

## Randomized, Double Blind, Prospective Comparative Study Of Safety And Efficacy Of Lornoxicam With Diclofenac In Osteoarthritis

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**Abstract:** Osteoarthritis is a degenerative disorder. It is more commonly affecting women and the severity of the disease depends on the age. It mostly affects the cervical, lumbosacral and knee joints. Osteoarthritis of knee joint seen in elderly people leads to impaired mobility. Life style modifications, exercise and analgesics can be tried for management of the disease before going to permanent cure by joint replacement surgery which is cost effective. Analgesics like diclofenac, lornoxicam are used in the reduction of inflammatory responses in joints. It was showed that lornoxicam is more beneficial and safest drug than diclofenac which may cause cardiovascular problem in chronic usage. The present study was conducted to compare the efficacy and safety of lornoxicam and diclofenac in newly diagnosed patients of osteoarthritis.

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### I. Introduction:

Osteoarthritis is highly prevalent and leading cause of disability in the elderly<sup>1</sup>. Severity of osteoarthritis increases with age. Osteoarthritis affects certain joints, including articular cartilage and subchondral bone. Commonly affected joints include the cervical and lumbosacral spine, hip, knee and first metatarsal phalangeal joint. In the hands, the distal and proximal interphalangeal joints and the bone of the thumb are often affected. Usually spared are the wrist, elbow, and ankle<sup>1,2</sup>. Symptoms may include joint pain, tenderness, stiffness and locking of affected joint and sometimes joint cavity effusion. In majority, large joints of human body are affected more than smaller joints. Among these larger joints, knee joint is most commonly affected<sup>3</sup>. Osteoarthritis is more common in women than in men and prevalence increases with age<sup>3</sup>. Osteoarthritis of knee is one of the five leading causes of disability among non-institutionalized adults and also is a leading cause of impaired mobility in elderly<sup>4</sup>. Apart from joint replacement surgery which is a permanent cure and costly; management of osteoarthritis knee generally involves a combination of exercise, lifestyle modification and analgesics. Diclofenac sodium and lornoxicam both are acid derivative analgesics which gets accumulated in the inflamed tissue like joints affected by osteoarthritis<sup>5</sup>. Diclofenac sodium is one of the most commonly prescribed drugs for the osteoarthritis knee. But, observational studies have shown the possibility of a cardiovascular risk from chronic therapy with diclofenac sodium<sup>6</sup>. Lornoxicam has come in Indian market since last few years. It is found to be a better alternative for management of conditions like post lumbar puncture pain, post tooth extraction pain but less information is available regarding its safety, efficacy and cost effectiveness in osteoarthritis knee<sup>6</sup>. As per the profile, if lornoxicam is really more beneficial than diclofenac sodium then it will be helpful in managing the patients of osteoarthritis more effectively. To confirm the same we planned this study<sup>3</sup>.

### II. Review of literature:

Osteoarthritis joint failure, a disease in which all structures of the joint have undergone pathologic changes. The pathologic hallmark of disease is hyaline articular cartilage loss<sup>1</sup>. This is accompanied by

1. Increasing thickness and sclerosis of the subchondral bony plate,
2. Outgrowth of osteophytes at the joint margin,
3. Stretching of the articular capsule,
4. Mild synovitis in many affected joints, and
5. Weakness of muscles bridging the joint.

Failures of joint protectors increases the risk of joint injury and osteoarthritis<sup>7</sup>. The first step in osteoarthritis treatment is patient education about the disease process, the extent of osteoarthritis, the prognosis and treatment options. Patients can be encouraged to access information from local or national units of the arthritis foundation<sup>8</sup>.

### **III. Materials and Methods:**

The present study was carried out in newly diagnosed patients of osteoarthritis attending the orthopaedics department of GOVERNMENT GENERAL HOSPITAL, RANGARAYA MEDICAL COLLEGE, KAKINADA, ANDHRA PRADESH. The protocol regarding the present study was submitted to the Institutional Ethics Committee and the permission was taken before starting the study. The study was conducted from January 2013 to September 2013. Written informed consent was taken before enrolment in English from participants of group-A and group-B according to Helsinki declaration.

