DRUG THERAPY PROBLEMS ASSOCIATED WITH ANTIBIOTICS PRESCRIPTIONS IN UNIVERSITY OF UYO HEALTH CENTRE, UYO, NIGERIA

Short title: "DRUG THERAPY PROBLEMS ASSOCIATED WITH ANTIBIOTICS"

ABSTRACT

Introduction: Antibiotic resistance has contributed as one of the greatest public health threats at present. This study aimed at identifying drug therapy problems (DTPs) associated with prescriptions of antibiotics to patients attending the University of Uyo Health Centre and presented a seminar as an intervention.

Method: A prospective observational study was carried out. One hundred (100) patient folders with 147 antibiotics prescriptions were used for the survey for the first-month collation of antibiotics prescriptions while one hundred and sixty (160) patient folders with 160 antibiotics prescriptions were used at the second -month of the survey. The seminar presentation on drug therapy problems associated with antibiotics prescriptions was held after the first -month of the survey. Data obtained were analyzed by using descriptive statistical tools such as frequency, mean, standard deviation and bar chart. The statistical analytical tool such as Chi-square test was used and significance was considered at p = 0.05.

Result: The first survey involved 147 prescriptions of antibiotics. Prescriptions with DTPs were 77 (52.4%) while the most frequently occurring DTPs were drug interactions (37.1%). The second survey involved 160 prescriptions while 112 (70%) prescriptions contained 209 DTPs. The most frequent DTPs were drug interactions (49.3%). The results also showed that antibiotics prescriptions containing DTPs were significantly higher in the follow-up survey (p=0.02) of the study. DTPs like inappropriate dosage frequency was significantly higher (p=0.04) in the follow-up survey.

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Conclusion: This study had indicated prevalence of DTPs. DTPs were drug interaction, inappropriate dosage frequency and unnecessary antibiotic prescriptions.

Keywords: Drug therapy problems, antibiotics, inappropriate prescription, antibiotics stewardship, antibiotic resistance.

Introduction

The United States National Coordinating Council for Medication Error Reporting and Prevention defines a drug therapy problem as:

"*any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer. Such events may be related to professional practice, healthcare products, procedures, and systems, including prescribing, order communication, product labeling, packaging, and nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use*" [1]. In outlining pharmacotherapy procedures, there are three stages where a drug therapy problem can be made such as the prescribing stage which occurs with the physician, dispensing stage that takes place at the pharmacy and the drug administration stage which occurs at the nursing unit.

Antibiotics are life-protecting medicines that are important in modern medicines, infections with pathogens that are resistant to first-line antibiotics can lead to treatment with some bioequivalent antibiotics that are expensive and cause severe adverse reactions. Antibiotic-resistant infections can lead to increased healthcare costs and consequently, to increased morbidity and mortality. The most important modifiable risk factor for antibiotic resistance is inappropriate prescribing of antibiotics. About half of outpatient antibiotic prescribing in humans might be inappropriate which included antibiotic selection, dosing, or duration and unnecessary antibiotic prescribing. It was reported that about 30% of outpatient antibiotic prescriptions in the United States were unnecessary [2]. A DTP rate of 42% was reported in a study in Sweden [3]. A systematic review that used an alternative approach to assessing DTP rates, found DTP rates of 3% at the

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dispensing stage. Outpatient prescriptions by general practitioners were associated with a 77% DTP rate [3].

Undesirable outcomes such as adverse drug reactions, drug-drug interactions, lack of efficacy, suboptimal patient adherence and poor quality of life, were patient experiences due to DTPs. Consequently, there were significant health and economic effects such as the increased use of health services, avoidable medication-related hospital admissions and death [3]. About 6-7% of hospital admissions seemed to be medication-related, while over two-thirds of these were considered avoidable DTPs [3].

A survey compared the factors associated with patient-reported DTPs in seven countries. It indicated that 11% of patients were observed with DTPs and risk factors such as poor coordination of care, cost-related barriers, medical services or medicines, co-morbidity and hospitalization, were responsible [4]. Some studies found that DTPs were linked with an increasing number of medications, children and elderly, and particular medications used in certain disease conditions such as musculoskeletal, oncology and immunosuppression, dermatology, ophthalmology, otolaryngologic conditions, infections and cardiovascular diseases [5, 6]. Acute febrile illness, respiratory and urinary infections were the prevalent infections in a study on antimicrobial drug therapy problems among patients in Northeast Ethiopia [7].

DTPs were classified into seven categories of problems by Shargel which were unnecessary drug therapy, wrong drug, dose too low, dose too high, adverse drug reaction, inappropriate adherence and needs additional drug therapy [8]. The first and the only published article in Africa at present on DTPs associated with antibiotics prescriptions also used Shargel's classification of DTPs. Their study was a retrospective study that focused on DTPs experienced by patients. The researchers collated data from folders of patients that attended the study site from September 2018 to February 2019. The study observed that forty percent of the participants experienced DTPs [7].

