



PAIN MANAGEMENT

WHAT IS PAIN ?

- Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage.
- Pain is a vital function of the nervous system in providing the body with a warning of potential or actual injury.
- Pain is a sensation transmitted from sensory nerves through the spinal cord to the sensory area of the cerebrum, where the sensation is perceived.

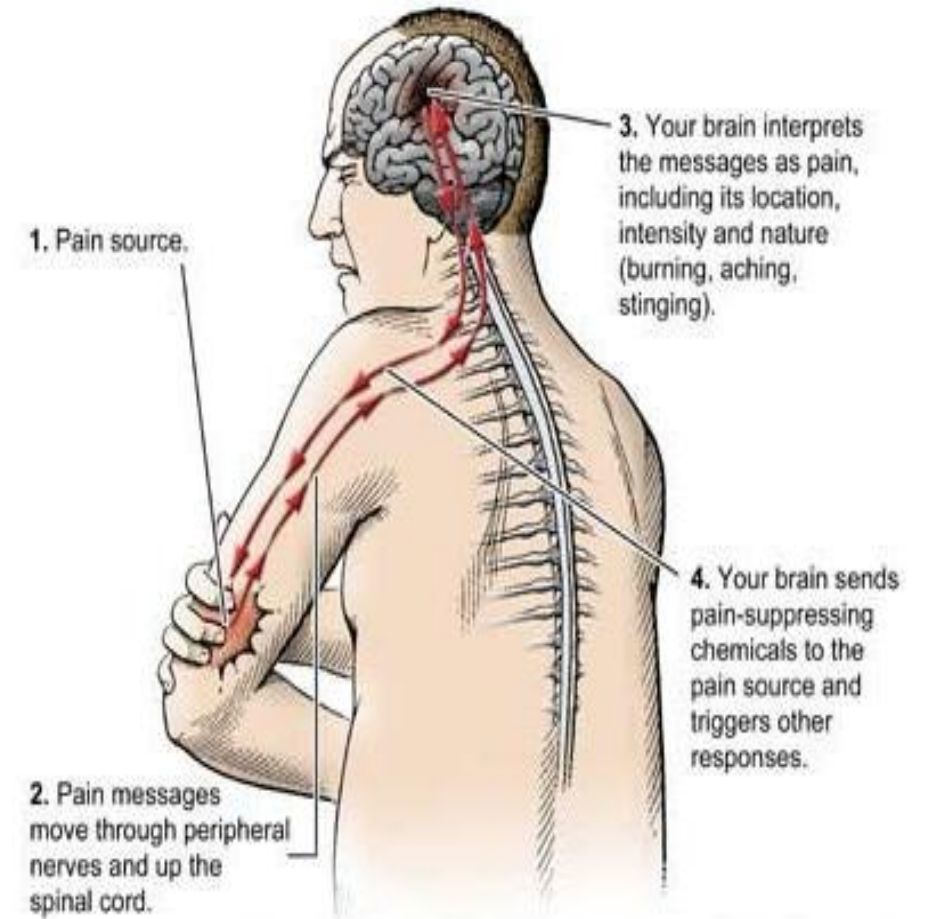


WHY IS PAIN AN IMPORTANT SYMPTOM?

- ✓ Pain is the most common symptom for which patients seek medical attention.
- ✓ Pain is a critical component of the body's ability to react to the damage.
- ✓ Pain is a rapid-warning relay, instructing the organs and principally the central nervous system to initiate reactions to minimize injury

PAIN MECHANISM AND TRANSMISSION

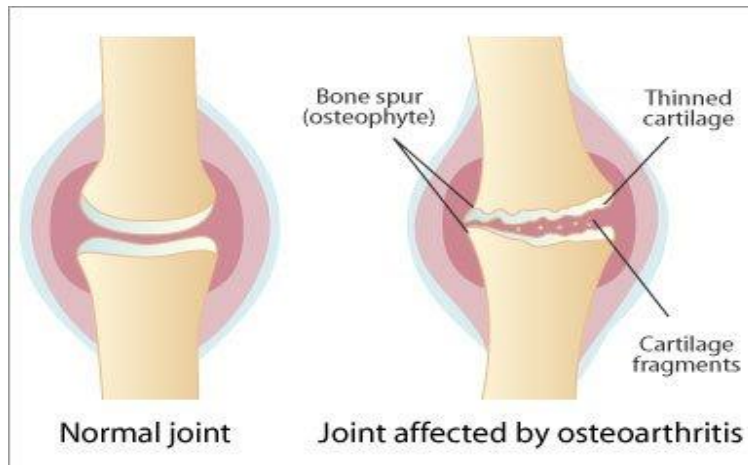
- Pain results from stimulation of peripheral receptors, which transmits impulses through pain pathways to the brain.
- Inflammatory mediators like prostaglandin's, leukotrienes, histamines etc produced in response to tissue damage produce peripheral sensitization so that receptors respond and perceive- -the pain.



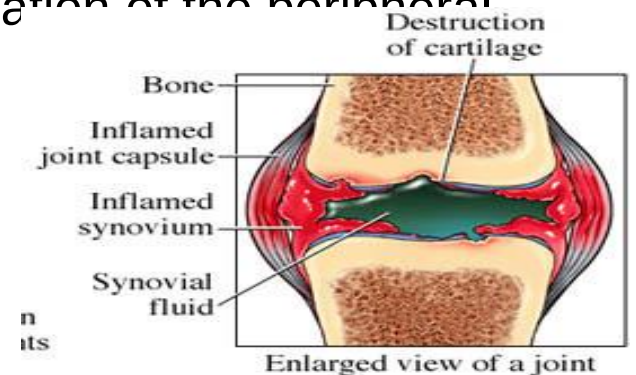
ARTHRITIS

Arthritis is an inflammation of a joint usually characterized by swelling, pain, and restriction of motion

Osteoarthritis is a degenerative joint disease characterized by pain and/or limitation of movement to the affected joints.



