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UTILIZATION OF ANTIMICROBIAL AGENTS IN FEDERAL NEURO-PSYCHIATRIC HOSPITAL, USELU, BENIN CITY, EDO STATE, NIGERIA

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ABSTRACT

The study evaluated the antimicrobial utilization pattern at the Federal Neuropsychiatric Hospital, Uselu, Benin City, Edo State, Nigeria, with a view to appraising the level of compliance of the hospital to WHO guidelines for rational use of antimicrobial agents. This was a retrospective, single site antibiotic evaluation study of case files of 210 patients who were admitted at the male and female in-patient medical wards of the hospital from 1st April to June 30th 2017. Data collection forms were used to collect the following information; patient demographics, diagnosis, name of prescribed antibiotics, antimicrobial treatment regimen, forms of combination therapy, laboratory investigation and cost of antibiotic utilization. All the case files of patients who were prescribed antibiotics during the study period were assessed. A total of 210 prescription encounters were evaluated. Patients aged 31-50 years were the highest recipients of antimicrobials while patients aged 11-20 years and above 80 years were the least recipients of antimicrobials. Respiratory and gastrointestinal tract infections accounted for the indications that received the highest number of antibiotic prescriptions among the 11 indications for antibiotic utilization. Penicillins were the most prescribed antibiotic singly and in combination. The average number of medicines per prescription was 3.5 and percentage of antibiotic prescriptions was 24.2%. Generic prescribing was at 48.0%, while laboratory investigations was 3.3% and the percentage cost of encounter was 40.5%. The percentage of antibiotic prescriptions and percentage cost of encounter were rational in comparison with WHO values. But the higher than recommended values for average number of drugs per encounter, low values of generic prescribing and laboratory investigations means prescribing was irrational. Thus, there was some level of irrational prescribing of antibiotics in the study centre and this could further worsen the burden of microbial resistances to these antibiotics.

KEYWORDS: **Antimicrobials, Prescription, Neuro-psychiatric setting, Utilization.**

INTRODUCTION

An antimicrobial is any substance of natural, semi-synthetic or synthetic origin that kills (bactericidal) or inhibits (bacteriostatic) the growth of microorganisms but causes little or no damage to the host. Antimicrobials include all agents that act against all types of microorganisms which include bacteria, viruses, fungi and protozoa [1].

Antimicrobial chemotherapy has been described as the main stay in the prevention and control of infectious diseases, thus quality use of these agents is important from both the clinical and public

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health perspectives. They are commonly prescribed by physicians in many health facilities, especially at the primary care level and their patterns of use vary between public and private sectors [2].

However, irrational use of medicines in general is prevalent in many health care systems, especially in developing countries, resulting in poly-pharmacy, overuse of antimicrobials and lack of compliance with standard treatment guidelines [3]. Irrational use of antimicrobials in both humans and animals has led to prescription errors, suboptimal empiric therapy, inappropriate combination therapy, inadequate dosing, as well as duration errors and apparent antibiotic or treatment failures [4,5]. Consideration of the potential antimicrobial resistance, tissue penetration, drug interactions, side effects and cost are among the factors which influence the prescription pattern and effectiveness of antimicrobial therapy [6].

In developing countries, antibiotics are prescribed for 44 - 97 % of hospitalized patients often unnecessarily or inappropriately [7]. Several socio-economic and behavioural factors are thought to contribute to the inappropriate use of antibiotics and consequently, to the increased incidence of bacterial resistance in developing countries [8].

The inappropriate use of antimicrobials is an important factor that has led to the emergence of antimicrobial resistance globally. Unless concerted action is taken to curb this problem, we might be at risk of returning to the pre-antimicrobial era. Hence, there is need for the implementing of standard guideline for rational prescribing. This research aimed at evaluating antimicrobial prescribing pattern at the Federal Neuro-psychiatric Hospital, Uselu, Benin City, with a view to determining the level of compliance of this study centre to the World Health Organization/International Network for the Rational Use of Drugs (WHO/INRUD) prescribing indicators on the rational use of antimicrobials.

MATERIALS AND METHODS

Study design

This retrospective, single site antibiotic evaluation study was conducted by collecting data using the World Health Organization/International Network for the Rational Use of Drugs (WHO/INRUD) prescribing indicators check list. Their standard values were used to measure the antibiotics prescribing pattern at the study centre [9].

Study area

The study was conducted at the Federal Neuro-Psychiatric Hospital (FNPH), Uselu, Benin City, Edo State, Nigeria. Edo State is located in the south-south geopolitical zone of Nigeria and occupies a land area of about 17,802 sq. km with a projected population of 4,235,595 in 2016. Benin City is the capital of the state and it is a large metropolitan city with a projected population of about 1.582 million inhabitants in 2017 [10].

