

PRESCRIBING PATTERN OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS AT THE OUTPATIENT PHARMACY DEPARTMENT OF A UNIVERSITY TEACHING HOSPITAL IN NIGERIA

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DOI: <http://dx.doi.org/10.4314/gmj.v49i1.5>

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Conflict of Interest: None declared

SUMMARY

Background: Non-steroidal Anti-inflammatory Drugs (NSAID), are among the most widely used and misused of all drugs. Though they provide symptomatic relief from pain and swelling in chronic joint diseases, they may cause renal impairment, especially in combination with other nephrotoxic agents.

Objectives: This study aimed to investigate the prescription pattern of NSAID in the Out-patient Pharmacy Department of Lagos University Teaching Hospital (LUTH), Nigeria.

Design: A total of 3800 prescriptions containing NSAIDs were analyzed for information on drug name, the number of NSAIDs per prescription, the presence of ACE inhibitors and diuretics alongside NSAIDs and NSAIDs prescribed in generic or brand names.

Results: The results showed that Aspirin was the most frequently prescribed NSAID (62.2%) and 68.4% of the NSAIDs prescriptions studied were written in generic names. The total number of drugs per prescription was in most cases 3 or greater (84.6%). There were statistically significant ($p \leq 0.05$) associations between the individual NSAID prescribed and whether they were prescribed in generics or brand names; individual NSAID prescribed and the frequency of co-prescription with an ACE inhibitor and a diuretic; types of NSAID prescribed and the cost in Naira.

Conclusion: Though most of the prescribers complied with WHO standard in their prescriptions *vis a vis* generic prescription, avoidance of polypharmacy and avoidance of drug interactions and contraindications, there is obvious need for interventional measures or strategies to improve rational prescribing for some of the prescribers tailored towards rational prescription and use of drugs

Keywords: NSAID, Prescription, Outpatient, Adverse reaction, Aspirin.

INTRODUCTION

Pain affects a person's quality of life and general functioning¹⁻² and it is the commonest reason for physician consultation.³ The treatment of both pain and inflammation is primarily through the use of Non-steroidal Anti-inflammatory Drugs. Non-steroidal Anti-inflammatory Drugs commonly called NSAIDs are among the most widely used and misused of all drugs.⁴ Most NSAIDs act as non-selective inhibitors of both the cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) isoenzymes.

NSAIDs provide symptomatic relief from pain and swelling in chronic joint diseases such as occur in rheumatoid arthritis and in more acute inflammatory conditions such as sports injuries, fractures, sprains, acute arthritic pains and other soft tissue injuries. They also provide relief from post-operative, dental and menstrual pain, and from the pain of headaches and migraine.⁵ They are also given to neonates whose ductus arteriosus did not close within 24 hours of birth.

There are different NSAID formulations available, including tablets, injections and gels, and most of these NSAIDs are available over the counter (there are now more than 50 different NSAIDs on the global market). They are often taken without prescription for some types of minor aches and pains that are not necessarily indicated for NSAIDs.⁶ However, it is important to note that virtually all NSAIDs, particularly the 'classic' NSAIDs, have significant unwanted effects, especially in the elderly; but the newer agents have fewer adverse effects.⁷ These agents may cause renal impairment, especially in combination with other nephrotoxic agents.

Renal failure has been recently known to be a risk if the patient is also concomitantly taking an ACE inhibitor and a diuretic - the so-called "triple whammy" effect.⁸ Liver problems are also possible with the long term use of NSAIDs.⁹

In Nigeria the exact number of prescriptions of NSAIDs-related hospitalization and deaths are not known, though their widespread use suggests that the adverse effects of these drugs are inevitable. Each year, 70 million prescriptions (NSAIDs) are dispensed in the United States, 20 million are dispensed in Great Britain and 10 million are dispensed in Canada.¹⁰

More so, the use of NSAIDs accounts for an estimated 76 000 hospitalizations and 7600 deaths in the United States¹¹ and 3897 hospitalizations and 365 deaths in Canada¹⁰ every year. These hospitalizations and deaths are majorly due to ulcer and gastrointestinal bleeding related to NSAID use. Irrational prescribing has further complicated the adverse effects from the use of NSAIDs.¹²

Therefore, this study aimed to investigate the prescription pattern of Non-steroidal Anti-inflammatory drugs (NSAIDs) in the Out-patient Pharmacy Department of Lagos University Teaching Hospital, Nigeria.