Rheumatoid Arthritis, an autoimmune disease of unknown etiology affects approximately 1% of the adult population. It is characterized by non-specific, usually symmetric inflammation of the peripheral joints.



MUSCULAR SPASM

- ✓ Muscular spasm occurs due to excessive muscular activity, which causes fatigue and damage to the muscles.
- ✓ The muscles are not able to relax properly and they remain in the state of contraction.
- ✓ A back spasm is the involuntary contraction or tensing of the muscles in the back.
- ✓ Heavy lifting is a common cause of back spasms.
- ✓ A ruptured or bulging disk in the vertebrae may also pressure a nerve, which can result in back pain.



TREATING LOWER BACK SPASMS

PHARMACOLOGICAL THERAPY

- Nonsteroidal anti-inflammatory drugs (NSAID)
- Muscle relaxants
- Injections of an anti-inflammatory medication (cortisone)



LOW BACK PAIN



- Low back pain (LBP) is a common disorder involving the muscles, nerves, and bones of the back.
- Low back pain may be classified by duration as acute (pain lasting less than 6 weeks), sub-chronic (6 to 12 weeks), or chronic (more than 12 weeks).
- Approximately 9 to 12% of people (632 million) have LBP at any given point in time, and nearly 25% report having it at some point over any one-month period.
- Difficulty most often begins between 20 and 40 years of age.

LOW BACK PAIN



- Men and women are equally affected.
- Muscle spasm-a typical feature of LBP.
- Low back pain may be the result of spinal diseases such as arachnoiditis, degenerative disc disease, epidural fibrosis, failed back surgery syndrome, lumbar disc herniation, osteoporosis and spinal stenosis.
- Back pain is often located in the lower back, but may extend to the thighs, calves, and even feet.

LOW BACK PAIN

- Affected areas may feel tender or sore to the touch, and the pain may increase with movement.
- This type of pain can be felt as a sharp pain, a burning sensation, or a dull muscular ache and can range from mildly uncomfortable to completely disabling.

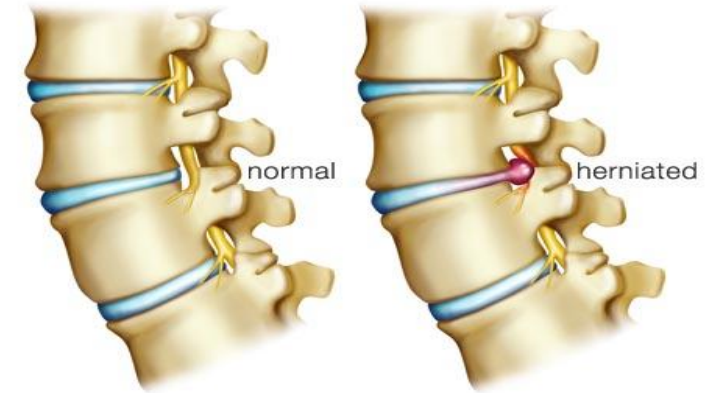
LOW BACK PAIN

CAUSES

- Obesity
- weight gain during pregnancy
- Stress
- Poor physical condition, poor posture and poor sleeping position.
- Physical causes like osteoarthritis, degeneration of the discs between the vertebrae or a spinal disc herniation

SYMPTOMS

- Dull aching pain
- Sharp pain
- Tingling or burning sensation
- Weakness in your legs or feet



A herniated disc as seen on MRI, one possible cause of low back pain

PREVENTION

NON PHARMACOLOGICAL THERAPY

- Exercise appears to be useful for preventing low back pain.
- Medium-firm mattresses are more beneficial for chronic pain than firm mattresses.
- Heat and/or cold therapy helps relieve most types of low back pain by reducing inflammation.

PHARMACOLOGICAL THERAPY

A wide variety of medications is available to help reduce lower back pain.

1. Opioid: e.g. Morphine, Pethidine, Dextropropoxyphene, Tramadol etc.

The Opioid group of drugs do not inhibit the prostaglandin formation. Hence, they are analgesics and do not have any anti-inflammatory activity.

These medications may have negative interactions with other drugs, and have a greater side effects, including dizziness, nausea, and constipation.

2. Corticosteroids :These drugs block the enzyme phospholipase and block the production of Arachidonic Acid.

These drugs may be considered for those with persistent sciatic pain.

PHARMACOLOGICAL THERAPY

3. **NSAIDs**: Inhibition of prostaglandin synthesis by cyclooxygenase is the principal mode of the analgesic and anti-inflammatory actions of NSAIDs.

NSAIDs are widely used to treat people with low back pain, especially people with acute back pain.

