CODEN (USA): IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.800681

Available online at: http://www.iajps.com *Case Study*

COMPARATIVE STUDY OF SAFETY,EFFICACY AND TOLERABILITY OF ACECLOFENAC VERSES DICLOFENAC IN OSTEOARTHRITIS PATIENTS ATTENDING A SECONDARY CARE HOSPITAL IN ANANTAPURAMU

Shaik Mohammad Arshad Ali*, Ottikunta Sowjanya and Dr.Yiragamreddy Samhitha Reddy

Pharm D,Department of Pharmacy Practice, Raghavendra Institute of Pharmacy Education and Research.

K.R.Palli Cross, Chiyyedu, Anantapur, Andhra Pradesh.

Abstract:

OBJECTIVE: Assess the safety, efficacy and tolerability of medication by using different scales. Compare the different disease management strategies adopted according to the disease relief achieved, adverse effects noticed.

MATERIAL AND METHODS: Patient diagnosed with OA were selected randomly and involved in the study after obtaining consent from them. Patient's interview was done to determine disease outcome before and after the treatment. Patient medication details, demographic details, lab investigations, x-ray of joints affected and adverse effects experienced by the patients were collected from the medication charts and from patient/attendant interview. The different disease management strategies adopted were then compared. The scores for different patient reported outcomes were than analyzed using Graphpad Instat 3.

RESULTS: The over all incidence of adverse effects in our study was 6% in Aceclofenac and 20% in Diclofenac group. Aceclofenac was well tolerated than Diclofenac in terms of epigastric pain, flatulence, abdominal pain and constipation.

CONCLUSION: Aceclofenac has anti-inflammatory and analgesic properties similar to those of Diclofenac, and gastrointestinal damage is less than that of Diclofenac. This might be due to preferential inhibition of COX-2. This study shows that Aceclofenac is safe, effective and well tolerated drug in osteoarthritic patients.

Key Words: *Aceclofenac, Diclofenac, NSAIDs VAS and WOMAC.*

Corresponding author:

Dr.Yiragamreddy Samhitha Reddy,

Pharm D, Department of Pharmacy Practice,
Raghavendra Institute of Pharmacy Education and Research.
K.R.Palli Cross, Chiyyedu, Anantapur, Andhra Pradesh.

QR code

Please cite this article in press as Y. Samhitha Reddy et al, ***Tolerability of Aceclofenac Verses Diclofenac in Osteoarthritis Patients Attending a Secondary Care Hospital in Anantapuramu****, Indo Am. J. P. Sci, 2017; 4(05).*

INTRODUCTION:

Osteoarthritis (OA) is one of the most common, chronic musculoskeletal inflammatory disorder which affects knee and hip joint in elderly people .Osteoarthritis is a disease of synovial joint characterized by cartilage loss with accompanying peri-articular bone response. Cartilage is a protein substance that serves as a "cushion" between the bones of the joints. Osteoarthritis is associated with pain and swelling which is a protective reaction of the vascularised tissue to injury, intended to eliminate the cause of cell injury as well as necrotic cells and tissues resulting from the injury and to initiate the repair of damage done to the tissue. Inflammation can be either acute or chronic[1].

Acute inflammation is characterized by 5 cardinal signs Rubar (redness), Calor (heat), Tumor (swelling), Dolar (pain), functiolaesa (loss of function).Pain is the main reason for visting the emergency department in more than 50% of cases[2] .

Osteoarthritis rarely occurs before the age of 40 but by the age of 65 at least 80% of the population have either clinical or radiographic evidence of osteoarthritis, its prevalence after the age of 65 is about 60% in men and 70% in women [1]. Osteoarthritis is a complex disorder with multiple risk factors, twin and family studies shows that genetic factors play a major role, particularly for hand and generalized Osteoarthritis, but also for hip and knee Osteoarthritis. The genes responsible remain to be unidentified. Knee Osteoarthritis is prevalent in all racial groups but hips, hand and generalized Osteoarthritis are particularly prevalent in causes. Osteoarthritis is more prevalent and more commonly symptomatic in women. Except at the hip where men are equally affected. Trauma is a recognized predisposing factor and repetitive adverse loading of joints during occupation or competitive sports also appears important, such as in farmer (hip OA), minors (Knee OA) and professional foot ballers (Knee OA)[22].

Risk factors for Osteoarthritis includes advanced age, female gender, genetic predisposition, obesity, and joint including trauma .Genes that encode collagen type II have been proposed as candidate genes for familial Osteoarthritis[1].

Table 1: Epidemological profile of Osteoarthritis

INDIA	USA	WORLD WIDE
Prevalence of 22% to 39%[19], 45% of women with age ≥ 65 years' shows symptoms.	46 million American adults (21% of the population) had arthritis, of which nearly 27 million had clinical Osteoarthritis[21].	100 million people worldwide suffer from Osteoarthritis[19].

.

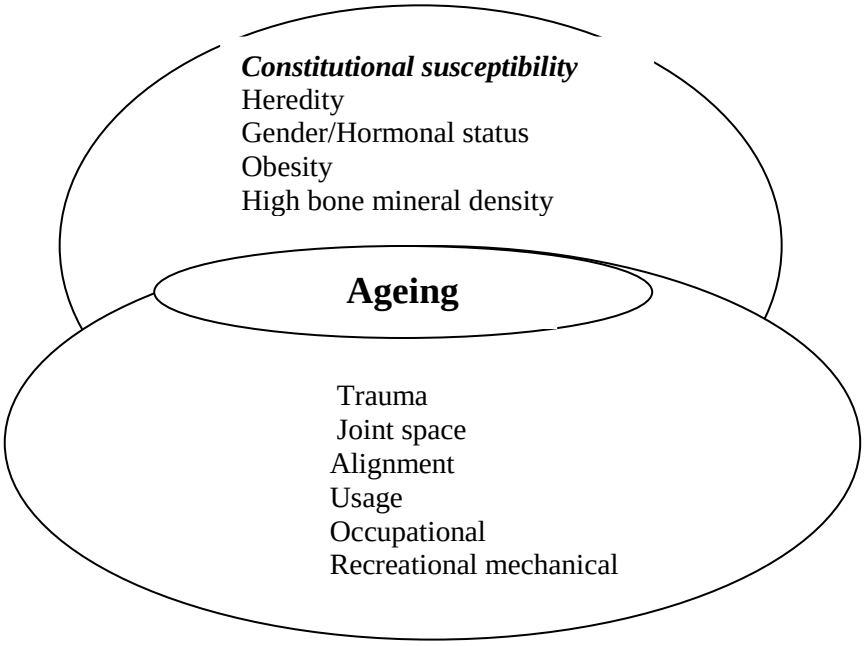

Fig 1: Risk factors for the development of Osteoarthritis [22]

Types of Osteoarthritis:
A) Primary Osteoarthritis
B) Secondary Osteoarthritis

Primary Osteoarthritis:
A) Idiopathic Osteoarthritis
B) Generalised (poly articular) Osteoarthritis

A. Idiopathic (Primary) Osteoarthritis :
- Localized (Monoarticular and Pauciarticular)Osteoarthritis involving
- Hands: DIP (Heberden's node), PIP (Bouchard's node), 1st carpometacarpel joint.
- Knee
- HIP(Primary OA of HIP is unknown in India)
- Spine (Apophyseal joint, inter vertebral joint)

B. Generalised (Poly articular) Osteoarthritis: Includes 3 or more of the above listed areas[23].

Secondary Osteoarthritis:

Etiology:
- Trauma
- Congenital/developmental disorders
  Eg: Perthe's, SCFE, DDH, varus/valgus deformity, bone dysplasias
- Metabolic disease
  Eg: Acromegaly, hyperparathyroidism, Diabetes mellitus, Obesity, Hypothyroidism.
- Calcium deposition diseases
  Eg: CPPD, Apatite Arthropathy.
- Other joint disease
  Eg: Fracture, AVN, Gout, Infection, Osteoporosis, Osteochondritis, Paget's disease[22,23].

Pattern of Joints Involved:
- Monoarticular/pauciarticular-Knee>Hip
- Poly articular-DIP (distal interphalangeal)
- Overall DIP commonest

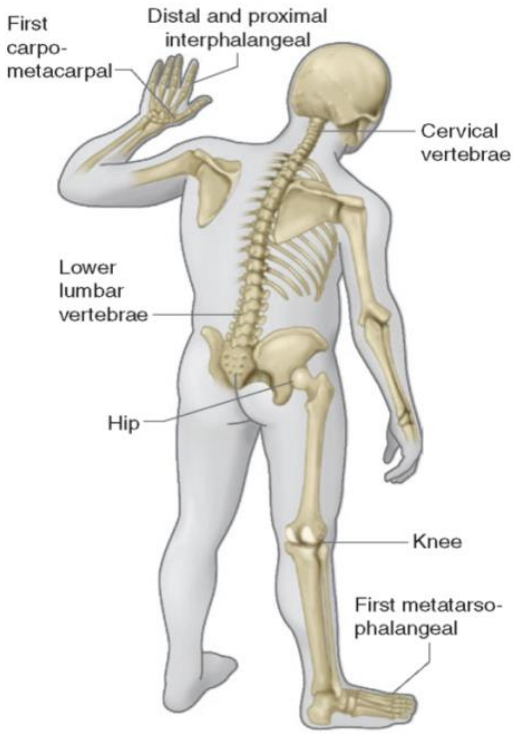

Fig 2: Joints involved in osteoarthritis[23]