#### **Inclusion criteria:**

1. Patients aged above 40 years with newly diagnosed osteoarthritis without any prior treatment.
2. Patients with severe pain and less deformity (stage I osteoarthritis)

#### **Exclusion criteria:**

1. Patients with cardiovascular diseases, and any bleeding disorders
2. Patients with gastrointestinal disorders like peptic ulcer etc.
3. Patients with hepatic or renal diseases
4. Patients with cancers
5. History of sensitivity or severe adverse reaction to NSAIDS
6. Patients with history of Diabetes mellitus,
7. Any concurrent condition like alcohol or drug abuse, disabling or terminal illness, personality or mental disorders,
8. Patients who are pregnant or nursing mothers
9. Concurrent therapy with medications like- ACE inhibitors, glucocorticoids, warfarin, salicylates etc.
10. Patients with other systemic illness.

#### **Methodology:**

115 patients fulfilling the inclusion criteria were chosen for the study. Only 50 cases were taken in each group keeping drop outs in mind. All the patients were randomly divided into two groups. Group A (Lornoxicam 8mg twice daily and 1 tablet of placebo is added) and Group B (Diclofenac 50mg thrice daily received) for a period 32 weeks.

Patients with acute osteoarthritis of the knee were selected and assessment of pain was done with the help of visual analogue scale. The Visual Analogue Scale (VAS) is a subjective measure of pain. It consists of a 10cm line with two end-points representing 'no pain' and 'worst pain imaginable'. Patients are asked to rate their pain by placing a mark on the line corresponding to their current level of pain. The distance along the line from the 'no pain' marker is then measured with a ruler giving a pain score out of 10.

#### **Statistical Analysis:**

The descriptive/demographic data is presented in tabular form and as mean  $\pm$  SD.

The analysis is done within the groups by paired 't' test for significance.

The analysis is done between the two study groups by unpaired 't' test for significance.

The statistical analysis is done by using GRAPHPAD PRISM VERSION 6.

### **IV. Results:**

All the results are compared between the 2 study groups:

Group A -	Lornoxicam
Group B -	Diclofenac

The mean pain score is compared at different periods of treatment in both groups (given in Table-1)

**Table -1 : Response to Treatment (unpaired ‘t’ test )**

Pain score	GROUP A (MEAN±SD)	GROUP B (MEAN±SD)	‘p’ value
BASELINE	7.6±1.03	7.76±1.02	—
4 <sup>th</sup> week	6.78±1.01	7.22±0.887	*
8 <sup>th</sup> week	6.06±0.93	6.76±0.846	*
16 <sup>th</sup> week	5.06±1.11	6.52±0.762	**
32 <sup>nd</sup> week	4.06±1.08	6.2±0.728	**

\* =< 0.05

\*\* = < 0.001

**Adverse drug reactions in each group:**

In the present study lornoxicam group had 66%(33 patients) and diclofenac group had 38%(19 patients)of one or more adverse drug reactions (given in Table-2).

**Table-2 :Adverse effectsin treated groups A and B**

Type of adverse effect	No.of patients Group-A(n=50)	No. of patients group-B(n=50)
Epigastric pain	21	11
Rashes	19	10
Nausea	18	13
Diarrhea	15	10
Headache	12	07
Vomitings	06	09
Bleeding	02	01
Others	10	02

**V. Discussion:**

Osteoarthritis is the most common type of arthritis. Its high prevalence, especially in the elderly and high rate of disability related to disease; make it a leading cause of disability in the elderly. Because of the ageing and obesity (a major risk factor), prevalence of osteoarthritis is on the rise. The present study is randomized double blind comparing Lornoxicam(8mg) and Diclofenac(50mg) in newly diagnosed patients with osteoarthritis. The principal aim was to study the efficacy and safety of both the drugs and compare them. In the present study, the maximum number of patients that is 72% of the total study group was in the age group 41-50 and 51-60 years .The remaining 23% patients were in the age group 61-70 years, and 2% of patients in age group 71-80years. The present study constituted both male and female patients with osteoarthritis. Osteoarthritis can be treated with Opioids in low doses, in patients who have no relief with acetaminophen, NSAIDs, intraarticular injections or topical therapy. They act by binding to different Opioid receptors in CNS and other tissues<sup>9</sup>. Long term use is not recommended because of their abuse potential..Acetaminophene acts by preventing prostaglandin synthesis by blocking the action of central COX. It is one of the safest analgesics but it has risks like hepatotoxicity and renal toxicity with long term use and chronic therapy with acetaminophene may intensify the anti coagulant effect in patients taking warfarin. COX-2 inhibitors can also be used in OA. But long term usage can increase the risk of MI and stroke by reducing prostaglandin I<sub>2</sub> production by vascular endothelium. Intra articular injections of glucocorticoids also have an excellent anti inflammatory effect but the expertisation of the clinician and risks of infection associated with their long term therapy limits their use in OA<sup>10</sup>. Intra articular injections of hyaluronic acid decreases pain by temporarily and modestly increasing the viscosity of synovial fluid. These agents are expensive because the treatment includes both drug costs and administration costs. As a result, hyaluronic acid injections are often used when there is demonstrable inefficacy with less expensive therapies. Diclofenac has analgesic, antipyretic, and anti-inflammatory activities. Diclofenac appears to reduce intracellular concentrations of free AA in leukocytes, perhaps by altering its release or uptake. Lornoxicam like other NSAIDs, inhibit both isoforms of COX in the same concentration range, that is, the ratio of COX-1 inhibition to COX-2 inhibition is 1:1. It readily penetrates into the synovial fluid.

