ORIGINAL ARTICLE

Pain Management in the Medical Specialty Clinics of a University Teaching Hospital: A Drug Utilization Study

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ABSTRACT

Background: The treatment of pain is largely determined by understanding the type of pain. A thorough understanding of analgesic prescriptions in specialized clinics may reflect the physicians' ability to effectively manage pain. This study aimed to investigate physicians' prescription pattern of analgesics and co-analgesics in a multispecialty internal medicine out-patient department.

Methods: This was a retrospective evaluation of dispensed medications containing analgesics and/or co-analgesics generated from the various specialized clinics of the Medical Out-Patient Department (MOPD) of the University of Benin Teaching Hospital from January 2021 to December 2021. These medications were classified according to the World Health Organization -Anatomic Therapeutic Chemical (WHO-ATC) classification system and evaluated using the WHO analgesic ladder and the guidelines for pain management in Nigeria. Data is presented descriptively.

Results: A total of 25837 medicines were dispensed during the period. Of which, 2311 (8.9%) were analgesics and co-analgesics. The mean age (SD) of patients issued these medicines was 63.6 (±13.8) years with majority aged 60 and above, 1592 (68.9%). Co-analgesics were the most dispensed medicines 1346 (58.2%) followed by non-opioids 705 (30.5%). Most NSAIDs dispensed were naproxen 112 (4.8%) while codeine was the most dispensed opioid 225 (9.7%). Majority of the non-opioid and co-analgesic prescriptions 742 (36.1%) were generated from the Neurology Clinic, while opioids were largely from Nephrology and Endocrinology Clinics 48 (18.5%).

Conclusion: The medical specialty clinics prescription pattern of analgesics suggests a rational approach to pain management. There is however a need to address the low utilization of opioid analgesics in pain management.

Keywords: Analgesics; Internal Medicine; Opioids; Pain management; Prescription drugs; Nigeria.

INTRODUCTION

The International Society for the Study of Pain defined pain as "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage or described in terms of such damage". [1] Pain is thus a subjective feeling which is usually distressing and reflects patients' experiences. In addition, it has a sensory, emotional and psychological component. The 3 main categories of chronic pain: nociceptive, nociplastic and neuropathic pain, and the knowledge of the type of pain determines to a large extent the treatment strategies.[1,2]

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Pain is a major contributor to the global burden of disease as musculoskeletal conditions typically characterized by pain is a major cause of disability. Over 1.71 billion people globally have musculoskeletal conditions worldwide.[3] There are also indirect costs attributable to the musculoskeletal conditions due to costs of medication, physical rehabilitation, as well as need for psychotherapy due to increased mental health issues.[3,4] The prevalence of pain ranged between18.1% to 28.2% in sub-Saharan Africa[5] and from 32.5%-73.5% in various Nigerian populations from a systematic review of low back pain prevalence, a commonly reported complaint in Nigeria. [6] Patients attending internal medicine clinics often have complex medical presentations, and multimorbidities[7] and pain presenting as headaches, back pain and osteoarthritis are among the commonest reasons for a medical consultation in the US.[8] Rheumatic disorders are also common in Africa with implications on

multimorbidity.[9] The contribution of chronic pain to existing chronic conditions such as hypertension, diabetes mellitus, stroke, attendant complications such as neuropathic pain from diabetes mellitus, osteoarthritis and other forms arthritis is mostly underestimated.[2] These have been shown to be associated with increased frailty, poorer quality of life and generally have poor outcomes. [2]

Multimodal management of pain including rational use of analgesics is advocated in routine ambulatory care in the Nigerian pain management guidelines,[10] which was patterned after the WHO analgesic ladder. It encourages a stepwise approach to pain management while considering the severity of the pain, non-opioids, opioids and co-analgesics including antidepressants, anticonvulsants) are useful in the management of nociceptive, nociclastic and neuropathic pain.[2,10] It has however been shown that many trainee physicians perceive that they lack the required depth for adequate pain management.[11] Again, studies have shown that opioid consumption is low in Nigeria, and in Africa as a whole. [12]

The literature regarding the prescription profile and utilization of analgesic medicines in Nigerian internal medicine settings is limited. Evaluating physicians' ability to manage pain effectively requires a thorough understanding of analgesic prescription patterns in outpatient clinics. The study therefore sought to determine the prescription pattern of analgesics and co-analgesics in a multispecialty internal medicine out-patient department.

