



**RANDOMISED COMPARATIVE STUDY OF ACECLOFENAC  
THIOLCHISIDE FIXED DOSE COMBINATION AGAINST  
ACECLOFENAC ALONE IN TREATMENT OF ACUTE NUCHAL  
PAIN: SAFETY AND EFFICACY ASSESSMENT**

**Sheikh Irfan Bashir\* and Shuja Rashid**

Medical officer and Surgeon, Trauma Super Speciality Hospital, Govt. Medical College, Srinagar, Kashmir, India.

Corresponding Author:- **Sheikh Irfan Bashir**

**E-mail:** sheikhirfanb@gmail.com

<p><b>Article Info</b>  <i>Received 05/11/2014</i>  <i>Revised 13/11/2014</i>  <i>Accepted 22/11/2014</i></p> <p><b>Key words:</b> Acute Nuchal Pain, Randomised Trial of Aceclofenac against Thiocolchiside combination, Treatment Acute Nuchal Pain, Neck Pain and NSAIDS, Neck Pain and Thiocolchiside.</p>	<p><b>ABSTRACT</b></p> <p>Nuchal pain is one of the most common reasons for consulting health care personnel. There are multiple modules to treat it, but all of them lack evidence. There have been no randomised trials for efficacy assessment of various drugs used in the treatment of nuchal pain. This study was conducted to assess efficacy and safety of Thiocolchiside Aceclofenac combination against Aceclofenac alone. Out of 145 patients randomised into two groups 138 completed the study. Patients were assessed by Visual Analogue Scale, Shafat’s Range of Motion Index and Shafat’s Nuchal Tenderness Index both before the start of treatment and on Tenth day of treatment. There was significant improvement in all scores in both groups. The combination therapy group showed better response in all scales than the aceclofenac alone group. The Shafat’s Range of Motion Index and Shafat’s Nuchal Tenderness Index showed significant improvement as compared to the Aceclofencac alone group with <math>P &lt; 0.01</math>. VAS showed better results in combination therapy than aceclofenac but the results were not statistically significant. All patients were given proton pump inhibitor during the treatment regime as a prophylactic measure for prevalent acid peptic disorder in the population. Few patients among combination therapy group developed dizziness with none of them requiring additional treatment. The study favours the use of thiocolchiside aceclofenac combination in the treatment of acute nuchal pain.</p>
--	--

**INTRODUCTION**

Neck pain is one of the most common reasons for the patients presenting to the out-patient Department. International figures indicate that at any point in time approximately 10–15% of the population will be suffering an episode of neck pain, and 40% will suffer neck pain during a 12-month period. About 40% of people suffer from neck pain during a 12-month period while 10-15% of the population in general do suffer from an episode of neck pain at any point of time [1]. According to International Association for the Study of Pain (IASP) Neck pain is defined as Pain perceived as arising from anywhere within the region bounded superiorly by the superior nuchal line,

inferiorly by an imaginary transverse line through the tip of the first thoracic spinous process and laterally by sagittal planes tangential to the lateral borders of the neck [2]. The term ‘acute’ refers to pain that has been present for less than three months; it does not refer to the severity or quality of pain [3]. Chronic pain is pain that has been present for at least three months [4].

Medications commonly used for the treatment of acute LBP include Acetaminophen, Methimazole and other Non-Steroidal Anti-Inflammatory drugs and muscle relaxants [5].



Same medications are usually used in cases of acute neck pain, but there are no or insufficient studies evaluating the use of Nsaids in the treatment of neck pain [6].

The use of nsaids accounts for 70% of medications used for pain. Aceclofenac is an orally administered phenyl acetic acid derivative with effects on a variety of inflammatory mediators [5]. It acts by inhibiting cyclooxygenase activity with a reduction in tissue production of prostaglandins like PGE2 and PgF2 alpha [7].

Thiocolchicoside is a semisynthetic derivative of colchicine, a natural glycoside of *superba gloriosa* [8]. This compound has a glycinomimetic activity hence used for myorelaxant property. Thiocolchiside produces muscle relaxation along with anti-inflammatory and analgesic effects. Hence present study was undertaken to compare the effect of fixed dose combination of Aceclofenac (100 mg) and Thiocolchicoside (4 mg) with Aceclofenac (100mg twice daily) alone in the treatment of acute neck pain.

## MATERIAL AND METHODS

In this ten day randomized prospective trial; 145 patients received the treatment for acute neck pain at the out-patient clinic in the department of Physical Medicine and rehabilitation. We compared the efficacy of Aceclofenac + Thiocolchicoside combination with Aceclofenac alone in the treatment of acute neck pain. The study was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki as revised in 2000. The study was approved by the Institutional Review Board after accepting their demand for the administration of proton pump inhibitor to all patients as a preventive measure for epigastralgia. Informed consent was obtained from each subject at recruitment. Out of the 145 patients included in the study only 138 patients completed the study.

### Inclusion criteria

All patients presenting to the Out-Patient Department with acute idiopathic neck pain in the age group of 18-55 yrs.

