Naproxen (Alone) Vs Tramadol Hydrochloride +Acetaminophen in the Management of Osteoarthritis of the Knee: A 13 Week Prospective Study at Tertiary Care Hospital

Batchu Pavani*, Tatinada Ramya Krishna, Thatikonda Neha, Kandimalla Krishna Vamsi, Voguri Bhanu Kalyan, Ganipisetti Ramesh, Satheesh S Gottipati, Puttagunta Srinivasa Babu

Department of Pharmacy Practice, Vignan Pharmacy College, Vadlamudi, Andhra Pradesh, INDIA.

ABSTRACT

Aim: The main aim of the study is to assess the effectiveness of Naproxen (Alone) Vs Tramadol Hydrochloride + Acetaminophen in the management of osteoarthritis of the knee. **Objectives:** To determine and evaluate effectiveness of drugs prescribed, Cost effectiveness analysis. **Methodology:** The present Prospective, Observational study with 100 subjects were from Orthopaedic department with Osteoarthritis of the knee. The subjects were selected on the basis of inclusion and exclusion criteria. The subjects were followed for every 14 days (2,4,6 weeks) and the severity of the pain was calculated by using Oxford knee score. All statistical analysis was carried out with SPSS software. **Results:** Paired *t*-test was calculated for two groups and the result was found to be statistically significant. When compared to Group B (Tramadol Hydrochloride + Acetaminophen), Group A (Naproxen) was found to be highly significant. **Conclusion:** Naproxen was ranked the most effective individual knee OA treatment for improving both pain and function followed by Tramadol Hydrochloride + Acetaminophen. Group B treatment shows cost effectiveness. Further research is required to investigate the use of these drugs in treating OA of the knee. Hence it is necessary to make awareness to physicians and pharmacists, therefore clinicians should promote the rational use of these drugs in the management of OA of the knee.

Key words: Osteoarthritis, Effectiveness, Oxford knee Score, Naproxen, Tramadol Hydrochloride + Acetaminophen.

INTRODUCTION

Osteoarthritis (OA) is the most common joint disease and is one of the 10 most disabling conditions in the United States and other developed nations.[1,2] Approximately 15% of the population is affected by OA, including 50% of those over 65 and 85% of those aged 75. Prevalence of OA increases with age. Prevalence for symptomatic knee OA is 5% for all persons over age 25, but 12 and for those over 55. Women exhibit a higher prevalence of knee OA than men and are at especially greater risk of hand OA, with 26% of women and 13% of men over age 70 affected.[3] Women are also more likely to have inflammatory OA of the proximal and distal inter-phalange joints of the hands, giving rise to the formation of Boucher and

heberden nodes, respectively.

The most common risk factors for the development of OA include:

- Obesity
- Occupation
- Participating in certain sports
- History of joint trauma
- Genetic factors

OA falls into two major etiologic classes. Primary OA (Idiopathic), the most common type, has no identifying cause. Sub-classes of Primary OA are localized OA, involving one or two sites and generalized OA affecting

three or more cells. Erosive OA is used to describe the presence of erosion and marked proliferation in the proximal and distal inter-phalange joints of the hands. Secondary OA is that associated with a known cause such as Rheumatoid or another inflammatory arthritis, trauma, metabolic or endocrine disorders and congenital factors.[4]

The diagnosis of OA is made through history, physical examination, characteristic radiographic findings and laboratory testing. The major diagnostic goals are to discriminate between primary and secondary OA and to clarify the joints involved, severity of joint involvement and response to prior therapies, providing basis for the treatment plan. The American College of Rheumatology has published traditional diagnostic criteria and decision trees for OA diagnosis.[5]

Patient management with OA starts with a diagnosis based on a detailed history, physical examination, radiographic observations and an assessment of the level of joint involvement. Treatment should be personalized to everyone. The goals are to educate patients, family members and caregivers; to alleviate pain and rigidity; to preserve or increase joint mobility; to restrict functional impairment and to retain or improve quality of life.[6] Treatment for all individuals with OA will start with patient education, physical or occupational therapy and, where applicable, weight loss or assistive devices.[7]