METHODOLOGY

The prescription data of analgesics prescribed at the Internal Medicine Consultants' Out-Patient Department (MOPD) of the University of Benin Teaching Hospital (UBTH) from January 2021 to December 2021 was obtained. The MOPD houses the major specialties in Internal Medicine, namely: Cardiology, Clinical Pharmacology, Therapeutics and Toxicology, Gastroenterology, Nephrology, Endocrinology and Metabolic medicine, Neurology, Rheumatology, Dermatology and Pulmonology. All specialties also offer general internal medicine coverage. The MOPD served approximately 22,000 patients in 2021. All clinics are run weekly and the MOPD Pharmacy keeps a record of all dispensed medications.

Data source: The MOPD pharmacy dispensing records was utilized in this study. This record contains information on all medicines prescribed to patients who attended any of the previously mentioned specialty clinics at the MOPD, and filled their prescription at the MOPD pharmacy. In this dispensing record, medicines are entered as single entities and for each registered medicine, details of the medicine-name, formulation, frequency of administration and duration of use are documented. Furthermore, the age, sex, documented diagnosis of the patient, and clinic attended are inputted as well.

Only adult patients (aged 18 years and above) who were prescribed analgesics and whose dispensing medications were found in the MOPD pharmacy during the period were included in the study. The analgesics studied were based on the analgesics in the guideline for the management of pain in Nigeria, and it included: Non-opioids analgesics, Opioids, and Co-analgesics or Adjuvants. [10]

Specifically, analgesics belonging to the following Anatomical Therapeutic Chemical Classification system (ATC) classes Level V were therefore included:

Non-opioids analgesics included in the study, had the following ATC codes/ names: Paracetamol (N02BE01).

Non-steroidal Anti-inflammatory Drugs (NSAIDs) - this includes both the non-selective cyclo-oxygenase (COX) inhibitors and selective COX2 inhibitors.

M01AB16 Aceclofenac; M01AB01 Indomethacin; M01AB05, M01AB55 Diclofenac; M01AB15 Ketorolac; M01AC02 Piroxicam; M01AE01 Ibuprofen; M01AE02, M01AE52 Naproxen; M01AE03 Ketoprofen; M01AH01 Celecoxib; M01AX05, M01AX25 Glucosamine/Chondroitin Sulphate; M02A Topical products for joint and muscular pain. [13]

Opioid analgesics included in the study, had the following ATC codes/names:

N02AA01 Morphine; N02AA05 Oxycodone; N02AA08, N02AA58 Dihydrocodeine; N02AA59 Codeine, combinations excluding psycholeptics; N02AB02 Pethidine; N02AB03 Fentanyl; N02AAD01 Pentazocine; N02AJ Opioids in combination with non-opioids analgesics-N02AJ06 Paracetamol with codeine; N02AJ15 Tramadol with other non-opioid analgesic and N02AX02 Tramadol.

Co-analgesics/Adjuvants included in the study also had the following WHO-ATC codes:

Gabapentinoids - N02BF01 Gabapentin; N02BF02 Pregabalin;

Muscle relaxants combined with NSAIDs/analgesics – M03BB53 Chlorzoxaxone combination excluding pyscholeptics; M03BC51 Orphenadrine citrate combinations.

Excluded from the study were corticosteroids, other muscle relaxants, drugs used in gout, bisphosphonates, and antidepressants which

may likely have other indications in a multispecialty clinic.

Information obtained for each drug included, drug name (generic names of all available analgesics dispensed during the period was obtained from the hospital pharmacy index where brand names were used). Also included were dose, frequency, formulation and duration of use of analgesics and co-analgesics.

Data analysis: The medications were classified into Non-opioids, Opioids and Co-analgesics (adjuvants) as described in the WHO analgesic ladder. They were also classified using the WHO-ATC level 5. The defined daily dose (DDD) of each drug which is defined as the assumed average maintenance dose per day for the main indication in adult patients for each drug was obtained from the WHO-ATC index.[13] The same DDD is often assigned for various dosage forms. Fixed dose combinations products DDD are counted and expressed as one daily dose irrespective of the number of active medications contained in the combination. However, some combined products are assigned the DDD for the main active ingredients. Topical products are not commonly assigned a DDD. The data are presented using means and frequencies. The median prescribed daily dose (PDD) of each drug was calculated and compared with the DDD for each drug. Categorical data was analyzed using chi-square, continuous variables with t-test, analysis of variance (ANOVA) and Tukey post hoc analysis conducted. Statistical significance accepted as $p < 0.05$.

