Original Article

A PROSPECTIVE STUDY OF SAFETY AND EFFICACY OF ORAL ANALGESICS IN THE MANAGEMENT OF ACUTE MUSCULOSKELETAL PAIN

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ABSTRACT

Objective: Musculoskeletal pain is a significant health problem in adolescents and challenging condition for clinicians and physicians. Acute musculoskeletal pain is sudden and severe which lasts less than 12 w. This study was aimed to assess the efficacy safety of oral analgesics in the management of the condition.

Methods: A Prospective study on oral analgesics prescribed routinely for this pain was conducted among 100 patients who attended OPD, at Area Hospital, Dharmavaram. 25 patients were included in each group; group a were given tramadol 100 mgOD, group B-paracetmol 500 mgBD, Group C-ibuprofen 200 mgBD and group D-dicolfenac 50 mgBD. The severity of pain assessed by Visual Analogue Scale (VAS) and Verbal Rating Scale (VRS). The data was analysed by using SPSS-21version.

Results: Number of subjects included in the analysis 100 who were divided equally into 4 groups. The improvement in pain relief as follows-Group a given tramadol 100 mg showed pain relief of 80%VAS and 84%VRS. Group b given paracetmol 500 mgBD-40% by VAS and VRS. Group c given ibuprofen 200 mgBD showed 60% by VAS and 68% by VRS. GROUP D given diclofenac 50 mgBD showed better improvement of pain relief i. e 88% by VAS and 96% by VRS, yet the p-value is 0.001, showing difference statistically significant.

Conclusion: Among all 4 groups, Tramadol and Diclofenac showed better response (80% and 84%;88 and 96% respectively). Diclofenac is non-opioid. Hence, considering safety and improvement in pain relief in acute musculoskeletal Pain, Oral Diclofenac is preferred analgesic of choice over oral tramadol, an opioid with an adverse drug reaction profile that includes rising BP, causing seizure and addiction liability.

Keywords: Acute musculoskeletal pain, Oral analgesics, Safety, Efficacy, Visual analogue scale, Verbal rating scale

INTRODUCTION

Musculoskeletal pain is a significant health problem in adolescents mainly affecting muscles, joints, ligaments and tendons due to injuries and sprains. Recent analysis of global prevalence is estimated to be approximately 1.71 billion [1]**.** Regardless of the age, gender or economic status many adults have experienced one or more episodes of musculoskeletal pain at sometimes of their lives It affects approximately 47% of general population. Poorly controlled musculoskeletal pain can have negative impact on quality of life and cause serious financial and social problems [2]. Specific disorders of musculoskeletal system may relate to different body regions and occupational work. Recent Global Burden Disease (GBD) studies showed that low back pain was leading cause of years lived with disability in most of the countries and musculoskeletal condition has as a group in non-communicable disease (NCD)-related disability burden [3].

Musculoskeletal pain consists of acute pain or chronic pain or focal or diffused as per International Association of study of Pain [4]. It is managed by clinicians such as general practitioners, physiotherapists, chiropractors and osteopaths. Non pharmacological treatments includes self-management advice and education, exercise therapy, manual therapy and psychosocial interventions, alternative therapies (e. g. acupuncture), and pharmacological interventions such as analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroid injections) [5]. The analgesics are classified into opioid and non-opioid analgesics. Non-opioid analgesics include Non-Steroidal Anti-inflammatory Drugs (NSAIDs) and Paracetamol; They reduce inflammation and pain by reducing the activity of cyclo-oxygenase (or COX) enzymes and inhibiting prostaglandin synthesis. NSAIDs are further divided into non-selective traditional non-steroidal anti-inflammatory drugs (NSAIDs) and selective cyclooxygenase (COX)-2 inhibitors. Side effects of oral opioid tramadol include nausea, vomiting, dizziness, dry mouth, sedation, and headache. sometimes, it can cause seizures and possibly exacerbate seizures in patients with predisposing factors, respiratory depression, rise in B. P and addiction liability,

whereas in non-opioids adverse effects are lesser side effects Hypersensitivity reactions occurred Elevation of hepatic transaminases in plasma by more than three times the upper normal limit, indicating significant liver damage, CNS effects, rashes, fluid retention, edema, and renal function impairment. The drug is not recommended for children, mothers, or pregnant women increased risk of hepatotoxicity [6].

