

## COMPARATIVE STUDY ON SAFETY AND EFFICACY OF CHLORZOXAZONE VERSUS THIOCOLCHICOSIDE IN COMBINATION WITH PARACETAMOL AND ACECLOFENAC IN PATIENTS WITH ACUTE LOW BACKACHE ASSOCIATED WITH MUSCLE SPASM

Ch. Anitha\*, G. A. Sravya Malika, K. Rani Samyuktha, S. K. Sharmila, S. Vara Prasad and P. Srinivasa Babu

Department of Pharmacy Practice, Vignan Pharmacy College, Vadlamudi, Guntur-522213, Andhra Pradesh, India.

\*Corresponding Author: Ch. Anitha

Department of Pharmacy Practice, Vignan Pharmacy College, Vadlamudi, Guntur-522213, Andhra Pradesh, India.

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### ABSTRACT

**Background:** The fixed dose combinations (FDCs) of muscle relaxants, non-steroidal anti-inflammatory drugs and paracetamol are commonly prescribed in the treatment of acute lower backache with muscle spasms. **Aim:** The present study was undertaken with the aim of comparing the safety and efficacy of FDCs of thiocholchicoside, aceclofenac & paracetamol versus chlorzoxazone, aceclofenac and paracetamol in patients with acute lower backache associated with muscle spasm. **Materials and Methods:** A total of 25 patients  $\geq 20$  years having low back pain of  $\leq 7$  days duration were randomly divided into two groups. Group A was prescribed chlorzoxazone (500 mg) + aceclofenac (100 mg) + paracetamol (325mg) while Group B was prescribed thiocholchicoside (4 mg) + aceclofenac (100 mg) + paracetamol (325 mg) orally twice daily for 7 days. Severity of pain at rest and on movement was recorded using visual analogue scale. Muscle spasm was evaluated by hand-to-floor distance. Readings were noted on day 1 (baseline) and day 7. **Results:** There was statistically significant reduction in severity of pain and muscle spasm on day 0 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 B than Group A. **Conclusion:** These findings confirm that FDC of thiocholchicoside, aceclofenac and paracetamol is a preferred option for patients with lower backache pain associated with muscle spasm.

**KEYWORDS:** Muscle Spasms, Acute Low Backache, Fixed Dose Combination, Finger to Floor Distance, Visual Analogue Scale.

### INTRODUCTION

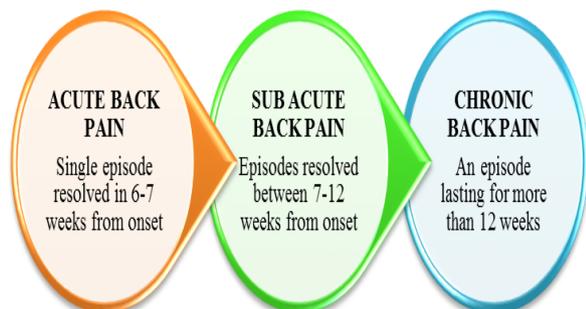
- According to the European Guidelines for prevention of low back pain, low back pain is defined as "pain and discomfort, localized below the costal margin and above the inferior gluteal folds, with or without leg pain" another definition, according to S.Kinkade, which resembles the European guidelines is that low back pain is "pain that occurs posteriorly in the region between the lower rib margin and the proximal thighs".
- Simply, low back pain is defined as symptomatic and a self-limiting condition characterised by pain, muscle spasm & stiffness.
- Typically the commonest area of back pain is the low back (lumbar region) & sometimes it spreads to buttocks, groin, upper thigh (posteriorly).
- Most of the back pains are caused by strain or sprain of the back muscles & ligaments.

- Low back pain (LBP) is the fifth most common reason for physician visits, which affects nearly 60-80% of people throughout their lifetime.
- The people that are mostly affected are within the age group of 25-60 years.
- The lifetime prevalence of low back pain is reported to be as high as 84%, and the prevalence of chronic low back pain is about 23%, with 11-12% of the population being disabled by low back pain.

#### Types of low back pain

- **Based on the symptom duration low back pain is classified as follows**
- **Acute LBP:** Back pain  $< 6$  weeks duration
- **Sub acute LBP:** Back pain  $> 6$  weeks but  $< 3$  months duration
- **Chronic LBP:** Back pain disabling the patient from some life activity  $> 3$  months

- **Recurrent LBP:** Acute LBP in a patient who has had previous episodes of LBP from a similar location, with asymptomatic intervening intervals.