The first step in OA treatment is patient education about the disease process, the extent of OA, prognosis and treatment options education is paramount in that OA is often seen as a disease of wear and tear and inevitable consequence of ageing for which nothing helps. In a number of programs, the benefits of patient education were recorded. Such services are implemented across a wide range of delivery methods: from qualified volunteers use telephone calls to community patient therapy groups, to one-on-one is training sessions with physical therapists or nurse educators. The long-term cost effectiveness of these patient education services is very critical for the sustainability

Excess weight raises the biomechanical stress on bearing joints and is the best single indicator of the need for eventual joint replacement.[8] Even a weight loss of 5 kg (11 lb) will reduce the load on a bearing joint. Weight loss is associated with symptoms of decrease and incapacity, although results vary.

Physical therapy with heat or cold therapies and exercise programs helps maintain and improve the range of motion in the joint and reduce pain and spasms in the muscle.

Warm baths or soak up of warm water will reduce pain and stiffness. To stop burns, patients should be warned not to fall asleep on the heat source or lie on it for more than brief periods. Strengthening exercise programs and quadriceps can enhance physical mobility and can minimize OA patients ' impairment, discomfort and analgesic use.[9] The therapist may assess muscle strength and stability of the joint and prescribe exercises and methods to protect the affected joint from excessive forces. The therapist may also provide assistive and orthotic aids for use during exercise or daily activities, such as canes, walkers, bracelets heel cups, splints, or insoles.

Surgery for OA patients with physical impairment and/or severe pain unresponsive to conventional therapy may be recommended. Criteria for total joint knee replacement (arthoplasty) were developed during a consensus conference of the National Institute of Health.[10] These guidelines for knee replacement were focused on critical literature review, as well as expert opinion. A partial or total arthoplasty can relieve pain and improve mobility for patients with advanced disease, with the best results after knee arthoplasty.

MATERIALS AND METHODS

Data source and Study design

The data was collected in a specially designed proforma for collecting patient details. The information was directly collected in out-patients prescription. We have used Oxford knee score for calculating the severity of pain. It is a Prospective Observational study and the study was carried out for duration of six months.

Study Population

The present Prospective, Observational study with 100 subjects were from orthopedic department with Osteoarthritis of the knee.
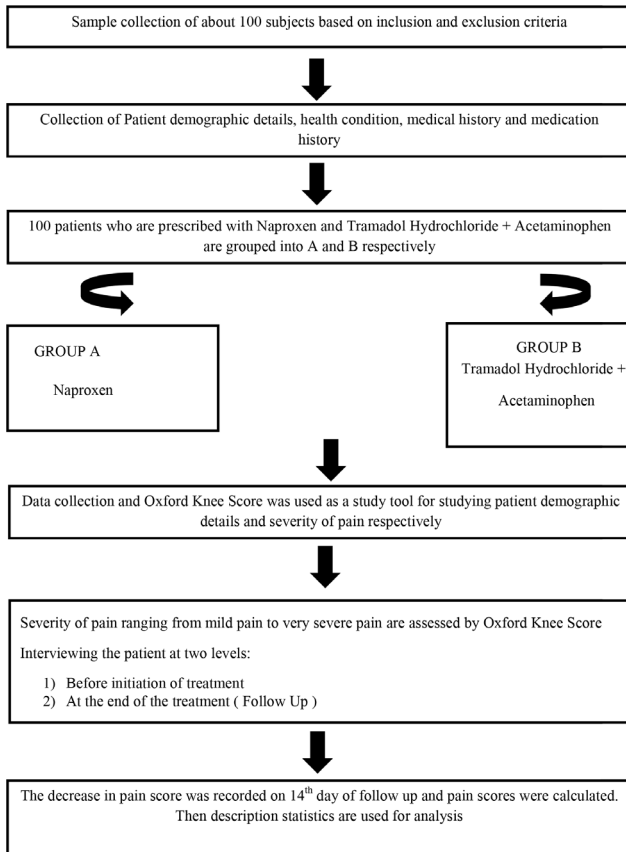
Inclusion criteria:-