This study was conducted on acute musculoskeletal pain or injuries in the patients who attended to the Area Hospital, Dharmavaram. Among 100 patients who attended to General O. P at Area Hospital were divided into 4 equal number of groups. The patients were randomly allocated to four groups, each group consists of 25 patients and treatment was given to GROUP A given Tramadol, GROUP B given Paracetamol, GROUP C were given Ibuprofen, GROUPD were given Diclofenac for one week and the pain intensity is assessed by using (VAS) visual analogue and follow up done after one week and by (VRS) Verbal Rating Scale. The Visual Analogue Scale (VAS) measures pain intensity from: 0(no pain) to 10 (worst pain record) [7], and the Verbal Rating Scale measures the pain severity from: 0 (no pain) to 5 (worst pain) [8]. The purpose of the study is to evaluate the safety and efficacy of oral analgesic opioid Tramadol and oral non-opioid analgesics Ibuprofen, Paracetamol, Diclofenac in the patients during the study based available benefits and harms of the treatment.

MATERIALS AND METHODS

Study centre: The study was conducted at Area Hospital, Dharmavaram who attended to General O. P

Study time: This was conducted in August 2023.

Study type: This study was a Prospective study.

Sample size: The study population consisted of total number of participants n=100.

Study period: The study was done for one week and follow up taken at the end of the week.
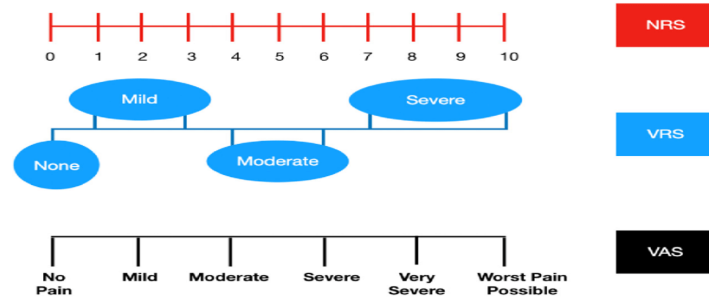
Fig. 1: Showing different scales assessing the pain severity

Methodology

After approval of the Institutional Ethics Committee (Protocol Number: 5-7-23, Dated 14/07/2023). After obtaining informed consent from the patients.

Study population and data collection

Total number of patients with age of 18-65 y of age were selected for the analysis. The relevant information's were recorded from the patient's case sheet.

Inclusion criteria

Patients had given informed consent, patients of 18-65y of age, patients who experienced pain of less than 7 d without any medication, patients who are affected with shoulder joints, elbow joints, low back pain, ligaments, tendons due to injuries and sprains for 2 w and sports injuries.

Exclusion criteria

Patients above 65 y of age, Patients who are not given informed consent, Patients with chronic musculoskeletal pain, Patients with ulcerations and perforations, Patients with severe illness of liver and kidney failure, Patients with chronic NSAIDS drug consumption, Patients with congestive heart failure, myocardial infarction, and stroke, Pregnant women, Children less than 18 y of age.

From the total population n=100 participants, the subjects were divided into divided into four equal groups randomly. The study participants were treated with Group A consists of 25 participants, were treated with oral opioid analgesic tramadol 100 mg once daily, Group B consists of 25 patients, were given oral non-opioid analgesic paracetamol 500 mg twice daily; Group C consists of 25 patients participants were given ibuprofen 200m g twice daily and Group D consists of 25 participants were given dicolfenac 50 mg twice daily. Patient s from the disease categories were assessed at baseline and at the end of the week based on the following parameters: pain intensity and pain relief. The primary efficacy parameter was reduction in pain intensity. The pain intensity was measured with a 0–10 VAS score and 0-5 VRS score (for overall pain, pain at rest, and pain on movement) for duration of period one week and follow up done at start of the week and at the end of the week by statistical analysis.