### Causes of lbp

- Low back is the second most common reason for the Americans to seek their health care providers. It is next to colds and flu.
- Back pain is usually felt after lifting a heavy object, on moving suddenly, sitting in a particular position for a longer period of time, or on getting injured.
- It is most often caused by a sudden injury to the muscles and ligaments supporting the back, which may lead to strain or sprain in the muscles and ligaments.

### Common Symptoms of Lower Back Problems

Low back pain is typically characterized by a combination of the following symptoms

- Dull, aching pain
  - Pain that travels to the buttocks, legs, and feet
  - Pain that is worse after prolonged sitting
  - Pain that feels better when changing positions
  - Pain that is worse after waking up and better after moving around
- Chlorzoxazone, a central muscle relaxant works by blocking nerve impulses or pain sensations that are sent to your brain. It inhibits degradation of mast cells, subsequently preventing the release of histamine and slow reacting substance of anaphylaxis, mediators of type 1 allergic reactions. It may also reduce the release of inflammatory leukotrienes. Chlorzoxazone may act by inhibiting calcium influx. The side-effects profile is similar to that of other muscle relaxants, except for a limited number of reported cases of significant hepatotoxicity particularly by chlorzoxazone.

Thiocolchicoside is a GABA-A receptor antagonist & semi-synthetic colchicoside (natural compound) derivative, which binds to GABA-A & strychnine sensitive glycine receptors. This results in the reduction of spasticity. It also has myorelaxant effects at the supraspinal level, via complex regulatory mechanisms. It has been reported that thiocolchicoside produces muscle relaxation without any subjective or objective sedative side-effects.

### METHODOLOGY

**Study Design:** This prospective, randomized, comparative drug study was undertaken in the outpatient department of orthopedics, Ramesh Hospitals, Guntur, Guntur Dt., Andhra Pradesh, India for a period of six months. The study protocol was approved by the institutional review board. Patients attending the outpatient department were screened and assessed according to the specified inclusion and exclusion criteria. A total of 100 eligible patients of both sexes having acute low back pain of moderate to severe intensity with muscle spasm were taken and willing to take medications as directed and come for follow-up were enrolled in the study. The written consent of patients was taken on inform consent form in the local language.

**Inclusion Criteria:** Patients of either sex (both males & females) of age  $\geq 20$  years with a history of Low Back Pain (LBP) & muscle spasm of  $\leq 7$  days were included in the study.

### Exclusion Criteria

- Patients with back pain due to malignancy, infection, osteoarthritis of hip or any other disease, back pain referred from other organs.
- Patients with a history of presence of peptic ulceration or GI bleeding or severe dyspepsia
- Patients allergic to NSAID's or skeletal muscle relaxants
- Patients suffering from asthma or other allergic disorders
- Patients treated with NSAID's or skeletal muscle relaxants for 3 days prior to study
- Patients on anticoagulant therapy
- Patients suffering from hepatic or renal impairment.
- Pregnant or lactating women were excluded from the study.

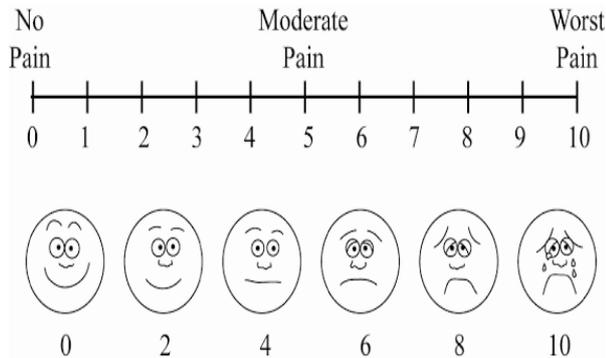
### Procedure

- Demographic data & relevant medical history was obtained from all patients prior to initiation of therapy.
- Patients were randomly divided into 2 groups: Group A & Group B, 50 each.
- Group A will be given a Fixed Dose Combination (FDC) of chlorzoxazone (500 mg), aceclofenac (100 mg) orally twice a day for 7 days.
- Group B will be given a Fixed Dose Combination (FDC) of thiocolchicoside (4 mg), aceclofenac (100 mg) orally twice a day for 7 days.
- Commercial available preparations were used.
- Patients were evaluated on day 0, day 3 & day 7 for severity of pain & muscle spasm.
- At each visit patients were asked to report any adverse event if present.
- Descriptive statistics were used for analysis.

