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Co- Prescription analysis of Analgesics in Orthopedic department in a tertiary care hospital

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Abstract: Nonsteroidal anti-inflammatory drugs (NSAIDs) are a class of analgesics that are frequently administered in clinical practice to treat pain and inflammation. This research was done to analyze the co- prescription of analgesics in orthopedic department of a tertiary care hospital. This hospital based prospective, observational study was carried out for 6 months. The pain score was assessed using visual analogue pain scale, and the rationality of medicines was assessed using medication adherence rating scale. The details of the patients were collected in the data collection form and results were analyzed using descriptive statistics. In this study it was seen that, majority of single class of analgesic i.e., "NSAIDS" were prescribed. In this, these are majorly prescribed to females. Most frequently prescribed analgesic combination was aceclofenac + paracetamol (21.09%). In visual analogue scale, 0 to 3(mild), 4 to 7 (moderate), 8 to 10(severe), majority of the patients showed moderate pain (51.05%) before the treatment, and majority of patients showed mild pain post-treatment. This improves the quality of life of patients (52%). From total 200 patients, females are more prone to analgesics, therefore, p- value is significant to females (0.045). The pharmacoeconomic burden was analyzed; the direct cost of the RTA patients was more (Rs. 62,535), while indirect cost (Rs. 8,349) and intangible costs (Rs. 21,650). The majority of patients were taking NSAIDs. Aceclofenac + paracetamol was prescribed more as compared to other class of drugs. In our findings it was also concluded that, the rational use of the medicines was higher.

Keywords: **Analgesics, Pharmacoeconomic Burden, WHO Indicators, Visual Analogue Scale**

INTRODUCTION

Pain is associated with adverse outcomes, subjective emotional experience linked to or explained in terms of actual or potential tissue damage. It is one of the most common symptoms that prompts people to seek medical help. Acute pain, which arises as a result of inflammation or tissue damage, plays a crucial function in preventing additional injury. Chronic pain serves no beneficial purpose and instead causes severe distress and suffering for the individual as well as having a societal impact. One of the most important aspects of pain processing is sensitization. The presence of pain is hypothesized to affect the nervous systems in response to tissue injury. This adaptive mechanism is referred as neuronal plasticity. Neuronal plasticity can cause long- term alterations in pathways effective in identifying and processing nociceptive impulses, resulting in chronic pain syndromes in some cases.[1] In several clinical and epidemiological research, one of the most common causes of ADRs is analgesics. The most prevalent ADRs are indicators of gastric poisoning, such as dyspepsia and bleeding. NSAID-related GI mortality is virtually entirely due to bleeding and perforation problems, which are becoming more common as people get older.[2]

People visit orthopedic experts for variety of reasons, including bone and joint pain. Pain can affect any bone or joint, but some are more susceptible to pain and disability than others. Some causes of bone and joint pain are minor and can be managed at home, but are more significant and require immediate action from doctors.[3] The pain in the bones can appear in a variety of ways. The most typical symptoms of this pain are deep, throbbing, or blistering pain. Although there are several disorders that can cause bone pain, the following are some of the most prevalent ones – Osteoporosis, mineral deficiency, bone cancer, infection, leukemia, bone discomfort can also be caused by injuries. Bone injuries such as breaks and deep bruising are prevalent.[3] Joint pain is typically an uncomfortable pain, but it can also show as stabbing pain with certain exercises and movements. Joint pain could be a symptom of a greater problem that needs to be addressed, or it could be an indication of something more serious. The following are among the most common causes of joint pain: osteoarthritis, rheumatoid arthritis, tendonitis, bursitis, joint effusions, sprains.[3]