Statistical analysis

All the collected patients data were charted in MS Excel and Descriptive Statistics was applied to interpret the findings. Analysis was done using the Chi-square test using SPSS 21 version software.

RESULTS

A total number of 100(n=100) patients enrolled in the study, there are no drop outs in the study Demographic data of gender were noted in total population; there was a female preponderance in our study design i. e 60% female population and 40% male population were given below table 1 and in fig. 2.

Table 1: Gender distribution in the population in the given below table

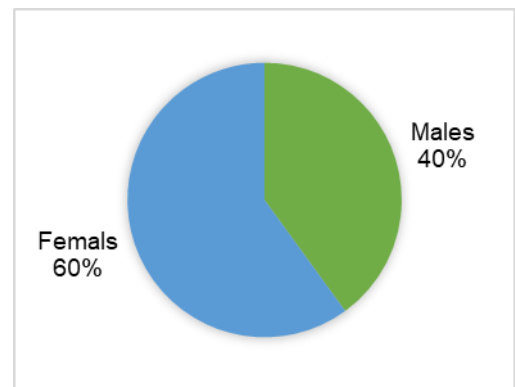| Gender distribution	Number of participants in the study (n=100)
Males	40%
Females	60%

Fig. 2: Pie depicts the gender distribution of subjects in the pie diagram given below

Demographic data of age noted from the study population of 100 patients, Few patients are in the age group of 18-28 y i.e., seven patients who have received the treatments and there are nineteen patients fell into the age group 29-38 y of age, twenty patients noticed into the age group of 39–48 y, highest number of patients were suffering with acute musculoskeletal pain were observed in the age group of 49-58 y of age i. e forty patients, and fourteen patients were noticed in the age group of 59-65 y population as shown in the tabular presentation and in the diagrammatic representation table 2 and in fig. 4, From the data given, obtained p-value is 0.999993.

Table 2: Age distribution in the population

Age distribution into four groups

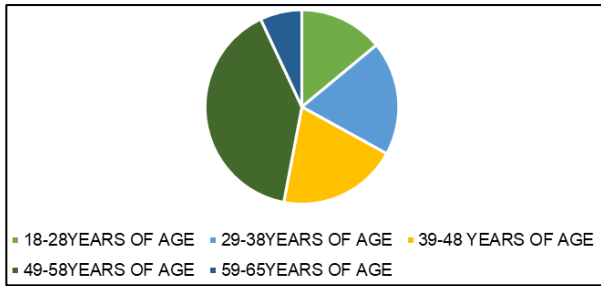| Age distribution	Group A	Group B	Group C	Group D	Rows total	P value
18-28 Y	2	2	1	2	7	0.999993
29-38 Y	5	4	5	5	19	
39-48 Y	5	5	5	5	20	
49-58 Y	10	10	10	10	40	
59-65 Y	3	4	4	3	14	
Columns total	25	25	25	25	100 (grand total)	

Fig. 3: Age distribution in the population shown in the pie diagram given below

The patients were divided into four groups, Group A, Group B, Group C and Group D given Tab tramadol 100 mg OD, Tab Paracetamol 500m g BD, Tab Ibuprofen 200 mg BD and Tab Diclofenac 50 mg BD respectively for 1 w after noting the baseline (Pre) VAS score and (pre) VRS score and later assessing the VAS score and VRS score after post medication. After taking the VAS and VRS scales at baseline.