1. Patients who are willing to participate in the study

2. Patient up to 55 years of age with osteoarthritis

3. Both gender of patient

Exclusion Criteria:-

1. Patient who are allergic to NSAIDs

2. Post Out Patient Cases

Plan of work

The study methodology was determined and protocol was prepared and ethical committee permission was taken.

Sample collection of about 100 subjects based on inclusion and exclusion criteria

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Collection of Patient demographic details, health condition, medical history and medication history

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100 patients who are prescribed with Naproxen and Tramadol Hydrochloride + Acetaminophen are grouped into A and B respectively

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GROUP A Naproxen	GROUP B Tramadol Hydrochloride + Acetaminophen

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Data collection and Oxford Knee Score was used as a study tool for studying patient demographic details and severity of pain respectively

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Severity of pain ranging from mild pain to very severe pain are assessed by Oxford Knee Score Interviewing the patient at two levels: 1) Before initiation of treatment 2) At the end of the treatment (Follow Up)

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The decrease in pain score was recorded on 14th day of follow up and pain scores were calculated. Then description statistics are used for analysis

Data collection

The notes of those patients with a diagnosis of Osteoarthritis were reviewed for the circumstances of their presentation, medical history, treatment and outcome. Specific details noted for each patient were: age at presentation, gender, all medications (with duration of treatment). Patient was reviewed for 14 days and follow up was done.

Statistical analysis

All statistical analysis was carried out with SPSS software. The Parametric patient data were analyzed statistically using paired *t*- test. A two tailed paired *t*-test was carried out to compare the drug therapy outcome before and after treatment. Data was expressed as the Mean ± SD. The efficacy data from all patients who received medication were analyzed on an intention to treat basis. The protocol violators are excluded from the protocol analysis. In addition, an end point analysis was performed on the data from all patients at their visit. A value of $p<0.05$ was considered to be significant.

RESULTS

GROUP A (NAPROXEN)

GROUP B (TRAMADOL HYDROCHLORIDE + ACETAMINOPHEN)

Demographic data for Group A & B was calculated as shown in Table 1.

Table 1: Demographic data in the treatment groups (Mean ± SD)		
Parameters	**Group A**	**Group B**
Number of Subjects	30	30
Male	11	14
Female	19	16
Age (Years)	50.37±3.728	51.70±3.640
Weight (Kg)	66.47±7.200	71.10±6.332

Oxford knee score in the two treatment groups at base line and after 1st, 2nd, and 3rd follow ups was calculated and shown in Table 2.

Table 2: Oxford knee score in the two treatment groups at base line and after 1st, 2nd and 3rd follow up (Mean ± SD).				
	Group A	Group B	Paired *t*-test *p*-Value	Significance
Base line	31.57±7.798	32.67±8.281	0.637	Not Significant
1st Follow up	33.93±7.432	30.73±8.538	0.168	Not Significant
2nd Follow up	38.13±8.063	30.90±9.571	.008	Significant
3rd Follow up	37.63±6.754	28.83±8.367	0.000276	Highly Significant

At 95% confidence interval *p* value <0.05 is considered to be significant and *p* value >0.05 is considered to be not significant.

Mean of three follow ups was compared with base line of Group A and Group B respectively. Paired T-test was calculated for two groups and the result was found to be statistically significant. When compared to Group B, Group A was found to be highly statistically significant as shown in Table 3.

Table 3: *t*-test for Baseline and means of three follow ups for both groups.			
	Base line	**Mean for three follow ups**	**Paired *t*-test *p*-Value**	**Significance**
Group A	31.57±7.798	36.23±7.137	*P*<0.05	Significant
Group B	32.67±8.281	29.87±8.869		Significant

At 95% confidence interval *p* value <0.05 is considered to be significant and *p* value >0.05 is considered to be not significant.