DRUGS USED FOR PAIN RELIEF

Most individuals use over the counter (OTC) pain drugs to address their joint pain on a symptomatic basis, often without their doctor's knowledge.[4] Pain relievers for arthritic, musculoskeletal and post-surgical pain are readily available. Analgesics or more commonly, painkillers are drugs that relieve pain in general.[5] Analgesics are the medications which relieves the pain sensation and unlike anesthesia it only alters the consciousness and that's why it is also known as painkillers. Analgesics including NSAIDS, Opioids are pain relievers, why NSAIDS being the most widely prescribed. They work by inhibiting COX-1 and COX-2 enzyme. COX-1 isoform enzyme inhibition is associated to NSAID negative effects, whereas COX-2 isoform enzyme inhibition is linked to their pharmacological qualities, such as analgesic and anti- inflammatory benefits.[6] Dermal non-steroidal anti-inflammatory medications (NSAIDs) and capsaicin are recommended as alternatives to or in combination with oral analgesics by the European League Against Rheumatism. [4]

One of the prescribing principles that promotes the sensible use of pharmaceuticals is prescriptions. It is a documented instruction from the clinician to the vendor on how to give the medicine. It acts as a conduit for communication between the doctor, dispenser, and medicine consumer regarding therapy or prophylaxes. [7]

Anticonvulsants (pregabalin and gabapentin, for example) and antidepressants (venlafaxine and duloxetine, for example) as adjunct painkillers that are shown to be useful in treating neuropathic pain.[8] Although combining opioids with other medications may enhance therapeutic intervention, some co-prescribing strategies have been implicated in the development of drug interactions and side effects. Drug-drug interactions (DDIs) are a major public health concern around the world, as they can result in unwanted side effects, lower patient quality of life, and increase hospitalization and healthcare costs. Polypharmacy is a significant risk factor for DDIs, is defined as prescribing five or more medicines on a daily basis in the literature. Polypharmacy and DDIs have long been associated with the older population. [9]

REVIEW OF LITERATURE

Pain is a prevalent chronic condition among the elderly, and it can result in decreased efficiency, despair, and a worse wellbeing. People complain less about discomfort as they get older.[10] Dermal analgesic medications are those that are administered to external areas like the skin or mucosa to treat pain.; they are either massaged on the skin or formed into patches or plasters that are put on the skin.[11] Topical analgesics are used to treat both acute (aches, acute back pain, tendonitis, muscular pains) and chronic (OA of the low back pain, knee or hand, and specific types of neuropathic pain). NSAIDs are given in the form of a spray, lotion, plaster, or gel topically to bare skin where they hurt. External NSAIDs penetrate the epidermis, reach tissues or joints, and inhibit the mechanisms that cause tissue pain. The concentrations of medicine in the bloodstream are substantially lower with local NSAIDs than with the same treatment taken orally. This minimizes the likelihood of unfavorable outcomes. [12]

OBJECTIVES

- To examine the co-prescription analysis of analgesics
- To examine the pain by visual analogue pain rating scale
- To analyze the medication adherence in patients
- To analyze the quality of life of patients
- To study the pharmacoeconomic burden of analgesics.

MATERIALS AND METHODS

The study was conducted in the orthopedic department at tertiary care hospital. To get the permission of the institutional ethical committee, the systemic protocol was followed, in which all the documents were submitted. This study was approved by institutional ethical committee.

Informed consents were obtained from all patients participating in the study.

SELECTION CRITERIA OF PATIENTS:

INCLUSION CRITERIA

Patients were selected with age of more than 18 years and also who are taking analgesics for their pain management. Patients who are taking other medications as well with analgesics were also included in this study. And also, patients who are attending Out-patient Department (OPD) and who are admitted in the In- Patient Department (IPD) were also included in this study by explaining them about the study and taking the consent of them for the same.

EXCLUSION CRITERIA

Patients who are below the age of 18 years and also who refuse to take part in the study were not included. Pregnant women and lactating mother were also excluded along with the cancer patients.

1. STUDY DESIGN AND PLACE

   This is a prospective, observational study, of a six-month duration in 2022, which was accomplished at Teerthanker Mahaveer Medical College and Research Centre, Moradabad.

2. STUDY POPULATION

   The patients receiving analgesics in the orthopedics department of the hospital.

