



Available online through

www.jbsoweb.com

ISSN 2321 - 6328

## Research Article

### A RANDOMIZED CONTROLLED TRIAL TO EVALUATE THE ANTI-INFLAMMATORY EFFECT OF *COMMIPHORA WIGHTII* IN COMBINATION WITH *CURCUMA LONGA* AGAINST DICLOFENAC POTASSIUM IN NON-SPECIFIC KNEE EFFUSION

Narinder Singh<sup>1</sup>, A. R. Bhattacharya<sup>2</sup>, Akhilesh Mishra<sup>3</sup>

<sup>1</sup>Lecturer, Department of Shalya Tantra, National Institute of Ayurveda, Jaipur, Rajasthan, India

<sup>2</sup>Reader, Department of Rog and Vikriti Vigyan, Ayurveda College, Mandi Gobindgarh, Punjab, India

<sup>3</sup>PG Scholar, Department of Shalya Tantra, National Institute of Ayurveda, Jaipur, Rajasthan, India

\*Corresponding Author Email: narinder.1973@gmail.com

Article Received on: 07/02/15 Accepted on: 17/03/15

DOI: 10.7897/2321-6328.03215

#### ABSTRACT

Knee effusion is an abnormal accumulation of the fluid in the knee capsule or the adjoining supra-patellar bursa secondary to the irritation/inflammation in the joint synovium. It is seen in approximately 8-10 % of the total patients suffering from osteo-arthritis. Kroṣṭukaśīrṣa described in Ayurveda, can be correlated with knee effusion. In Present clinical trial an effort has been made to evaluate anti-inflammatory effect of *Commiphora wightii* in combination with *Curcuma longa* against Diclofenac potassium [NSAID's] in Non-specific knee effusion. Total twenty two, clinically diagnosed patients of Non-specific knee effusion were selected for the present clinical trial excluding drop out 20 patients were assorted in to two groups Trial Group and control Groups. Trial Group 10 patients were given crude extract of *Commiphora wightii* 500 mg along with *Curcuma longa* 500 mg in a separate capsule twice a day continuously for 8 weeks orally. In Control Group patients were given Diclofenac Potassium 50 mg twice a day continuously for 2 weeks orally. It was assessed that Diclofenac potassium was significantly better in the outcomes in comparison to the trial drugs *Commiphora wightii* (Guggulu) and *Curcuma longa* (Haridra) when compared at the end of two weeks of start of the trial. Trial drugs *Commiphora wightii* (Guggulu) and *Curcuma longa* (Haridra) are also having outcomes of comparative extent to Diclofenac Potassium when administered continuously for further 6 weeks i.e. total 8 weeks.

**Keywords:** Knee effusion, Kroṣṭukaśīrṣa, *Commiphora wightii*, *Curcuma longa*, Diclofenac Potassium.

#### INTRODUCTION

In current scenario Osteo-arthritis of knees could appropriately be included under the category of life style disorders. The condition is often reported at very young age in comparison to the previous statistic<sup>1</sup>. This could be attributed to early degenerative changes affecting knee joint architecture owing to excessive body weight leading to excessive wear tear of articular cartilage and sub chondral bone, trivial or evident trauma to the knee joint affecting the joint synovium<sup>2</sup>. As reported 8-10 % of the total cases of osteo-arthritis affecting knee joint, present with the complaint of swollen knees owing to abnormal accumulation of synovial secretions secondary to synovitis. This condition could rationally be included under the heading of Non-specific knee joint effusion<sup>3-5</sup>. Ayurveda is a system of health science known since the time immemorial. The condition of non-specific knee effusion can well be considered comparable to kroṣṭukaśīrṣa mentioned under the vāta-vyādhi. Ācārya Suśruta<sup>6</sup> has described severe pain (mahāruja), Swelling