Despite universal agreement that antibiotic overprescribing is a problem, the continuous overprescribing of antibiotics continues. Antibiotic use has been linked to rising rates of antimicrobial resistance and disruption of the gut micro-biome which led to *Clostridium difficile*

Comment [Ma9]: The same ref are being used throughout. Author should do more literature review to add on appropriate references

Comment [Ma10]: Same ref

Comment [Ma11]: Citation is not appropriate (Shargel et al)

Comment [Ma12]: Unnecessary details

infections, allergic reactions and increased healthcare costs [9,10]. A study estimated that at least 30% of antibiotics prescribed in US outpatient settings were unnecessary [11]. Another report cited a slightly higher figure across a variety of healthcare settings [12]. These findings with the fact that there were very few drugs in development to target resistant bacteria, suggested a future threat in which common infections could become lethal [11]. This study aimed at identifying DTPs associated with prescriptions of antibiotics to patients attending the University of Uyo Health Centre and presented a seminar as an intervention.

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METHODS

Study design

This was a prospective and observational study that included a collection of data from the folders of the patients that attended the University of Uyo Health Centre.

Study setting

The study was done at the University of Uyo Health Centre, Uyo, Akwa-Ibom State, Nigeria, which is a primary healthcare facility.

Study population/ Sample

Folders of study participants including both male and female patients who received antibiotics prescriptions from the primary healthcare facility in May-June 2019 and July – August 2019 were used for the collation of data.

Sample size calculation

The University of Uyo Health Centre is a 20-bed hospital with about 100 patients attending the clinic daily. The confidence level used was 95% while the confidence interval used was 5. Online sample size calculator, The Survey System [13], was used to determine the sample size. The sample size calculation was based on the single population proportion formula [14] below:

Comment [Ma15]: Do you mean margin of error is 5%?

Sample size, $n = \frac{z^2*(p)*(1-p)}{}$

C^2

The report from the University of Uyo Health Centre indicated that average one hundred (100) patients received antibiotics prescriptions. Since the population of patients receiving antibiotics prescription at the University Health Centre was below ten thousand (10,000), adjusted sample size calculation with a reduction formula was used as indicated below:

$$\frac{n*N}{n+N}$$

$$= 80$$

The sample size calculated was 80 persons.

It is important to state that this survey was not focused on the study participants but the pattern of antibiotics prescriptions by prescribers at the Health Centre. Therefore the study was designed to survey all patients' folders that contained antibiotic prescriptions within the period of the survey on a daily basis as patients attended the University of Uyo Health Centre. However, folders of patients that did not contain antibiotics prescriptions for each day of the survey were not considered because it was not included in the objectives of the study. Cippole's classification of DTPs was not used for this study because it contains sources of DTPs that originated from Physicians, Pharmacists, Patients and Nurses. This study focused on DTPs that were originated from only Physicians; hence, Shargel's classification of DTPs was more suitable for this study.

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Inclusion criteria:

Only patients' folders containing antibiotics prescriptions were used.

Exclusion criteria:

Non-antibiotics prescriptions in patients' folders were not used for the survey.

Comment [Ma17]: Indicate whether OPD or inpatient folders were used or both

Data collection instrument

Patients' folders were retrieved from Doctors' consulting rooms after consultation by trained graduating pharmacy students.

Data collection method

Patients' folders were retrieved from physicians' consulting rooms after consultation daily by trained graduating pharmacy students for one month. The folders containing antibiotics prescriptions were sorted out from other patients' folders and were used for the study.

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Information about the date, sex, age, folders' no, staff, student, height, weight, ethnicity, marital status, complaints, diagnosis, laboratory results and medicines were obtained from the patients' folders before the folders were returned to the record section daily. British National Formulary (BNF), Medscape and Epocrates were used for assessing the probability of drug interactions and other DTPs. DTP is considered as any undesirable event experienced by a patient related to drug therapy that interferes with achieving desired pharmacological goals [7]. DTPs were identified through the following procedures:

i. Disease conditions of the patients were identified.
ii. Consideration for antibiotics was not based on prescription antibiotics or non-prescription antibiotics. All antibiotics were considered.
iii. Disease conditions were compared with prescribed antibiotics for contraindication.
iv. The weight and age of patients with the prescribed dose of antibiotics were compared with the standard dose in official books like BNF to determine if a dose was under-dose or overdose.
v. All prescribed drugs in a prescription were also compared with one another to determine their compatibility and drug interaction.
vi. The complains made by patients were also compared with the prescribed drugs for effective treatment.
vii. Physiological conditions such as breastfeeding, pregnancy and special population like "the elderly" among the patients were compared with the prescribed dose and drugs.

