

Comparison of efficacy and tolerability of aceclofenac and diclofenac in osteoarthritis of knee joint

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ABSTRACT

Background: Osteoarthritis is a slowly progressive disorder associated with a hyaline cartilage loss. Non-steroidal anti-inflammatory drugs play a pertinent role in management of osteoarthritis.

Objectives: The study was carried out for the comparison of efficacy and tolerability of Aceclofenac and Diclofenac in patients of osteoarthritis of knee joint.

Material and Methods: It is a randomised parallel group double blinded study. The study included 60 patients of confirmed osteoarthritis of knee joint, 30 patients were given Aceclofenac and 30 patients were given Diclofenac after food for 8 weeks and the patients were evaluated and compared statistically for pain intensity by VAS Score, Joint tenderness, Swelling, Erythema, Pain on movement, Functional capacity and Overall Assessment on LIKERT Scale.

Results: Both the drugs caused marked improvements in the parameters of - Pain intensity, Joint tenderness, Swelling, Erythema, Pain on movement of OA knee joint but there was increased improvement in all the parameters with aceclofenac.

Conclusion: Aceclofenac is the NSAID of choice in the osteoarthritis of knee joint as compare to Diclofenac.

Key Words: NSAID, osteoarthritis, aceclofenac, diclofenac, joint

Introduction

Osteoarthritis is a chronic progressive articular erosive disorder which is due to alterations in the biochemical and metabolic dimensions, affecting mainly the weight bearing joints, most commonly seen late in life. [1] It usually has no systematic manifestations. It has significant association with overweight, Race, and Occupation and among them long term obesity is the causative factor. [2, 3] Osteoarthritis (OA) is the most common form of arthritis, accounting for approximately 75% of the disease and ranking among the top ten causes of disability worldwide. [4] Age is a major determinant of OA. OA is 13% in adult population but reaches 70% mark in above 65 years. [5]

Diagnosis can be made with clinical investigations but is confirmed with X-ray using defined criteria. Combination of

orally administered Non steroidal anti-inflammatory drugs and non pharmacological intervention like regular exercise, reducing weight plays an important role in treatment of osteoarthritis. In the Framingham study in subjects tracked longitudinally weight change over time affected the risk of developing osteoarthritis, those who gained were at increased risk and those who lost weight lowered the risk but medications remain a primary source in India, some noted one beings Diclofenac and Aceclofenac. [6,7]

Diclofenac, an aryl acetic acid derivative, anti-inflammatory, analgesic properties, somewhat COX -2 selective, being selectively maintained in synovial fluid 3 hours longer than in plasma, is a choicest drug for osteoarthritis. [8] It has a direct effect on ongoing hyperalgesia in addition to blocking COX. [9] The analgesic

is independent of a central or peripheral opioid effect but is based on locally activated nitric oxide.

Aceclofenac, an orally administered phenyl acetic acid derivative with anti-inflammatory and analgesic action. It does not inhibit any COX forms.^[10] It has additional properties of inhibition of interleukin 1 and tumour necrosis factor – besides stimulating cartilage matrix synthesis, so is a better manager of acute and chronic pain conditions.^[11]

The present study was carried out to evaluate the efficacy and tolerability of Aceclofenac for treatment of osteoarthritis knee joint compared to Diclofenac.

Material and methods

A randomised parallel group double blind study was conducted after having approval from ethics committee. 60 patients of either sex ageing between 30-75 years with confirmed osteoarthritis of knee joint (unilateral or bilateral), reporting to OPD of Orthopaedics department of Gian Sagar Medical College, Patiala were recruited. Informed Consent was obtained from all the patients after fully explaining the procedure to them. Patients were divided into two groups after satisfying the inclusion and exclusion criteria. 30 patients of Group 1 were given aceclofenac [100 mg bd] and 30 patients of Group 2 were given diclofenac [50 mg tds] for 8 weeks.