NSAIDS

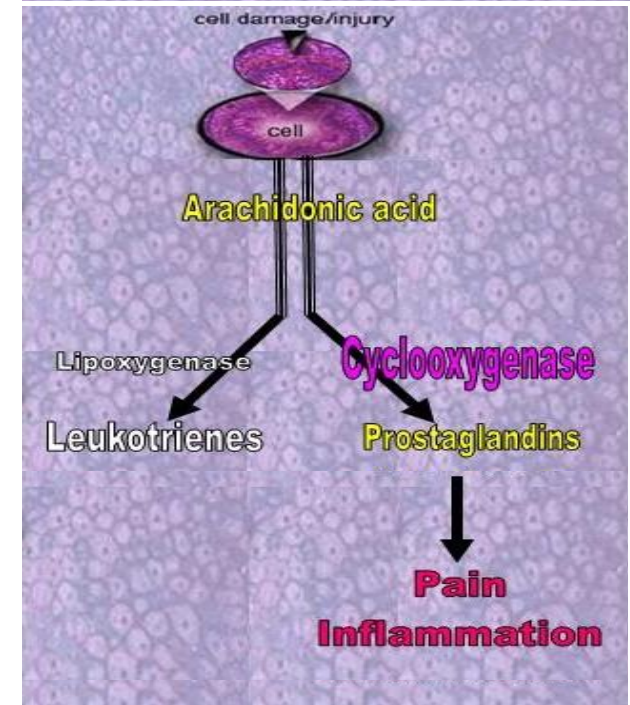
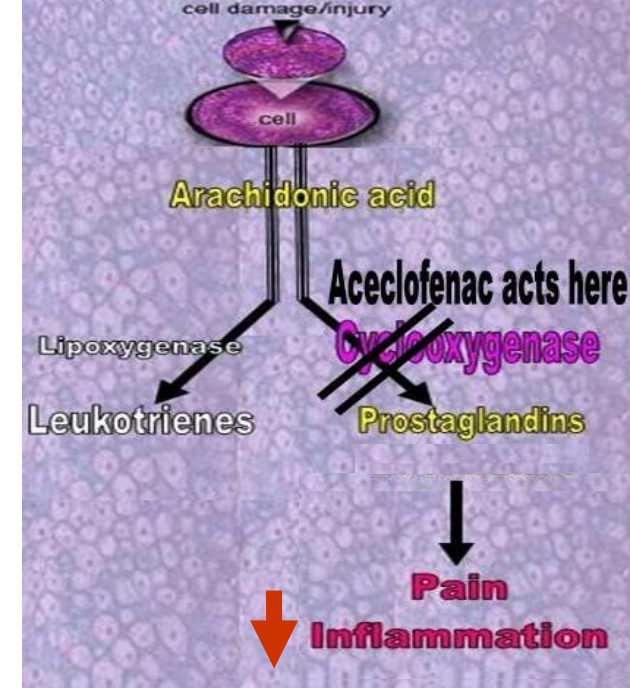
- Most commonly prescribed drugs
- Act as analgesics and anti-inflammatory agents
- Guidelines say “Use lowest effective dose or intermittent dosing if symptoms are intermittent, then try full doses if patient’s response is insufficient”.

ACECLOFENAC : A NOVEL NSAID

1. Aceclofenac is a non-steroidal anti-inflammatory drug
2. Acts specifically on inflammatory sites and thereby decreases the inflammation.
3. It is highly effective as an anti-inflammatory drug for various inflammatory conditions.

MECHANISM_OF ACTION

- Aceclofenac -Inhibits PGE-2 production
- Aceclofenac is also a NSAID with greater COX-2 specificity when compared to Diclofenac sodium.
- Aceclofenac inhibits cyclooxygenase (COX) activity
- Thereby suppress PGE-2 production



ACECLOFENAC -INHIBITS IL-1BETA AND TNF

- At site of inflammation, IL-1 β and TNF released
- IL-1 β & TNF produce PGE-2
- Aceclofenac inhibits IL-1 β and TNF
- Thereby it blocks PGE-2 secretion at the site of inflammation

Aceclofenac



Inhibition of IL-1 β & TNF



Inhibition of PGE2 by blocking COX



**Anti-inflammatory
action**

SUMMARY OF THE MECHANISM

Mechanism	Resultant effect
Inhibits PGE-2 secretion	↓ Inflammation
Inhibits interleukins and TNF	↓ Inflammation
Inhibits neutrophil adhesion & motility	↓ Inflammation
Inhibits IL-1 β & stimulates Glycosaminoglycan (GAG) synthesis Inhibits metalloproteinase production	Maintenance of cartilage matrix.

ACECLOFENAC VS DICLOFENAC

- Aceclofenac statistically superior to diclofenac in efficacy parameters in osteoarthritis patients
- Aceclofenac statistically superior to diclofenac in terms of epigastric discomfort, dyspepsia and abdominal pain.
- Compliance better with aceclofenac

PHARMACOKINETICS

- Bioavailability is almost 100%.
- Peak plasma concentrations are reached approximately 1.25 to 3 hours
- Half Life is 4 to 4.5 hrs
- Protein-bound (>99.7%).
- Aceclofenac penetrates into the synovial fluid, where the concentrations reach approximately 60% of those in plasma.
- Approximately two-thirds of the administered dose is excreted via the urine, mainly as conjugated hydroxymetabolites. Only 1% of an oral single dose is excreted unchanged.
- T_{max} is 1.25- 3 hrs

DOSAGE

Maximum recommended dose is 200 mg daily, taken as two separate 100 mg doses, one tablet in the morning and one in the evening.

Elderly

- Generally no dose reduction necessary.

Children

- Safety & Efficacy not established.
- Hepatic insufficiency
- Mild to moderate - 100 mg daily.



INDICATIONS

- In conditions associated with Pain and Inflammation
- Aceclofenac is primarily indicated in conditions like Ankylosing spondylitis, Osteoarthritis, Rheumatoid arthritis.