Age wise distribution

Out of 60 Subjects maximum no. of subjects with Osteoarthritis were in the age group of 50-55 (36) followed by age group of 45-50 (18) and the least in the age group of 40-45 (6) as shown in Table 4 & Figure 1.

Table 4: Age wise distribution.

Age(years)	Group a	Group b
40-45	4	2
45-50	10	8
50-55	16	20
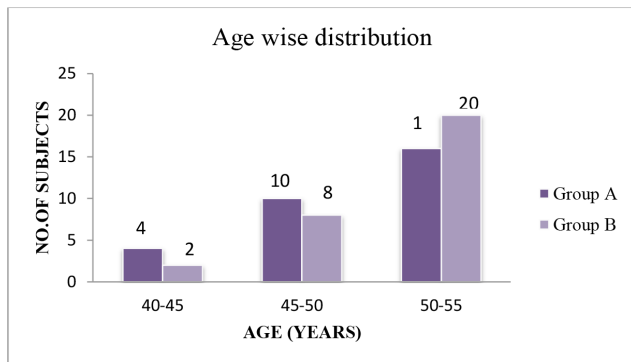
Figure 1: Age wise distribution.

Gender wise distribution

Out of 60 subjects, maximum no. of subjects with Osteoarthritis was found in females rather than males. When compared to males, females are more likely to develop Osteoarthritis shown in Table 5 & Figure 2.

Table 5: Gender wise distribution.

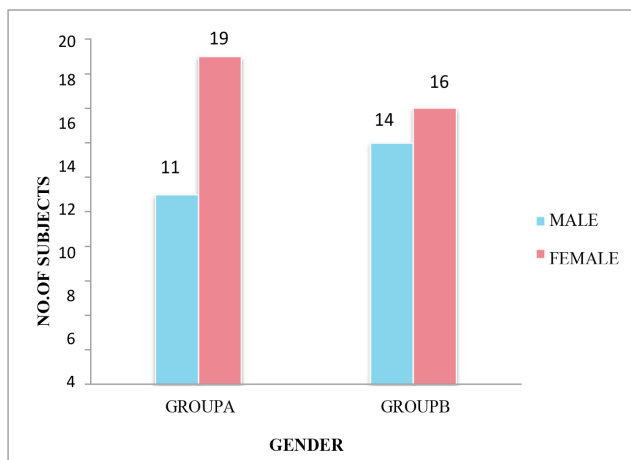| Gender	Group A	Group B
Male	11	14
Female	19	16

Figure 2: Gender wise distribution.

Occupational Status

In out of 60 subjects, more no. of house wife (22) with Osteoarthritis are reported followed by farmer (16), teacher (9), driver (5), daily labor (5) and industrialist (3) as shown in Table 6 & Figure 3.

Table 6: Occupational Status.

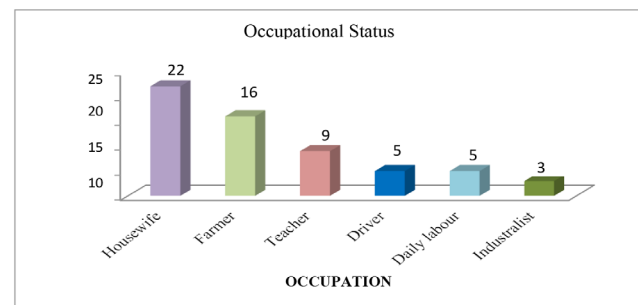| Occupation	No of Subjects
House Wife	22
Farmer	16
Teacher	9
Driver	5
Daily Labor	5
Industralist	3

Figure 3: Occupational Status.

Pre-treatment Severity

The below numerical table (Before initiation of therapy) in both groups A and B shows that the more no. of subjects with moderate severity of knee pain were reported followed by severe, mild and very severe shown in Table 7 and Figure 4.