METHODS

Study Area

Lagos University Teaching Hospital (LUTH) is one of the largest Teaching Hospitals in Nigeria, located in the South-west region of the country. Lagos is one of Nigeria's most populated states and the principal economic centre in Nigeria. LUTH has many pharmacy units, one of which is the Out-patient Pharmacy Department (OPD), where the prescriptions written by the doctors of patients who have no need for immediate hospitalization or who have been discharged are dispensed. The total number of residents, medical officers and consultant doctors in various disciplines in LUTH is about 800. All these doctors in one way or the other prescribe NSAIDs depending on the complaints and presentation of the patients.

Study Design

Ethical approval was obtained from the Research Ethics Committee of the Lagos University Teaching Hospital, Lagos-Nigeria. All prescriptions from July 2009 to January 2010 were obtained from the Out-patient Pharmacy Department prescription bank. The prescriptions containing NSAIDs were separated from those without NSAIDs.

A total of 3800 prescriptions containing NSAIDs were analyzed for information like the drug name and strength, the quantity prescribed, the number of NSAIDs per prescription, the total number of each NSAID prescribed, the presence of ACE inhibitors and diuretics alongside with NSAIDs, the presence of anticoagulants in the prescriptions, the number of drugs in each prescription, formulation of NSAIDs prescribed and NSAIDs prescribed in generic or brand names. The total number of prescriptions whether containing NSAIDs or not was also noted.

Data analysis

The 3800 prescriptions obtained from the study were analyzed using the EPI-INFO 2002 software programme. The data was presented in pie-chart and frequency distribution tables with percentages, and chi-square analysis was used to test the significance at $p < 0.05$.

RESULTS

The results obtained showed that 3800 (22 %) prescriptions contained NSAIDs out of the total 17, 300 (100%) prescriptions during the period of the study.

Table 1 shows that Aspirin was the most frequently prescribed NSAID (62.2%) followed by Diclofenac potassium (13.7%) and Tenoxicam and Piroxicam were least prescribed (0.1%). Salicylates were the highest prescribed class of NSAIDs (62.2%), followed by Acetic acid derivatives (23.1%), Propionic acid derivatives (14.1%), Cox-2-selective inhibitors (0.6%) and the enolic acid derivatives were the least prescribed (0.1%).

Table 1 Distribution of NSAID prescribed

NSAID	Frequency	Percentage
Aspirin	2364	62.2
Celecoxib	20	0.5
Ibuprofen	331	8.7
Diclofenac Potassium	521	13.7
Ketoprofen	37	1.0
Diclofenac Sodium	360	9.5
Naproxen	162	4.3
Piroxian	3	0.1
Tenoxicam	2	0.1
Total	3800	100

Table 2 shows that 68.4% of the NSAIDs prescriptions studied were written in generic while 31.6% were written in brand names. Furthermore, the tablet/ capsule formulations were the major forms by which the NSAIDs were prescribed (97.9%).

Formulations of NSAIDs in injections and syrups account for 0.1 % and 0.5 % respectively. Most of the prescriptions had only one NSAID per prescription (96.2 %), however, some of the prescriptions contained two or more NSAIDs (3.8%).