Federal Neuro-Psychiatric Hospital is a specialty hospital which renders professional health care services in areas such as: general adult psychiatry, general medical services/National Health Insurance Scheme (NHIS), emergency psychiatry, community psychiatry, addiction and drug abuse, early intervention, medical imaging and radio-diagnosis. The hospital provides a friendly, specialized and qualitative psychiatry and rehabilitative care for the mentally ill in their social environment and delivered by professionals using the most modern equipment. The study was conducted in the male and female in-patient medical wards using case notes of patients admitted into the wards from April 01, 2017 to June 30, 2017.

Sample size selection

Following ethical approval from the ethical committee of the Federal Neuro-Psychiatric Hospital, a total of 5,500 prescriptions that were dispensed between April 01, 2017 to June 30, 2017 at the male and female in-patient medical wards of the hospital were assessed. Patients whose prescriptions contained antimicrobial agents were included in the study and those without antimicrobial agents were excluded. From the total number of prescriptions assessed, 210 prescriptions were selected.

Data collection

Patient information were collected with a data collection form and these included; age, sex, occupation, infection diagnosed/treated, name of antibiotics prescribed, name of other drugs prescribed, duration of therapy, cost, co-morbid condition, evidence of diagnostic laboratory investigations, antibiotics dosages, dosage of other drugs and hypersensitivity. Rational use of antimicrobial agents at the hospital was evaluated by measuring the indicator variables for rational antibiotic utilization as outlined by the World Health Organization/International Network for the Rational Use of Drugs (WHO/INRUD) prescribing indicators for antimicrobial utilization [9].

Data analysis

Using Microsoft Excel 2010, the data collected were analyzed with descriptive statistical analysis and

transformed into frequency counts, means and percentages.

RESULTS

A total number of 210 patients had their antimicrobial therapy evaluated; 129 (61.4%) were female while the mean age of the patients was 20.9 years. The age groups of 31-40 and 41-50 years were the highest recipients of antimicrobial agents (21.4% each) while 11-20 and 81-90 years age groups were the lowest recipients (2.4% each) (Table 1). The most commonly prescribed classes of antimicrobial agents at the wards were the penicillins (41.3%) while the aminoglycosides (0.4%), lincosamides (0.4%) and nitrobenzenes (0.4%) were the least prescribed classes (Figure 1).

A total of 11 different indications were encountered in the study (Table 2). Respiratory and gastrointestinal tracts infections were the most prevalent, accounting for 48.8 and 21.7% respectively in females and 48.2 and 22.2% respectively in males. There were no prevalence of sepsis and wound infections in male patients and eye and joint infections in female patients.

Out of the 210 prescriptions reviewed, 68.6% of the prescriptions were single antimicrobial agents and 31.4% combination antimicrobial agents were encountered (Table 3 and 4). While the penicillins (61.1%) were found to be the most prescribed single antimicrobial agents, penicillins + 5-nitroimidazoles (31.8%) was found to be the most prescribed combination therapy, followed by the fluoroquinolones + 5-nitroimidazoles (12.1%) (Table 3 and 4).

Only 7 (3.3%) patients that received antimicrobial therapy had records of laboratory investigations conducted prior to antibiotic prescription.

In the study, a total cost of antibiotics utilized by the patients during the period of study was one hundred and seventy-four thousand, four hundred and fifty-one naira (₦174,451.00). Amoxicillin/Clavulanic acid capsules accounted for the highest cost of antibiotics (₦61,130) (Table 5).

A comparison of the prescribing indicators in the hospital wards to that of WHO standard values showed the following; the average number of drugs per prescription (3.5), percentage of antimicrobial per prescription (24.2%), percentage of drugs prescribed in generics (48.0%), percentage cost of encounter (40.6%) and laboratory investigation (3.3%) (Table 6).

DISCUSSION

The antimicrobial prescription pattern at the male and female in-patient medical wards of the Federal Neuro-Psychiatric Hospital, Uselu, Benin City was evaluated in this study. Results showed a partial level of compliance to the WHO/INRUD prescribing indicators on the rational use of antimicrobials with all the prescribing indices falling out of range of the standard WHO values except the percentage of antimicrobial per prescription indicator.