Table 7: Pre-treatment Severity at base line.

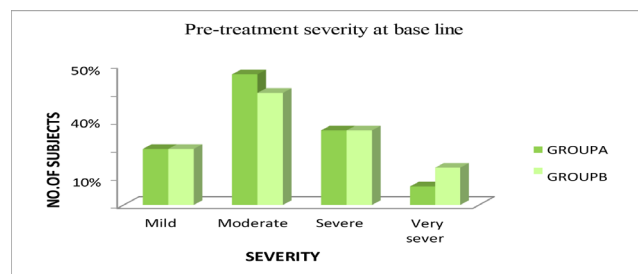| Severity	Group A	Group B
Mild (12)	6 (20%)	6 (20%)
Moderate(26)	14 (46.6%)	12 (40%)
Severe(16)	8 (26.6%)	8 (26.6%)
Very severe(6)	2 (6.60%)	4 (13.3%)

Figure 4: Pre-treatment severity at baseline.

Post treatment reduction of severity (Group A)

The below graphical representation shows, in Group A out of 6 Mild subjects 4 were relieved and 2 were not relieved, in case of 14 Moderate subjects 13 were relieved and 1 were not-relieved, in case of 8 Severe subjects 2 were relieved and 6 were not relieved and in case of 2 Very severe subjects 1 were relieved and 1 were not relieved as shown in Table 8 and Figure 5.

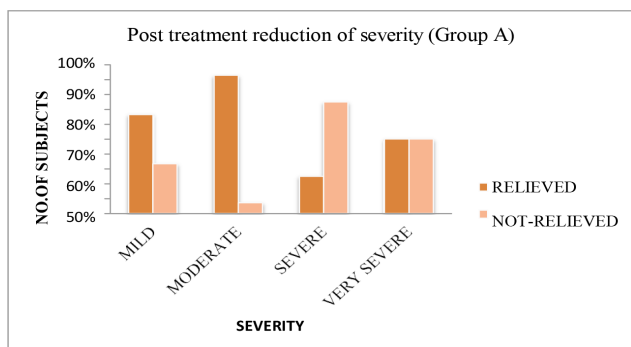|		Relieved	Not- Relieved
Table 8: Post treatment reduction of severity (Group A).			
Group A (*n*=30)	Mild (6)	4 (66.6%)	2 (33.3%)
	Moderate (14)	13 (92.8%)	1 (7.14%)
	Severe (8)	2 (25%)	6 (75%)
	Very severe (2)	1 (50%)	1 (50%)

Figure 5: Post treatment reduction of severity (Group A).

Post treatment reduction of severity (Group B)

The below graphical representation shows, in Group B out of 6 Mild subjects 4 were relieved and 2 were not-relieved, in case of 12 Moderate subjects 6 were relieved and 6 were not- relieved, in case of 8 Severe subjects 3 were relieved and 5 were not relieved and in case of 4 Very severe subjects 1 were relieved and 3 were not relieved as shown in Table 9 & Figure 6.

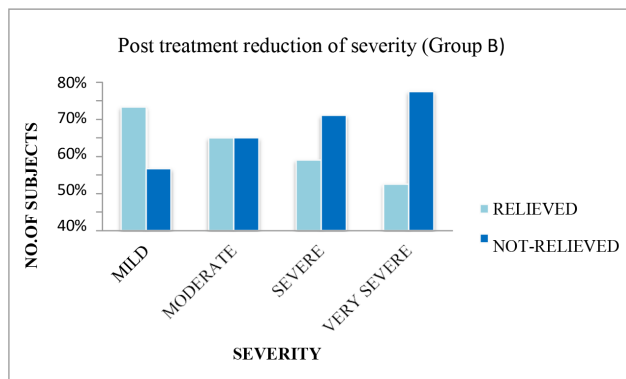|		Relieved	Not- Relieved
Table 9: Post treatment reduction of severity (Group B).			
Group B (n=30)	Mild (6)	4 (66.6%)	2 (33.3%)
	Moderate (12)	6 (50%)	6 (50%)
	Severe (8)	3 (37.5%)	5 (62.5%)
	Very severe (4)	1 (25%)	3 (75%)

Figure 6: Post treatment reduction of severity (Group B).