3. SAMPLE SIZE

   Sample size technique-

   $n = z^2p(100-p)/e^2$

   $n = (1.96)^2\ 15.4(100-15.4)/5^2$

   $n = 200$

4. Questionnaire was made and was also validated. Along with questionnaire study information sheet and the consent form was also taken for the patients.

5. INTERPRETATION OF RESULTS STATISTICAL ANALYSIS

   MS- excel and the Statistical Package for Social Sciences (SPSS) 22.0 were used. A chi square test was applied to show association.

6. DATA COLLECTION

   Data collection was done using the tools used Visual Analogue Scale, Medication Adherence Rating Scale -10, Quantitative Analgesic Questionnaire, Quality of Life scale.

7. Presentation and publication of the report was done.

8. Documentation was done.

RESULT & DISCUSSION

The current investigation made a number of noteworthy observations.

Table 1 Study population criteria

S. No.	Characteristics	Mean	Standard deviation
1.	Age	40.985	2.47
2.	Weight	64.383	4.07
3.	Height	1.62	0.375
4.	BMI	24.53	1.247

Table 2 Frequency distribution according to Gender

S. No.	Gender	Frequency	Percentage
1.	Male	85	42.5%
2.	Female	115	57.5%

Table 3 Distribution according to Diagnosis

Diagnosis	Number of cases	Percentage
Rheumatic Pain	147	73.05%
RTA	33	16.05%
Spondylitis	20	10.00%

Table 4 Distribution of Study group

S. No.	Class	Number	Percentage
1.	NSAIDS	76	38.00
2.	NSAIDS+OPIOIDS	55	27.50
3.	NSAIDS+STERIODS	39	19.50
4.	NSAIDS+OPIOIDS+STERIODS	30	15.00

Table 5 Drugs used in orthopedics patients

Drugs	Number	Percentage
Aceclofenac + PCM	89	21.09%
Paracetamol	50	11.84%
Diclofenac	39	9.24%
Naproxen	11	2.60%
Etoricoxib	6	1.42%
Hydrocortisone	32	7.58%
Prednisolone	23	5.45%
Budesonides	11	2.60%
Tramadol	42	11.37%
Tapentadol	30	7.10%

Table 6 Association of study group with gender

Study Group		Gender		SD	P-value
		Male	Female		
NSAIDS	No.	31	45	11.92	0.045
	%	15.50	22.50		
NSAIDS+OPIOIDS	No.	25	30		
	%	12.50	15.00		
NSAIDS+STERIODS	No.	17	22		
	%	8.50	11.00		
NSAIDS+OPIOIDS+STERIODS	No.	12	18		
	%	6.00	9.00		

Table 7 Intensity of pain according to VAS scoring

Class	Pre- treatment		Post treatment	
	Number	%	Number	%
Mild	10	5.00	10	60.00
Moderate	103	51.05	103	39.05
Severe	87	43.05	87	0.5

Parameter	Mean	SD	P-value
Pre- treatment	125.0375 ±12.709	12.96	0.49
Post- treatment	145.7143 ±22.976	31.01	

Table 8 Assess the medication adherence according to MARs-10

S. No.	Questionnaire	Number	Percentage
1.	Forget medication?	23	11.50
2.	Careless about medication?	20	10.00
3.	Stop medication, when feel better?	10	5.00
4.	Stop medication, when feel worse?	12	6.00
5.	Take medication only when sick?	32	16.00
6.	Unnatural for mind & body?	8	4.00
7.	Thoughts clear about medication?	40	20.00
8.	Can prevent getting sick?	4	2.00

9.	Feel weird	15	7.50
10.	Feel tired & sluggish	36	18.00

Table 9 Pharmacoeconomics burden for orthopaedic patients

Table – 9.1

Cost	Rheumatic Pain	RTA	Spondylitis
Number of preventable cases	147	33	20
Cost of intervention	1,08,927	62,535	14,820
Avoided expenditure on illness	11,760	8,349	1,600
Prophylaxis per avoided case	00	21,650	00