Pathophysiology:

Mechanisms involved:

- Osteoarthritis is classified as primary if the etiology is unknown and secondary when degenerative joint changes occur in response to a recognized local or systemic factor.
- The cause of secondary Osteoarthritis are listed, developmental abnormalities are believed to be of major importance in the aetiology of Osteoarthritis of the hip, and collagen gene defects have been identified in a few families in whom familial, premature, polyarticular Osteoarthritis is associated with an epiphyseal or Spondylo epiphyseal dysplasia. Epidemological surveys suggest that physical factors involved in occupations such as farming are important determinants in hip Osteoarthritis. Abnormal surface contacts and weight-bearing alignments lead to increased local mechanical stress and wear. Past traumatic malignent and incongruity of joint are well established as important predisposing causes of premature Osteoarthritis.
- Metabolic diseases lead to degeneration of cartilage by very different mechanisms .In Alkaptonuria (Ochronosis) a genetically determined defect of homogentisic acid oxidase results in the collagen rendering it brittle and prone to mechanical degradation. Crystal deposition of calcium pyrophosphate dehydrates or hydroxyopalite may alter the properties of cartilage matrix directly but crystal formation usually follows the matrix changes.
- It is uncertain whether the degenerative joint disease seen in acromegaly is a consequence of joint incongruity following cartilage overgrowth or whether the endocrine disturbance results in a mechanically defective matrix. Paget's disease, Gowcher's disease and various diseases associated with aseptic necrosis result in pathological changes in subchondral bone, with consequent altered stresses on the overlying articular cartilage. Thus Osteoarthritis can be the end result of disorders in which normal cartilage matrix fails secondary to abnormal mechanical loads.
- Current concepts of the pathogenesis of Osteoarthritis are based on the assumption that, whatever the provoking cause, the final pathway of changes in articular cartilage is identical. Two mechanical hypotheses meant consideration. The first suggests that the initiating event is fatigue fracture of the collagen fiber network, which is followed by increased hydration of the articular cartilage with unraveling of the proteoglycons and loss of proteoglycone into the synovial fluid. There is some evidence of augmented metalloproteinase activity and indirect evidence of a putative aggrecanose but collagen may also be lost as a result of mechanical attrition.
- The alternative hypothesis suggests that the initial lesions are micro fracture of the subchondral bone following repetitive loading. Healing of these micro fractures leads to significant loss of resilience of the subchondral bone, which in turn creates a shear stress gradient in the adjacent articular cartilage. As the process evolves the cartilage surface becomes fibrillated and deep clefts appear, with reduplication and proliferation of chondrocytes within them, simultaneous proliferative changes commence at the joint margins, with formation of osteophytes. Eventually articular cartilage is lost altogether in areas of maximum mechanical stress and the underlying bone becomes hardened and eburnated cysts may form but bony ankylosis does not occur. The associated biochemical changes in articular cartilage are.

Biochemical Changes Occurring in Osteoarthritis Cartilage:

- ↑ H_2O
- ↓ Collagen, Proteoglycone, monomer size, Hyaluronate, Keratan sulphate, and Chondroitin sulphate.
- ↑ Chondroitin 4:6 ratio
- Expression of fetal Chondroitin sulphate epitopes
- ↑ Collagen and proteoglycone synthesis
- ↑ Aggrecanase, stromelysin and collagenase.

The molecular mechanism of damage of cartilage in Osteoarthritis appears to be the breakdown of collagen type2, probably by IL-1, TNF and nitric oxide.

Pathologic changes occurs at

1) Articular Cartilages
2) Adjacent bones and
3) Synovium.

1) Articular cartilage:

The regressive changes are most marked in the weight-bearing region of articular cartilage. Initially, there is loss of cartilaginous matrix (proteoglycons) resulting in progressive loss of normal metachromosia. This is followed by focal loss of chondrocytes, and at other places, proliferation of chondrocytes forming clusters. Further progression of the process causes loosening, flaking and fissuring of the articular cartilage resulting in breaking off of pieces of cartilage exposing subchondral bone. Radiologically, this progressive loss of cartilage is apparent as narrowed joint space.

2) Bone:
The denuded subchondral bone appears like polished ivory. There is death of superficial osteocytes and increased osteoclastic activity causing rarefraction, microcyst formation and occasionally microfractures of the subjacent bone. These changes results in remodeling of boric and changes in the shape of joint surface leading to flattening and mushroom-like appearance of the articular end of the bone . The margins of the joints respond to cartilage damage by osteophyte or spur formation. These are cartilaginous out growths at the joint margins which later get ossified. Osteophytes give the appearance of lipping of the affected joint. Loosened and fragmented osteophytes may form free 'joint mice' or loose bodies.

3) Synovium:
Initially, there are no pathological changes in the synovium but in advanced cases there is low-grade chronic synovitis and villous hypertrophy. There may be some amount of synovial effusion associated with chronic synovitis[25].

Diagnosis:

☆ Radiological Features:

X-ray:

X-ray is so characteristic that other forms of imaging are seldom necessary. The four cardinal signs are:

- A symmetrical loss of cartilage causing narrowing of joint space (earliest feature)
- Sclerosis of subchondral bone under the area of cartilage loss
- Cystic lesion close to articular surface
- Osteophytes at the margins of joint, loose bodies and deformities can be there [23].

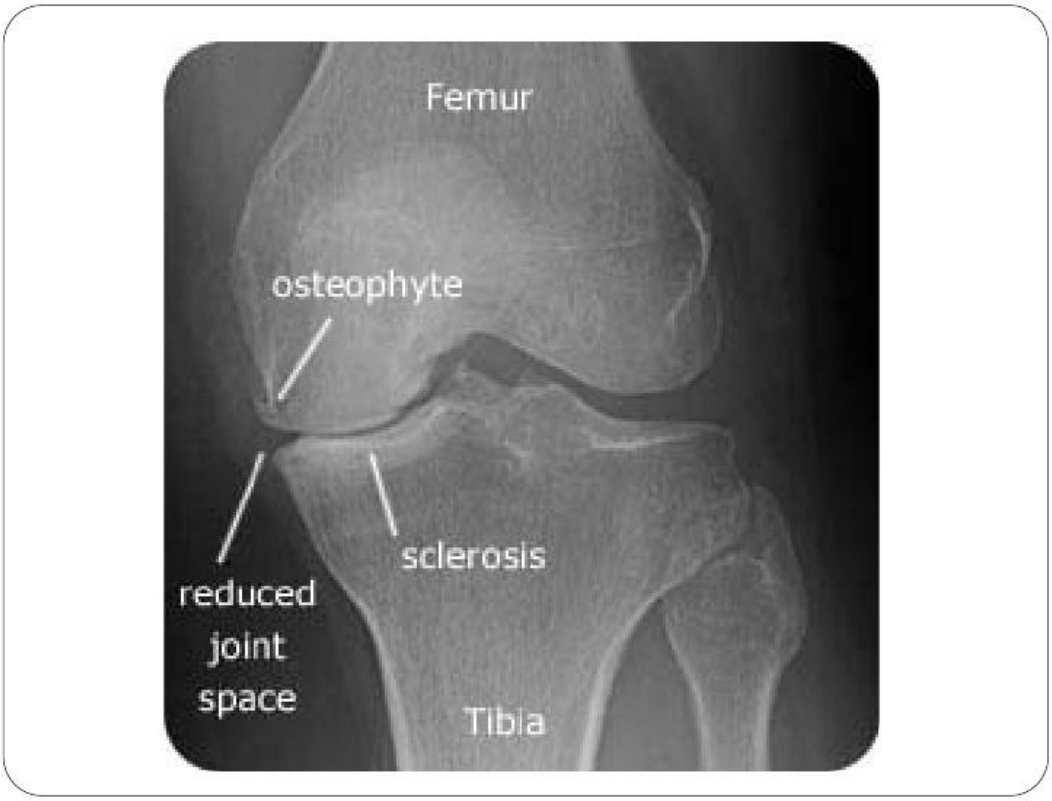

Fig 3: Radiological changes in Osteoarthritis joint

Treatment:

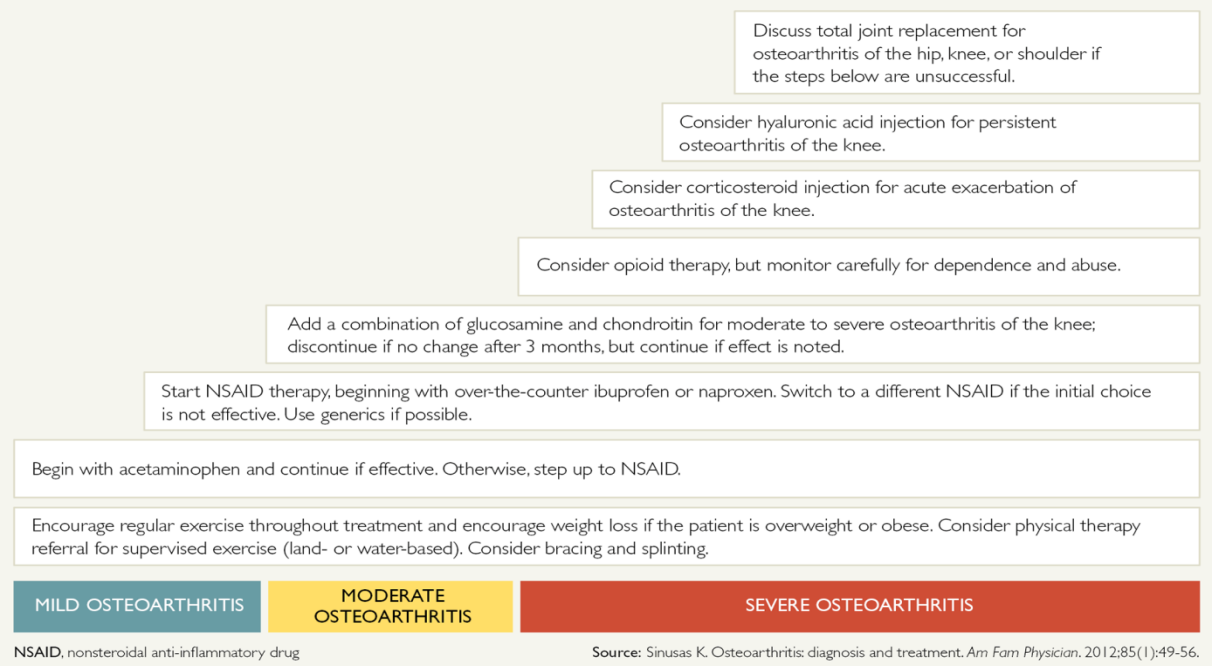

Fig 4: Treatment option in Osteoarthritis management[24]

The FBS, ESR and CRP are normal in Osteoarthritis. Synovial fluid aspirated from Osteoarthritis knees shows variable characteristics but is predominantly viscous with low turbidity; accompanying CPPD and basic calcium phosphate may also be identified. Radio isotope bone scans performed for other reasons often show, as an incidental finding, discrete increased uptake on Osteoarthritis joints due to bone remodeling.

Unexplained early-onset Osteoarthritis requires additional investigation, guided by the suspected underlying condition. X-rays may show typical features of dysplasia or avascular necrosis, widening of joint space in acromegaly, multiple cysts and chondrocalcinosis in haemochromatosis or disorganized architecture in neuropathic joints [22].

Principles followed during the process are:-

Full explanation of the condition:

- Estimation relevant risk factors (obesity, heredity, and trauma).
- discussion of prognosis(good for nodal hand OA, more optimistic for knee than hip OA)
- **Exercise** :

This should cover both strengthening and aerobic exercise, preferably with reinforcement by a physiotherapist.

- **Reduction of adverse mechanical factors :**

This includes weight loss if Obese, Shock-absorbing foot wear, Pacing of activities, use of walking sticks for painful knee or hip

Osteoarthritis or provision of built-up shoes to equalize leg length.

- **Drug therapy**:

Give an initial trial of paracetamol and consider the addition of a topical NSAIDS, and then capsaicin, for knee and hand Osteoarthritis. If required, consider escalating to combined analgesics or oral NSAIDs.

Opiates may occasionally be required. For temporary benefit of moderate to severe pain consider intra-articular injection of corticosteroid and local physical therapies such as heat or cold. At present there are licensed disease modifying drugs for Osteoarthritis, but the measures above may reduce structural progression as well as improve symptoms.

- **Surgery** :

Surgery should be considered for patients with Osteoarthritis whose pain, Stiffness and reduced function impact significantly on their quality Of life and are refractory to non-surgical care and adjunctive treatments. Osteotomy may prolong the life of malaligned joint replacement, however, can transform the quality of life of people with severe knee or hip Osteoarthritis. Surgery for refractory Osteoarthritis should be considered before prolonged and established functional limitation and severe pain,

since these may compromise the surgical outcome. Patient-specific factors such as age, gender, smoking and pressure of obesity, should not be barriers to referral for joint replacement.

Total joint replacement is required for the minority of people with large joint Osteoarthritis. Over 95% of joint replacements continue to function well into the second decade after surgery and most provide life-long pain free function. However, approximately 1 in 5 patients are not satisfied with the outcome, and a minority gets little or no improvement in pain following surgery [22].

The evidence supporting Non-Pharmacologic therapies is spores and is mainly limited to the treatment of knee osteoarthritis. A Cochrane review from 2001 concluded that land based therapeutic exercise seemed to reduce pain and improves function in symptomatic Osteoarthritis of the knee .Orally administered NSAIDS play an important role in the symptomatic management of Osteoarthritis[1] .It is estimated that more than 30 million people worldwide take NSAIDS[1] .

While NSAIDS are effective in the management of pain and inflammation in a large number of condition including Osteoarthritis, it is now well established that they are associated with the development of upper gastrointestinal(GI) damage including mucosal erosions, ulcers and life-threatening condition like perforations and hemorrhage .This led to the development of cyclooxygenese-2(COX-2) inhibitors . The potential advantage of COX-2 inhibitors is that they have fewer adverse effects on the gastrointestinal tract as a result of having less inhibitory effect on the gastro protective prostaglandins produced by COX-1 enzymes in the gastrointestinal tract .this advantage of COX-2 selective NSAIDS has been demonstrated in many trials, however, the cardiovascular safety of these drugs was found to be controversial [1].

Diclofenac appear to have anti-inflammatory, anti-pyretic, and analgesic properties, which are thought to be mediated by cyclooxygenase (COX) enzyme. COX-1is involved in 'house keeping' activities, such as mediating normal platelet function, regulating renal blood flow and providing cytoprotection of the gastric mucosa. COX-2 is involved in the response to tissue damage and mediates inflammation and pain. The COX-2 inhibitors are more selective in their inhibition of COX-2 relative to COX-1. The COX-2 inhibitors have been associated with higher rates of cardiovascular adverse events and it is hypothesized that this effect is a result of relative COX-2, COX-1 inhibition. While Diclofenac is a traditional NSAID, it does display a preferential inhibition of COX-2 compared to COX-1. Maximum dose is –150mg daily. Side effects of Diclofenac are peptic ulcer perforation, obstruction & bleeding, myocardial infarction, heart failure, coronary heart disease [26].

Aceclofenac inhibits synthesis of the inflammatory cytokines like interleukin (IL-1), Tumor necrosis factor (TNF) and prostaglandin E_2 (PGE_2) production. Aceclofenac is an effective analgesic and anti-inflammatory agent provides symptomatic relief in a variety of painful conditions .Aceclofenac appears to be particularly well tolerated among the NSAIDS with a lower incidence of gastrointestinal adverse effects this good tolerability profile results in a reduced withdrawal rate and greater compliance with treatment. Since long-term NSAIDS treatment is indicated for osteoarthritis the ideal agent should have good efficacy and a low propensity to cause adverse events.

Positive points of Aceclofenac over Diclofenac are good Tolerability of Aceclofenac was better than with Diclofenac experienced gastrointestinal adverse events, incidence of treatment related diarrhoea was less with Aceclofenac than the Diclofenac'

Hence the present study was carried out in osteoarthritis patients receiving Aceclofenac and Diclofenac [1], to establish safety, efficacy, and tolerability of these drugs which are used majorly in the treatment of Osteoarthritis.

Literature Review

Anand R, Kanaki, Rajesh S, Patil, Jeevangi Santosh Kumar, Ravi D, and mala have performed a study titled 'Comparative study of Safety, Efficacy, and Tolerability of Aceclofenac verses Diclofenac in Osteoarthritis Patient's and it was published in Journal of Evolution of medical and Dental science in 2013. The purpose of the study was to compare the long term NSAIDs treatment is indicated for Osteoarthritis, the ideal agent should have good efficacy and a low propensity to cause adverse events Aceclofenac has anti-inflammatory and analgesic property similar to those of Diclofenac and gastrointestinal damage is less than that of Diclofenac. This may be due to preferential inhibition of COX-2. This study shows that Aceclofenac is a safer, effective and well tolerated drug for Osteoarthritis.

*Richa Garg, Shafiqa Aslam, Anil Garg and Rani Walia have performed a randomized prospective, titled 'A prospective comparative study of serratiopeptidase and Aceclofenac in upper and lower limb soft tissue Trauma cases' and it was published in International Journal of Pharmacology and Pharmaceutical Technology in 2012.*The purpose of the study is to compare the Serratiopeptidase and Aceclofenac in upper and lower limb soft tissue trauma cases. In the present study Serratiopeptidase

showed significant anti-inflammatory effect and mild analgesic effect. None of the patient was required to be put on another analgesic or any alteration in treatment. Aceclofenac showed superior analgesic effect as compared to serratiopeptidase. Mild to moderate adverse effects were reported. The most common adverse effect reported was dyspepsia. All were mild and did not require any alteration or discontinuation of treatment.

Patil Pramod Reddy, Jaida Jyothirmai, Palani Anuradha, B Anandam and Rao Kateshwar have performed a study titled 'A comparative study of efficacy and safety of Diclofenac and Aceclofenac in the treatment of Osteoarthritis patients' and it was published in Journal of delivary and therapeutics in 2012. The aim of the study was to compare an efficacy and safety of Diclofenac and Aceclofenac in the treatment of Osteoarthritis patients. Analysis of Aceclofenac over Diclofenac in Osteoarthritis. Because single blinding was a limitation, the findings of this study can be confirmed by multicentric, randomized, double blinded large population studies.