### Exclusion criteria

Patients with neck pain with any of the following;

1. Symptoms and signs of infection (e.g. fever, night sweats)
2. History of trauma
3. Use of corticosteroids
4. Past history of malignancy
5. Age > 50 years
6. Failure to improve with treatment
7. Unexplained weight loss
8. Dysphagia, headache, vomiting
9. Neurological symptoms in the limbs
10. Cerebrovascular symptoms or signs, anticoagulant use
11. Cardiovascular risk factors, transient ischaemic attack

Patients who fulfilled the inclusion and exclusion criteria were randomised into two groups, Group A and Group B. Group A patients received Aceclofenac 100 mg + Thiocolchiside 4 mg, while group B patients received Aceclofenac 100 mg tablets. Both the groups received medicine as twice daily dosages for a period of 10 days.

History, demographic and anthropometric parameters were recorded for all patients. All patients were assessed by Visual Analogue Scale (0-10 points), Shafat's Range of Motion Index for nuchal pain (S ROM I) and Shafat's Nuchal Tenderness Index (S NTI) for nuchal muscle tenderness.

Visual analogue scale (VAS), Shafat's Range of Motion index for nuchal pain (S ROM I) and Shafat's Nuchal Tenderness index (S NTI), was evaluated at patient recruitment and on 10<sup>th</sup> day of treatment. Pain assessment was recorded on a 10 point scale where a score of 0, corresponds to no pain while a score of 10 corresponds to worst possible pain.

Severity of pain on movement was assessed on (S ROM I) 5 point scale as-

0: All movements free

1: Mild pain in single plane of movement (either extension, flexion, sideways bending, or sideways rotation).

2: mild to moderate pain in two or more planes of movement.

3: moderate to severe pain in one or more planes of motion.

4: Incapacitating pain with any tried movement of the cervical spine.

Severity of nuchal region tenderness was assessed by (S NTI) 5 point scale as:-

0: No Tenderness.

1: Mild tenderness on palpation on one side.

2: moderate to severe tenderness on palpation on one side.

3: mild to moderate tenderness on palpation on both sides.

4: severe tenderness on palpation on both ligamentum nuchae or along spinous processes.

Detailed history was collected from all patients regarding development of any side effects or drug allergy whatsoever.

Efficacy and safety analysis was done for all patients included in the study. Patients from both the study groups were evaluated at baseline for homogeneity with respect to demographics and disease characteristics. The basic descriptive statistics was calculated. Safety and efficacy outcome was calculated on day 0 and day 10. Statistical analysis was performed with Student's t test using graph pad instat 3. Descriptive statistics were determined by calculation of the mean and standard deviation ( $\pm$ SD) and statistical significance was defined as  $P < 0.01$ .

## RESULTS

A total of 145 patients randomised into two groups with group A comprising of 74 patients and group B comprising of 71 patients were included in the study. 7



patients were lost in the follow up; out of which 4 patients were from Group A and 3 patients from group B. So the total number of patients who completed the study were 138 with 70 patients in Group A while 68 patients in group B. The demographics of both the groups were comparable as in table 1.

Mean age range in group A and group B were 36.74 and 36.33 respectively. There were 70 patients in group A and 68 patients in group B who completed the study with 28 males in both groups while 42 and 40 females in group A and group B.

All the patients included in the study showed significant improvement in pain. As per the visual analogue scale the improvement in pain score was better in Group A (Thiocolchiside+ Aceclofenac) than Group B (Aceclofenac only) though it was not statistically significant (table 2). Mean VAS score of group B was 0.5 while that of group A was 0.41 on tenth day of treatment showing better improvement in pain with combination therapy.

Overall assessment of patient for Shafat’s Range of Motion Index showed significant improvement in both the groups while range of movement score was much better in the

Thiocolchiside + Aceclofenac group, showing marked improvement in range of motion and the difference is statistically significant  $P < 0.01$ . as in table 3.

Both the groups showed significant improvement in the Shafat’s nuchal tenderness index after treatment whether it be monotherapy with aceclofenac or combination therapy with Aceclofenac + Thiocolchiside. Though both therapies lead to improvement in the tenderness but the combination therapy lead to better patient response and the difference in the two groups is statistically significant with  $p < 0.01$ . as in table 4.

**Safety**

Among all the patients involved in the study only two patients and both from the combination therapy group developed dyspepsia for which an antacid gel was given twice daily until continuation of therapy. Four patients from combination therapy group complained of mild dizziness. None patient other than these developed any adverse event. Though as per the recommendation of the ethical committee all the patients were given proton pump inhibitor every day before breakfast until the continuation of the therapy because of the prevalent dyspepsia in the people of the state of Jammu and Kashmir.