Ethical approval (ADM/EE/A/VOL. VII/148311 669) was obtained from the UBTH Ethics and Research Committee.

RESULTS

A total of 25837 prescribed medicines were dispensed during the period, of which 2311 (8.9%) were eligible prescription of analgesics and co-analgesics. The analgesics were dispensed more to females than males 1622 (70.2%). The mean age (SD) was 63.6 (13.8) years ranging from 18-102 years and majority of the patients were aged 60 and above 1592(68.9%). Hypertension was the most prevalent disease condition noticed in the dispensing records 817(35.4%) and Co-analgesics were the most prescribed medicines 1346(58.2%), (Table 1).

The most prescribed non-opioid was paracetamol 213(9.2%) and the most prescribed NSAID was Naproxen (either as a single agent or in combination with esomeprazole) 112(4.8%), and according to the ATC classification, codeine and paracetamol combination was the most prescribed opioid 225(9.7%). A high proportion were fixed dose combination medicines 1127(48.7%), and this included naproxen with esomeprazole, codeine with paracetamol. Table 2. The gabapentinoids were the most prescribed co-analgesic agents in the study with pregabalin alone or in combination with methylcobalamin-829(35.9%), Table 3.

Comparing the DDD with the average prescribed daily dose (PDD), majority of the drugs were prescribed in doses less than the average maintenance dose (DDD) for pain relief. Non-opioids were prescribed for short durations (median duration of 7 days) and opioids were prescribed to the oldest age group 61 and above (64.5%).

Table 1: Characteristics of prescribed analgesics in the internal medicine clinic of a Teaching Hospital in Southern Nigeria

Characteristic	n (%)
Sex	
Male	689 (29.8)
Female	1622 (70.2)
Age group	
18-39	141 (6.1)
40-59	578 (25.0)
60-102	1592 (68.9)
Proportion of prescription from various Specialty clinics	
Neurology	786 (34.0)
Endocrinology	502 (21.7)
Cardiology	421(18.2)
Pulmonology	173 (7.5)
Nephrology	145 (6.3)
Clinical Pharmacology and Therapeutics	143 (6.2)
Gastroenterology	73 (3.2)
Rheumatology	55 (2.4)
Dermatology	13 (0.6)
Type of analgesic group prescribed	
Non-opioids	705 (30.5)
Opioids	260 (11.3)
Co-analgesics	1346 (58.2)

n=2311

Table 2: Classes of prescribed analgesics in the Internal Medicine clinics (MOPD) of a Teaching Hospital in Southern Nigeria

	Frequency	ATC Code	DDD (g)	PDD (g)	Duration (days)
Non-opioids					
Paracetamol	213 (9.2)	N02BE01	3	3	3
NSAIDS					
Naproxen/Esomeprazole	72 (3.1)	M01AE52	0.5	1	12
Naproxen	40 (1.7)	M01AE02	0.5	1	10
Celecoxib	69 (3.0)	M01AH01	0.2	0.2	7
Diclofenac potassium	39 (1.7)	M01AB05	0.1	0.2	5
Diclofenac /Misoprostol	14 (1.4)	M01AB55	0.1	0.15	14
Diclofenac sodium	4 (0.2)	M01AB05	0.1	0.075	5
Diclofenac sodium/Vitamin B1/B6/B12	2 (0.1)	M01AB55	0.1	0.1	26
Diclofenac sodium/ Cholestyramine	1 (0.04)	M01AB55	0.1	0.075	10
Ibuprofen	38 (1.7)	M01AE01	1.2	0.8	5
Aceclofenac	16 (0.7)	M01AB16	0.2	0.2	10
Aceclofenac/paracetamol	3 (0.1)	N02BE51	-	1	7
Indometacin	2 (0.1)	M01AB01	0.1	0.06	18
Glucosamine/Chondroitin	15 (0.6)	M01AX(05/25)	1.5	0.5	21
Topical agents					
Diclofenac gel	167 (7.2)	M02AA15	-	-	14
Methyl salicylate ointment	7 (0.3)	M02AC	-	-	14
Ketoprofen gel	1 (0.04)	M02AA10	-	-	14
Diclofenac/Methylsalicylate ointment	1 (0.04)	M02AA15	-	-	30
Opioids					
Codeine and Paracetamol (8mg/500mg)	200 (8.6)	N02AJ06	-	-	10
Codeine and Paracetamol (30mg/500mg)	25 (1.1)	N02AJ06	3	2	10
Tramadol capsule	21 (1.0)	N02AX02	0.3	0.05	10
Dihydrocodeine tablet 30mg	12 (0.5)	N02AA08	0.15	0.06	8.50
Pentazocine injection	1 (0.04)	N02AD01	0.2	0.03	1
Tramadol hydrochloride injection	1 (0.04)	N02AX02	0.3	0.05	3