Table 2 Pattern of NSAID prescription

Name used for prescription of NSAID	Frequency	Percentage
Generic	2600	68.4
Brand	1200	31.6
Total	3800	100
Form of NSAID prescribed		
Tablet/Capsule	3720	97.9
Eye drop	15	0.4
Topical gel	41	1.1
Syrup	20	0.5
Injection	4	0.1
Total	3800	100
Number of NSAID per prescription		
1	3657	96.2
≥ 2	143	3.8
Total	3800	100
Mean number of drugs per prescription		
	4.3 ± 1.8	
Median number of drugs per prescription		
	4	
Total number of drugs per prescription		
1	175	4.6
2	410	10.8
3	784	20.6
4	914	24.1
5	650	17.1
≥ 6	867	22.0
Total	3800	100

The total number of drugs per prescription was in most cases 3 or greater (84.6%) and the mean number of drugs per prescription is 4.3± 1.8. The results revealed that only 0.5 % NSAIDs were prescribed with an anti-coagulant while 20.8 % of NSAIDs were prescribed along with an ACE inhibitor and a diuretic.

Table 3 Association between type of NSAID prescribed and the name used for prescription

Type of NSAID	Name used for prescription of NSAID (%)		
	Generic	Brand	Total
Aspirin	1888 (79.9)	476 (20.1)	2364
Ibuprofen	327 (98.8)	4 (1.2)	331
Diclofenac Potassium	245 (47.0)	276 (53.0)	521
Diclofenac Sodium	67 (18.6)	293 (81.4)	360
Naproxen	47 (29.0)	115 (71.0)	162
Others	26 (41.9)	36 (58.1)	62

$\chi^2 = 944.92, df, 5, p = 0.00$

Table 3 shows a statistically significant ($p \leq 0.05$) association between the individual NSAID prescribed and whether they were prescribed in generics or

brand names. Aspirin (79.9 %), Diclofenac potassium (47 %), Diclofenac sodium (18.6%) and Naproxen (29%) were prescribed in generic.

The results on Table 4 also illustrate a statistically significant ($p \leq 0.05$) association between the individual NSAID prescribed and the frequency of co-prescription with an ACE inhibitor and a diuretic. Aspirin (31.9%), ibuprofen (2.1%), Diclofenac potassium (3.3%) and Diclofenac sodium (2.5%) were prescribed with ACE inhibitor and a diuretic.

Table 4 Association between type of NSAID prescribed and whether it was prescribed with ACE inhibitor plus diuretic

Type of NSAID	NSAID was prescribed with ACE inhibitor + diuretic (%)		
	Yes	No	Total
Aspirin	753 (31.9)	1611 (68.1)	2364
Ibuprofen	7 (2.1)	324 (97.9)	331
Diclofenac Potassium	17 (3.3)	504 (96.7)	521
Diclofenac Sodium	9 (2.5)	351 (97.5)	360
Naproxen	0 (0)	162 (100)	162
Others	3 (4.8)	59 (95.2)	62

$\chi^2 = 468.65, df, 5, p = 0.00$

Table 5 reveals a significant ($p \leq 0.05$) association between the types of NSAID prescribed and the cost in Naira (N). The cost of Aspirin (96.6%), ibuprofen (92.4%), Diclofenac potassium (50.9%), Diclofenac sodium (32.8%) and Naproxen (5.6%) prescribed were less than N500.

Table 5 Association between type of NSAID prescribed and cost of NSAID

Type of NSAID	Cost of NSAID in Naira (%)		
	≤ 500	> 500	Total
Aspirin	2284 (96.6)	80 (2.4)	2364
Ibuprofen	306 (92.4)	25 (7.6)	331
Diclofenac Potassium	265 (50.9)	256 (49.1)	521
Diclofenac Sodium	118 (32.8)	242 (67.2)	360
Naproxen	9 (5.6)	153 (94.4)	162
Others	11 (17.7)	51 (82.3)	62

$\chi^2 = 1842.15, df, 5, p = 0.00$

DISCUSSION

Lagos University Teaching Hospital (LUTH) is one of the several tertiary institutions in Nigeria established mainly for the purpose of conducting research, training and performing clinical services. Conducting studies showing the prescription patterns of different drugs would discourage less effective and irrational use of drugs.