Based on the pain intensity assessment was done by the VAS using statistical analysis. Out of 100 participants, the baseline assessment of the Group A showed participants who responded to treatment 20(16.75) [0.63] i.e 80%, and not responded to the treatment, i.e. 5 (8.25) [1.28] i. e 1.25%, Group B showed participants who responded to treatment10 (16.75) [2.72] i. e 40%and who not responded to treatment 15 (8.25) [5.52] i. e 60%, Group C showed the response with treatment in patients15(16.75) [0.18] i. e 60% and who not responded 10 (8.25)[0.37] i. e 40%, Group D showed responded 22(16.75) [1.65] i. e 88% and who not responded 3 (8.25) [3.34] i. e 0.75%, we observed the efficacy of the drugs by VAS after post medication, there is no much statistical difference in the treatment with Group B and Group C. GROUP A and Group D, both the groups showed the better efficacy in pain by reducing the pain intensity in participants, but greater efficacy showed by Group D P value obtained from VAS scores of the total population *P value of VAS is 0.00131* ☐ ²value is 15.6943*.

Data compared who are responded to medication and not responded to medication in the study participants for VAS scale were given below and the p-value were given in tabular presentation table 3 and the histogram representation of data given below in fig. 4.

Table 3: Visual analogue scale difference at the start of the week and at the end of the week

Total number of patients =100	Response shown	Not responded	Row totals
Group A tramadol	20 (16.75) [0.63]	5 (8.25) [1.28]	25
Group B paracetamol	10 (16.75) [2.72]	15 (8.25) [5.52]	25
Group C ibuprofen	15(16.75) [0.18]	10 (8.25) [0.37]	25
Group D diclofenac	22(16.75) [1.65]	3 (8.25) [3.34]	25
Column Totals	67	33	100 (Grand Total)

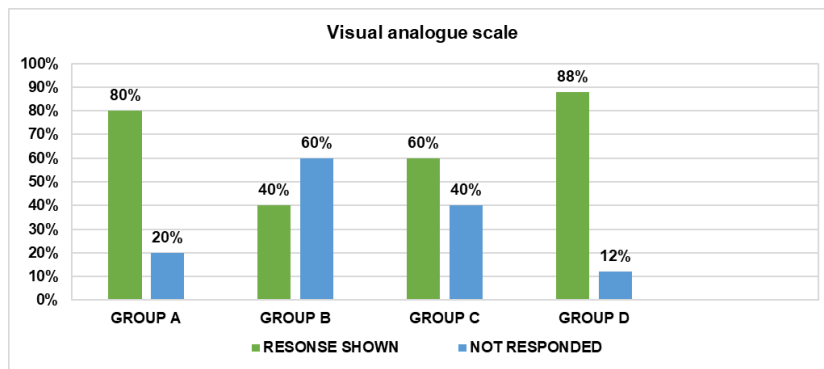The ☐² value is 15.6943 and* p value is 0.00131*

Fig. 4: Bar diagram showing vas differences responded and not responded to treatment

Based on the pain intensity assessment was done by the Verbal Rating Scale using the statistical analysis. Out of 100 participants, the baseline assessment of Group A showed responded 21 (18.00) [0.50] i. e 84% and not responded to treatment 4 (7.00) [1.29] i. e 16% and Group B responded to medication 10(18.00) [3.56] i. e 40% and not responded 15 (7.00) [9.14] i. e, 60%, Group C responded to medication17 (18.00) [0.06] i. e 68% and not responded to medication 8 (7.00) [0.14] i. e 32%., Group D we observed the efficacy of the drugs by VRS after post medication no much difference with the Groups B and C in the response with the drugs from the study. GROUP A and Group D, both the groups showed better efficacy in improving the symptoms by reducing the pain intensity in patients, showed in the statistical analysis, but Group D showed greater response than Group A showed from the data given, P value obtained from VRS scores *P value of VRS is 0.000071*☐² value value is 21.8254

Data who responded to medication and not responded to medication were given below and the p values were given in tabular presentation table 4 and histogram presentation of data given below in fig. 5.