(śopha) like kroṣṭukmūrdhvāta (Gross swelling like head of jackle) as the symptoms of kroṣṭukaśīrṣa. In this way, the disease kroṣṭukaśīrṣa can be defined as a disease of jānu-sandhi (knee Joint) with symptoms of śopha-jānumadhyamahārūjasthūla- kroṣṭukmūrdhvāta. Description of Kroṣṭukaśīrṣa as per various reference texts (Ayu.) viz. Suśruta Samhitā: (1000-1500 B.C.) Ācārya Ḍalhaṇa<sup>7</sup> commentator of Suśruta Samhitā, Aṣṭāṅga Hṛdaya<sup>8</sup> (6<sup>th</sup> Century), Mādhava Nidāna<sup>9</sup> (7<sup>th</sup> Century), Chakradatta (11<sup>th</sup> Century) Sarangdhara (13<sup>th</sup> Century)<sup>10</sup>, Yogratnākar, Bhāvaprakāśa (16<sup>th</sup> Century)<sup>11</sup>, Kṛṣṇarambhaṭṭa (20<sup>th</sup> Century). In kroṣṭukaśīrṣathe main presenting feature is swelling of the knee joint caused by vitiated vāta and rakta. Vitiated vāta doṣa in association with vitiated rakta doṣa get stationed in knee joint completing the pathogenesis of the kroṣṭukaśīrṣa<sup>12</sup>. This pathogenesis leads to the development of the main clinical features i.e. throbbing pain, hyperesthesia, numbness etc. various Ācārya describes kroṣṭukaśīrṣa as a joint disorder in which knee joint have an inflammation like a jackal's head.

Table 1: Differential Diagnosis

Factor	Kroṣṭukaśīrṣa (OA knees with gross Knee effusion)	Sandhigata-vāta (osteoarthritis)	Āmavāta (R. A)	Vātarakta (Gouty arthritis)
Āmaprādhānya	Absent	Absent	Present	Absent
Jvara	Absent	Absent	Present	Absent
Hrdgaurava	Absent	Absent	Present	Absent
Prone age		Old Age	Any age	
Vedanā	Tīvra	At Prasarana Akunchana Pravritti	Vrischik Dansha Vātaand, Sanchari	Mushika, Damshavat, Vedana
śoṭha	kroṣṭrukaśīrṣavat	Vatapurna Dritisparsha	Sarvanga and Sandhigata	Mandal Yukta
Sandhi (affected)	Only Janu	Vatapurna Dritisparsha	Big Sandhi	Small Sandhi
Upaśaya	RaktaShodhana	Abyanga	Ruksha Svedana	Raktasodhna

### Kroṣṭukaśīrṣa Cikitsā (Management principle)

Kroṣṭukaśīrṣa is a vātika disease, mainly occurs due to dhātukṣaya or āvaraṇa<sup>5</sup>, so general treatment of vātavyādhi can be adopted. Common treatment like Snehana, Svedana, mṛdusamśodhana, basti and vātahara auśadha, āhara and vihāra may also be applicable in kroṣṭukaśīrṣa. kroṣṭukaśīrṣa is a vātavyādhi<sup>6</sup> in this disease gudūchī and triphlā should be used with śudha-guggulu otherwise milk with eraṇḍa oil or vidhāracūrṇa should be used for treatment he also mentioned that it is essential to do śīrāvedha and vātavyādhi treatment in kroṣṭukaśīrṣa. Thus, keeping in view above discussed facts; the present work *Commiphora wightii* (Guggulu) along with *Curcuma longa* (Haridra) against Diclofenac potassium [NSAID'S] on Non-specific knee effusion was carried out.

### Aims and Objective

#### Primary Aims

- To assess the therapeutic efficacy of crude extract of *Commiphora wightii* along with *Curcuma longa* on Non-specific knee effusion.
- To compare the therapeutic efficacy of above mentioned formulations with that of Diclofenac Potassium (NSAID'S) given orally on Non-specific knee effusion.

#### Secondary Aims

- To study the incidence of knee effusion among the patients having Non-specific arthritis of knees.
- To study the various aspect of Non-specific knee effusion with special reference to similar entities described in Ayurveda in comprehensive details.
- To make available cheap, economic and side effect free formulation/regimen for the treatment of Non-specific knee effusion.
- To obtain and analyze any information regarding the toxicity/adverse effects of crude extract of *Commiphora wightii* along with *Curcuma longa* in proposed dosages.

### MATERIALS AND METHODS

Total 22 patients were registered for study. Two patients dropped out during study due to various reasons; so all observations were made on 10 patients each in the two groups.

**Time Frame:** 40 weeks.

**Duration of trial:** 8 weeks in trial group and 2 weeks in control group.

**Follow up:** 32 weeks.

### Inclusion Criteria

- Patients in the age group 15-65 years of either gender having non-specific knee effusion.
- Patient who were willing for trial and ready to give written informed consent.
- Patients were selected randomly irrespective of economical, educational and marital status.