**Table 1. Demographics of group A and group B patients**

Group	Mean Age (range)	Males	Females	Total
Group A (Thiocolchiside+ Aceclofenac)	36.74 (26-52)	28	42	70
Group B (Aceclofenac only)	36.33 (26-50)	28	40	68

**Table 2. Comparison of improvement in pain as per visual analogue scale among the group A and group B patients**

Mean VAS score	Group A	Group B	Difference of mean	P value
Day 0	6.60± 1.39	6.59± 1.38	0.01	$P > 0.01$
Day 10	0.41±0.49	0.5±0.61	0.09	$P > 0.01$
Difference of mean	6.19	6.09	-	-
P value	$P < 0.01$	$P < 0.01$	-	-

**Table 3. Comparison of shafat's range of motion index among the group A and group B patients**

Mean S ROM I	Group A	Group B	Difference of mean	P value
Day 0	2±1.01	2.03± 1.02	0.03	$P > 0.01$
Day 10	0.31±0.47	0.68± 0.53	0.37	$P < 0.01$
Difference of mean	1.69	1.35	-	-
P value	$P < 0.01$	$P < 0.01$	-	-

**Table 4. Comparison of shafat's nuchal tenderness index among the group A and group B patients**

Mean S NTI	Group A	Group B	Difference of mean	P value
Day 0	1.66± 1.07	1.59± 1.01	0.07	$P > 0.01$
Day 10	0.28±0.45	0.53± 0.55	0.25	$P < 0.01$
Difference of mean	1.38	1.06	-	-
P value	$P < 0.01$	$P < 0.01$	-	-

**DISCUSSION**

Nuchal pain is one of the most common reasons to consult healthcare providers world over. NSAIDs being the most frequently medicines used. There is increased use of Thiocolchiside for the same. To our knowledge there is no randomized study to show evidence based approach for the

same in English literature. In the present study patients with nuchal pain were randomly allocated two groups. Both the groups were comparable as regards to baseline demographics and disease characteristics. Patients were evaluated for the severity of nuchal pain using VAS. There



has been significant improvement in the VAS on tenth day of therapy in both the groups, though the combination therapy group showed more improvement in the VAS than monotherapy while the difference was not statistically significant  $p > 0.01$ . These results are in accordance with the results of Pareek A et al [9]. All Patients were evaluated for pain during range of motion by S ROM I at baseline and on 10<sup>th</sup> day of therapy. Both the groups showed significant improvement in the index after receiving therapy, though the improvement was significantly better in the group receiving combination therapy of Thiocolchiside and Aceclofenac with  $P < 0.01$ , which is in accordance with Pareek A et al [9]. However results of Sachdeva et al showed decrease in pain on movement more

pronounced in Thiocolchiside group but not statistically significant which they themselves ascribe to lesser number of patients [10]. Nuchal tenderness was assessed by S NTI. The baseline evaluation showed similar characteristics in both the groups while evaluation on tenth day showed statistically significant improvement in the Thiocolchiside Aceclofenac group as compared to Aceclofenac group with  $P < 0.01$ , though both treatment groups showed improvement in tenderness after receiving treatment.

#### ACKNOWLEDGEMENT

We thank Ms. Surayya Pandit for her contribution to preparing this article. No funding whatsoever has been received from any individual or organisation.

#### REFERENCES

1. Ariens GAM, Borghouts AJ, Koes BW (1999). Neck pain. In: Crombie IK (ed). *Epidemiology of Pain. IASP Press: Seattle*, 235–255.
2. Merskey H, Bogduk N, editors. (1994). Classification of chronic pain. Descriptions of chronic pain syndromes and definitions of pain terms. 2nd ed. *Seattle: IASP Press*, 11.
3. Merskey H. (1979). Pain terms: a list with definitions and notes on usage recommended by the IASP Subcommittee on Taxonomy. *Pain*, 6, 249–252.
4. Merskey H, Bogduk N (eds) (1994). Classification of Chronic Pain. Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms (2nd Edition). *IASP Press: Seattle*, 210.
5. Malmivaara A, Hakkinen U, Auro T, et al. (1995). The treatment of acute low back pain – bed rest, exercises, or ordinary activity? *New England Journal of Medicine*, 332, 351–355.
6. Evidence-based Management of Acute Musculoskeletal Pain. Australian Acute Musculoskeletal Pain Guidelines Group; A Guide for clinicians: Australian Academic Press PTY LTD, 35-43.
7. Colin Dolery: (1999). Therapeutic drugs 2<sup>nd</sup> ed. Churchill livingstone, D88-89.
8. Umalkar AR, Bavaskar SR, Yewale PN. (2011). Thiocolchiside as muscle relaxant: a review. *International Journal of Pharmacy and Biological Sciences*, 193, 364-371.
9. Pareek A, Chandurkar N, et al. (2009). Aceclofenac – Tizanidine in the treatment of Acute Low Back pain: A Double blind, Double–Dummy, randomized, Multicentric, comparative study against Aceclofenac alone. *European Spine Journal*, 10, 1007/s00586-009-1019-4.
10. Ankita A Desai, Punam D Sachdeva, Bhoomi D, Arora. (2011). A comparative study of combined use of Aceclofenac along with Thiocolchiside and Aceclofenac alone in patients diagnosed of low back pain. *An International Journal of Pharmaceutical Sciences*, 2(2), 141-150.