The high occurrence of female in the study centre also implies that more females than males received antimicrobial therapy. This could be attributed to the fact that women are at higher risk of contracting infections than their male counterparts as a result of their physiologic makeup, anatomical structures, biological differences, social inequities, sociocultural constraints, and educational background. [11,12]. Reports from similar studies in other countries have documented that women more often visit their general practitioner than men and visitation rate has been linked to antibiotic prescribing. Gender has also been documented as a key determinant of antibiotic prescribing as studies across primary care facilities in nine high-income countries found that women received more antibiotics than men in all age groups except those above 75 years [13-16]. Similarly, across English and Welsh primary care facilities the rate of antibiotic prescribing has been found to be 40.0% higher in female than in male patients [17].

A total of 11 indications were recorded of which respiratory and gastrointestinal tracts infections were the highest with the number of female patients almost twice that of the male patients. The number of indications reported is high considering that the study centre is a specialty hospital and not a general hospital catering for all forms of infections. Again, the number of indications may be the result of the states of the patients who were not able to take care of themselves prior to admission as these infections were not contracted while they were in admission at the hospital. Additionally, the high number of female patients with infections also justifies the higher use of antibiotic in females than in male patients.

The class of antimicrobial most frequently prescribed were the penicillins either singly or in combination with clavulanic acid, followed by 5-nitroimidazole and cephalosporin. Penicillins and cephalosporins have continued to be a mainstay of therapy in hospitals because of their broad spectrum of activity, clinical efficacy and favorable tolerability profiles as well as their availability and affordability [18]. However, recent surveys in Europe and the US have found that the most frequently prescribed antibiotics were fluoroquinolones, penicillins, and aminoglycosides

Table 1: Demographics of patients prescribed with antimicrobial agents

Characteristics	Frequency	Percentage
Gender		
Male	81	38.6
Female	129	61.4
Age (years)		
≤ 10	22	10.5
11-20	5	2.4
21-30	31	14.8
31-40	45	21.4
41-50	45	21.4
51-60	32	15.2
61-70	18	8.6
71-80	7	3.3
> 80	5	2.4

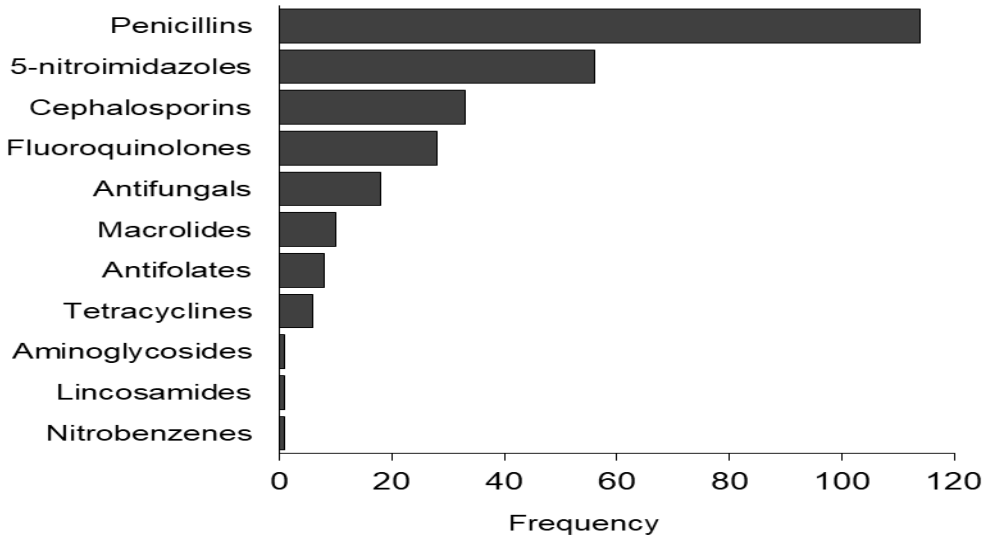

Figure 1: Antimicrobial prescriptions in patients at the hospital wards.

Table 2: Indications for antimicrobial prescription in patients at the hospital wards

Indication	Females	Males
RRT infections	63(48.8%)	39(48.2%)
GIT infections	28(21.7%)	18(22.2%)
GUT infections	24(18.6%)	7(8.6%)
Skin infections	6(4.7%)	8(9.9%)
Ear infections	2(1.5%)	5(6.2%)
Sepsis	2(1.5%)	0
Wound infections	2(1.5%)	0
Tooth infections	1(0.8%)	1(1.2%)
GIT + RRT infections	1(0.8%)	1(1.2%)
Eye infections	0	1(1.2%)
Joint infections	0	1(1.2%)

RRT; Respiratory tract, GIT; Gastrointestinal tract, GUT; Genitourinary tract

Table 3: Antimicrobial mono (single) therapy in patients at the hospital wards (n = 144)