Table – 9.2

Cost effectiveness ratio

Case/Drug	Cost	Survival	Ratio
Rheumatic Pain	1,20,687	145	832.32
RTA	92,534	30	3084.46
Spondylitis	16,420	19	864.21

Table 10 Assessment of patient QOL

Class	Pre-treatment		Post- treatment	
	Number	Frequency	Number	Frequency
Worst	150	75.00	150	3.00
Better	48	24.00	48	45.00
Best	2	1.00	2	52.00

Parameter	Mean	SD	P-value
Pre- treatment	130 ±13.665	15.81	0.026
Post- treatment	146.8 ±20.454	33.00	

1. BMI

High BMI (>27 kg/m2) was associated with an increased risk of discomfort, most notably amongst elders with osteoarthritis. The relationship between BMI and pain differed according to the MSD (musculoskeletal disorders), with a stronger relationship in the osteoarthritis group and a less obvious relationship in the back and low back pain groups.[13] In current study a positive correlation was established between BMI and increased risk of pain in Rheumatic pain, RTA and Spondylitis. The data was significant with (SD – 1.247).

2. DIAGNOSTIC CONDITIONS

Fractures are among the biggest prominent orthopedic concerns in India, with 6.8 million people getting care. Fractures are one of the most prominent reasons for prescribing diclofenac.[13] In this study it was concluded that majority of the patients were of Rheumatic pain (73.05%) while other conditions were RTA (16%) and Spondylitis (10%).

3. INDICATION

NSAIDS accounted for 157 (53.77%), combination analgesics (nonopioid and NSAIDS) for 132 (45.20%), and centrally acting synthetic opioid analgesics, such as tramadol, for 1.03% of the 292 analgesics.[13] In this study, the preponderance of analgesic users was prescribed a single type of analgesic drug i.e., NSAIDS, followed by NSAIDS + OPIOIDS, NSAIDS + STEROIDS and then NSAIDS + OPIOIDS + STEROIDS. Aceclofenac and Paracetamol co-prescriptions were most usually prescribed to 21.09% of patients. Non-opioid analgesics (e.g., paracetamol and NSAIDs) and opioid analgesics are frequently used to treat CNMP (Chronic non-malignant pain).

Analgesics are used by two-thirds of patients with CNMP, according to a recent European survey.[14] Prescription opiates were associated with more than one-third of fatal opioid-related fatalities in 2017–2018, while more than 40% of nonfatal overdose victims had previously obtained an opioid prescription.[13] Whereas, in our study we concluded that tramadol is highly prescribed opioid analgesic (11.37%) followed by tapentadol (7.10%) in the previous six months.

Narcotic Analgesics are taken at medical doses to relieve pain and induce sleep. Increased doses of this analgesic medicine can cause unconsciousness, convulsions, and death.[15] Throughout the 12-month period, treatment with opioids versus nonopioid drugs failed to demonstrate substantially improved results in pain-related function in people with persistent back pain or hip or knee OA pain. Gabapentin and Pregabalin are being authorized by the FDA for the management of neuropathic pain.[16]