Patients were confirmed of osteoarthritis Radiologically by following features^[12]

- Narrowing of joint spaces
- Altered bone contour
- Bone sclerosis [subchondral sclerosis]
- Bone cysts [sub chondral cysts]
- Periarticular calcification
- Osteophytes and spurs

- Soft tissue changes [small effusions, calcification, and soft-tissue swelling]

Exclusion criteria:^[10, 13]

- Patients with renal or cardiac disorder
- Patients with active gastrointestinal ulceration
- Patients with hepatic or coagulation disorders
- Patients receiving antineoplastic agents, corticosteroids, gold salts penicillamine, colchicine, anticoagulants, and antimalarials within one month from their date of inclusion in the study.
- Patients of rheumatic arthritis, gout, or post traumatic osteoarthritis of knee
- Patients of previous hypersensitivity to NSAIDs
- Pregnant women and nursing mothers
- Female patients taking contraceptives
- All unstable patients suffering from any kind of serious ailments
- Patients scheduled for knee replacement therapy

At the end of the eight weeks the patients were analysed in the following areas according to the clinical features seen^[14]

- Pain Intensity
- Joint tenderness
- Swelling
- Erythema
- Pain on movement
- Functional capacity
- Overall assessment

Functional Capacity was measured by: Likert version of five point scale

- 0 – none
- 1 – mild
- 2 – Moderate
- 3 – Severe
- 4 – extreme

Pain was measured by Visual Analogue Scale [VAS]: a standardized vertical scale from 0 – 100 [least pain 0, maximum pain 100]

Adverse effects of the drugs were noted: in particular reference to gastric discomforts like:

- Epigastric pain
- Abdominal pain
- Dyspepsia
- Heartburn
- Indigestion
- Vomiting
- Episodes of haemetemesis/perforation/peritonitis or any serious sequel

Compliance of the patients as much as possible was maintained and recorded [preferably by number of used and unused pills in pack counting method]. The results were statistically analysed by using student t test and chi square.

Results

The group 1 consisted of 30 patients taking aceclofenac out of which 18 were

female and 12 were male, 30 patients in Group 2 consisted of 21 female and 9 male. In Group 1, 23 patients[76.7%] reported an improvement in pain intensity and joint tenderness respectively, 18[60%] showed improvement in swelling, 13[43.3%] showed improvement in erythema, 24 patients[80%] showed improvement in pain on movement and 23 patients[76.7%] showed improvement in functional capacity with Aceclofenac, whereas in Group 2, 19 patients[63.3%] showed improvement in pain intensity, 20 [66.7%] showed improvement in joint tenderness, 16[53.3%] showed improvement in swelling, 11 [36.67%] showed improvement in erythema, 21[70%] showed improvement in pain on movement and 20[66.7%] showed improvement in Functional capacity with Diclofenac. [Table 1] There was no significant difference in improvement in efficacy amongst Aceclofenac and Diclofenac [Table 2]

Table: 1 Drug efficacy

Parameters	Mean score at start of treatment	Mean score at end of treatment	P Vale
Aceclofenac			
P1	2.73±0.08	1.60±0.13	<0.001
JT	2.60±0.10	1.53±0.12	<0.001
S	2.16±0.11	1.16±0.12	<0.001
E	1.60±0.09	1.10±0.08	0.002
PM	2.70±0.08	1.46±0.17	<0.001
FC	2.83±0.06	1.70±0.15	<0.001
OS	2.63±0.08	1.56±0.14	<0.001
Diclofenac			
PI	2.70± 0.08	2.00± 0.12	<0.001
JT	2.50± 0.09	1.83± 0.13	<0.001
S	2.00± 0.09	1.26± 0.13	<0.001
E	1.66± 0.08	1.16± 0.13	0.031
PM	2.83± 0.06	1.76± 0.15	<0.001
FC	2.80± 0.07	1.96± 0.13	<0.001
OS	2.73± 0.08	1.93± 0.14	<0.001

Table: 2 Drug efficacy comparison amongst themselves

PARAMETER	X2 [CHI SQUARE VALUE]	P VALUE
P1	1.27	>0.05
JT	0.73	>0.05
S	0.27	>0.05
E	0.27	>0.05
PM	0.8	>0.05
FC	0.74	>0.05
O	0.34	>0.05

PI = Pain intensity, JT = Joint tenderness, S=Swelling, E=Erythema, PM = Pain on movement, VAS = Visual analogue scale, FC=Functional capacity, OS=Overall status