Class of antimicrobials	Type of antimicrobials	Frequency	Percentage
Penicillins (61.1%)	Amoxicillin	44	30.6
	Amoxicillin/Clavulanic acid	39	27.1
	Ampicillin/Cloxacillin	5	3.4
5-nitroimidazoles (2.8%)	Metronidazole	3	2.1
	Ornidazole	1	0.7
Fluoroquinolones (9.0%)	Ciprofloxacin	8	5.6
	Levofloxaacin	5	3.4
Antifungals (9.0%)	Clotrimazole	11	7.6
	Ketoconazole	2	1.4
Cephalosporins (13.9%)	Cefuroxime	14	9.7
	Cefixime	1	0.7
	Ceftriaxone	4	2.8
	Cefixime/Clavulanic acid	1	0.7
Macrolides (2.1%)	Azithromycin	1	0.7
	Erythromycin	2	1.4
Aminoglycosides (0.7%)	Gentamicin	1	0.7
Antifolates (1.4%)	Sulphamethoxazole/Trimethoprim	2	1.4

Table 4: Antimicrobial combination therapy in patients at the hospital wards (n = 66)

Antimicrobial class	Frequency	Percentage
Aminoglycoside + antifungal	7	10.6
Antifungal + 5-nitroimidazole	1	1.5
Antifungal + tetracycline	1	1.5
Cephalosporin + 5-nitroimidazole	7	10.6
Cephalosporin + macrolide	1	1.5
Cephalosporin + penicillin	1	1.5
Cephalosporin + penicillin + 5-nitroimidazole	2	3.1
Cephalosporin + fluoroquinolone + 5-nitroimidazole	1	1.5
Cephalosporin + fluoroquinolone + 5-nitroimidazole + tetracycline	1	1.5
Fluoroquinolone + chloramphenicol	1	1.5
Fluoroquinolone + lincosamide	1	1.5
Fluoroquinolone + 5-nitroimidazole	8	12.1
Fluoroquinolone + 5-nitroimidazole + tetracycline	4	6.1
Fluoroquinolone + antifungal + 5-nitroimidazole	1	1.5
Fluoroquinolone + tetracycline	1	1.5
5-nitroimidazole + macrolide	5	7.7
5-nitroimidazole + tetracycline	1	1.5
Penicillin + macrolide	1	1.5
Penicillin + 5-nitroimidazole	21	31.8

Table 5: Cost of prescribed antimicrobials at the wards in the hospital

Antibiotics prescribed	Unit	Unit price (₦)	Total number	Total price (₦)	Percentage
Amoxicillin	Cap	18	743	13370	7.66
Metronidazole	Tab	5	898	4490	2.57
Metronidazole	Susp	120	1	120	0.07
Metronidazole	Infusion	120	29	3480	2.00
Amoxicillin/Clavulanic acid	Cap	85	719	61130	35.04
Amoxicillin/Clavulanic acid	Susp	1050	6	6300	3.61
Ampicillin/Cloxacillin	Cap	12	107	1280	0.73
Azithromycin	Tab	120	5	600	0.34
Cefixime	Tab	150	15	2270	1.30
Ceftriaxone	Vial	680	34	23120	13.25
Ceftriaxone	Tab	1135	10	11045	6.33
Ciprofloxacin	Tab	1000	5	5000	2.87
Clarithromycin	Tab	135	148	20020	11.48
Doxycyclin	Cap	6	70	420	0.24
Erythromycin	Cap	23	40	945	0.54
Gentamicin	Vial	25	2	50	0.03
Chloramphenicol	Drop	300	1	300	0.17
Levofloxacin	Tab	780	7	5720	3.28
Clotrimazole	Tab	6	164	985	0.57
Ornidazole	Tab	120	84	10080	5.79
Secnidazole	Tab	300	1	300	0.17
Ketoconazole	Cream	420	1	420	0.24
Cotrimoxazole	Tab	6	126	756	0.43
Ciprofloxacin	Drop	850	1	850	0.49
Clindamycin	Tab	100	14	1400	0.80
Total			**3231**	**174451**	**100**

1USD = ₦310

Table 6: Comparison of prescribing indicator at the hospital wards with WHO values

Prescribing indicators	Hospital wards	WHO value
Average number of drugs per prescription	3.5	1.6 - 1.8
Percentage of antimicrobial per prescription	24.2	20.0 - 26.8
Percentage of drugs prescribed in generic	48.0	100
Percentage cost of encounter	40.5	20 - 40
Laboratory investigation (%)	3.3	100

[19,20].