ATC- WHO-Anatomical Therapeutic Chemical Classification, PDD-Prescribed daily dose, DDD- Defined Daily Dose

The duration of treatment of the co-analgesics were statistically significantly different from the non-opioids and opioids (Anova=723.4, p<0.001) and on Tukey post hoc analysis, the co-analgesics were significantly different from the others. (p=<0.001). Also, neurology and endocrinology clinics prescribed the highest proportion of co-analgesics in this study, 900/1346(76.8%) Table 4.

DISCUSSION

In this study of analgesic and co-analgesic use in the internal medicine clinics, co-analgesics were the most prescribed group of medicines. Among the non-opioids paracetamol was the most prescribed followed by naproxen. There were however few prescriptions of opioids in the study, with and paracetamol/codeine been the most prescribed. Majority of the patients' prescribed analgesics were older than 60 years of age and largely females. Non-opioids were prescribed for short periods in and notable was the near absence of injections in this study,

Paracetamol was extensively prescribed in this study, consistent with findings from other global studies where it remains a predominant choice for analgesia. [14] Its widespread use can be attributed to factors such as affordability and accessibility, coupled with its proven efficacy across various conditions including low back pain. Given that many patients at internal medicine clinics have co-existing medical conditions that contraindicate NSAID use, paracetamol emerges as a preferred alternative. Furthermore, the study highlighted a prevalent use of paracetamol combinations, emphasizing the importance of clear patient information to mitigate the risk of medication errors.

The majority of the study population were elderly individuals, this is not unexpected as chronic pain tend to increase with aging, increased occurrence of degenerative bone diseases and other chronic conditions such as diabetic neuropathy in the elderly.[15]

Table 3: Co-analgesic medications prescribed at the Internal medicine clinics of a Teaching Hospital in Southern Nigeria

Co-analgesics (Other Analgesic)	Frequency (n=2311) n (%)	ATC Code	DDD (g)	PDD (g)	Duration (days)
Pregabalin	392 (17.0)	N02BF02	0.3	0.075	42
Pregabalin/Methylcobalamin	437 (18.9)	N02BF02	0.3	0.075	56
Gabapentin	161 (7.0)	N02BF01	1.8	0.3	42
Gabapentin/Nortriptyline	144 (6.2)	N02BF01	1.8	0.4	84
Gabapentin/Methylcobalamin	206 (8.9)	N02BF01	1.8	0.3	49
Paracetamol/Orphenadrine	6 (0.6)	M03BC51	-	3	3
Chlorzoxazone/Paracetamol/ Aceclofenac	1 (0.1)	M03BB53	-	1	3

ATC- WHO-Anatomical Therapeutic Chemical Classification, PDD- Prescribed daily dose, DDD-Defined Daily Dose

Table 4: Association between analgesic groups and demographic characteristics of analgesic prescriptions at the MOPD of a Teaching Hospital in Southern Nigeria