Although no consensus definition for polypharmacy has emerged; the definition imbibed describes polypharmacy as the concomitant use of 3 or more drugs or the use of more drugs than indicated.¹³ In this present study, a high percentage of the prescriptions studied were discovered to contain 3 or more drugs. This observation is clear enough to conclude that polypharmacy is prevalent among the studied prescriptions. Average number of drugs per prescription observed in Tanzania was 2.4 as compared to 4.3 observed in this study in Nigeria.¹⁴

These data are consistent with the general observation in Nigerian communities where people take numerous drugs daily. The aforementioned event may be due to limited knowledge or experience of the prescribing doctors in therapeutics. Polypharmacy, which is a form of irrational drug use can increase the risk of adverse reaction of drugs and drug interaction.¹⁵

This study has shown that NSAIDs were contained in about 22% of the total number of studied prescriptions, hence it can be inferred that one of every five prescriptions contained NSAIDs. This observation is consistent with the earlier study of Carson & Willet⁴, which showed NSAIDs to be some of the widely prescribed and used drugs. As a matter of fact, NSAIDs are drugs that are generally misused and owned by most Nigerians without doctors' prescriptions.

It is a known fact that the route of drug administration affects the therapeutic outcome, the onset of action as well as the adverse effects produced. It has been revealed from this study that most of the NSAIDs were prescribed for oral administration and the oral administration of NSAIDs is always associated with gastrointestinal ulcerations.

This may explain the high incidence of GIT side effects that have been observed with NSAIDs usage.¹⁶ There may be need for the co-administration of cytoprotective agents with NSAIDs and appropriate counseling of patients to always take NSAIDs after meal.

Prescriptions written in generics have special importance in rational use of drugs as regards to cost, safety and efficacy by permitting the identification of the products by their scientific names.¹⁷ It also makes the prescribers, dispensers and users to easily choose between many alternatives in terms of quality, price or convenience.

The results of this study revealed 68.4 % of drugs prescribed in Nigeria in generics as compared to 20 % in Cyprus.¹⁸ This is quite an encouraging observation but there is need for improvement so as to comply with the World Health Organization's standard that ALL prescriptions must be written in generics.

Pressure from pharmaceutical companies may be one of the reasons for the writing of brand names thus, there is need to discourage the pharmaceutical companies from unethical influence of doctors' prescription pattern and for doctors' to also exercise their ethical and professional rights in prescribing drugs. As long as the pharmaceutical companies influence the prescriptions of doctors', the rate of irrational drug use will continue and the irrationality in drug use is always at the expense of the patients' safety.

In most of the cases as seen in this study, only one NSAID was prescribed per prescription, however, a few had 2 or more NSAIDs prescribed together. Taking two or more different NSAIDs may not be therapeutically beneficial. Such practice multiplies the toxicities of NSAIDs with no evidence of improvement in efficacy.¹⁹ The studies of Thomas⁸ and Rabinowitz & Van-Thiel⁹ showed that the risk of severe drug reactions causing injury to the liver and acute renal failure was 6 to 7 times higher in reported cases of simultaneous use of two NSAIDs.

There was also statistically significant ($p \leq 0.05$) association between the individual NSAID prescribed and the frequency of co-prescription with an ACE inhibitor and a diuretic. A recent study has shown the contraindication that exists in the co-administration of NSAIDs, diuretics and angiotensin converting enzyme inhibitors (ACEIs) which may result in drug-induced renal failure.⁸ The use of NSAIDs especially aspirin with anticoagulants is contraindicated; however it was observed that though contraindicated, NSAIDs (0.5 %) were prescribed with anticoagulants in a few cases in this study.

The statistically significant ($p \leq 0.05$) association that was observed between the types of NSAIDs prescribed and the cost in Naira may justify the result of aspirin as the most frequently prescribed NSAID (62.2%) as it is extremely cheap. The frequent prescription of aspirin may also be due to the role of this drug in cardiovascular diseases especially in the prevention of platelets aggregation.

CONCLUSION

There is obvious need for adequate training in rational prescribing to inculcate in the prescribers the appropriate habits tailored towards rational prescription and use of drugs. More importantly, the consultants and senior doctors should regularly review the prescriptions of their resident doctors and junior doctors so as to identify the appropriateness of their prescriptions.

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