### Criteria for Evaluation

#### Primary efficacy measures: Pain assessment scale

Assessment of intensity of pain at rest & pain on movement was carried out on day 0 (visit-1, baseline) & day 7 (visit-2) by means of 10cm visual analogue scale (VAS) as reported by a patient between 0 (no pain) & 10 (unbearable pain).



#### Muscle spasm assessment: Finger to floor distance.

It was measured by flexion at the hip joint in a standing position. The patients were told to bend down as far as possible without bending the knees & try to touch the floor with their fingers. The remaining distance between the floor & fingertips was measured by ruler in centimeters.



**Safety measures:** Side effects such as tiredness, drowsiness, dizziness & alertness were noted based on history, observations of adverse reactions.

#### Secondary efficacy measure

Efficacy evaluation was evaluated based on a 4-point scale marked as excellent/good/average/poor.

### STATISTICAL ANALYSIS

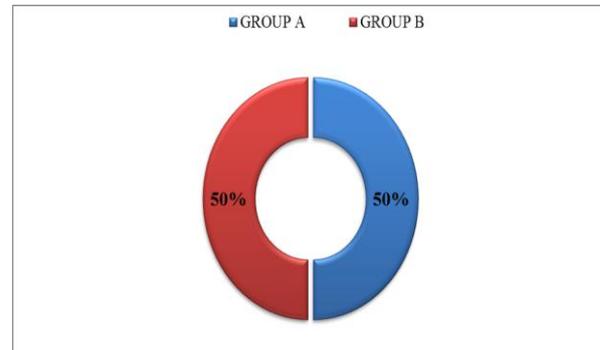
Comparison was done in both inter group between baseline and day 7 values and expressed in mean  $\pm$  standard deviation. Then the data was pooled and analyzed. One-way analysis of variance (ANOVA) was applied in the intra group analysis for pain at rest, pain on movement and Finger to Floor Distance (FFD).

### RESULTS

**Table. 1: Distribution of subjects with acute back ache & muscle spasms into groups.**

Total	Group A	Group B
88	44	44

**Inference:** 88 subjects were included in the study so far, of which 44 of them were taken in to group A (Chlorzoxazone + Aceclofenac + Paracetamol) & group B (Thiocolchicoside + Aceclofenac + Paracetamol).

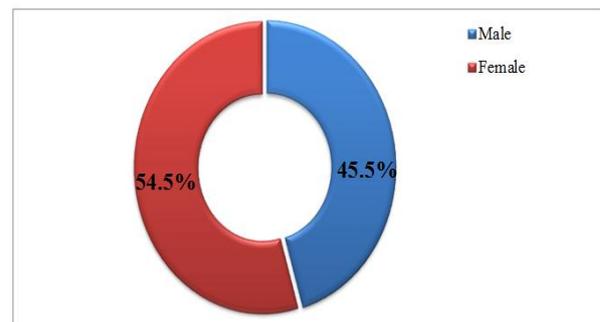


**Figure. 1: Representation of distribution of subjects with acute low back ache & muscle spasms.**

**Table. 2: Gender wise distribution of subjects with acute back ache & muscle spasms.**

Gender	Group-A	Group-B	Total (%)
Male	20	20	40 (45.5%)
Female	24	24	48(54.5%)

**Inference:** Out of 44 subjects included so far the prevalence of acute low back ache with muscle spasms was more in females(48) than in males(40).

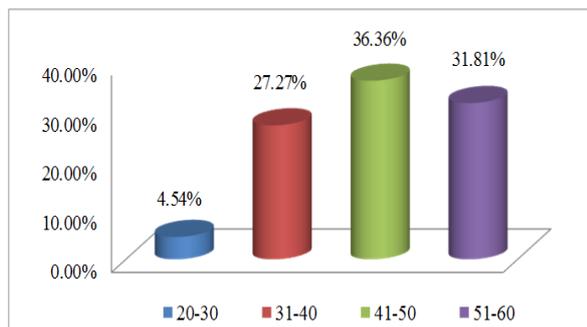


**Figure. 2: Representation of gender wise distribution of subjects with acute low back ache & muscle spasms.**

**Table. 3: Age wise distribution of subjects with acute back ache & muscle spasms.**

Age	Group-A	Group-B	Total (%)
20-30	4	0	4 (4.5%)
31-40	16	8	24 (27.27%)
41-50	12	20	32 (36.36%)
51-60	12	16	28 (31.81%)

**Inference:** Out of 88 subjects included so far 32 subjects (36.36%) were between age group 41-50, 28 subjects (31.81%) were between age group 51-60, 24 subjects (27.27%) were between age group 31-40 & 4 subjects were between age group 20-30.