	Non-opioids n-705	Opioids n-260	Co-Analgesics n-1346	Test /p-value
Median duration (days)	7	10	56	Anova=723.4, p<0.001
Sex				
Male (%)	193 (27.4)	70 (26.9)	426 (31.6)	X^2=5.21, p=0.07
Female (%)	512 (72.6)	190 (73.1)	920 (68.4)	
Age group				
18-39	71 (10.1)	17 (6.5)	53 (3.9)	X^2=34.2 p<0.001
40-59	179 (25.4)	53 (20.4)	346 (25.7)	
60-103	455 (64.5)	190 (73.1)	947 (70.4)	
Specialty Clinics				
Neurology	202 (28.7)	44 (16.9)	540 (40.1)	X^2=382.2, p<0.001
Endocrinology	94 (13.3)	48 (18.5)	360 (36.7)	
Cardiology	150 (21.3)	38 (14.6)	233 (17.3)	
Pulmonology	114 (16.2)	6 (2.3)	53 (3.9)	
Nephrology	53 (7.5)	48 (18.5)	44 (3.3)	
Clinical Pharmacology and Therapeutics	32 (4.5)	38 (14.6)	73 (5.4)	
Gastroenterology	34 (4.8)	23 (8.8)	16 (1.2)	
Rheumatology	21 (3.0)	15 (5.8)	19 (1.4)	
Dermatology	5 (0.7)	0 (0.0)	8 (0.6)	

Pain is also a common complaint in the elderly as observed in a study, pain significantly impacts the activities of daily living in elderly patient, and therefore use of analgesics may be more in this subgroup. Another study had also shown that multi-morbidities are very common in the elderly in this setting, mainly cerebrovascular accidents, hypertensive disorders and diabetes mellitus being the commonest.[16]

Elderly patients received more opioids in this study in contrast to what subsisted in a German study where dipyrone was the commonest analgesic prescribed to the elderly.[17] This suggests that elderly patients in this cohort likely presented with moderate to severe pain necessitating opioid therapy. However, the doses of opioids prescribed were generally below the expected average maintenance levels. Factors influencing these prescriptions include physician discretion and patient-specific considerations, highlighting the necessity for a critical evaluation of opioid dosing practices. Concerns regarding misuse and dependence may contribute to the conservative opioid prescribing observed. Additionally, opioids were identified as the most commonly prescribed class of medications in another study involving elderly patients.[18]

Younger patients were more likely to receive non-opioids potentially due to the lower risk of gastrointestinal adverse effects associated NSAIDs, they also may have fewer morbidities, as such the risks associated with worsening cardiovascular is reduced. Naproxen emerged as the most prescribed NSAID in this study, likely influenced by studies demonstrating its lower

risk for cardiovascular events, compared with other NSAIDs.[19] However, a meta-analysis has also shown that all NSAIDs, naproxen inclusive are associated with an increased risk of myocardial infarction.[20] Naproxen was also the most prescribed in a Colombian study.[21] Conversely, some studies have reported diclofenac as the most commonly prescribed NSAID. [14,22]

Evaluating analgesic prescriptions pattern in any clinical setting provides insight into the alignment between physicians' assessment of pain presentation, adherence to pain severity guidelines, medication knowledge, and drug availability.[1] The predominance of co-analgesics prescribed in this study suggests a significant prevalence of neuropathic pain among patients. It is noteworthy the neurology and endocrinology clinics contributed over 70% of co-analgesic prescriptions reflecting an increasing recognition of this condition in chronic care settings. The observed proportion of co-analgesic prescriptions warrants further research into the underlying morbidities and medication tolerability, particularly in light of concerns regarding potential abuse and misuse.[23] In contrast, a separate study in general practice reported a lower utilization rate of gabapentinoids.[24]

A notable finding in this study was the frequent use of fixed-dose combination products, despite recommendations against their use due to increased medication costs.[25] However, these combinations were specifically prescribed to enhance therapeutic effectiveness in managing pain and reduce the pill burden on patients with multiple underlying health conditions. Adherence to Nigeria's drug policy requirements is crucial for maintaining essential medications within the community and fostering trust in the healthcare system. On a positive note, injections were infrequently prescribed in this study, highlighting the contributions of previous advocacy for rational medicine use in specialty clinics.

Limitations: The dispensing records lacked detailed consultation encounter information, preventing access to the clinical impressions that guided the prescriptions. Furthermore, the study did not identify patients who received two or more analgesics simultaneously.

Conclusion: The medical specialty clinics prescription pattern of analgesic suggests a rational approach to pain management with the different classes of drug. However, there is still a low utilization of opioids compared to other medications, and a high proportion of fixed dose combination products prescribing. Furthermore, the gabapentinoids are increasingly being used for possible neuropathic pain in the specialty clinics. These calls for increased advocacy into ensuring rational prescriptions as

well as indicate the need for more research into factors limiting opioid use in outpatient departments, as well as rationality in the use of gabapentinoids.

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