate+severe) | 100 | 60.78 | -39.22 | -39.22 | 0.0001 |
| Pain score (mean±SD) | 75.77 ±10.73 | 32.11 ±10.48 | -43.66 | -57.62 | 0.0001 |
| Ankle Swelling (mean±SD score) | 32.82 ±3.05 | 28.97 ±2.48 | -3.85 | -11.73 | 0.0001 |
| Knee Swelling (mean±SD score) | 37.21 ±1.22 | 33.38 ±1.17 | -3.83 | -10.29 | 0.0001 |
| Tenderness (%) | 91.67 | 35 | -56.67 | -61.82 | 0.0001 |
| Redness (%) | 81.67 | 56.67 | -25.00 | -30.61 | 0.0079 |
| Distance walked (mean±SD meters) | 16.25 ±5.77 | 27.96 ±6.50 | +11.71 | +72.06 | 0.0001 |
| Range of motion (mean±SD degrees) | 45.64 ±19.13 | 88.61 ±23.21 | +42.97 | +94.15 | 0.0001 |

***Cont...*** **Table no 4 -Summary table showing effect of leech therapy on important parameters**

| | | | | | |
|---|---|---|---|---|---|
| Rise in local temp (%) | 91.87 | 35 | -56.87 | -61.90 | 0.0001 |
| ESR (mean ±SD mm/hr) | 50.95 ±7.74 | 45.7 ±7.60 | -5.25 | -10.30 | 0.0001 |
| CRP (mean±SD mg/dL) | 21.24 ±5.08 | 16.24 ±4.65 | -5.00 | -23.54 | 0.0001 |

*Relative (%) change from baseline= (Absolute change/Baseline value)*100

. **Overall Effect of leech therapy was found significant on all important Subjective parameters and objective parameters. Though significant but effect size was observed small (around 10%) for swelling and ESR, whereas it was large (>30%) for all other parameters.**

Results-The table no 4 above reflects the overall effect of leech therapy on the clinical assessment parameters like pain, swelling, redness, tenderness, rise in local temperature, restricted movement and walking effect. The effect of therapy was also assessed on pathological parameters like inflammatory markers CRP and ESR at the end of 10 leech sessions on alternate days. The overall effect was assessed on day 21 of therapy.that shows significant effect on all the important parameters statistically with p values =0.0001 which is highly significant. Maximum relative change was found in walking effect in the patients of RA which is found to be 72.06%. The relative change in pain score is found to be 39,22%. In Swelling it was found to be 57.62% in knee and 11.73% in ankles. The relative change in tenderness and redness on joints are found to be 61.82% and 30.61% respectively. The relative change in range of motion is 94.15% and in rise in local temperature,it is found to be 61.90%.

Discussion-These findings are the outcome of the anti-inflammatory and analgesic effect of enzymes in leech salivary gland secreions like bdellins, eglins, factor Xa inhibitor, protease inhibitors, tryptase inhibitors, Cathepsin G, histamine like substance, Hyaluronidase,carboxypeptidase inhibitors,acetyl choline,and Anesthetic substance, and anti-coagulant substance called Hirudin and hirustasin which cumulatively give the relative change effects of reduction in pain, swelling, redness, tenderness, rise in local temperature, and improved walking effect stated as above ay p=0.0001 level of significance. The combined effect of the multiple bioactive salivary secretions like pain killer action, analgesic anti-inflammatory action, anesthetic properties, thrombolytic effect, tissue rejuvenation effect, anti-ischemic effect, renders the improvement in the pain, swelling, stiffness of the joint and improvement in the restricted movement of joint[13]

As Leech therapy is effective in giving pain relief, reducing swelling, redness, tenderness and local warmth is also reduced improving the restricted movement of joints of lower limb. Singh et al state that all the improved characters play a combined role on the walking effect of the patient thereby improving the quality of life of the patient

Results-The relative change in CRP after leech therapy is found to be 23.54% which is found to be highly significant .The relative change in ESR levels is found to be 10.30% which is statistically somewhat less significant.

Discussion-These findings can be justified by the fact that Overall anti -inflammatory effect of leech therapy by the virtue of various enzymes in its salivary gland secretions gives the reducing effect on inflammatory markers.[14] Besides, the difference in the rate of reduction of both CRP and ESR can be justified by the fact that plasma half-life of ESR is up to certain weeks to 2 to 3 months, while that of CRP is 19 hours. Hence for plasma ESR levels to reduce, takes a long span of time which may be in months, because even if the disease process is over ESR is found to be high with other confounders

in coexistence. CRP on the other hand is a protein which increases when the inflammatory process is activated in the body with peak plasma levels for 19 hours and regression later. Hence it is the rate of synthesis which determines the response to treatment.[15] Hence after 10 sittings of leech therapy, if CRP levels are deterred by 23.54% then it is found to be a significant difference with arrest of inflammatory process at a certain level. CRP being a specific marker of inflammation, is a significant finding as a regressed marker after treatment with leech therapy.[16]

Limitations of the present study-

As the effect of leech therapy on CRP and ESR could be found to render statistically significant but parametrically less significant results, it can be used as an adjuvant therapy in the treatment of Aamvata.

Immediate post-doctoral Research direction & Suggested future studies-

Ø This study should be done on large population**.**

Ø Multicentric, Interdisciplinary research with RCT design should bconducted.

Achievable translatory component:

Ø Many patients suffering from Rheumatoid Arthritis(*Aamvata*) having inflammatory arthritis and painful joints along with features of stiffness and inability to walk can be effectively treated with Leech therapy on Joints.

Ø CRP is a marker of inflammation which is significantly attainable by treatment with leech therapy.

Declaration of new knowledge generated:

Ø Leech Therapy is significantly effective in decreasing the CRP to a significant level and ESR to considerable levels and effectively renders pain relief to the patients of Rheumatoid Arthritis.

**Ethical Clearance-** Taken from Institutional ethics committee, JNMC, Saongi, Wardha, in 2016

**Source of Funding-** Self

**Conflict of Interest** - Nil.

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