Shelgel A, Sehgal VK, and Singh R conducted a randamised parallel group double blinded study as an article titled 'Comparison of efficacy and tolerability of Aceclofenac and Diclofenac in Osteoarthritis of knee joint' it was published in 2015. The study was conducted to compare an efficacy and tolerability of Aceclofenac and Diclofenac in Osteoarthritis of knee Joint. The both drugs caused marked improvements in all the parameters of symptom complex of OA knee joint, the virtue of their wide spread use remaining validated, but the effects of anyone 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 safety assumed and quoted that Aceclofenac can replace Diclofenac as the NSAID of choice in Osteoarthritis of knee joint.

Dr. Malik Muhammad Yasin Awan, Dr. Ijaz Ahmad and Prof. Dr. Amer Aziz conducted a study entitled 'Efficacy and safety of Aceclofenac in the treatment: A randomized double-blind comparative clinical trial verses Diclofenac' and published in the Professional Medical Journal in 2014. On the basis of observations made in this study, we can safely conclude: Aceclofenac is effective and effective and reliable drug for the treatment of Osteoarthritis in the Pakistani Population. Aceclofenac is safe and possesses an excellent gastrointestinal tolerability profile.

Faizal Vohra and Asawari Raut conducted a study entitled 'Comparative efficacy, safety and tolerability of Diclofenac and Aceclofenac in musculoskeletal pain management: A systemic review' and published in Indian Journal of pain in 2016. These studies performed also showed that Aceclofenac was more tolerable compared to Diclofenac with lower incidence of GIAEs including abdominal pain and dyspepsia. One study reported that Diclofenac is cost-effective compared to Aceclofenac; however, Aceclofenac has a better efficacy and tolerability in the patients that makes Aceclofenac a drug of choice. Use of assessment scales can be helpful in assessing the pain intensity and measuring the efficacy of the drug. This review concludes that Aceclofenac is a better choice compared to Diclofenac in reducing the pain in musculoskeletal disorders with lower incidence of AEs, providing better patient compliance and better tolerability.

*Sung-Hun Lee, Chang-Dong Han, KK-Hwan Yang, and Chul-Won Ha have performed a study titled 'Prescription pattern of NSAIDs and the patients in clinical practice in Korea' it was published in the Korean Academy of Medical sciences in 2011.*Multiple case-control population and database studies have confirmed that use of NSAIDs increases the risk of significant GI complications (Eg: Bleeding, Hospitalization, Surgery) from 3.5 fold overall about half of Korean Orthopaedic patients receiving NSAIDs are at high or very high risk for NSAID-induced GI complications, physician's prescription pattern for NSAIDs appears to be inconsiderate. Physician's considerate prescription of NSAIDS with well-understanding of each patient's GI risk factors is strongly encouraged in order to maximize cost effectiveness as well as to prevent serious GI complications in Korea.

K. P. Patnaik, P. Das, S. Hota, B. N. Mohapatra, S. Mohapatra, S. Nayak and S. Panigrahi have performed a study titled 'Comparative safety and cost effective analysis between Aceclofenac, Lornaxicam and Diclofenac in patients of musculoskeletal disorder' and it was published in International Journal of Pharmaceutical sciences and research in 2012. The aim of the study was to compare safety and cost effective analysis. This study showed that the GIAE (Gastro intestinal adverse events) i.e. dyspepsia, abdominal pain, vomiting etc were maximum i.e. 20% with Diclofenac which was significantly higher than GIAE with Lornaxicam-10% and Aceclofenac 8%, but there was no significant difference between incidence of AE with Lornaxicam and Aceclofenac, finds that better GI safety profile of Aceclofenac in comparison to Diclofenac.

Kudaravalli Jyothsna and Narayan Deshpande in their study titled 'Efficacy and safety of Diclofenac sodium and Aceclofenac in controlling post extraction Dental pain: A randomized open Label comparative study 'published in Journal of Pharmacology and Toxicology in 2011. Evaluated the efficacy and safety of Diclofenac sodium and Aceclofenac in controlling post extraction Dental pain. The study proved that Aceclofenac has a rapid onset and prolonged pain relief and statistically significant analgesic effect in the immediate post operative period of 8h in comparision to Diclofenac sodium. Aceclofenac has a better gastrointestinal profile than Diclofenac sodium.

Pravin Kumar INGLE, Prakash H patil, and Vibhavari Lathi have performed a study title 'study of rational prescribing and dispening of prescriptions with non-steroid anti-inflammatory drugs in orthopedic outpatient department' and it was published in Asian journal of pharmaceutical and clinical research in 2015. The study was conducted to study of rational prescribing and dispensing of prescriptions with NSAIDS in orthopedic OPD. The data obtained from the present study, it was found that although the use of low risks traditional NSAIDS, CO-prescriptions of antacids, supplements are some of the positive points in the management pattern. The prescription should be educated about generic prescribing which may have a multitude of benefits including cost minimization. The study suggests that there is the immense scope of improvement in prescribing and dispensing in the hospitals to achieve standards of rational prescribing.

E. Batlle-Gualda, J. Roman Ivorra and so on was conduct a study entitled 'Aceclofenac vs Paracetamol in the Management of symptomatic Osteoarthritis of the knee: a double- blind 6-week randomized controlled trial and it was published in Osteoarthritis and cartilage in 2007. They performed a study on symptomatic management with Aceclofenac and Paracetamol in Osteoarthritis of the knee. In this 6-week study Aceclofenac was superior to Paracetamol in pain reduction and functional improvement in symptomatic patients with OA of the knee, with no significant difference in tolerability. This finding give additional support to the notion that NSAIDs may be more effective than simple analgesics in OA patients, especially when used in short term.

Shankar PR, Pai R, Dubey AK, and Upadhyay DK conduct a study entitled 'Prescribing Patterns in the Orthopedics outpatient department in a teaching hospital in Pokhara, Western Nepal' Published in Kathmandu University Medical Journal in 2007. Evaluated the percentage of prescribing by generic name was low and efforts to encourage prescribing by generic name was low and efforts to encourage prescribing by generic name should be initiated. The average cost may be high for a poor country like Nepal. The prescribing of topical NSAIDs and of glucosamine sulfate may have been partly responsible for this. The drugs were prescribed for a relatively longer duration of time. The percentage of encounters with an antibiotic and an injection prescribed was low. This is a welcome sign and has to be encouraged. The use of FDCs was low. Anomalies were noted in some of the prescribiptions. Education interventions to improve prescribing for doctors at different levels may be required.

Taruma Sharma, S. Putta, and D. C. Dhasmama have performed a study title 'Prescribing pattern of NSAIDs in Orthopedic OPD of a Tertiary care Teaching Hospital in Uttaranchal, published in journal of medical education and research in 2006. The study was conducted to evaluate the prescribing pattern of NSAIDs in Orthopedic OPD. The selective NSAIDs are costlier than the non-selective NSAIDs, the cost of therapy per prescription to the patient is lower as the selective NSAIDs need not be complimented with concomitant therapy with gastro protective agents. Initial trials showed superiority of COX-2 selective drugs over non-selective drugs but clinical experience has put their safety in question. The withdrawal of Rafecoxib and Valdecoxib by the manufacturing company, in lieu of causing cardiovascular side effects, has probably changed the prescribing pattern of NSAIDs. The choice of COX-2 selective inhibitors for a particular patient should be based upon a number of factors including relative efficacy, toxicity, concomitant disease states, patients, age, renal function and cost.

Mohamed Ahmed, Nahid Ali, Zia ur Rahman and Md. Misbahullah khan have performed a study titled 'A study on prescribing pattern in the management of arthritis in the department of orthopedics and it was published in journal of Der pharmacia Lettre in 2012. The purpose of study was to compare the prescribing patterns in the management of arthritis in the department of orthopedics. The results showed that out of 92 patients, 53 (57.60%) patients were males and 39 (42.31%) patients were females. Whereas, the gender distribution in OA patients shows that out of 75 patients, 49 (65.33%) patients were males and 26 (34.66%) patients were females. Whereas the gender distribution of RA patients shows that out of 15 patients, 13 (86.66%) patients were females and 2 (13.33%) patients were male. The overall drug usage in this study revealed that a total of 193 drugs were prescribed. Out of which, Diclofenac was most prescribed [72(37.30%)] followed by paracetamol in [40(20.72%)], Tramadol in [16(8.29%)], Nimesulide in [15(7.77%)], hydroxyl choloquine in [13(6.73%)], Aceclofenac in

[9(4.66%)], Methotrexate in [8(4.14%)], Prednisolone in [7(3.62%)], Etoricoxib in [6(3.1%)], Deflazacort in [3(1.55%)], Ibuprofen in [2(1.03%)], Indomethacin in [1(0.51%)] and Colchicine in [1(0.51%)] patients. So the purpose of the study to analyze the current prescribing pattern in the management of the Arthritis.

Singh V, Yadav P and Deolekar P in their study titled 'Current trends of prescribing patterns of NSAIDs in an Orthopaedic OPD in a teaching hospital' it was published in International journal of Pharma and Bio sciences in 2014. The aim of study was to know the current trends of prescribing patterns of NSAIDs in an Orthopaedic OPD in a teaching hospital. This study documented a non-selective NSAIDs accounted for (45.71%) total drugs prescribed. FDCs (19.19%) were more commonly prescribed than monotherapy (14.39%). Paracetamol (15.12%) was the commonly prescribed NSAIDs in FDCs and Diclofenac (11.77%) is the most commonly non-selective NSAID in monotherapy. 97.66% of patients were prescribed gastro protective drugs. Non selective NSAIDs were commonly co-prescribed with gastro protective. Proton pump inhibitors (27%) most frequently co-prescribed with NSAIDs.