The mean pain score with lornoxicam is 6.78±1.01 with significant difference (P<0.05) compared to diclofenac mean pain score 7.22±0.887 at the end of 4<sup>th</sup> week of the study. The mean pain score with lornoxicam is 4.06±1.08 with significant difference (P< 0.001) compared to Diclofenac mean pain score 6.2±0.728 at the end of 32<sup>nd</sup> week of the study. During the study, adverse drug reaction like epigastric pain, nausea etc were reported in both groups. This was managed by tab. ranitidine 8<sup>th</sup> hourly for 5 days and these patients showed their willingness to continue in study and successfully completed full duration of study. None of the patients developed cardiovascular adverse reactions like edema or increase in blood pressure. Similar results were shown by Vadgama, Vishalkumar K. et al, in their study “A randomized, controlled clinical trial comparing efficacy,

safety and cost effectiveness of lornoxicam with diclofenac sodium in patients of osteoarthritis knee” there was statistically significant difference between reduction of pain assessed by visual analogue scale (68.09 % reduction in group L as compared to 45.45 % reduction in group D at 2 months;  $P < 0.05$  and 80.89% reduction in group L as compared to 45.45 % reduction in group D at 3 months;  $P < 0.001$ ). Mean pain score of group L was less than results of group D after 2 and 3 months of treatment. Balfour JA et al in their review article stated that lornoxicam alone is studied for its pharmacology and therapeutic potential found lornoxicam is as effective as opiod analgesics and NSAIDs in relieving pain post operatively. Rosenow DE et al in their study lornoxicam verses morphine in relieving post operative pain stated that lornoxicam is as effective as morphine in relieving pain post operatively.

**In the present study the effect of lornoxicam increased over the period of study. The reduction in pain score is 47% at the end of the study with Lornoxicam and for Diclofenac it is 21%.**

Probable reason of this effect is that lornoxicam inhibits human polymorphonuclear cell migration induced by f -myeloperoxidase, IL-8 and substance P which are some of the important chemotactic mediators of inflammation. As it is clinically difficult to study the effect of a drug on articular cartilage, it should be confirmed with advanced procedures like arthroscopy. However, as this was a pilot study with limited sample size and relative short study duration, more studies with larger sample size, longer duration, and blinding techniques are necessary to substantiate our observations. Though lornoxicam is costlier than diclofenac, lornoxicam is more preferred because it is more effective in reducing pain in patients with acute osteoarthritis

## VI. Conclusion:

Based on the results obtained and the points mentioned in the discussion, the present study concludes that both lornoxicam and diclofenac reduced pain, but lornoxicam significantly relieves pain of osteoarthritis knee more than diclofenac sodium throughout the study period of 32 weeks<sup>11</sup>.

- There is a statistically significant decrease in mean pain score with lornoxicam compared to diclofenac ( $p < 0.001$ )<sup>12</sup>.
- So, we can conclude from our study findings that lornoxicam is efficacious compared to diclofenac sodium in reducing pain in patients with osteoarthritis.

In terms of safety, though lornoxicam has a little higher rate of gastrointestinal side effects (66%) than Diclofenac (38%) and costlier, it is more preferred for the treatment of osteoarthritis as pain alleviation is more important.

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