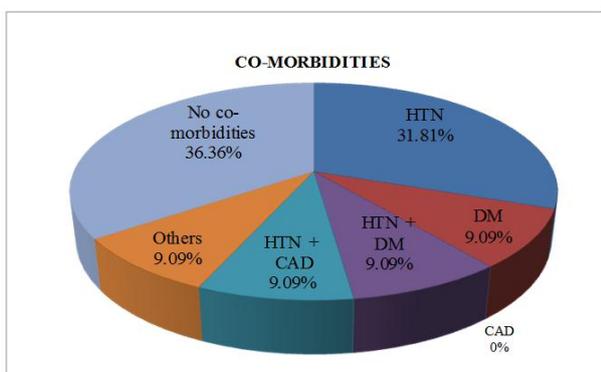


**Figure. 3:** Representation of age wise distribution of subjects with acute low back ache & muscle spasms.

**Table. 4:** Distribution of subjects with acute back ache & muscle spasms based on co-morbidities.

CO-Morbidity Condition	Group-A	Group-B	Total (%)
HTN	16	12	28 (31.81%)
DM	4	4	8 (9.09%)
CAD	0	0	0 (0%)
HTN + DM	4	4	8 (9.09%)
HTN + CAD	4	4	8 (9.09%)
Others	0	8	8 (9.09%)
No co-morbidities	16	16	32 (36.36%)

**Inference:** Out of 88 subjects included so far 32 subjects with no-comorbidities (36.36%) were observed, followed by 28 hypertensive subjects (31.81%), 8 subjects with DM, 8 with HTN+DM, 8 with HTN+CAD, 8 with other co-morbidities.

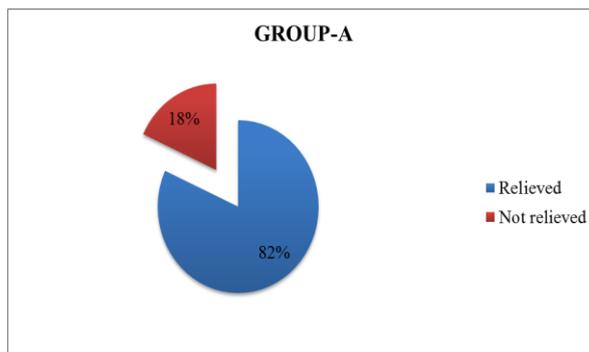


**Figure. 4:** Representation of distribution of subjects with acute low back ache & muscle spasms based on co-morbidities.

**Table. 5:** Post treatment reduction in severity of pain in Group-A.

Severity	Group A	Relieved	Not Relieved
MILD	12	12	0
MODERATE	20	16	4
SEVERE	12	8	4
TOTAL	44	36 (81.81%)	8 (18.18%)

**Inference:** According to the above statistical representation, in group A out of 12 mild patients 12 were relieved, while that of 20 moderate patients 16 were relieved & 4 were not relieved of pain & in 12 severe patients 8 were relieved of pain & 4 were not relieved.

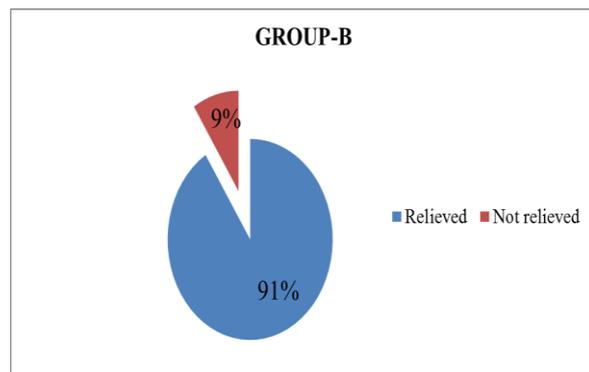


**Figure. 5:** Representation of post treatment severity in reduction of pain.

**Table. 6:** Post treatment reduction in severity of pain in Group-B.

Severity	Group B	Relieved	Not Relieved
Mild	12	12	0
Moderate	16	16	0
Severe	16	12	4
Total	44	40 (90.9%)	4 (9.09%)

**Inference:** According to the above statistical representation, in group B out of 12 mild patients 12 were relieved, while that of 16 moderate patients 16 were relieved & in 16 severe patients 12 were relieved of pain & 4 were not relieved.