SIDE EFFECTS

- Diarrhoea
- Nausea
- Dyspepsia
- Abdominal pain
- Dizziness
- Rashes
- Blood dyscrasias are rare

SALIENT FEATURES

- Aceclofenac is a NSAID that is effective in the treatment of painful and inflammatory conditions.
- Aceclofenac is associated with significantly fewer adverse events compared with other NSAIDs.
- Effective in the treatment of both chronic and acute inflammatory and degenerative diseases compared with other NSAID therapies.
- Therefore, Aceclofenac is the treatment of choice for patients and physicians in the management of inflammatory pain.

THIOCOLCHICOSIDE

Thiocolchicoside is a muscle relaxant with anti-inflammatory and analgesic actions.

MECHANISM OF ACTION

➤ It has an affinity for the inhibitory glycine and gamma- amino butyric acid (GABA) -A receptors i.e., have glycomimetic and gaba mimetic activity, therefore shows muscle relaxant action.

➤ The GABAA receptor (GABAAR) is an ionotropic receptor and ligand-gated ion channel. Thiocolchicoside binds to the GABAAR and activates it, leading to an increase in chloride current.

➤ Glycine Receptors (GlycR) are also ionotropic receptors and ligand-gated ion channels. Thiocolchicoside binds to the GlycR and activates it, leading to an increase in chloride current.

Plays a major role of neurotransmission in the spinal cord and peripheral nervous system. It is free from sedation effects possible due to non-interference with nicotinic receptors.

PHARMACOKINETICS

- Peak plasma concentration: 17 ng/ml
- Elimination $t_{1/2}$ - 5-6 h.
- T_{max} = 0.4 h
- Absorption: Rapidly absorbed
- Half life: 1.5h
- Terminal half-lives ranged from 2.4 to 2.7 h in plasma and from 3.2 to 3.7 h in urine.
- Distribution - estimated around 42.7 L.

DOSAGE

- Oral : Adult: - 4mg bid can be increased maximum upto 16 mg/day.

INDICATION

- Pain associated with spasm

SIDE EFFECTS

- Includes nausea, allergy and vasovagal reactions

FIXED DOSE COMBINATION OF ACECLOFENAC & THIOCOLCHICOSIDE

COMPOSITION:



ACECLOFENAC : 100MG

THIOCOLCHICOSIDE : 4/8MG

FIXED DOSE COMBINATION OF ACECLOFENAC AND THIOCOLCHICOSIDE

- Aceclofenac has an excellent efficacy as it easily penetrates into inflammatory tissues of joints and the like, and thus exhibits an excellent action of inhibiting prostaglandin production, as compared to other anti-inflammatory analgesic drugs.
- Thiocolchicoside is a muscle relaxant, anti-inflammatory and analgesic, used for the treatment of orthopedic, traumatic and rheumatologic disorders.

RATIONALE OF COMBINATION

- Aceclofenac inhibits cyclooxygenase (COX) activity and suppresses the PGE2 production .
- Thiocolchicoside modulates chemokine and prostanoid production and inhibits neutrophil and endothelial cell adhesion molecules.
- Aceclofenac has analgesic and anti-inflammatory properties.
- Thiocolchicoside produces muscle relaxation.
- Hence, combination of aceclofenac and thiocolchicoside can be considered in patients having pain, inflammation, spasm and low back pain.

INDICATION

- Pain associated with inflammation and spasms
- Ankylosing spondylitis,
- Torticollitis

DOSAGE

- One tablet twice daily after food for 5-7days.

ADVERSE EFFECTS

- The most common adverse effects were somnolence, fatigue, dry mouth, pharyngitis.

CONTRAINDI CATIONS

- Hypersensitivity to Thiocolchicoside or Aceclofenac or any component of the tablet.
- Severe heart failure or severely impaired hepatic or renal organ function and during the last three months of pregnancy.