4. PHARMACOECONOMIC BURDEN

Naproxen and ibuprofen-containing treatments are far more effective and cost-effective than opioids, celecoxib, or SOC in individuals with multiple comorbidities. The economic cost of injury is substantial, implying that there is significant potential for cost reductions through injury prevention. To further prioritize investing in injury prevention, there is a requirement of consistent approach to economic evaluation of injury. The cost of injury varied greatly, with mean expenses ranging from $14 to $17 400 USD. In terms of injury-prevention strategies, the cost per disability adjusted life year prevented varies from US$10.90 for speed bump installation to US$17 000 for driving while intoxicated and breath testing programs in Africa.[17] In our study after economic evaluation was done, in RTA direct costs (Rs. 62,535), while indirect cost (Rs. 8,349) and intangible cost is (Rs. 21,650). RTA patients' costs per prescription (Rs. 3084.46). Mean expenses (without therapy) for the infliximab group are expected to be pound 17,240, a saving of 31%. As a result, some of the treatment cost was offset by other resource savings (pound 7888), leaving an incremental cost of pound 6214. For the first year of treatment, the cost per QALY gained is £35,400. When treatment is expected to last the entire two years, the cost per QALY is pound 32,800. The cost per QALY is reduced to pound 17,300 when infliximab infusions are administered every 8 weeks rather than every 6 weeks. The long-term model estimates the cost per QALY at £9600. After economic evaluation was done, it was observed the direct cost for patients with Spondylitis (Rs. 14,820), while indirect costs are (Rs. 1600) with no intangible costs. Spondylitis's patient's costs per prescription is (Rs. 864.21). Infliximab treatment for one year in individuals with long-standing aggressive arthritis demonstrated a satisfactory therapeutic impact but dramatically increased medical expenses. Work disability costs did not reduce significantly. Employing infliximab in the early phases of chronic arthritis may avoid job impairment in the long run, lowering the total cost to society. The average cost of hospital hospitalizations to the rheumatology department for causes other than infliximab infusions increased from €2332 to €4751.[18,19] When compared to other biological medicines, the cost of Rituximab (50.4) was high. The cost of NSAIDs is around 2.36 percent of the overall medicine cost for the month. In this study patients of Rheumatic Pain per prescription costs (Rs.832.32), with direct cost (Rs. 1,08,927), indirect cost (Rs. 11,760) with no intangible costs.

5. QUALITY OF LIFE ASSESSMENT

Visual Analogue Pain Scale is used for measuring the intensity of pain. The intensity is measured from 0 to 10 range. In our study we divided these ranges in three categories i.e., mild, moderate, severe. We found that before medication, the majority of patients had moderate pain (51.05%), whereas after treatment, the majority of patients had mild pain (60.00%). This shows that p – value is non-significant to post –treatment (0.49). During the pain patients' quality of life suffers. In this study it shows that before the treatment patients have worst quality of life (75.00%) and after the treatment patients have best quality of life (52.00%). This implies that p- value is significant to post – treatment.

When implemented in conjunction with suitable acquisition regulations and robust prescribing practices, the essential medicines list has been found to increase the quality and cost-effectiveness of healthcare provision. Prescriptions from the nationwide essential medications list or plan for the style of hospital being assessed are used to assess how well processes comply to a national drug policy.[11] In this study it was seen that Paracetamol, Hydrocortisone, Prednisolone, Budesonide prescribed to the patients was according to the

World Health Organization indicators, whereas, Aceclofenac, Diclofenac and Tramadol was prescribed according to the Essential Drug List.

The MARS is a self-reporting multidimensional questionnaire with ten items that describe three aspects: medication adherence behavior (items 1-4), attitude about taking medication (items 5-8), and unpleasant side effects and attitudes regarding analgesic medication (items 9-10). Medication adherence behavior determines the frequency and duration of medicine use during therapy. In our study it was seen that 11.50% patients forget to take their medications. 20% patients said that their thoughts are clearer about medications and 16% patients said that they take medications only when they feel sick. And 18% patients report fatigue. QAQ analysis was done to check the adherence in patients attending the orthopedic department and it was observed that 69.05% patients were adhere to the patients, while, only 30.05% were non- adhere.

CONCLUSION

This study demonstrated that the patients who are attending the orthopedic department at a tertiary care hospital for management of different bone conditions have been treated with single class of analgesics (NSAIDS) more as compared to others. Aceclofenac + Paracetamol in combination have been prescribed more as compared to other drugs. The majority of the patients were females, who had visited the orthopedic department the most. Majority of the patients have moderate pain before the treatment but after taking medications majority of the patients have mild pain. In our findings it was also concluded that, the rational use of the medicines was higher. In case of quality of life, it was seen that majority of patients' quality of life has improved after treatment. Pharmacoeconomic burden of the patients with RTA was more as compared to rheumatic pain and spondylitis patients.

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