**Figure. 6:** Representation of post treatment severity in reduction of pain.

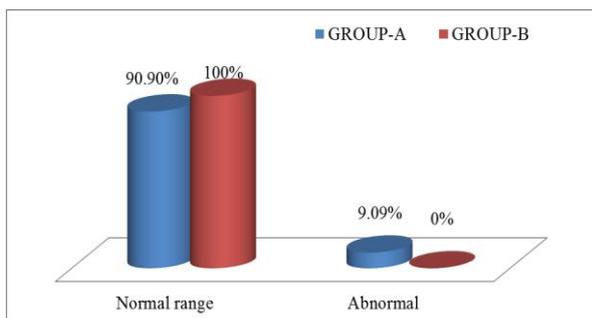
**Table. 7: Post treatment reduction in severity of pain.**

Severity	Group A	Relieved	Not Relieved	Group B	Relieved	Not Relieved
Mild (1-3)	12	12	0	12	12	0
Moderate (4-6)	20	16	4	16	16	0
Severe (7-8)	12	8	4	16	12	4

**Table. 8: Comparison of alterations in LFT between group-A & group-B.**

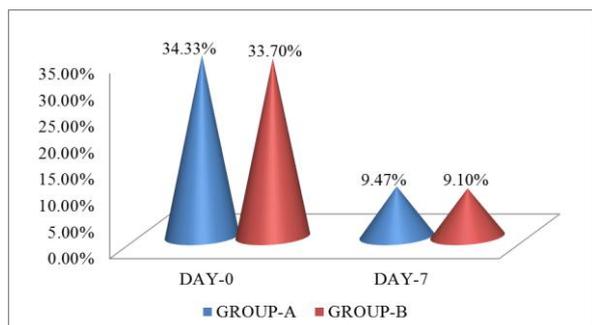
LFT's	Group-A	Group-B
Normal range	40 (90.9%)	44 (100%)
Abnormal	4 (9.09%)	0 (0%)

**Inference:** According to the above statistical representation, out of 44 subjects in group-A there was no alteration of LFT in 40 subjects (90.9%) & an alteration of LFT in 4 subjects (9.09%), in case of group-B none of them showed an altered LFT

**Figure. 7: Representation of alterations in LFT between group-A & group-B.****Table. 9: Comparison of FFD reduction in subjects of group-A & group-B (from day-0 to day-7).**

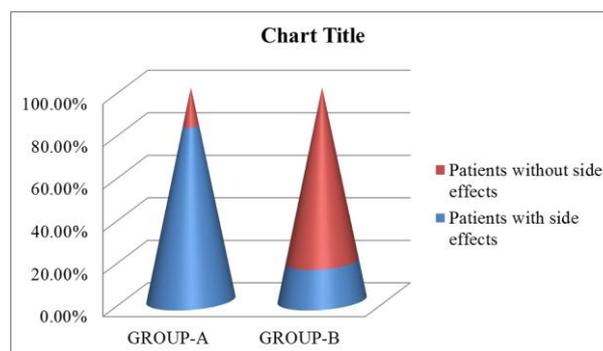
Average Hand to Floor Distance of Patients On	Group-A	Group-B
DAY-0	34.33%	33.7%
DAY-7	9.47%	9.1%

**Inference:** According to the above statistical representation, the average FFD of group-A subjects on day-0 was 34.33% & it got reduced to 9.47%, similarly in group-B patients FFD got reduced from 33.7% to 9.1%.

**Figure. 8: Representation of FFD reduction between the subjects of group-A & group-B.****Table. 10: Comparison of side effects experienced by subjects between the groups.**

	Group-A	Group-B
Patients with side effects	36 (81.81%)	8 (18.18%)
Patients without side effects	8 (18.18%)	36 (81.81%)

**Inference:** According to the above statistical representation, 36 out of 44 subjects experienced side effects in group-A & 8 out of 44 subjects experienced side effects in group-B.