CLINICAL STUDIES

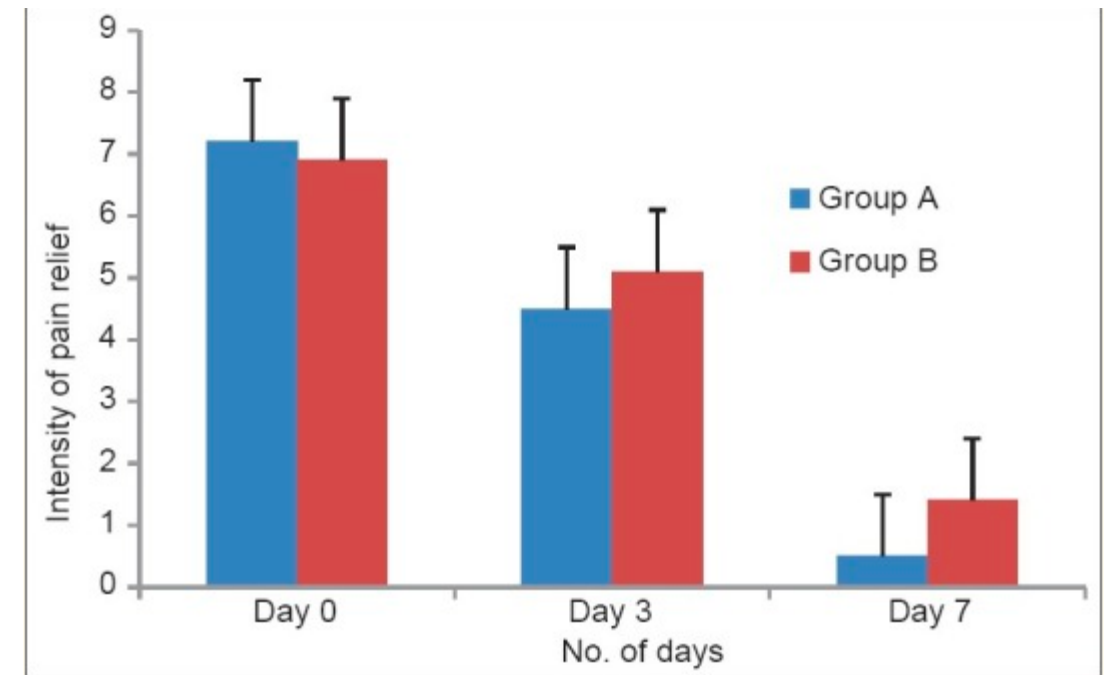
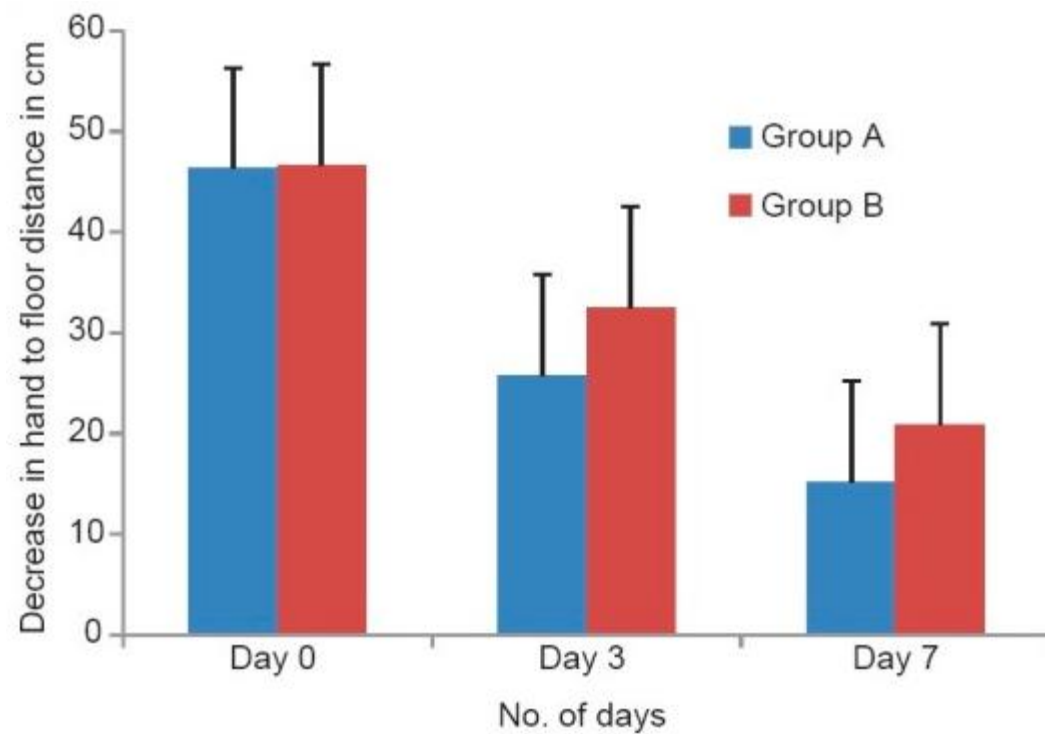
FIXED DOSE COMBINATION OF THIOCOLCHICOSIDE AND ACECLOFENAC VERSUS CHLORZOXAZONE, ACECLOFENAC AND PARACETAMOL IN PATIENTS WITH ACUTE LOWER BACKACHE ASSOCIATED WITH MUSCLE SPASM

Methods:

- 100 patients between ages range from 18 and 55 years having low back pain of ≤ 7 days duration were randomly divided into two groups.
- Group A was prescribed thiocolchicoside (4 mg) + aceclofenac (100 mg)
- Group B was prescribed chlorzoxazone (500 mg) + aceclofenac (100 mg) + paracetamol (325 mg) orally twice daily for 7 days.

Outcome:

- There was statistically significant reduction in severity of pain and muscle spasm on day 3 and day 7 in both groups.
- There was no statistically significant difference in pain relief and muscle spasm among the treatment groups but clinically showed better improvement in the Group A.
- The adverse drug reactions occurring during study showed a statistically significant better safety profile in the Group A than Group B



Pain intensity	Baseline (%)	Day 3 (%)	P	Day 7 (%)	P
Group A	8.5 (100)	6.1 (71.7)	0.001	1.3 (15.2)	0.001
Group B	8.9 (100)	6.2 (77.3)	0.001	2.7 (30.7)	0.001

Pain was evaluated by means of 10-cm VAS; VAS: Visual analogue scale

These findings confirm that FDC of thiocolchicoside and aceclofenac is a preferred option for patients with lower backache pain associated with muscle spasm.