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After one month of data collection, the results of the survey were disclosed to the medical practitioners at the University of Uyo Health Centre during seminar presentation as our

intervention. The purpose of the seminar presentation was to acquaint the prescribers of the common drug therapy problems that were observed with the prescriptions of antibiotics at the University of Uyo Health Centre. The seminar presentation involved the display of the first-survey results on DTPs associated with the prescriptions of antibiotics. All Physicians, Pharmacists, Laboratory Scientists and Radiologists at the University of Uyo Health Centre were invited for the seminar presentation with one week of notice from the Centre Administrator. The Pharmacists were also alerted of the common drug therapy problems to prevent their occurrence. The laboratory scientists and radiologists were invited to the seminar to inform them of the importance of proper diagnostic procedures and availability of required diagnostic materials. Seminar presentation activities included the following:

i. Invited healthcare professionals were seated in the Conference room.
ii. The principal investigator presented the audio-visual seminar on DTPs associated with the prescriptions of antibiotics.
iii. The results of the first survey of the study were presented as evidence of DTPs in the Centre.
iv. Impacts of DTPs such as antimicrobial resistance among others were emphasized.
v. Measures to prevent DTPs associated with antibiotic prescriptions in the Centre like the formation of an Antibiotics Monitoring Committee was emphasized.
vi. Guidelines and policy on the prescriptions of antibiotics by CDC were also advised.

Then, a follow-up survey was undertaken subsequently for another one month to assess the impact of the seminar presentation on antibiotics prescriptions in the University of Uyo Health Centre. DTPs were categorized based on guidelines described by Shargel [8]. The criteria for the classification of DTPs were applied by the principal investigator of the study who is a registered Pharmacist. DTPs were also reviewed by another registered Pharmacist.

Comment [Ma20]: Clearly indicate the criteria and its basis

Ethical consideration

Ethical approval was obtained from the Ethical Committee of the University of Uyo Health Centre before the commencement of the study. The Ethical Approval letter reference number: UU/DHS/EC/VOL.1/004. The principles of Helsinki were followed in all aspects of the study.

Data analysis

Data obtained were saved in the Microsoft word format. Descriptive analytic tools such as mean, frequency, standard deviation were used to present the results. The statistical analytic tool such as Pearson Chi-square test was used for analysis. Statistical significance was considered at $p \leq 0.05$, the confidence interval was 95%. Online social science statistics (The Survey system, 2019, version 10.5) was used [13].

Comment [Ma21]: What software analytical tool was used as Ms. Word Is not used for analysis

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RESULTS

First phase survey

The results showed that in the first phase of the study, one hundred patient folders were surveyed for the study. The folders included folders of forty-four (44) male patients and fifty-six (56) female patients who attended the clinic and collected antibiotics containing prescriptions in the month of review. A total number of one hundred and forty-seven (147) antibiotics prescriptions were surveyed at the first phase. Seventy-seven (52.4%) of the prescriptions contained drug therapy problems. The most frequently occurring drug therapy problems identified in the antibiotics-containing prescriptions were drug interactions (37.1%), inappropriate dosage frequency (23.7%) and unnecessary medication (22.7%) respectively (Table 1).

Comment [Ma23]: Typographical error

Seminar presentation as an intervention

Forty healthcare professionals were selected for the seminar presentation; thirty-three percent (33%) of them were represented at the seminar. The proportion of the healthcare professionals in attendance were Pharmacy technicians (43%) followed by Pharmacists (40%) and medical doctors (36%) respectively (Table 2). Discussion at the seminar was focused on the results displayed in Table 1. Emphasis was also made on the consequences of inappropriate antibiotic prescriptions without proper diagnosis. Only three (3) of the prescribers had postgraduate education while nine (9) of the prescribers had very few medical practice experiences (Table 2).

Second phase (Follow-up) survey

The results showed that in the second phase of the study, one hundred and sixty (160) patient folders were surveyed for the antibiotics-containing prescriptions which included one hundred and two (102) folders for the female and forty-eight (48) folders for the male. A total number of 160 antibiotics prescriptions were obtained at this follow-up survey. Out of the 160 antibiotics-containing prescriptions in the month of review, 112 (70%) prescriptions contained 209 drug therapy problems. The most frequently occurring drug therapy problems in the second phase of the study were drug interactions (49.3%), inappropriate dosage duration (19.1%) and inappropriate dosage frequency (11.5%) (Table 3).

The results also showed that there was no significant variation (p=0.53) between the number of antibiotics prescriptions in the first survey and that of the follow-up survey while antibiotics prescription containing DTPs was significantly higher in the second phase (p=0.02) of the study. Drug therapy problem like inappropriate dosage frequency was significantly higher (p=0.04) in the second phase of the study (Table 4). The rate of increase of errors per prescription was higher in prescriptions containing more than 2 errors per prescription (Figure 1).