Alaa Rostom, Lawrence Goldkind, and Loren Laine. Have performed a study titled 'Non steroidal Anti-inflammatory drugs and hepatic toxicity: A systemic review of randamized controlled trials in Arthritis patients' and it was published in the Clinical Gastroenterology and Hepatology in 2005. The aim of the study is Non-steroidal Anti-inflammatory drugs (NSAIDs) might cause hepatic side effects, but the frequency of these laboratory and clinical side effects is uncertain. The commonly used NSAIDs that we studied, ibuprofen, naproxen, meloxicam, celecoxib, and Valdecoxib were associated with rates of aminotransferase elevations in the range of that seen with placebo. Two of the NSAIDs studied, Diclofenac and Rafecoxib, had higher rates of aminotransferase elevation compared to the placebo and the other NSAIDs studied. None of the medications, including the 2 with higher rates of aminotransferase elevations, were associated with increased rates of liver-related serious clinical events, hospitalization, or deaths.

Ullal SD, Narendranath S, Kamath RK, Kamath SU and Amarnath D have performed a study titled 'Prescribing pattern for Osteoarthritis in a tertiary care hospital' and it was published in journa of clinical and diagnostic research in 2010. They performed the cross-sectionally for six months from an Orthopaedic outpatient unit in a tertiary care hospital. Prescriptions of all 154 patients were analysed, out of which 66(43%) were male and 88(57%) female. 153(99%) patients were affected with Osteoarthritis of the knee alone, either unilateral or bilateral. In one patient along with the knees, the right wrist was also involved. 39 patients were newly diagnosed cases of Osteoarthritis, 115 were old cases. This study has found that in the treatment of Osteoarthritis NSAIDs especially oral Diclofenac is the most preferred drug. Paracetamol SYSADOA and topical NSAIDs are being under-prescribed.

R. Asha Latha, K. Srinivasu, M. Ananda Babu Naik and Jaya Chandra Reddy have conducted a study entitled 'A study of prescribing pattern of non-steroidal anti-inflammatory drugs in Orthopedic outpatient department at a teritarycare hospital and it was published in Journal of Evolution of Medical and Dental sciences in 2015. A prospective, non-interventional cross sectional [observational] study was carried out in orthopedic outpatient department in Govt.General Hospital, Anantapuramu. Data collection was done by taking 100 prescriptions. Prescription included 35% of Non-traumatic musculoskeletal pain, 25% post traumatic pain, 10% Osteoarthritis, 30% post-operative pain, 5% Ankylosing Spondylitis, degenerative diseases of spine. Rheumatoid arthritis 1% Neuralgia. NSAIDs prescribed were Aceclofenac 45%, Etodolac 20%, Diclofenac 24%, and Ibuprofen 11%. Patient information was inadequate in most prescription. Duration of study was short. Hence effect a seasonal variation on NSAID prescription could not be determined. Calcium supplements and multi vitamins were used as nutritional supplements. Methotrexate was used as disease modifying anti-rheumatoid drug [DMARD] in 4 rheumatoid arthritis patients. Glucosamine with diacerein was used in 15 patients in Osteoarthritis the former drug claimed to prevent cartilage erosion and the latter supposed to be cytokine modulator with potential anti-inflammatory action. Further large scale research is required for detailed evoluation of NSAID prescription pattern. Continuing medical education regarding appropriate use of NSAIDS, knowledge of potential adverse effects and standard prescription guidelines will play pivotal role in rational prescription of NSAIDs. It is also essential to encourage and promote generic prescribing to reduce the cost of therapy.

AIM AND OBJECTIVE:

Aim

To study the safety, efficacy and tolerability of Aceclofenac and Diclofenac in osteoarthritis by referring the prescriptions/medication orders, and by using WOMAC and VAS scales in outpatients and inpatients.

Objective

- Assess the safety, efficacy and tolerability of medication by using different scales.
- Compare the different disease management strategies adopted according to the disease relief achieved, adverse effects noticed.

METHODOLOGY:

Study Design:-

Prospective, observational study

Study site:-

It was decided to carry out this study in Sri Anand hospital, Anantapuramu.

Study Criteria:-

- **Inclusion Criteria**
  - Male and female patient who were ≥40 years of age diagnosed with OA.
- **Exclusive Criteria**
  - Patient with other rheumatic disease and out patient's pregnant and lactating women.

Study Duration:-

The study was planned to be conducted in Sri Anand hospital for a period of 6months from January 2016 to June 2016.

Source of Data:-

- Patient Medication Chart.
- Patient profile form.
- Patient and attendant interview.

Study procedure:-

Patient diagnosed with OA were selected randomly and involved in the study after obtaining consent from them. Patient's interview was done to determine disease outcome before and after the treatment. Patient medication details, demographic details, lab investigations, x-ray of joints affected and adverse effects experienced by the patients were collected from the medication charts and from patient/attendant interview. The different disease management strategies adopted were then compared. The scores for different patient reported outcomes were than analyzed using Graphpad Instat 3.

Forms used for study:-

- Demographic detail form
- Scales
  - WOMAC Scale
  - VAS

RESULTS:

Sample:

Age Wise Distrubution:

Data was collected for a total of 115 patients. Out of which 22 patients where from the age group of 35-45 years, 42 patients between the age of 45-55 years, 27 patients in between the age of 55-65 years and 24 patients are >65 years of old. The percentage of a study sample was calculated and mentioned in below table 2.

Table 2: Age wise distribution

S. No	Age (years)	No. of patients	Percentage
1	35-45	22	19.13%
2	45-55	42	36.52%
3	55-65	27	23.47%
4	>65	24	20.86%

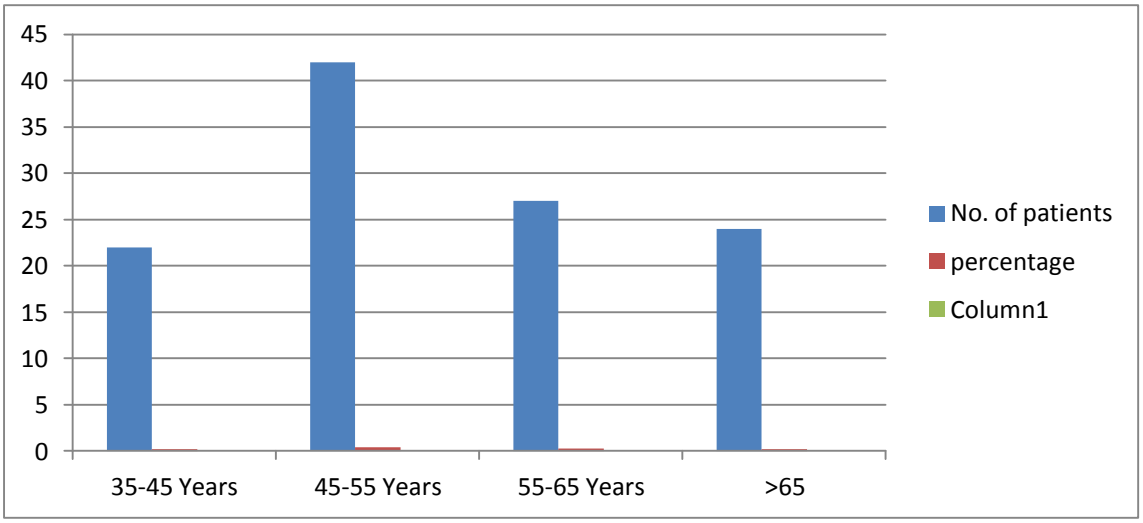

Fig 5: Age wise distribution

Gender Wise Distribution in Patien:
The study sample included 44 male (38.26%) and 71 female (62.60%) patients.

Table 3: Gender wise distribution

S. No	Gender	Frequency	Percentage
1	Male	44	38.26%
2	Female	71	62.60%
	Total	115	100%

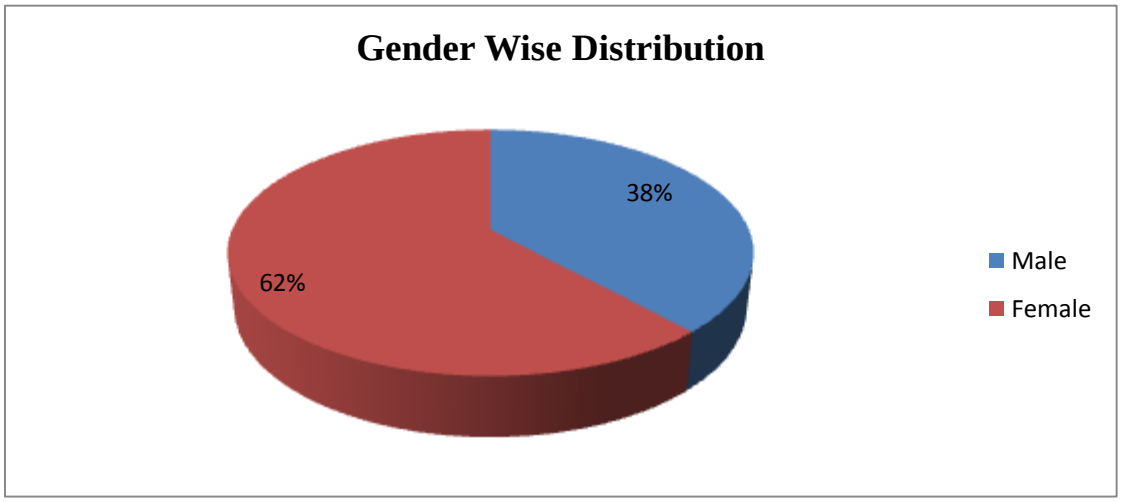

Fig 6 : Gender wise distribution

Demographic data:
Treatment for the patients in the study Aceclofenac (90) and Diclofenac (25) and their distribution had been male and female given in table 4.