EFFICACY AND SAFETY OF ACECLOFENAC IN OSTEOARTHRITIS: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

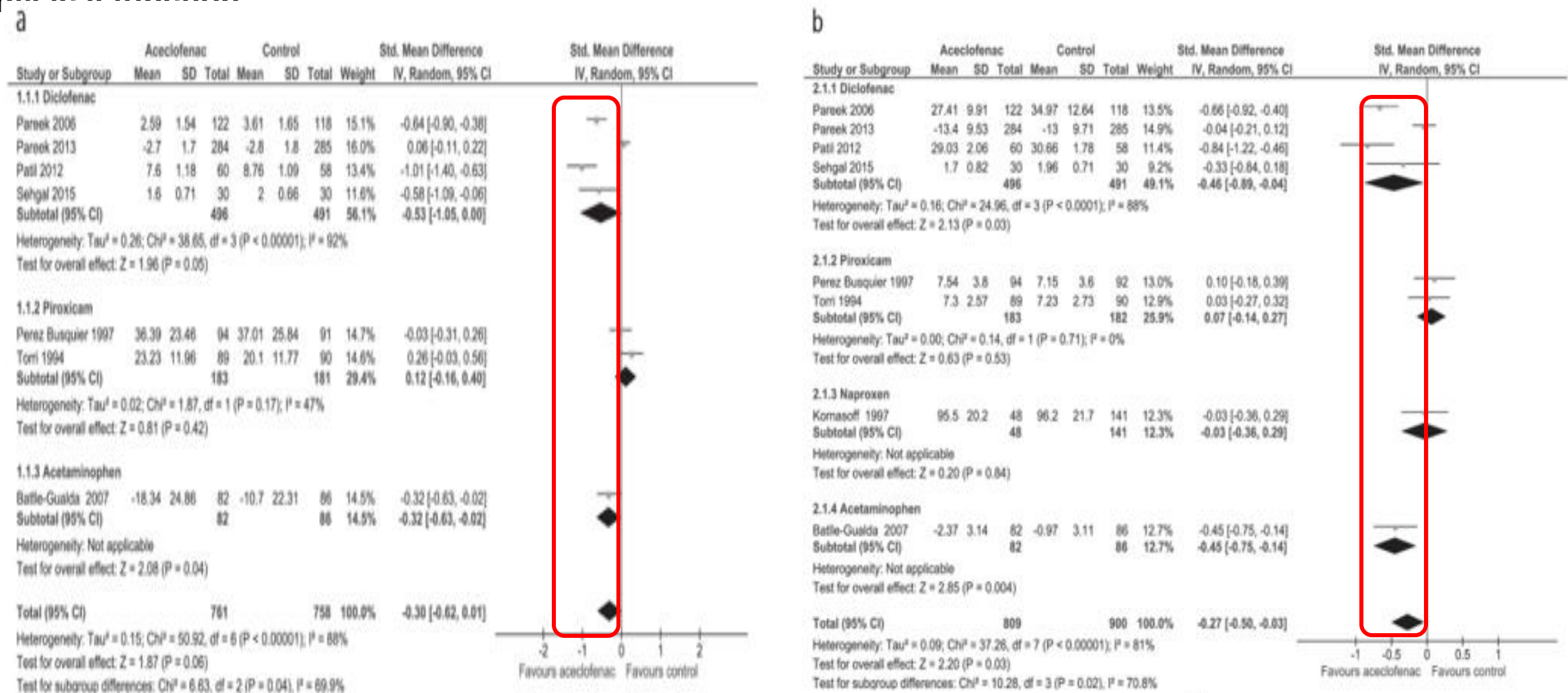
Methods:

- Randomized controlled trials evaluating efficacy and/or safety of aceclofenac compared with control interventions (NSAIDs or acetaminophen) in patients with osteoarthritis.

Outcome:

- Aceclofenac was more beneficial than control interventions in improving physical function.
- Less gastrointestinal adverse events for aceclofenac than in control interventions
- No difference in overall adverse events occurrence and dropout rate between aceclofenac and control interventions.

Forest plot of the comparison between aceclofenac and control for the efficacy outcome a) pain scale b) physical function



Favouring Aceclofenac

ACECLOFENAC AND THIOCOLCHICOSIDE AGAINST ACECLOFENAC ALONE IN LOW BACK PAIN

Methods:

- Patients with acute low back pain receiving either aceclofenac 100 mg or a combination of aceclofenac 100 mg and thiocolchicoside 4 mg twice daily were enrolled in the study and were divided into two groups of 50 each.
- The primary efficacy parameter was pain intensity measured on a visual analogue scale.

Outcome:

- There was a reduction in pain intensity in both the groups and the reduction was more significant in the combination group ($p < 0.001$). Adverse effects reported in both the groups were found to be comparable

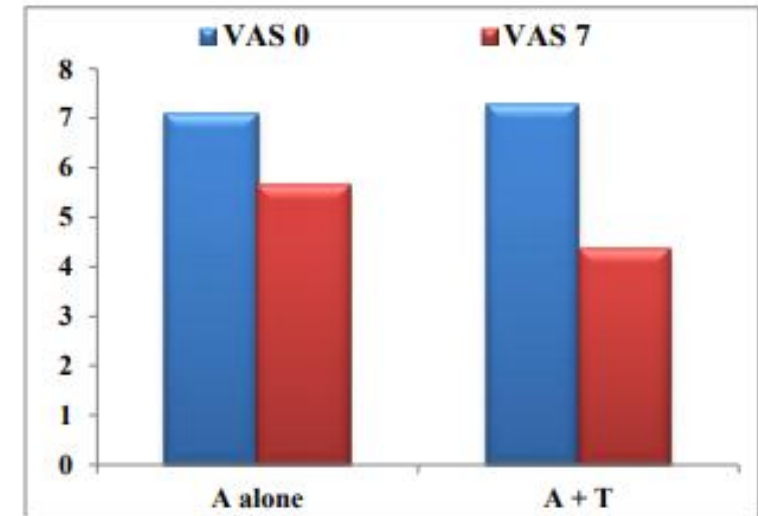


Figure 1: Comparison of baseline and final vas score in the study groups.