### Exclusion Criteria

- Patients suffering from Knee effusion due to specific arthritis of knee joints.
- Patient with the history of recent trauma to knees.
- Excessively tense knee effusion.
- Patient having haemarthrosis of knees.
- Patient having known hypersensitivity to diclofenac potassium.
- Patient having pre-existing asthma, urticarial or other allergic type/adverse reactions on medication with steroids or other NSAIDs.

### Sample Size

22 Subjects diagnosed for Non-specific knee effusion,

### Source

Subject selected from O.P.D. / I.P.D. at P.G. Department of Shalya-Tantra, N.I.A. Jaipur, India.

### Ethical Clearance

The study was approved by Departmental Research Committee (DRC) PG studies as per NIA No. F 154(1) Academics /2011/3014 Dated. 12-04-11.

### Informed Consent

The study explained clearly to the subjects and their signed, written informed consent was taken before starting the trial.

### Investigations

The following investigations were carried out before starting the research work.

- X-ray knee joint (AP and LAT view)
- Hematological investigation-Hb, ESR, TLC, DLC, Sugar (F and PP)

- Serological investigations
- R.A Factor
- ASLO Titer
- CRP
- Serum uric acid
- Urine examination (routine and microscopic)
- Cytology of diagnostic aspirate.
- ELISA for Tuberculosis (If required)
- Synovial Biopsy (if required)

### Grouping

After thorough evaluation including complete clinical examination routine investigations 20 patients of Non-specific knee effusion has been selected for trial. These have been randomly divided in two groups of 10 patients each.

#### • Trial Group

Patient had been given crude extract of *Commiphora wightii* 500 mg and *Curcuma longa* 500 mg in a separate capsule twice a day continuously for 8 weeks orally.

#### • Control Group

Patients had been given Diclofenac potassium 50 mg twice a day continuously for 2 weeks orally. Crape bandage application was advised to the patients of both the groups at the time of weight bearing. *Commiphora wightii* 500 mg and *Curcuma longa* 500 mg were procured and supplied by the form of capsules by the GMP certified NIA Pharmacy. Diclofenac potassium 50 mg (Ethical group) had been procured from the market.

### Assessment

- The inter group comparison between Trial group and Control group had been observed and analysed statistically after two weeks from the commencement of the trial.
- Intervention has been continued for further six weeks with Trial group only and outcomes have been observed and analysed after eight weeks from the commencement of the trial.
- The inter group comparison among Trial group (on intervention for 8 weeks) and control group (on intervention for 2 weeks) has been observed and analysed statistically after eight weeks from the commencement of the trial.

### Assessment Criteria

Assessment was done on starting of trial and then as per schedule mentioned above on following criteria's:

- Pain - VAS
- Tenderness - Ritchie index
- Walking distance - In meters
- Swelling circumferential variation in c. m. (at particular level)
- Improvement in ROM

### OBSERVATIONS AND RESULTS

The observation of this study went like this: Total 22 patients were registered for study. Two patients dropped out during study due to various reasons so all results were made on 10 patients each in the two groups.

Table 2: Average relief of sign and symptom on 2 weeks

Sign and symptom	Overall relief Trial group After 2 weeks	Overall relief Control group After 2 weeks
Pain	17 %	65 %
Tenderness	45 %	62 %
Effusion	43 %	77 %
Rang of movement	24 %	35 %
Walking distance	12 %	48 %

Table 3: The intergroup comparison during overall treatment

Sign/Symptom	Trial group After 8 weeks	Trial group After 2 weeks	p-value	Result
Pain	62 %	65 %	0.1727	NS
Tenderness	58 %	62 %	0.6959	NS
Effusion	72 %	77 %	0.3771	NS
Range of movement	34 %	35 %	0.9952	NS
Walking distance	43 %	48 %	0.8515	NS