Table 4: VRS showing difference responded and not responded to the medication at the end of the week

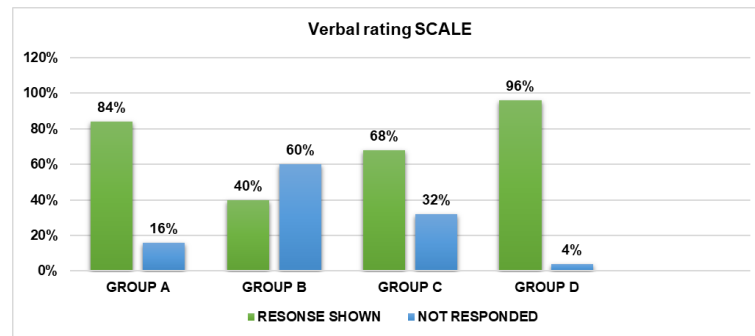| Groups	Responded	Not responded	*Row totals*
Group a tramadol	21 (18.00) [0.50]	4 (7.00) [1.29]	25
Group b paracetamol	10(18.00) [3.56]	15 (7.00) [9.14]	25
Group c ibuprofen	17 (18.00) [0.06]	8 (7.00) [0.14]	25
Group d diclofenac	24 (18.00) [2.00]	1 (7.00) [5.14]	25
Column totals	72	28	100 (Grand Total)

Fig. 5: Histogram showing verbal rating scale difference at the start of the week and at the end of the week

Table 5: Adverse effects with oral analgesics tramadol, paracetamol, ibuprofen, and diclofenac medication during the study period

Group A		Group B		Group C		Group D	
Adverse effects		Adverse effects		Adverse effects		Adverse effects	
Addiction liability	8	Stomach pain	1	Nausea, Vomiting	4	Stomach pain	5
Dizziness	2	Loss of appetite	5	Diarrhoea	5	Bloating	8
Headache	4	Tiredness	3	Constipation	8	Constipation	7
Drowsiness	8	Itching	2	Bloating	7	Diarrhoea	5
Nausea and vomiting	10			Epigastric pain	7	Dizziness	3
Constipation	9			Headache	6	Drowsiness	2
Dry mouth	5			Dizziness	11	Headache	4
Sweating	4			Skin rash	4	Itching	2
Seizures	2			Decreased appetite	10		
Raised B. P.	4						

Group A tramadol

Showed side effects with 32% addiction liability, 8% dizziness, 16% headache, drowsiness 32%, nausea and vomiting 40%, constipation 36%, dry mouth 20%, sweating 16%, seizures 4%, raised B. P 16%.

Group B paracetamol

Showed side effects as follows: stomach pain 4%, loss of appetite 20%, tiredness 12%, itching 8%

Group C ibuprofen

Showed side effects of nausea and vomiting 16%, diarrhoea 20%, constipation 32%, bloating 28%, epigastric pain 28%, headache 24%, dizziness 44%, skin rash 16%, decreased appetite 40%.

Group D diclofenac

Showed side effects stomach pain 20%, bloating 32%, constipation 28%, diarrhoea 20%, dizziness 12%, drowsiness 8%, headache 16%, itching 4% during the study period and symptomatic medication given and fewer side effects were self-resolved by participants.

P value<0.05 is significant and* P value>0.05* is NOT significant. Obtained values were *P value of VAS scale-0.00131* and *P value of VRS scale-0.000071*, hence *p value obtained<0.05* is statistically significant and χ^2 value for VAS value-15.6943 obtained and for the VRS scale χ^2 value-21.8254

DISCUSSION

Acute Musculoskeletal pain posing a major health problem. This present study was conducted at Dharmavaram, Urban health centre, Andhra pradesh to study the effectiveness of different analgesic groups in acute musculoskeletal pains like lower back pain, ligaments injuries, sports injuries, and shoulder joints pains, elbow joint pains due to injuries or sprains which affecting daily routine activities. The primary outcome of study was to reduce pain intensity based on the Scales VAS and VRS for duration of one week and follow up after one week. The results of this study indicates relatively more improvement in symptoms in oral diclofenac group D than other analgesics.