THIOCOLCHICOSIDE AND ACECLOFENAC SUSTAINED-RELEASE COMBINATION THERAPY IN MUSCULOSKELETAL INFLAMMATORY PAIN

Methods:

- 442 patients fixed-dose combination of aceclofenac (200 mg) and thicolchicoside (8 mg)-sustained-release capsules was orally administered once daily for 2 weeks..

Outcome:

- The treatment led to significant pain reduction from the baseline noted with visual analog score at the 1st week itself.
- After 2 weeks of treatment, the mean pain score declined by 90%, joint tenderness improved in 90% of the patients, and the mean joint mobility scores were near normal in most of the patients.
- Furthermore, at the end of the treatment, nearly all of the patients were symptom free.
- No serious adverse events were reported

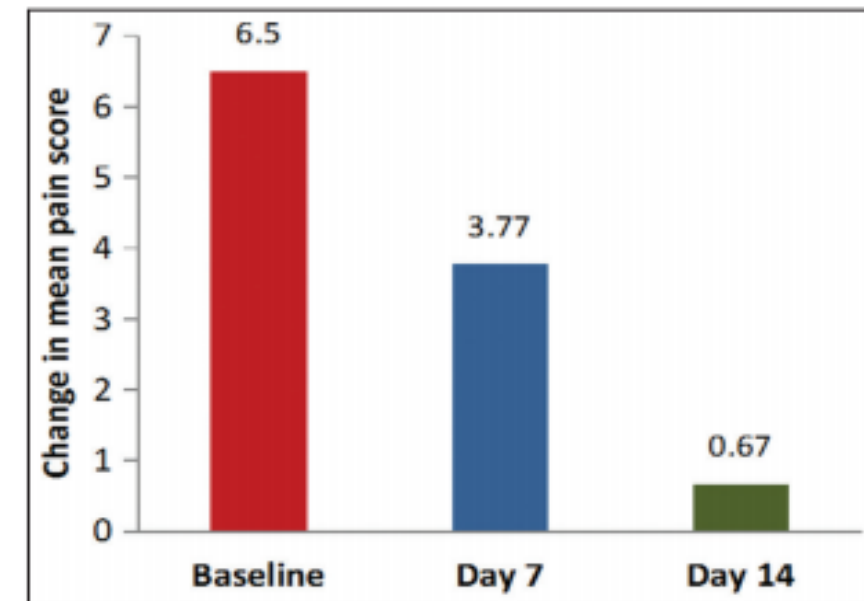


Figure 1: Change in the mean pain score

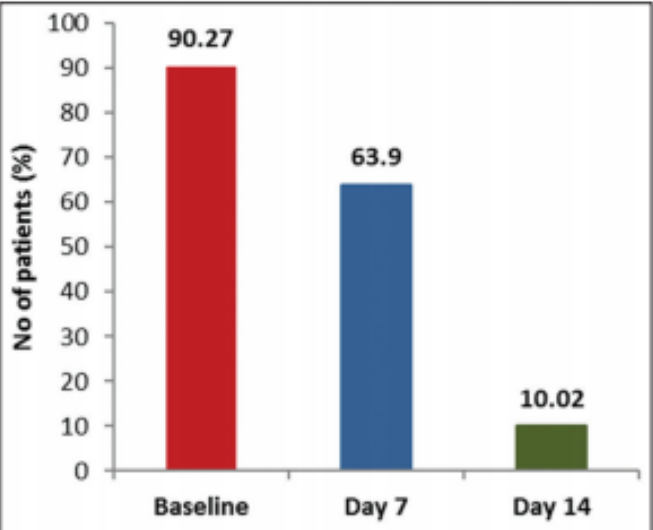


Figure 2: Effect on joint tenderness

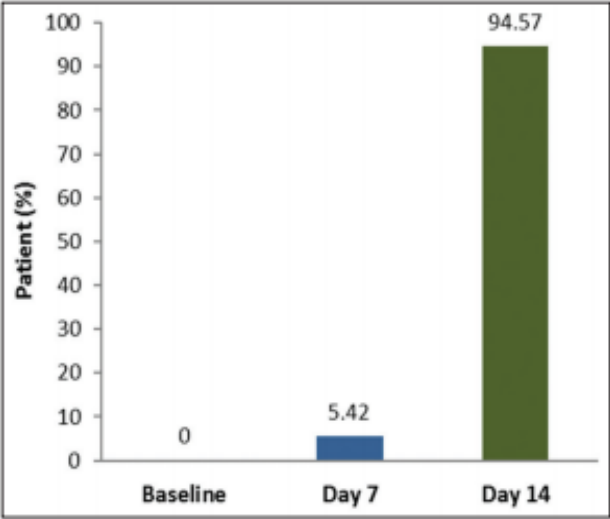


Figure 4: Time needed by the patients to be symptom free

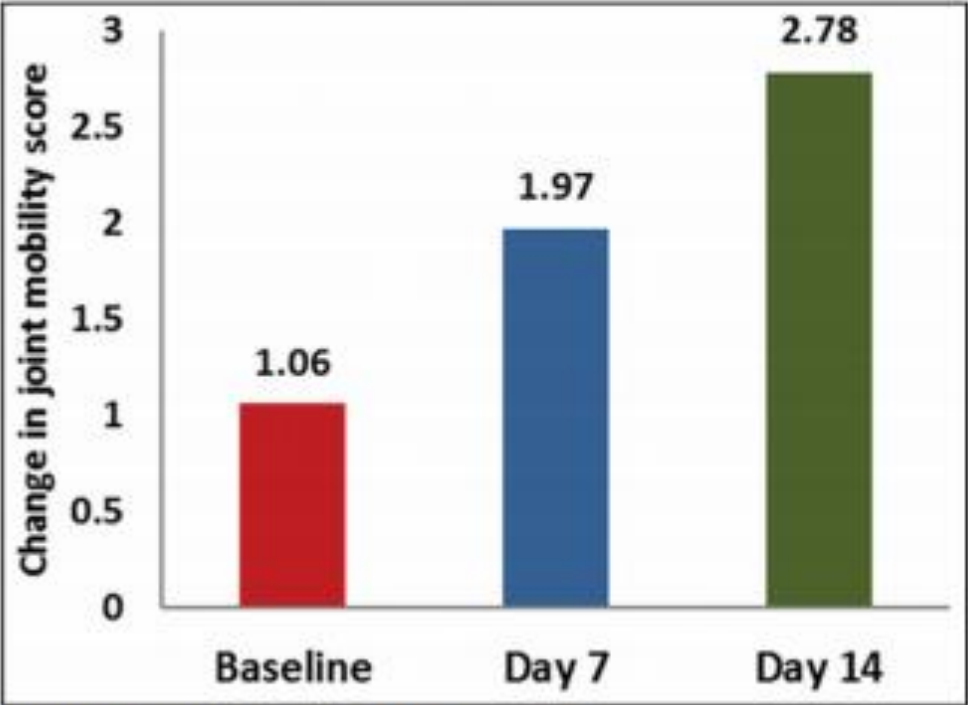


Figure 3: Effect on the joint mobility score

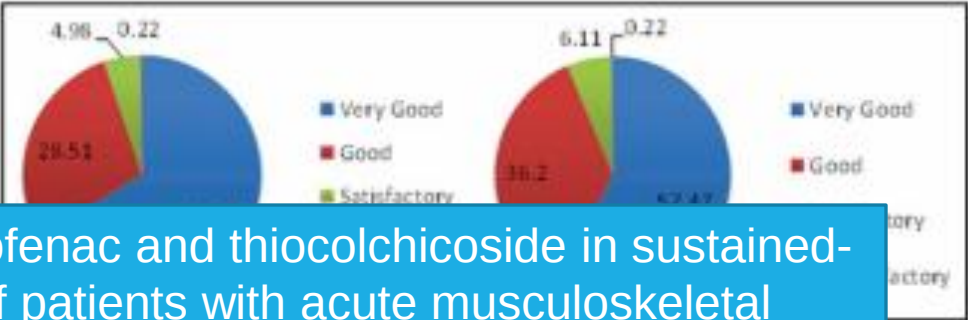
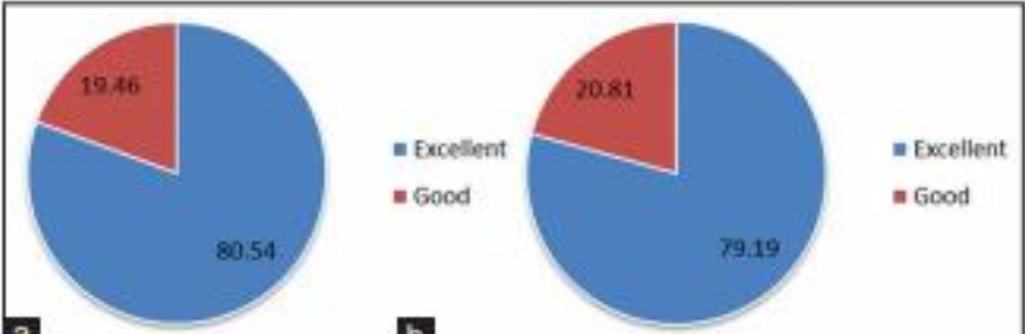


Figure 5: Overall global assessment of efficacy by physicians (a) and patients (b)

The current study confirms that fixed-dose combination of aceclofenac and thiocolchicoside in sustained-release form is effective and well tolerated in the treatment of patients with acute musculoskeletal