Amoxicillin (29.4%) is the most prescribed antibiotics associated with DTPs followed by amoxicillin + clavulanic acid (23.5%) and ofloxacin (10.3%) respectively. Malaria (49.2%) is the most diagnosed infection associated with DTPs followed by Upper respiratory tract infection (URTI) (32.2%) and peptic ulcer (5.1%) (Table 5). The most used antibiotics class associated with DTPs was penicillin (29.4%) followed by enhanced beta-lactamase penicillin (25%) and fluoroquinolone (19.1%) (Figure 2). Enhanced beta-lactamase penicillins are penicillins that are protected from the effect of beta-lactamase enzymes in the gastro-intestinal tract.

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Table 1: Baseline data summary

S/N	Characteristics	Frequency	Percent
	Male	44	44
	Female	56	56
	Total	100	100
	Prescription		
	No of Antibiotics prescription	147	
	Antibiotics prescriptions containing DTPs	77	52.4%
	Antibiotics prescriptions without DTPs	70	47.6%
	Drug therapy problems (DTPs)		
	Drug interaction	36	37.1%
	Overdosing	8	8.2%
	Under-dosing	3	3.1%
	Required antibiotics (but not indicated)	0	0%
	Inappropriate dosage duration	2	2.1%
	Inappropriate dosage frequency	23	23.7%
	Contraindication	3	3.1%
	Unnecessary medication	22	22.7%
	Total no of errors (DTPs)	97	

Comment [Ma27]: The 97 total errors is different from the 77 error mentioned earlier. Explain this

Table 2: Attendance of the healthcare professionals at the seminar presentation

Professionals	Total no of staff at UHC	No of staff that attended the seminar presentation (Percent)	Qualifications of antibiotics prescribers	Frequency (percent)	Ranks of antibiotics prescribers	Frequency (percent)
Medical doctors	11	4 (36)	First degree	11 (100)	Director	1 (9.1)
Pharmacists	5	2 (40)	Second degree	1 (9.1)	Chief Medical Officer	1 (9.1)
Pharmacy technicians	7	3 (43)	Third degree	0	Principal Medical Officer	5 (45.5)
Assistant Pharmacists	7	2 (29)	Fellowship	2 (18.2)	Medical Officer	4 (36.4)
Laboratory scientist	4	1 (25)				
Radiologist	6	1 (17)				
Total	40	13 (33)				

Table 3: Follow-up data summary

S/N	Characteristics	Frequency	Percent
	Male	58	36.3%
	Female	102	63.7%
	Total	160	
	Prescription		
	No of Antibiotics prescriptions	160	
	Antibiotics prescriptions containing DTPs	112	70.0%
	Antibiotics prescriptions without DTPs	48	30%
	Drug therapy problems (DTPs)		
	Drug interaction	103	49.3%
	Overdosing	15	7.2%
	Under-dosing	6	2.9%
	Required antibiotics (but not indicated)	3	0%
	Inappropriate dosage duration	40	19.1%
	Inappropriate dosage frequency	24	11.5%
	Contraindication	0	0%
	Unnecessary medication	18	8.6%
	Total no of DTPs	209	

Comment [Ma28]: Same here. Explain

Table 4: Comparison of antibiotics prescription

S/N	Characteristics	First phase	Second phase	Comparison
	Male	14.6±18.7	19.3±13.7	p= 0.007
	Female	18.6±23	34±23.3	p= 0.014
	Total	33.3±41.7	53.3±36.2	p= 0.0002
	Prescription			
	No of Antibiotics prescription	147	160	
	Antibiotics prescription	49±39.5	53.3±36.2	p=0.53
	Antibiotics prescriptions containing DTPs	25.6±13.8	37.3±28.3	p=0.02
	Antibiotics prescriptions without DTPs	23.3±25.8	16±7.9	p= 0.37
	Drug therapy problems (DTPs)			
	Drug interaction	12±6	34.3±22.2	p= 0.225
	Overdosing	2.6±3.0	5±5.5	p= 0.93
	Under-dosing	1.0±1.7	2±2	p= 0.92
	Required antibiotics (but not indicated)	0	1±1	p= 0.70
	Inappropriate dosage duration	0.6±1.1	13.3±4.7	p=0.88
	Inappropriate dosage frequency	7.6±6.1	8±10.3	p=0.04
	Contraindication	1±1	0	p= 0.70
	Unnecessary medication	7.3±7.5	6±1.7	p=0.1
	Total no of errors (DTPs)	97	209	

Comment [Ma29]: This should statement the type of analysis

Table 5: Composition of prescribed drugs and diagnosed diseases associated with DTPs