**Figure. 9: Representation of side effects experienced by subjects between the groups.****Table. 11: Comparison of side effects experienced by subjects between the groups.**

Side Effect	Group-A	Group-B
Drowsiness/dizziness	32 (72.72%)	0 (0%)
Sedation	32 (72.72%)	0 (0%)
GI discomfort	16 (36.36%)	8 (18.18%)
Hepatic dysfunction	4 (9.09%)	0 (0%)

**Inference:** According to the above statistical representation, 32 subjects of group-A experienced drowsiness/dizziness, sedation individually, 16 experienced GI discomfort & a subject experienced hepatic dysfunction Out of 44 group-B subjects 8 of them experienced GI discomfort & 36 experienced none.

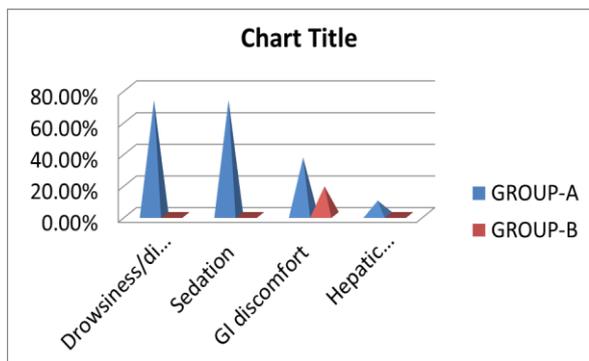


Figure. 10: Representation of side effects experienced by subjects between the groups.

Table. 12: Combined effects experienced by subjects of group-A.

Side Effect	Group-A
Drowsiness/dizziness + Sedation (D+S)	16 (36.36%)
Drowsiness/dizziness + Sedation + GI discomfort (D+S+G)	12 (27.27%)
GI discomfort (G)	4 (9.09%)
Drowsiness/dizziness + Sedation + Hepatic dysfunction (D+S+H)	4 (9.09%)
None (N)	8 (18.18%)

**Inference:** According to the above statistical representation 36.36% experienced D+S, 27.27% experienced D+S+G, 18.18% haven't experienced any side effects & 9.09% experienced G & D+S+H individually.

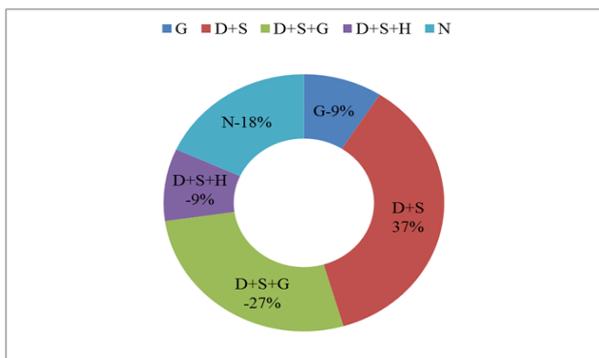


Figure. 11: Representation of combined effects experienced by subjects of group-A.

Table. 13: Comparison of secondary efficacy measurement between the groups.

	Excellent	Good	Average	Poor
Group-A	12 (27.27%)	16 (36.36%)	12 (27.27%)	4 (9.09%)
Group-B	20 (45.45%)	16 (36.36%)	4 (9.09%)	4 (9.09%)

**Inference:** According to the above statistical representation 20 subjects of group A & 12 subjects of group-B perception towards the therapy was excellent,

16 in both the groups perception was good, 12 in group A & 4 in group B perception was average & 4 subjects in each group perception was poor.

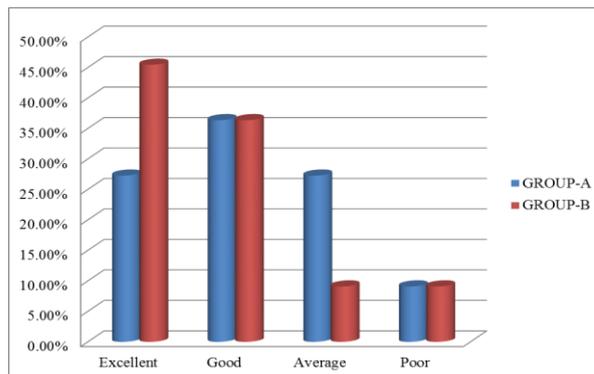


Figure. 12: Representation of secondary efficacy measurement between the groups.

**CONCLUSION**

- There was no statistically significant difference in pain relief & muscle spasm among the treatment groups but clinically showed better improvement in GROUP-B.
- The adverse drug reactions occurring during study showed a statistically significant better safety profile in the GROUP-B than GROUP-A.
- These findings till now confirm that FDC of thiocolchicoside, aceclofenac & paracetamol is a preferred option for patients with acute low backache associated with muscle spasm.

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