Table 4 : Demographic data in the treatment groups [mean ± SD]

S. no	Parameters	Aceclofenac group [n=90]	Diclofenac group [n=25]	Test statistics
1	No. of patients	90	25	----
2	Male: female	36:54	8:17	----
3	Age [Years]	55.65±9.083	48.84±5.34	<0.0001

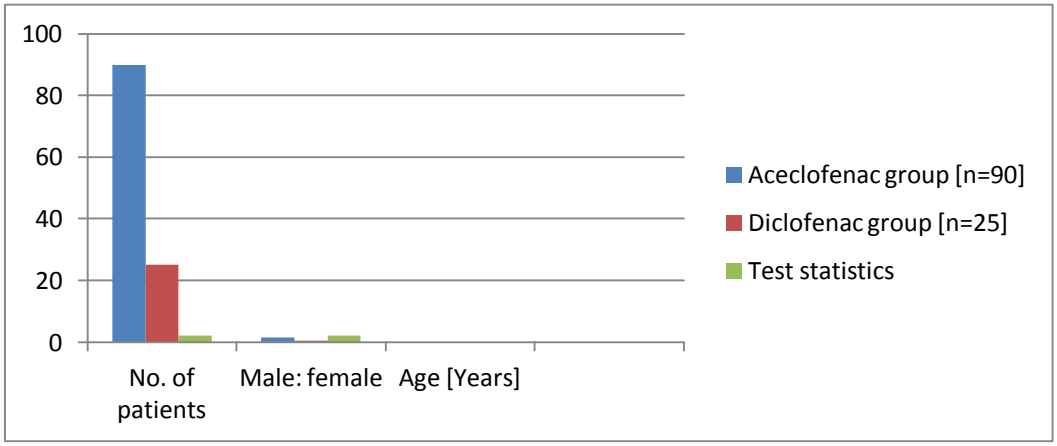

Fig 7: Demographic data in the treatment groups [mean ± SD]

Types of Joints Affected:
During the study period joints had been affected among them male were bilaterally 13 (11.30%), unilaterally 31 (26.95%) and females 29 (25.21%) bilaterally, 42 (36.52%) unilateral.

Table 5: Comparision of joints affected in male and female

S. No	Gender	Bilateral Osteoarthritis (Knee)	Unilateral Osteoarthritis (Knee)	Total
1	Male	13 (11.30%)	31 (26.95%)	44 (38.26%)
2	Female	29 (25.21%)	42 (36.52%)	71 (61.73%)
	Total	42 (36.52%)	73 (63.47%)	115 (100%)

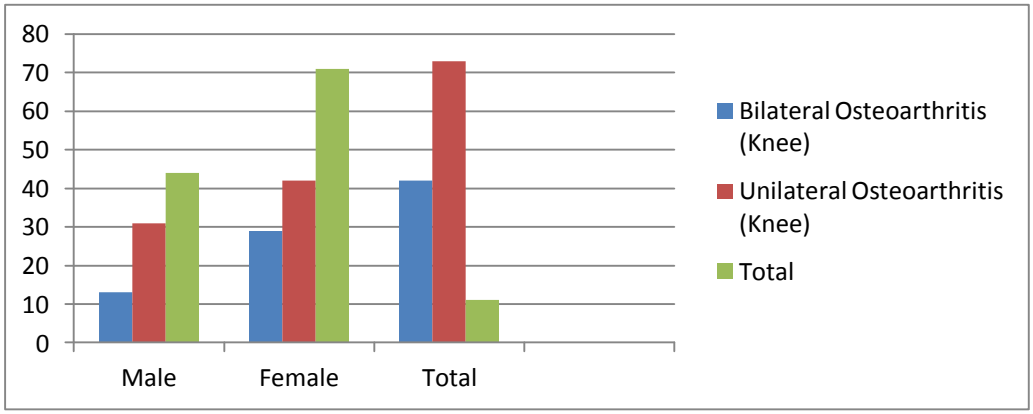

Fig 8: Comparision of joints affected in male and female

Prescription pattern of Aceclofenac, Diclofenac:
Aceclofenac and Diclofenac are prescribed in total patients of male and female as, 36 Aceclofenac and Diclofenac in male and 54 Aceclofenac, 17 Diclofenac in females.

Table 6: Prescription pattern of Aceclofenac, Diclofenac

S. No	Gender	Aceclofenac	Diclofenac	Total
1	**Male**	36	8	44
2	**Female**	54	17	71
	Total	90 (78%)	25 (21%)	115 (100%)

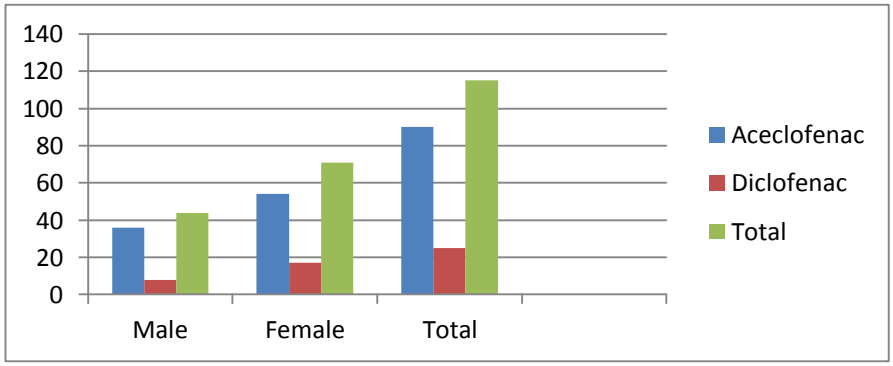

Fig 9: Prescription pattern of Aceclofenac & Diclofenac

Pain Severity:
Pain scores were collected from each patients before and after treatment using WOMAC scale and VAS scales. Pain level were classified as 0= None, 1= Slight, 2= Moderate, 3= very, 4= Extremely for WOMAC, with VAS scale the pain was recorded at a scale of 0-10 with 0 indicating no pain 10 indicating worst possible pain. The pain scores before and after treatment of Aceclofenac and Diclofenac was statistically evaluated using unpaired T-test.

Table 7: WOMAC scores in the two treatment group at baseline and after 1st visit and 2nd visit [mean ± SD]

S. no		Aceclofenac group	Diclofenac group	Unpaired t-test p-valve
1	Baseline	71.54±10.515	72.52±14.58	<0.0001
2	1st visit	52.144±10.787	57.44±15.80	<0.0001
3	2nd visit	35.177±9.210	38.16±15.26	<0.0001

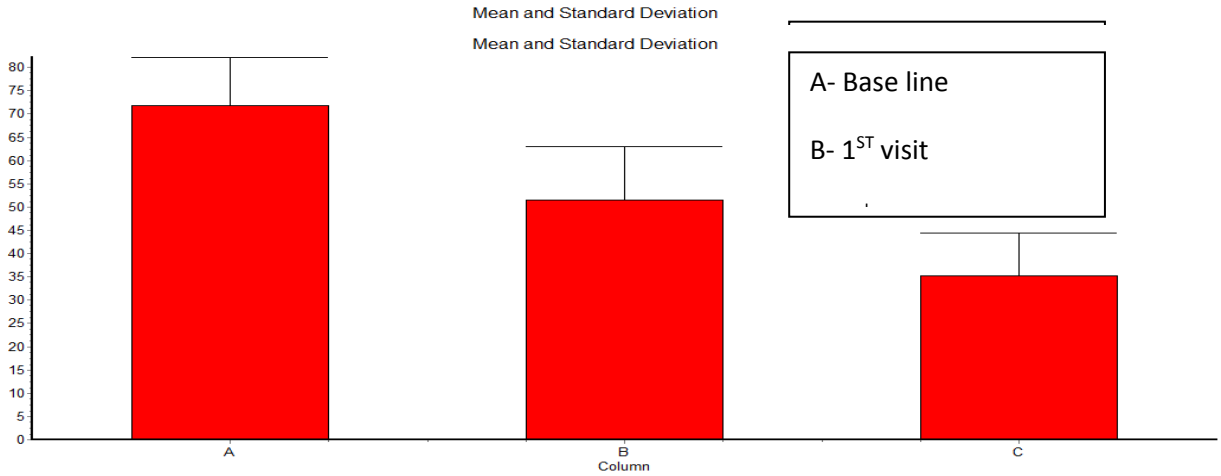

Fig 10: Comparision of mean and SD at baseline, 1st visit, 2nd visit [Diclofenac group]