DISCUSSION

Naproxen and Tramadol Hydrochloride + Acetaminophen were the most widely prescribed drugs in the management of osteoarthritis of the knee. Nonsteroidal Anti-inflammatory Drugs (NSAIDs) are at the cornerstone of treatment of OA. Many professional societies suggest that use of NSAIDs or tramadol, a lower potency opioid, for primary pharmacologic management of Knee OA. NSAIDs are superior in subjects with moderate to severe pain, but the disparities between NSAIDs and acetaminophen were small in subjects with mild intensity pain. Naproxen was ranked the most effective in individual knee OA treatment for improving both pain and function.

Naproxen and Tramadol Hydrochloride + Acetaminophen were effective in Osteoarthritis knee pain relief. In present study, comparison was done to compare the effectiveness of the drugs prescribed i.e. Naproxen and Tramadol Hydrochloride + Acetaminophen. Severity of the pain in OA knee patient was assessed using Oxford Knee Score between two groups. The baseline score were recorded before the initiation of treatment, three follow ups was done for every 14 days for each patient.

Based upon inclusion and exclusion criteria, out of 100 subjects 60 subjects were included in the study and 40 subjects were excluded. Subjects who were prescribed with Naproxen are categorized as Group A and subjects who were prescribed with Tramadol hydrochloride + Acetaminophen are categorized as Group B. Mean of three follow ups was compared with base line of Group A and Group B respectively. Paired *t*-test was calculated for two groups and the result was found to be statistically significant. When compared to Group B (Tramadol Hydrochloride + Acetaminophen), Group A (Naproxen) was found to be highly statistically significant.

CONCLUSION

The incidence of Osteoarthritis is increasing in the present scenario due to modernization, Lack of exercise, Obesity. Naproxen and Tramadol Hydrochloride with Acetaminophen has anti-inflammatory properties, as tramadol hydrochloride is an opioid long term use of these medications may leads to side effects.

Naproxen is effective for moderate to severe Pain with fewer side effects when compared to Tramadol Hydrochloride with Acetaminophen up to 55 years of age. Naproxen was ranked the most effective individual knee OA treatment for improving both pain and function followed by Tramadol Hydrochloride with Acetaminophen.

Finally according to the study Naproxen 500mg twice daily is advised for moderate to severe pain.

Further research is required to investigate the use of these drugs in treating OA of the knee. Hence it is necessary to make an awareness to physicians and pharmacists, therefore clinicians should promote the rational use of these drugs in the management of OA of the knee.

Cost Effectiveness Analysis was done for both the groups and the results were found to be:

i. Using ACER it was found that the additional benefit gained by using Group A costs INR 480.3 (594.8-114.5).

ii. The incremental cost for each additional cure with Group B costs INR 1008.

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We would like to bring to light those who have helped us in completion of this work without which this work would not have reached its destination.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

OA: Osteoarthritis; **NSAIDs:** Nonsteroidal Anti-inflammatory Drugs ; **ACER:** Average Cost Effectiveness ratio.

SUMMARY

Naproxen and Tramadol Hydrochloride + Acetaminophen were the most widely prescribed drugs in the management of osteoarthritis of the knee. Non-steroidal anti-inflammatory (NSAIDs) are at the cornerstone of treatment of OA. Many professional societies suggest that use of NSAIDs or tramadol, a lower potency opioid, for primary pharmacologic management of Knee OA. NSAIDs are superior in subjects with moderate to severe pain, but the disparities between NSAIDs and acetaminophen were small in subjects with mild intensity pain. Naproxen was ranked the most effective in individual knee OA treatment for improving both pain and function.

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