The results from our study showed that oral analgesic diclofenac treatment given at a low dose taking twice daily according to the patient's need for a maximum of 1 w, assessed by the subjects, showed effectiveness and safety in patients with mild or moderate musculoskeletal pain expressed overall satisfaction with the treatment. Almost similar satisfaction rates were registered for time to the onset of pain relief, amount and duration of pain relief, and satisfaction with the treatment tramadol 100 mg once daily expressed. These findings are not consistent in the study by us. The studies previously reported by polly. E. bijur *et al.*, the results indicate there was no difference in the efficacy of opioid and non-opioid combination analgesics or in satisfaction with analgesics for Emergency Department patients with musculoskeletal pain. They didn't detect the specified difference in change in pain,1.3 Numerous Rating Scale units, that would indicate the superiority of any treatment over another. None of the test results of efficacy or satisfaction were statistically significant [9]. In our study, there was also no much difference of opioids and non-opioids, but non-opioids are well tolerated than opioids group participants

Another study by Nikose *et al.*, treatment groups showed pain reduction and improvement in spinal function. Ibuprofen+paracetamol group showed faster and worthwhile improvement in pain relief score, which was significant. Progressive improvement in spinal mobility was seen in both groups but was slightly higher in Ibuprofen+paracetamol Group. Ibuprofen+paracetamol group showed fewer adverse events causing it more tolerable as compared to diclofenac sodium. At final assessment 70.8% of Ibuprofen+paracetamol group rated their tolerability as "VERY GOOD" as compared to 50.89% of those in diclofenac sodium group. Moreover, Ibuprofen+Paracetamol shows a trend towards superiority in its tolerability and efficacy compared to diclofenac sodium [10]. When compared to our study, we have given single dosage forms of drugs given to Group B paracetamol administrated at dosage of 500 mgBD and Group C Ibuprofen administrated at dosage of 200 mg BD doses for the patients showed less significant pain relief in patients with acute musculoskeletal pain. In a meta-analysis study by Moore *et al.*, single doses of ibuprofen 200 mg and 400 mg typically produce good pain relief in more people than paracetamol 1000 mg in almost all circumstances. The priority in acute pain, including headache and period pain, is for a high degree of pain relief, ideally delivered quickly. These are common conditions, with most people not consulting a professional,

but treating ibuprofen was shown to be consistently superior to paracetamol in a range of conditions [11]. In the similary way, based on our study groups participants, Group B oral analgesic paracetamol 500 mg BD showed lesser response than that of Group C oral analgesic Ibuprofen 200 mg BD doses given for a duration period of one week to Acute musculoskeletal pain participants in the study.

According to aronson *et al.*, other treatment alternatives for pain management also have associated risks; for example, acetaminophen is associated with liver toxicity and severe cutaneous reactions; other treatment alternatives include opioids, which could be highly addictive, for example, in a cross-sectional study of chronic pain patients, the prevalence of addiction was 14% [12]. In our study, as in Group B and C, we observed the side effects like headaches, nausea, gastric irritation common with both groups. Group D also showed the nausea gastric irritation. which are self-resolved by the patients and there were many side effects with Group A tramadol 100 mg OD dizziness, rise in b. p, seizures, addiction liability, depression.

Another study by Sy Man *et al.*, The analgesic effect of paracetamol is no different than that of NSAIDs. This finding is of great financial and clinical significance. From a health service perspective, analgesic agents are being prescribed in large quantities, which are a considerable drain on the healthcare budget. Therefore, an inexpensive, effective analgesic with fewer side effects may be welcomed by physicians and health service providers. No patient developed major side effects with NSAIDs [13]. There many conflicts in the studies previously mentioned though the paracetamol is found easily in government hospitals such as Area Hospitals, PHC centres, there is no significant pain relief in the patients who received the GROUP B Paracetamol with acute musculoskeletal pain due in local region at Dharmavaram.