### DISCUSSION

The most common signs and symptoms observed in trial subjects were pain, swelling (effusion) and tenderness. To assess the signs and symptoms, after a thorough discussion in departmental research committee assessment criteria has been graded accordingly as per their characters. The aim of this clinical study is to assess the anti-inflammatory effect of *Commiphora wightii* along with *Curcuma longa* against Diclofenac potassium [NSAID'S] on Non-specific knee effusion, through various assessment criteria i.e. pain, tenderness, effusion, range of movements (ROM) and walking distance. After 2 week of treatment % relief of pain in Trial group was 17 % and in control group it was 65 %. These

observations show that there is a considerable difference in the relief of symptoms between Trial group and Control group. This can be due to the proven anti-inflammatory action of the Diclofenac Potassium in comparison to the Shallaki, Guggulu and Haridra. On further continuation of the intervention in trial group for further 6 weeks i.e. after 8 weeks of treatment % relief in pain in trial group was 62 %. Hence this observations show that trial drugs Guggulu along with Haridra is also having anti-inflammatory action of comparative extent with Diclofenac Potassium, When administered continuously for further 6 weeks i.e. total 8 weeks. But it has been observed that Diclofenac potassium for two weeks produces unwanted effect in most of the patient in control Group, like indigestion, diarrhea, dry mouth, anorexia, palpitation as shown in Table below.

Table 4

S. No.	Symptoms	No of patient
1	Indigestion	5
2	Diarrhoea	1
3	Anorexia	2
4	Dry mouth	1
5	Not reported any Side effect	1

After 2 weeks treatment % relief in tenderness in trial group 45 % and in control group was 62 %. This observations shows that % of relief in tenderness in control group is comparatively much better. This again can be attributed to the prompt relief in Control group owing to the potent anti-Inflammatory property of Diclofenac Potassium. On further continuation of the intervention in trial group for 6 weeks i.e. after 8 weeks of treatment % relief in tenderness in Trial group was 58 %. The observations again suggest that crude extract of *Commiphora wightii* 500 mg and *Curcuma longa* 500 mg also having anti-inflammatory action of comparative extent with Diclofenac Potassium, When administered continuously for further 6 weeks i.e. total 8 weeks. And after statistical analysis for the results during continuous administration of Diclofenac potassium for 2 weeks when compared with 8 weeks administration of *Commiphora wightii* 500 mg and *Curcuma longa* 500 mg, difference in the % relief in tenderness between Trial group and Control group appears to be insignificant. After 2 weeks of treatment % relief in effusion in Trial group was 43 % and in control group it was 77 %. This observations shows that % of relief in effusion in Control group is comparatively much better than Trial group. On further continuation of the intervention in trial groups for 6 weeks i.e. after 8 weeks, of treatment % relief in effusion in Trial group was 72 % (p value 0.0002). Again after statistical analysis of the results during continuous administration of Diclofenac potassium for 2 weeks when compared with 8 weeks administration of *Commiphora wightii* 500 mg and *Curcuma longa* 500 mg, in the trial group difference in the % relief ofin effusion between Trial group and control group is insignificant. During assessment of range of movement after 2 week in Trial group % of relief was 24 % and in Control group it was 35 %. This result also shows that relief of symptoms in Control group is comparatively much better than Trial group. On further continuation of the intervention in trial group for 6 weeks i.e. after 8 weeks, in Trial group % of relief in term of the range of movements was 34 %.

Again after statistical analysis of the results during continuous administration of Diclofenac potassium for 2 weeks when compared with 8 weeks administration of *Commiphora wightii* 500 mg and *Curcuma longa* 500 mg in the trial group, difference in the relief of % in the range of movement in between Trial group and Control group is insignificant. After 2 week of treatment % relief in walking distance in Trial group was 12 % and in control group it was 48 %. The results in Control group are significantly better in comparison to Trial group. Again after statistical analysis of the results during continuous administration of Diclofenac potassium for 2 weeks when compared with 8 weeks administration of *Commiphora wightii* 500 mg and *Curcuma longa* 500 mg in the trial group, difference in the relief of % in walking distance, between Trial group (43 %) and Control group (48 %) is insignificant.

#### Pharmacological Action

Anti-inflammatory effects of Guggulu could be attributed to the influence i.e. down-regulation of the expression of mediators of inflammation, including interleukins, transcription factors and cytokines. Guggulsterone demonstrated a significant effect

against inflammatory mediators. Guggulu is able to suppress the activation of nF-kB via interfering with various activators such as hydrogen peroxide, TNF-a, phorbol ester. NF-kB, a transcription factor, is known as a significant pro-inflammatory. Guggulsterones also appear to reduce circulating levels of pro-inflammatory cytokines and markers such as IL-1b, IL-2 and TNF-a. Guggulsterones are also able to reduce Cyclooxygenase-2 (COX<sub>2</sub>) mRNA levels and suppress its TNF $\alpha$  mediated induction (activation). *Curcuma longa* owing to its active principle also inhibit the activity and synthesis of the enzymes implicated in inflammation, such as, cyclooxygenase-2 and 5-lipoxygenase. Its anti-inflammatory action may also be attributed to inhibition of pro-inflammatory leukotrienes, prostaglandins and arachidonic acid, as well as its influence on neutrophilic activity during inflammatory states. Along with the curcuminoids, the volatile oils present in turmeric are also responsible for the anti-inflammatory activity.