S/N	PRESCRIBED DRUGS	FREQUENCY (%)	DIAGNOSED DISEASES	FREQUENCY (%)
1	Amoxicillin	40 (29.4)	Malaria	58 (49.2)
2	Amoxicillin+Clavulanic acid	32 (23.5)	URTI	38 (32.2)
3	Ofloxacin	14 (10.3)	Peptic Ulcer	6 (5.1)
4	Ciprofloxacin	12 (8.8)	UTI	4 (3.4)
5	Fluconazole	12 (8.8)	Skin rash	2 (1.7)
6	Tinidazole	8 (5.9)	Hemorrhoid	2 (1.7)
7	Metronidazole	6 (4.4)	Gastroenteritis	2 (1.7)
8	Erythromycin	4 (2.9)	Asthma	2 (1.7)
9	Clotrimazole	4 (2.9)	Fever	2 (1.7)
10	Ampicillin + Cloxacillin	2 (1.5)	Insomnia	2 (1.7)
11	Cefuroxime	2 (1.5)		
	Total	136	Total	118

URTI: Upper respiratory tract infection, UTI: Urinary tract infection

Comment [Ma30]: This is not enhanced beta lactamase. Its penicillin with beta lactamase inhibitor combination

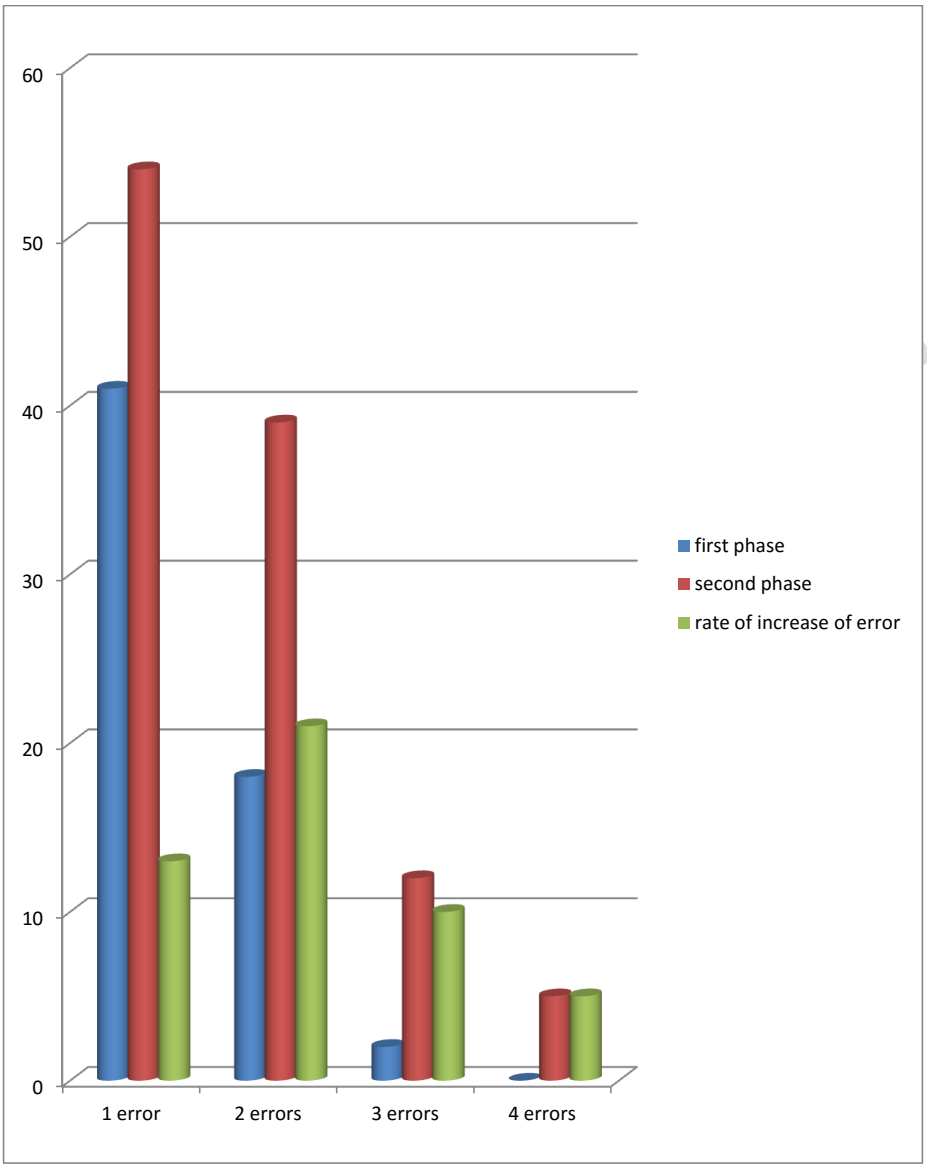

Figure 1: Number of errors per prescription

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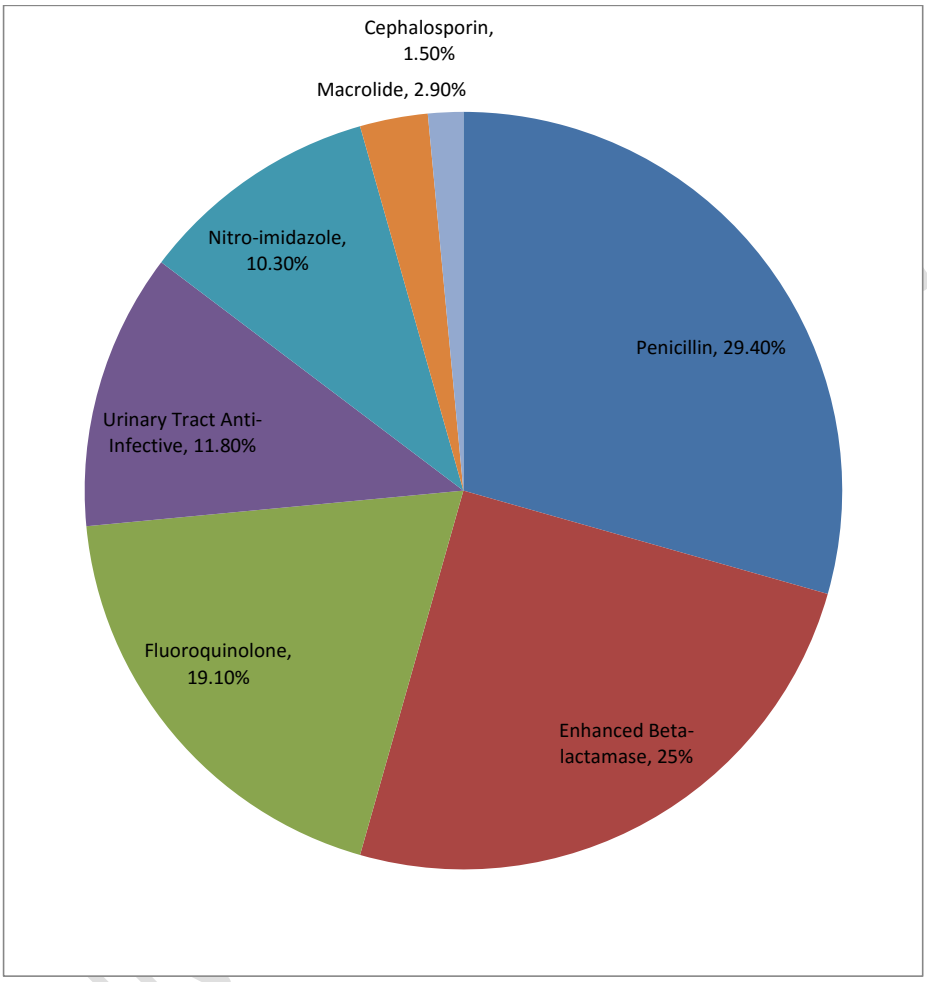

Figure 2: Prescribed Antibiotics Class

DISCUSSION

Effects of inappropriate prescriptions previously reported

Antibiotic resistance is among the greatest public health threats today, leading to an estimated 2 million infections and 23,000 deaths per year in the United States of America. Antimicrobial resistance is one of our most serious health threats. Infections by resistant bacteria are now very common, and some pathogens have even become resistant to multiple types or classes of antibiotics. The loss of effective antibiotics will undermine our ability to fight infectious diseases. If alternative treatments exist, research showed that patients with resistant infections would likely die; survivors had significantly longer hospital stays, delayed recuperation, and long-term disability. Efforts to prevent such threats