FIXED DOSE COMBINATION OF ACECLOFENAC + PARACETAMOL + THIOCOLCHICOSIDE IN THE TREATMENT OF ACUTE LOW BACK PAIN

Methods:

- Thirty-five patients, age being 18 to 76 years suffering from acute low back pain were enrolled in the study. Study drug containing aceclofenac 100 mg + thiocolchicoside 4 mg + paracetamol 500 mg was prescribed twice daily for a duration of 7 days.

Outcome:

- Intensity of pain at rest during movement and at night was significantly reduced by the combination compared to baseline.
- The mobility assessment revealed a statistically significant improvement in hand-to-floor distance on the 3rd and 7th day as compared to baseline with combination.
- Result of this study showed that aceclofenac + thiocolchicoside + paracetamol significantly reduced intensity of pain and improve the mobility of the patients.

SALIENT FEATURES OF DOLOWIN TC

- Analgesics and muscle relaxants are commonly prescribed in combination for the treatment of low back pain.
- NSAIDs and skeletal muscle relaxants are effective in Low Back Pain(LBP) for short term pain relief.
- Hence, combining Thiocolchicoside, an effective muscle relaxant and Aceclofenac, a potent cox-2 selective NSAID shall be an ideal Fixed Dose Combination which can be indicated in conditions of pain associated with muscle spasms.
- It can be given as a single tablet to the patient.

thank you