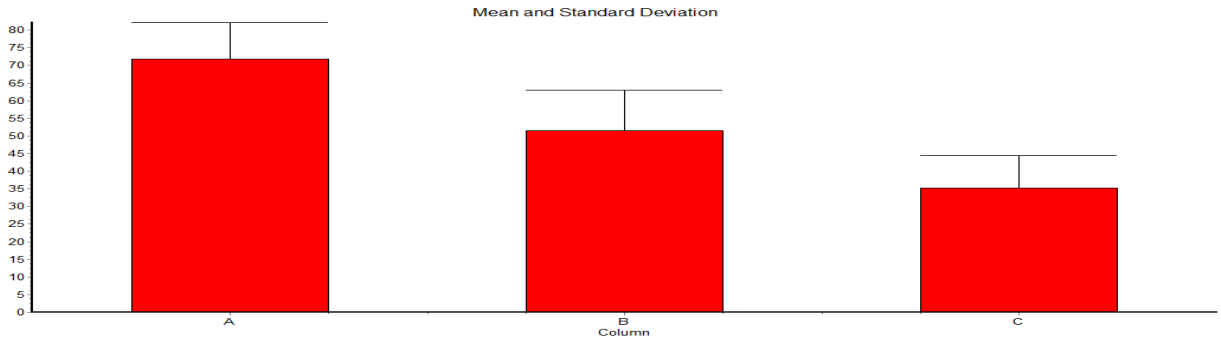

Fig 11: Comparision of mean and SD at baseline, 1st visit, 2nd visit [Aceclofenac group]

Table 8: Visual analogue scale (VAS) score for pain in the two treatment group at baseline, after 1st visit and 2nd visit treatment [mean ± SD]

S. no		Aceclofenac group	Diclofenac group
1	Baseline	4.16 ± 2.483	4.16 ± 2.48
2	1st visit	3.5 ± 2.618	4.16 ± 2.63
3	2nd visit	3.16 ± 2.639	4.16 ± 3.656

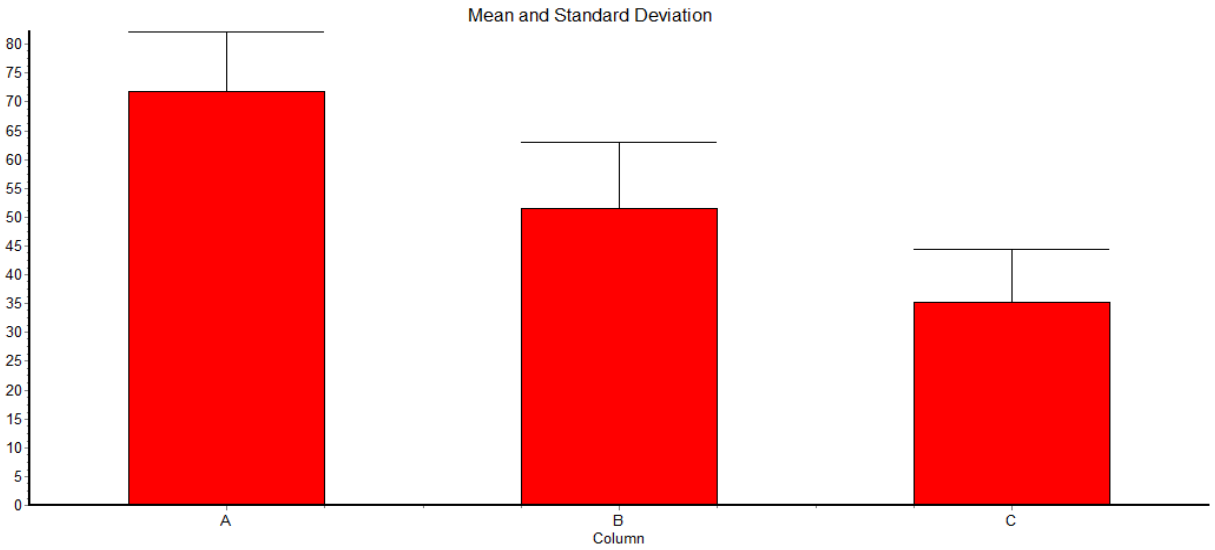

Fig 12: Visual analogue scale (VAS) score for pain in Aceclofenac group

Outcomes:

Outcome was graded as high, moderate and mild for efficacy and as good, moderate and poor for tolerability in two treatment groups.

Table 9: Outcome of therapy as assessed by physician in the two treatment group after 2nd visit of treatment.

		Aceclofenac n [%]	Diclofenac n [%]
Efficacy	**High**	49 (54%)	9 (36%)
	Moderate	36 (40%)	11 (44%)
	Mild	5 (5%)	5 (20%)
Tolerability	**Good**	51 (56%)	7 (28%)
	Moderate	37 (41%)	8 (32%)
	Poor	2 (2%)	9 (36%)

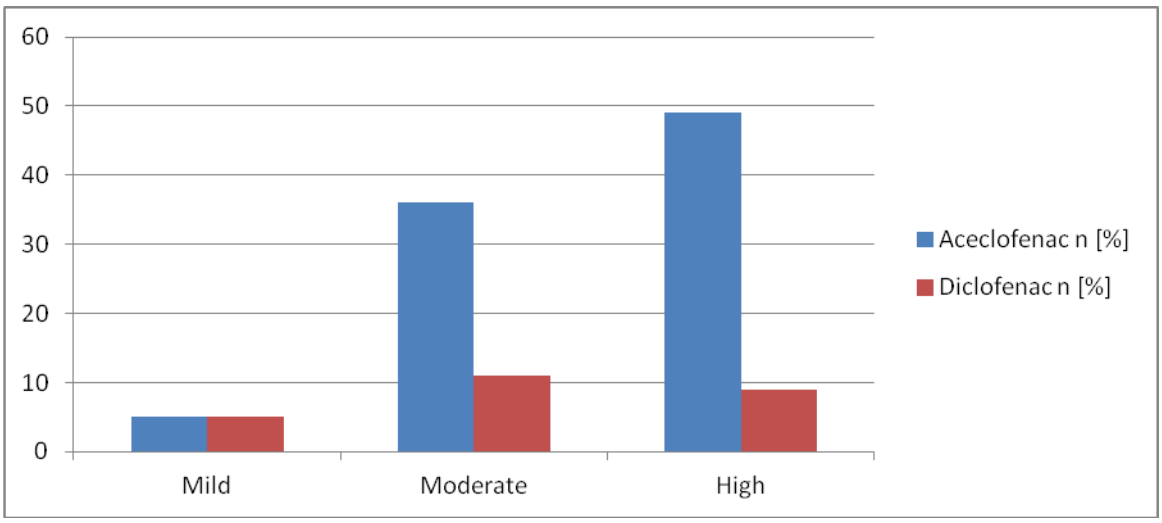

Fig 13: Comparision of efficacy in Aceclofenac and Diclofenac

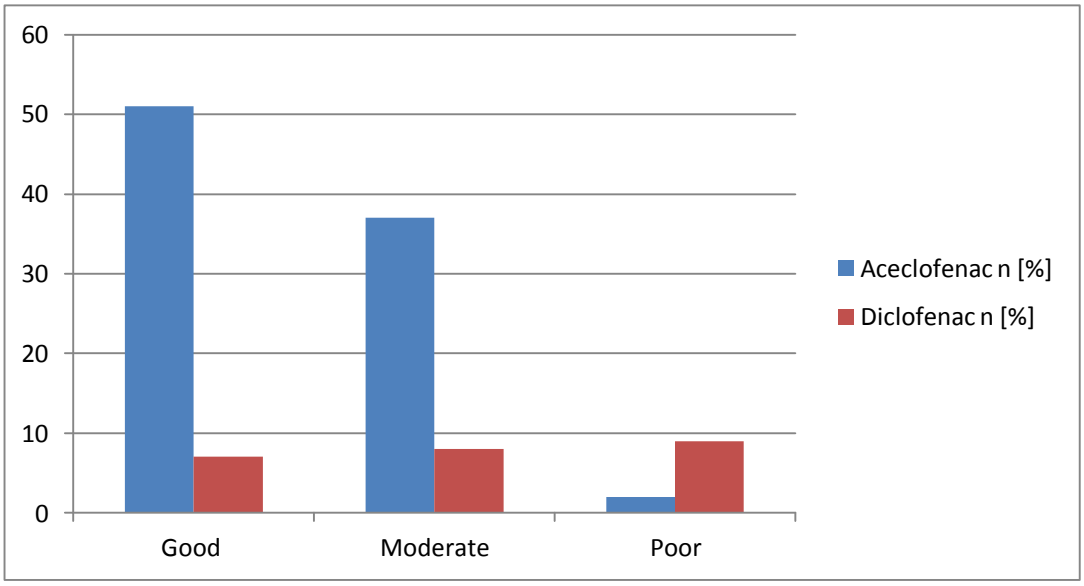

Fig 14: Comparision of Tolerability in Aceclofenac and Diclofenac

Adverse Effect:

Common adverse effects for Aceclofenac and Diclofenac includes Vomiting, Epigastric pain, GI bleeding, Flatulence, Constipation, Abdominal pain, Headache, GI ulcers. Out of which patients in the two treatment groups experienced epigastric pain, flatulence, abdominal pain, constipation which was presented in the table 10.