lie on the foundation of proven public health strategies such as immunization, infection control, protecting the food supply, antibiotic stewardship, and reducing person-to-person spread through screening, treatment and education [15]. The rate of antibiotic resistance could be reduced through the prevention of inappropriate prescribing of antibiotics. Minimizing unnecessary antibiotic use would be the best way to reduce the risk of adverse drug events from antibiotics [15].

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Prevalence of inappropriate prescriptions at the facility

More than half of the antibiotics prescriptions (52.4%) in the first month of this study involved drug therapy problems. Some of the observed drug therapy problems were prescribing antibiotics for ten days for undiagnosed infections without any laboratory investigations, the combination of antibiotics with anti-malaria drugs which were liable to reduce the absorption of antibiotics in the gastrointestinal tracts, wrong dosage frequency of antibiotics eg ampicillin+cloxacillin capsule prescribed to be taken thrice daily instead of the usual every six hours. This observation is supported by the report of previous studies which affirmed a high prevalence rate of drug therapy problems in countries like the United Kingdom, Sweden and Mexico with 12%, 42% and 58% respectively [3]. The rate of antibiotics prescriptions with DTPs (52.4%) was higher in this study than that of other countries with exception of Mexico [3]. Another observational study conducted in 700bed University hospitals in Barcelona Spain had indicated a DTP rate of 45.1%. In their study, medication reconciliation was responsible for 38.4% of DTPs [16]. In our study, the DTPs