Nitroimidazole was observed to be the second most commonly prescribed antimicrobial in this study. This could be due to their activity against wide range of anaerobic bacteria such as *Bacteroides fragilis*, and gram-positive anaerobic bacteria, such as *Clostridium difficile* [21]. They are also known to have favourable pharmacokinetic and pharmacodynamic properties, low cost and reduced adverse effects [22]. This is in agreement with a similar study conducted by Abu-Saeed and colleagues in a secondary health facility in Abuja, Nigeria which also reported a high prescription rate for metronidazole (30.0%) [23]. In accordance with international guidelines, metronidazole is also a component of multidrug regimens (e.g, in combination with omeprazole, clarithromycin, and amoxicillin) for therapy of *Helicobacter pylori* infections, such as gastroduodenal ulcers [24].

From the most frequently prescribed antimicrobial combination therapy in this study, it can be deduced that penicilllins and metronidazoles are more readily available than other potent and generic antimicrobials such as perfloxacin, methicillin and vancomycin which were not prescribed at all. It has been reported that these popular, cheaper and readily available broad-spectrum antimicrobial agents are more commonly affected by bacterial resistance in developing countries [25]. However, the relationship between antibiotic use and the emergence and spread of resistance is a complex one. Resistance of pathogens to these readily available and commonly used drugs would definitely result in high cost of treatment, longer hospital stay and therapeutic failure, which might lead to life-threatening diseases and more deaths [26]. The observed combination of bacteriostatic agents with antimicrobials that act on rapidly growing cells as seen in (penicillins + macrolides, cephalosporins + macrolides) is unjustifiable. Existing data have demonstrated antagonism between bacteriostatic agent and antimicrobials that act on rapidly dividing cells [27].

The low incidence of laboratory investigation prior to medications observed could be attributable to the specialized nature of the hospital whose primary objectives are psychiatry and rehabilitative care, hence may lack a diagnostic laboratory or a well-equipped one to carry out these antimicrobial susceptibility laboratory investigations. A survey of the pattern of antibiotic use in the Family Medicine Department of a tertiary hospital in Sokoto, North-Western Nigeria revealed that about one-fifth of the patients had laboratory investigation carried out [28]. A similar study has suggested two possible reasons for the increased resistance to antibiotics observed in the Benin City metropolis, being the prescription of antibiotics without laboratory guidance and over the counter sales of antibiotics without prescription [29]. Results from laboratory investigations are supposed to help the prescribing physician in making definitive diagnoses and reduce high rate of empirical treatment. A quick switch in antibiotic therapy from a broad-spectrum antibiotic to a narrow-spectrum agent is important once the causative organism has been identified from the laboratory results, in order to limit the development of resistance which had resulted in increased morbidity, mortality, as well as increased cost of health care [30].

In the prescription of antibiotics, it is most often preferred to minimize the number of antibiotics per prescription in order to curtail the risk of interaction, resistance and cost to the barest minimum in order to achieve optimum clinical outcome as well as adherence. In this study the average number of drugs per encounter was 3.5, this far exceeds the recommended WHO range of 1.6-1.8% indicating poor prescribing practice. Similar value as that recorded in this study has been reported both in Ghana and India [31, 32]. This practice maybe ascribed to empirical antimicrobial use and lack of adherence to guidelines on rational prescribing. The compliance of the study centre to the percentage of antimicrobial per prescription and percentage cost per encounter is indicative of a level of rational prescribing at the hospital. This is expected as the indications necessitating antimicrobial therapy were infections secondary to the cause of admission at the hospital. A 100% prescription by generic name is expected by WHO, however poor adherence to this was observed in this study as only 48.0% of the total prescriptions were in generics. Generic prescribing has been reported to decrease cost and encourage optimum adherence [33].

Finally, a number of limitations were encountered in the course of the study and one of them was arriving at the sample size of 600 prescriptions recommended by WHO for such study. Being a specialized hospital, the number of daily prescriptions containing antimicrobial agents were few. Another limitation was the time constraints of the study. The three months course of the study was not enough to generate 600 antimicrobial prescription encounters. A nine months to a year study period would have been ideal.

CONCLUSION

This study revealed that the antimicrobial utilization pattern of the physicians in the study centre was in partial compliance with the World Health Organization antibiotics prescribing indicators. The centre had a higher average number of drugs per encounter, a lower percentage of antimicrobials prescribed as generics and laboratory investigations. There was compliance in the percentage of antimicrobial per prescription and the percentage cost per encounter. The penicillins were the most prescribed followed by the nitroimidazoles and the major indications for antibiotics were respiratory and gastrointestinal tract infections. Thus, it is most important that Federal Neuro-Psychiatric Hospital, Uselu, Benin City imbibes the culture of adherence to WHO guidelines and policies on rational use of antimicrobial agents.

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