Table: 3 Comparison of drug tolerability and safety profile

ADVERSE EFFECT	ACECLOFENAC	%	DICLOFENAC	%	X2	p value
ABDOMINAL PAIN	5	16.67	6	20	0.11	>0.05
CONSTIPATION	3	10	4	13.33	0.16	>0.05
DIARRHOEA	1	3.33	4	20	1.96	>0.05
DYSPEPSIA	4	13.33	6	20	0.48	>0.05
EPIGASTRIC PAIN	10	33.33	11	36.67	0.07	>0.05
FLATULENCE	4	13.33	1	3.33	1.9	>0.05
HEART BURN	12	40	13	43.33	0.06	>0.05
INDIGESTION	6	20	8	26.67	0.37	>0.05
NAUSEA	3	10	3	10		
VOMITING	2	6.67	2	6.67		
HEADACHE	1	3.33	1	3.33		
TIREDNESS	1	3.33	2	6.67	0.35	>0.05

There was no significant difference found in adverse effects like Abdominal Pain, Constipation, Diarrhoea, Dyspepsia, Epigastric Pain, Flatulence, HeartBurn, Indigestion, Nausea, Vomiting, Headache and Tiredness [Table 3]

Discussion

Over the past few decades the problem of osteoarthritis has increased and prevalence of osteoarthritis has led to a growing recognition of need to recognise the difference between commonly used drugs- Aceclofenac and Diclofenac. Functional status was assessed by VAS

[visual analogue scale] and Likert five point scale on the parameters of Pain intensity, Joint tenderness, Swelling, Erythema, Pain on movement, Functional capacity and Overall assessment.

74.5% patients having aceclofenac showed improvement in pain intensity in a study conducted by Ward et al. [15] The study of Kornasoff et al showed 76.2% improvement [16] which are similar (76.7%) with our findings. 59% of patient taking diclofenac showed improvement in pain intensity [15] which are almost similar (63.3%) to our study. 72.4% patients taking aceclofenac showed improvement

in joint tenderness as compare to diclofenac (59%).^[15] Our study also showed almost similar results with aceclofenac (76.7%) and diclofenac (63.3%)

58.3% patients taking aceclofenac showed improvement in swelling as compare to diclofenac 59%.^[15] Our study showed improvement in 76.7% patients taking aceclofenac and 63.3% in diclofenac group.

The study of Kornasoff et al showed that 43.4 % patients taking aceclofenac showed improvement in erythema as compare to naproxen^[16] The study of Ward et al showed that 23.4 % patients taking aceclofenac showed improvement in erythema as compare to diclofenac.^[15] Similarly, our study also showed approximate same results (43.3%) with aceclofenac.

The study of Diaz et al showed that there was significant improvement in pain on movement in patients of OA knee taking aceclofenac as compare to diclofenac.^[17] The study of Kornasoff et al showed that there was significant improvement in pain on movements in [78%] patients taking aceclofenac as compare to naproxen.^[16] Similarly, our study showed significant results (80%) with aceclofenac.

The study of Ward et al showed that 74.5% patients showed improvement in functional capacity with aceclofenac as compare to diclofenac.^[15] Gualda et al in his study observed that there was significant improvement in pain and functional capacity with aceclofenac as compare to acetaminophen.^[18] Our study showed approximate same results (76.7%) with aceclofenac.

It can be said that both of these drugs, with so widespread use in the indian scenario, are definitely successful relievers of symptom complex of OA knee on all the fronts. Though statistically no

significant difference could be seen between the two, a general tendency of increased relief could be seen with aceclofenac in all the parameters so put to test.

The difference in the adverse effect profile was not statistically significant, except for diarrhoea. Apart from this there is clear cut tendency of lesser gastrointestinal side effects with aceclofenac than diclofenac. Therefore it can be said that both these drugs are well tolerated but the tolerability of aceclofenac is better.

Conclusion

The results showed that both the drugs caused marked improvements in all the parameters of symptom complex of OA knee joint, the virtue of their widespread use remaining validated, but the effects of any one was not significantly greater than the other, but a tendency of increased improvement in all the parameters was observed with aceclofenac.

Furthermore, Aceclofenac, a relatively selective enhancer of glycosaminoglycan synthesis, was found to have a less tendency towards the well documented gastrointestinal side effects of NSAIDs, especially in relation to diclofenac as seen in the study. Therefore it can be safely assumed and quoted that aceclofenac can replace diclofenac as the NSAID of choice in the osteoarthritis of knee joint.

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