Table 10: Adverse effects observed in the Aceclofenac group and Diclofenac group

S. no	Adverse effects	Aceclofenac adverse effect patients	Diclofenac adverse effect patients
1	Epigastric pain	6	5
2	Flatulence	3	2
3	Abdominal pain	4	3
4	Constipation	2	1

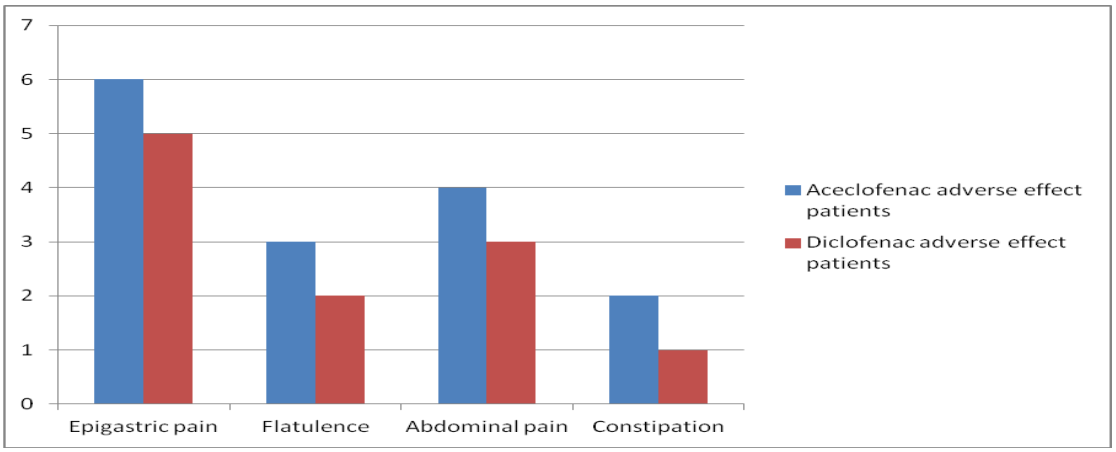

Fig 15: Adverse effect observed in Aceclofenac group and Diclofenac group

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 recognize the difference between commonly used drugs-Aceclofenac and Diclofenac. Until recently the new COX-2 selective inhibitors have been increasingly used. They have equal efficacy to standard NSAIDs. However the cardiovascular safety of these drugs was found to be controversial.

Aceclofenac has been evaluated in international studies and is indicated for the relief of pain and inflammation associated with Osteoarthritis, Rheumatoid arthritis, Ankylosing Spondylitis. This study not only evaluates its efficacy and tolerability in patients but also compare it with Diclofenac which is of the widely used drug for chronic pain.

In one study improvement was seen in VAS and WOMAC osteoarthritis index with both drugs. But the improvement with Aceclofenac was found to be better in comparision to Diclofenac.

In a study Aceclofenac is superior to Diclofenac in decreasing joint tenderness scores similar to previous studies by Pareek A et al 2006 and Ward DE et al 1995.

Aceclofenac was better than Diclofenac in improving the disease and investigator response to therapy, which is supported by previous studies done by Ward DE et al 1995.

The anti-inflammatory effects of Aceclofenac have been shown due to inhibition of various mediators like IL-1B, IL-6 and tumor necrosis factor in human osteoarthritic synovial cells and human articular chondrocytes, inhibition of PGE_2 via cyclooxygenase inhibition after intracellular metabolism.

The overall incidence of adverse effects in our study was 6% in Aceclofenac and 20% in Diclofenac group. Aceclofenac was well tolerated than Diclofenac in terms of epigastric pain, flatulence, abdominal pain and constipation.

CONCLUSION:

Analysis of results of all the parameters of safety and efficacy explores the probable superiority of Aceclofenac over Diclofenac in osteoarthritis.

Long term NSAIDs treatment is indicated for osteoarthritis, the ideal agent should have good efficacy and low propensity to cause adverse effect.

Our results concluded that Aceclofenac has anti-inflammatory and analgesic properties similar to those of Diclofenac, and gastrointestinal damage is less than that of Diclofenac. This might be due to preferential inhibition of COX-2. This study shows that Aceclofenac is safe, effective and well tolerated drug in osteoarthritic patients.

REFERENCES:

1.Anand R, Kanaki, Rajesh S, Patil, Jeevangi Santosh Kumar, Ravi D, and mala. Comparative study of Safety, Efficacy, and Tolerability of Aceclofenac verses Diclofenac in Osteoarthritis Patient's. Journal of Evolution of medical and Dental science, 2013; vol 2: page-2432.

2.Richa Garg, Shafiqa Aslam, Anil Garg and Rani Walia. A prospective comparative study of serratiopeptidase and Aceclofenac in upper and lower limb soft tissue Trauma cases. International Journal of Pharmacology and Pharmaceutical Technology, 2012; vol-1.

3.Patil Pramod Reddy, Jaida Jyothirmai, Palani Anuradha, B Anandam and Rao Kateshwar. A comparative study of efficacy and safety of Diclofenac and Aceclofenac in the treatment of Osteoarthritis patients. Journal of delivary and therapeutics, 2012; 2(4): 139-143.

4.Shelgel A, Sehgal VK, and Singh R. Comparison of efficacy and tolerability of Aceclofenac and Diclofenac in Osteoarthritis of knee joint. 2015; 4(2).

5.Dr. Malik Muhammad Yasin Awan, Dr. Ijaz Ahmad, Prof. Dr. Amer Aziz. Efficacy and safety of Aceclofenac in the treatment: A randomized double-blind comparative clinical trial verses Diclofenac. Professional Medical Journal, 2014; 21(3): 471-476.

6.Faizal Vohra and Asawari Raut. Comparative efficacy, safety and tolerability of Diclofenac and Aceclofenac in musculoskeletal pain management: A systemic review. Indian Journal of pain, 2016.

7.Sung-Hun Lee, Chang-Dong Han, KK-Hwan Yang, and Chul-Won Ha. Prescription pattern of NSAIDs and the patients in clinical practice in Korea. Korean Academy of Medical sciences, 2011; 26: 561-567.

8.K. P. Patnaik, P. Das, S. Hota, B. N. Mohapatra, S. Mohapatra, S. Nayak and S. Panigrahi. Comparative safety and cost effective analysis between Aceclofenac, Lornaxicam and Diclofenac in patients of musculoskeletal disorder. International Journal of Pharmaceutical sciences and research, 2012; vol-3.

9.Kudaravalli Jyothsna and Narayan Deshpande. Efficacy and safety of Diclofenac sodium and Aceclofenac in controlling post extraction Dental pain: A randomized open Label comparative study. Journal of Pharmacology and Toxicology, 2011.

10.Pravin Kumar INGLE, Prakash H patil, and Vibhavari Lathi. Study of rational prescribing and dispening of prescriptions with non-steroid anti-inflammatory drugs in orthopedic outpatient department. Asian journal of pharmaceutical and clinical research, 2015; vol-8.

11.E. Batlle-Gualda, J. Roman Ivorra and so on. Aceclofenac vs Paracetamol in the Management of symptomatic Osteoarthritis of the knee: a double-

blind 6-week randomized controlled trial. Osteoarthritis and cartilage, 2007; 15(8).
12.Shankar PR, Pai R, Dubey AK, and Upadhyay DK. Prescribing Patterns in the Orthopedics outpatient department in a teaching hospital in Pokhara, Western Nepal. Kathmandu University Medical Journal, 2007; vol-5: 16-21.
13.Taruma Sharma, S. Putta, and D. C. Dhasmama. Prescribing pattern of NSAIDs in Orthopedic OPD of a Tertiary care teaching Hospital in Uttaranchal. Journal of medical education and research, 2006; vol-3.
14.Mohamed Ahmed, Nahid Ali, Zia ur Rahman and Md. Misbahullah khan. A study on prescribing pattern in the management of arthritis in the department of orthopedics. Journal of Der pharmacia Lettre, 2012; 4(1): 5-27.
15.Singh V, Yadav P and Deolekar P. Current trends of prescribing patterns of NSAIDs in an Orthopaedic OPD in a teaching hospital. International journal of Pharma and Bio sciences, 2014; 5(2): 486-491.
16.ALAA Rostom, Lawrence Goldkind, and Loren Laine. Non-steroidal anti-inflammatory drugs and hepatic toxicity: A systemic review of randamized controlled trials in arthritis patients. Clinical gastroenterology and hepatology, 2005; 3: 489-498.
17.Ullal SD, Narendra Nath, Kamath RK, Pai MRSM, Kamath SU, Savur Amarnath D. Prescribing pattern for Osteoarthritis in a tertiary care hospital. Journal of clinical and diagnostic research, 2010; (4): 2421-2426.
18.R. Asha Latha, K. Srinivasu, M. Ananda Babu Naik, Jaya Chandra Reddy. A study of prescribing pattern of non-steroidal anti-inflammatory drugs in orthopedic outpatient department at a tertiary care hospital, 2012; vol-4: 559-564.
19.M. S. Radha and M. R. Gangadhar. Prevalence of knee Osteoarthritis patients in Mysore city Karnataka. 2015; vol-6: 3316-3320.
20.Dr. Abhijit Khan Vilkar, MS. Aruna Deshpande, Dr. Aditi Agashe, Dr. Amal Mamkar, Dr. Dhanamjay Pathak. Study to find the prevalence of knee Osteoarthritis in the Indian population and factors associated with it. 2013.
21.Johanne Martel-Pelletier and Jean-Pierre Pelletier. Epidemology of Osteoarthritis. 2011; 1-26.
22.Davidson's principles and practice of medicine, 21st edition. Musculoskeletal disease by M. Doherty, S. H. Ralston, 2010.
23.Apurv Mehra. Orthopedics quick review, 2nd edition, 2013.
24.Sinusas k. Osteoarthritis diagnosis and treatment. Am Fam physician. 2012; 85(1): 49-56.
25.Harsha Mohan. Text book of pathology; 6th edition, 2010.
26.Australian Government, Department of health therapeutic goods administration, 2014; version 2-1.