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included drug interactions, inappropriate dosage frequency and unnecessary medication. These were associated risk factors for antibiotics resistance and drug adverse events which might lead to a reduced quality of life of the patients. A previous study had indicated that inappropriate drug selection, inappropriate dosage frequency and duration, and unnecessary medication were responsible for antibiotics resistance [17]. A report had shown that antibiotics were known to be powerful, safe and helpful drugs in fighting disease, but sometimes could be harmful. Antibiotics were reported to cause side effects such as allergic reactions and also interfered with the action of other drugs taken by the patient for another condition [15]. Moreover, taking antibiotics through requested prescriptions of antibiotics or non-empirical prescriptions of antibiotics when it was not needed would probably lead to the development of antibiotic resistance. When resistance develops, antibiotics would not be able to stop future infections [15].

Response of healthcare professionals

More than half of the antibiotics prescribers at the University of Uyo Health Centre did not attend the seminar presentation. The few antibiotics prescribers and other healthcare team members at the seminar widely accept our intervention. The intervention emphasized the prevalence of DTPs at the Centre which was acknowledged by the antibiotics prescribers during the seminar presentation. The observed DTPs of the study were disclosed at the seminar presentation which suggested that the inadequate knowledge of the global trend of the antimicrobial stewardship program, which is a major approach to preventing inappropriate prescription of antibiotics. It was clear that this medium would not be adequate for the dissemination of information on drug therapy problems to the prescribers of antibiotics at the University Health Centre as many of them were not in the meeting. After an elaborate discussion on antibiotics stewardship program during the seminar presentation, the antibiotics prescribers acknowledged the need for the antibiotics stewardship program at the University of Uyo Health Centre. The antibiotics prescribers at the seminar presentation also declared their commitment to laboratory investigation before prescription of antibiotics except in an emergency. In consonance with our observations, a previous study indicated that prescribing antibiotics when they were not needed or prescribing the wrong antibiotics in outpatient settings such as doctors' offices were common observations. It also emphasized that doctors might not order laboratory tests to confirm that bacteria were the cause of infections; therefore antibiotics might be unnecessarily

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prescribed. It also indicated that patients demanded treatment for conditions such as cold when antibiotics would not be needed and would not help. Likewise, healthcare providers could be too willing to satisfy patient's expectations for antibiotic prescriptions [18]. It was reported that CDC set up "the Get Smart program" to improve antibiotic prescribing and use in both outpatient and inpatient settings. The program was set up to inform local public health authorities of messages and resources for improving antibiotic use [19]. A higher proportion of DTPs was observed in the follow-up survey because many patients received antibiotics prescriptions, most of the antibiotics prescribers did not attend the seminar, thereby were unaware of DTPs situation at the Centre. Moreover, the majority of the antibiotics prescribers at the Centre did not have post-graduate qualifications and their years of medical experience were still few. Pearson *et al.*, had earlier reported that antibiotic prescribers had challenges of access to information on antibiotics use and antimicrobial resistance [18]. These factors could have led to the increased DTPs during the follow-up survey. However, the repetition of antibiotics prescriptions for some patients that were observed in the first survey was completely avoided during the follow-up survey in response to the seminar presentation.

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Trends of drug therapy problems at the facility

There were many antibiotics prescriptions at the second survey because it coincided with the resumption of the second semester academic activities after barely a month mid-session break. There was no significant variation in the number of the prescriptions of antibiotics used in the two surveys. Most of the physicians were not in attendance during the seminar presentation and were also involved in the prescription of antibiotics at the follow-up survey of the study. The observed increased number of prescriptions of antibiotics consequently led to a profound increase in the number of observed drug therapy problems which mostly included drug interactions, inappropriate dosage duration and inappropriate dosage frequency. The increase in number of prescriptions of antibiotics could be due to influence from patients and medical representatives of Pharmaceutical Companies promoting pharmaceutical products. Pearson *et al*., had earlier reported that medical representatives promoting pharmaceutical products in the hospitals directly motivated prescribers of antibiotics [18]. The observed DTPs in this study were potential causes of drug adverse reactions and antibiotics resistance. This observation was in consonance with an earlier report on mortality and morbidity [17].