According to study by Kurita GP *et al.*, Restrictive use of NSAIDs due to the decade-old debate on associated Cardiovascular risks has led to a drastic increase in opioid prescriptions drug class use, associated with diversion, abuse, overdose, and even deaths due to respiratory depression [14]. In our study design, there are minor adverse effects with GROUP B, Group C, Group D and with the Group D major adverse reactions noticed like rise in B. p, addiction liability, depression, dizziness, seizures.

Based on the previous study by Eric E. Bondar sky MD *et al.*, they did not find that an oral combination of acetaminophen ibuprofen was more effective at relieving the pain associated with acute musculoskeletal injuries in adult ED patients than either acetaminophen or ibuprofen alone [15]. Accordingly in our study design showed less response in pain-relieving participants with Group c Ibuprofen 200 mg BD.

In one of the other studies, the tolerability of tramadol in the treatment of OA found that long-term treatment with tramadol once daily was generally safe in cases of OA. Tramadol is an analgesic that has incredible use in acute pain, chronic pain, cancer pain, etc., mostly due to its dual mode of action [16]. Similarly, we observed in our study, there was the pain relieving rapidly in the patients with acute musculoskeletal pain in GROUP A individuals caused addiction liability and other side effects.

Previously, there was study by Auad A, **a**dditionally, the combination tramadol-diclofenac showed a significantly greater reduction in pain intensity and was well tolerated compared with tramadol-paracetamol, resulting in better analgesia in patients suffering from moderate to severe pain due to acute musculoskeletal conditions, at all the dose regimens, significantly (*P*<0.005) improved pain relief and was well tolerated in patients with acute inflammatory pain of moderate to severe intensity [17]. Even though we have goven single dosage of the drugs we have observed the same efficacy with the Group A and Group D.

One of study by Shukla, diclofenac provide effective and better analgesia in immediate post operative pain than tramadol. Also, tramadol needs more frequent administration [18].

In our study similar findings are present, subjects are satisified more with the treatment of oral tramadol once daily and oral diclofenac

given twice daily than the paracetamol and ibuprofen, the adverse reactions are very mild with diclofenac i. e nausea gastric irritation, which are self-resolved whereas with oral tramadol the adverse reactions like rise in Bp and addiction liability are more common and not self-resolved, and with the ibuprofen when given twice daily,60% pain relieved by visual analogue scale and 68% pain relieved by verbal rating scale. using the visual analogue scale and verbal rating scale, paracetamol has an extremely low percentage of pain relief 40% each.

Hence, we conclude that Group D Diclofenac 50 mg BD showed better effectiveness in the treatment of the acute musculoskeletal pain than that of Group A Tramadol 100 mg OD.

LIMITATIONS AND THE STRENGTHS OF THE STUDY

In our study many limitations found but major limitation of the study was sample size is very small and Duration of the study and follow up was lesser period. Hence we could not find accurate adverse drug reactions. Subjects are well tolerated with the treatment and feel stress relief due to short term course.

CONCLUSION

The aim of this study is to reduce the pain in the acute musculoskeletal pain showed that with the methods used for the treatment of acute musculoskeletal pain, among all 100 patients GROUP A, GROUP B, GROUP C, GROUP D, Oral analgesics Tramadol and Diclofenac showed better improvement in symptoms 80% by Visual Analogue Scale and 84%Verbal Rating Scale 88% Visual Analogue Scale and 96% Verbal Rating Scale respectively). oral DICLOFENAC is a non-opioid. Hence, considering safety and improvement in the pain relief in Acute musculoskeletal Pain, Oral DICLOFENAC is preferred as the analgesic of choice over oral TRAMADOL, an Opioid with Adverse drug reaction profile that includes causing a rise in BP, seizures and addiction liability

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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