#### CONCLUSION

The entity in question can be correlated with the kroštukaširša. Pain and swelling were the two important and troublesome symptoms of knee effusion which sought an immediate clinical attention. Diclofenac potassium was significantly better in the outcomes in comparison to the trial drugs *Commiphora wightii* 500 mg along with *Curcuma longa* 500 mg when compared at the end of two weeks of start of the trial while Trial drug *Commiphora wightii* 500 mg along with *Curcuma longa* 500 mg is also having outcomes of comparative extent to Diclofenac Potassium, When administered continuously for further 6 weeks i.e. total 8 weeks. It is observed in this study that continuous administration of Diclofenac potassium for 2 weeks when compared with 8 weeks administration of *Commiphora wightii* 500 mg along with *Curcuma longa* 500 mg in the trial group, difference in the % relief in between Trial Group and Control Trial group appears to be insignificant. No adverse effect of drug *Commiphora wightii* 500 mg along with *Curcuma longa* 500 mg has been reported by the patients during the course of treatment. But in Control Group some side effect of drug noticed during the course of treatment.

#### REFERENCES

1. John Ebnezar. Text book of Orthopaedics First Edition, Apoorva Publications, Bangalore 560076; 1996.
2. Mc Gahan JP, Shoji H. Knee effusions. J Fam Practice; 1977.
3. Graham J Goldman JA. Fat droplets and synovial fluid leukocytosis in traumatic arthritis. Arthritis Rheum 1978; 21: 76. <http://dx.doi.org/10.1002/art.1780210113>
4. Hardy RM, Wallace LH. Arthrocentesis and synovial membrane biopsy. Vet Clin North Am 1974; 4: 449. [http://dx.doi.org/10.1016/S0091-0279\(74\)50044-9](http://dx.doi.org/10.1016/S0091-0279(74)50044-9)
5. Harris EL Jr. Role of collagenases in joint destruction, Sokoloff L (ed): The Joints and Synovial Fluid. New York, Academic Press; 1978.
6. Vaidya Yadavji Trikmaji Acharya and Narayana Rama Arya: Sushruta Samhita with Nibandhasamgraha

- Commentary; of Sri. Dalhanacharya and Nyayachandrika Panjika of Sri Gayadasacharya on Nidanasthanal. Edited by. Choukhamba Orientalia.
7. Shashtri Kavirj Ambika Dutta. Suśruta Samhitā Nidāna sthāna-adhyāya-1/76, Ayurveda Tatwa Sandeepika Hindi commentary Varanasi Chaukhamba Sanskrit Sansthaan Edition 11; p. 182.
  8. Upadhyayadunandan Aṣṭāṅga Hṛdaya, Vidyotini nidanstan 15/52, Hindi commentary Varanasi Chaukhamba Sanskrit Sansthaan Edition; 2003. p. 211.
  9. Upadhyayadunandan: Mādhava Nidānavātavyādhinidāna shlok no 58. Hindi commentary Varanasi Chaukhamba Sanskrit Sansthaan Edition; 2003. p. 56.
  10. Sarangdhara in under section of vatroga shlok no 107; p. 44.
  11. Bhāvaprakāśa in madhyamkhaṇḍaadhyāya 24 vātavyādhiadhikāra śloka number 9/10
  12. Bhashagratna Kaviraj Kunjalal. MRAS. Sushruta Samhita (Text with English translation) Vol. - I and II: 2<sup>nd</sup> edition; 1963.

**Cite this article as:**

Narinder Singh, A. R. Bhattacharya, Akhilesh Mishra. A randomized controlled trial to evaluate the anti-inflammatory effect of *Commiphora wightii* in combination with *Curcuma longa* against diclofenac potassium in non-specific knee effusion. J Biol Sci Opin 2015;3(2):68-72 <http://dx.doi.org/10.7897/2321-6328.03215>

Source of support: Nil; Conflict of interest: None Declared