The prescription of antibiotics at the University of Uyo Health Centre majorly involved significant drug therapy problems of which inappropriate dosage frequency was the most prominent. This suggests that the University community could be subjected to a future alarming therapeutic failure of antibiotics due to antibiotic resistance. This could be worsened as the laboratory section lacked basic reagents for diagnostic investigations. Any antibiotic use could be a potential for side effects. Some antibiotics could lead to side effects that would be severe, disabling, and even deadly. Adverse Drug Events had been reported from the use of medication which included allergic reactions and side effects due to over-medication and medication errors. Using the right antibiotic, at the right time, dose, and duration would protect people and help slow the development of antibiotic resistance and the spread of germs. Unnecessary antibiotic use could also pose for antibiotic-resistant germs, which could affect other people [20]. A previous study indicated that twenty percent of all hospitalized patients who received an antibiotic experienced an adverse drug event [21]. In the community, antibiotic-associated adverse events had been reported to often require emergency treatment. Among children, antibiotics were reported in 46 percent of emergency department visits for adverse drug events [22]. Among adults, antibiotics were reported in 14 percent of emergency department visits for adverse drug events [23]. Any antibiotic use would be the potential harm; therefore, clinicians should prescribe antibiotics to their patients only when the benefits outweigh the potential risks.

Future problems requiring immediate attention

The increase in the number of patients attending the University of Uyo Health Centre would be of concern because of the alarming increase in the rate of errors per prescription. The rate of errors per prescription was beyond proportion for antibiotics prescriptions with more than two-drug therapy problems. This was a major concern for health practitioners at the Centre to ensure that appropriate measures were put in place to prevent drug therapy problems, especially drug adverse reactions and antibiotic resistance. Hicks *et al*., suggested that possible antibiotic resistance in a community where drug therapy problems persist [17]. In our study, the effects of DTPs were not followed up on the health outcomes of the patients whose folders were used because it was not in the objectives of the study and the period of the study was too short to follow-up the patients. This is the limitation of our study. Bacterial resistance problems caused by gram-negative pathogens were usually worrisome due to resistance to nearly all drugs that

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would be considered for treatment [15]. This study indicated significant drug therapy problems with antibiotic prescriptions in the University of Uyo Health Centre which had prompted the set up of antibiotic stewardship committee at the Centre. Preventing infections from developing would reduce the number of antibiotics used. This reduction in antibiotic use would slow the pace of antibiotic resistance. Preventing infections would also prevent the spread of resistant bacteria. Antibiotic-resistant infections could be prevented in healthcare settings. Antibiotic resistance in healthcare settings is a significant threat to public health.

CDC had worked to prevent antibiotic resistance in healthcare settings by providing a system to track resistance and prescribing patterns at national, regional, and local levels; and guidance to healthcare facilities interested in better antibiotic use. Tracking CDC's National Healthcare Safety Network (NHSN) was used by health care facilities to electronically report infections, antibiotic use, and resistance. Data currently submitted by hospitals to NHSN would allow facilities, states, and regions the ability to track and benchmark antibiotic resistance in bacteria responsible for many healthcare-associated infections. As more hospitals submitted data to the new NHSN Antibiotic Use and Resistance Module, it would be possible to track and benchmark antibiotic resistance in all bacteria, as well as track antibiotic usage. This information would help facilities to target areas of concern, required for improvement. National reference laboratory would test bacteria samples from around the country to detect new and emerging resistance patterns that would affect patient health. This reference testing also would provide an early warning of new resistance that would have the potential to spread across the nation and that requires public health action.

Therefore, doctors and other health professionals around the world are increasingly adopting the principles of responsible antibiotic use, often called antibiotic stewardship. Stewardship is a commitment to always use antibiotics only when they are necessary to treat, prevent disease, choose the right antibiotics and administer them in the right way in every case. Effective stewardship program ensures that every patient gets the maximum benefit from antibiotics, avoids unnecessary harm from allergic reactions and side effects, and helps preserve the life-saving potential of these drugs for the future. Efforts to improve the responsible use of antibiotics have not only demonstrated these benefits but have also been shown to improve outcomes and save healthcare facilities money in pharmacy costs [15].

Patients could be protected by healthcare providers from antibiotic-resistant germs such as bacteria and fungi, which could cause difficult and sometimes impossible-to-treat infections. The following measures should be employed, infection prevention and control recommendations, educate patients on ways to prevent spread, treatment guidelines should be followed. The CDC's Core Elements of Antibiotic Stewardship ensure appropriate antibiotic use [20].

Study limitation

There was a possibility that the whole prescriptions generated at the healthcare were not accessed by researchers. Lack of total response to the intervention by the healthcare professionals also limited the effect of the intervention in the study outcome. The study did not follow-up patients whose folders were used for the manifestation of DTPs' outcomes.

CONCLUSION

The observed drug therapy problems in this study were drug interactions, inappropriate dosage frequency and unnecessary prescription of antibiotics. There was no improvement in drug therapy problems despite seminar presentation as an intervention except that repetitions of antibiotics for certain patients were stopped at the follow-up survey. Further study is required to find better measures of intervention as solution to the drug therapy problems.

However, the impact of this study has resulted in the establishment of the Antimicrobial Stewardship Committee at the University of Uyo Health Centre to control and monitor the use of antibiotics.

RECOMMENDATION

Support for the newly established Antibiotic Stewardship Committee by all prescribers and other healthcare professionals are hereby recommended.

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