INDIAN JOURNAL OF SCIENCE AND TECHNOLOGY

RESEARCH ARTICLE

Improving Antibiotic Use in Surgical Care: Impact of Clinical Pharmacist Interventions on Optimizing Patient Therapy

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OPEN ACCESS

Received: 13-01-2022
Accepted: 02-08-2022
Published: 27-08-2022

Citation: Kuruvilla AV, Ramesh M, Madhu CP (2022) Improving Antibiotic Use in Surgical Care: Impact of Clinical Pharmacist Interventions on Optimizing Patient Therapy. Indian Journal of Science and Technology 15(33): 1634-1641. https://doi.org/10.17485/IJST/v15i33.100

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Funding: None

Competing Interests: None

Published By Indian Society for Education and Environment (iSee)

ISSN
Print: 0974-6846
Electronic: 0974-5645

Abstract

Objectives: To assess the nature of drug-related problems (DRPs) associated with antibiotic use and to evaluate the level of significance of clinical pharmacist interventions in surgical care. **Methods:** This prospective interventional study was carried out for 1 year in the wards of General Surgery. The in-patients were followed daily and reviewed for DRPs. The identified DRPs were categorized according to the Hepler and Strand classification. Drug-related problems other than those in Hepler and Strand classification were categorized separately based on medical literature and clinical practice evidence. The identified DRPs were conveyed and discussed by the clinical pharmacist with the surgeon, and ideal suggestions for further action. A bivariate logistic regression analysis was performed to identify the predictors of the DRPs associated with antibiotic use. **Findings:** Of the 614 patients, 64.49% were males. 414 DRPs were identified, wherein improper duration of drug use (20.86%) was the most common DRP. The significance level of pharmacist intervention was found to be 'major' in 49% of cases. The incidence of DRPs associated with antibiotic use was 67.42%. The rate of acceptance of pharmacist interventions was 99%. A strong association between the occurrence of DRPs and age, the presence of two co-morbid conditions, the intake of two and three antibiotics, and length of stay (LOS) of 6–10 and 16–20 days ($P < 0.05$) was noted. **Conclusion:** Even though antibiotics are necessary for surgical management, their vigilant use is warranted. The clinical pharmacist plays an enormous role in optimizing antibiotic therapy in surgical patient care. **Novelty:** To the best of our knowledge, such an interventional study of its kind that exclusively focused on the surgery ward was not conducted in India previously, and not many studies of a similar kind have been carried out in other parts of the world that have assessed the prevalence and frequency of DRPs related to antibiotic use, the predictors associated with the DRPs, the role of clinical pharmacists in the surgery ward, and the acceptance rate of pharmacist interventions by the surgeons. Here, an attempt to identify the predictors of drug-related problems associated with antibiotic use was made to help prevent and resolve drug-related problems earlier, thereby

promising optimized therapy. Also, it highlights the importance of a clinical pharmacist's role in surgical care regarding patient safety.

Keywords: Antibiotics; Surgery; Clinical Pharmacist; Predictors; Interventions; Drug Related Problems

1 Introduction

Antibiotics have become an inevitable component in surgical care, where these are used for treating or preventing infections more than any other ward. Even with the advancements in preventive strategies, fear of a rise in surgical infection rate is because of the occurrence of more lengthy surgeries or performed with more complexity, a growing number of elderly, diabetics, and immune-compromised patients, which is associated with markable morbidity and mortality[1–3].

However, it is deplorable that approximately half of the patients receive antibiotics unnecessarily or inappropriately as a result of inappropriate prescription for antibiotic prophylaxis, the continuation of empirical therapy in stable patients, although cultures show no bacterial growth and unawareness about the patterns of susceptibility of common pathogens. Inappropriate use of antibiotics paves the way for Drug-Related Problems (DRPs), Surgical Site Infections (SSIs), morbidity, mortality, and antibiotic resistance, thereby increasing the cost of treatment and hospital stay[4–8]. Literature reviews concerning DRPs indicated that among the medications prescribed in the surgery ward, antibiotics contributed the most (73.8%) towards DRPs[1]. In addition, in a study conducted in the surgical wards of Jimma University Medical Centre, Ethiopia, for 3 months, DRPs related to antibiotic use were found in 69.3% of the 300 study participants[8]. This being the case, it requires early identification and resolution[1].

Clinical pharmacists are well known for their expertise in detecting, resolving, and preventing drug-related problems. Despite this, few or no clinical pharmacists were allocated to the surgery ward, presuming that the prevalence of DRPs in this ward was lower. Therefore, it is vital to assign clinical pharmacists to every hospital ward and to accept them as a part of the multi-disciplinary health care team to provide patient care[1]. Even though antimicrobials are prescribed more frequently in developing countries than any other drug class, regardless of the nature of the infection, very few studies were conducted to determine the prevalence of DRPs related to antibiotic use in developing countries[9].

Studies conducted to date have not thrown much light on the real-time practice as they have limitations such as following retrospective or prospective observational study designs or prospective study design with narrow inclusion criteria and small sample size conducted for a short period, medication-oriented rather than patient-centred approach. Few have assessed the medical fraternity's acceptance rate of pharmacist interventions. Also, this study is intended to contribute to the documentation of pharmacist interventions which is paramount for the further expansion and recognition of Clinical pharmacists.

Hence, to the best of our knowledge, such an interventional study that exclusively focused on the Surgery ward was not conducted in India previously. Not many studies of a similar kind were carried out in other parts of the world as well that assessed the prevalence and frequency of DRPs related to antibiotic use, the predictors associated with the DRPs, the role of clinical pharmacists in the Surgery ward, and the acceptance rate of pharmacist interventions by the surgeons.

2 Method

2.1 Design of Study and Ethical Approval

This prospective interventional study was carried out for 1 year by the clinical pharmacist in the general surgery wards of a multi-speciality tertiary care hospital in India after obtaining ethics approval from the Institutional Human Ethics Committee of JSS College of Pharmacy, Mysuru.

2.2 Selection of participants

All in-patients were reviewed daily for antibiotic prescriptions, and those prescribed at least one antibiotic were enrolled after obtaining their informed consent. Patients who had a hospital stay of less than a day were excluded.

2.3 Data collection

The patient demographics, diagnoses, co-morbid conditions, and antibiotic treatment regimens were recorded in detail by reviewing the respective patient treatment charts and other relevant records with the help of a suitably designed data collection form. The diagnoses were coded using the International Classification of Disease (ICD-10), and the antibiotics were coded according to the WHO- Anatomical Therapeutic Classification (ATC) Code.

2.4 Drug-Related Problems (DRPs)

All in-patients on antibiotics were followed daily and reviewed for DRPs. If a DRP was identified, it was conveyed and discussed by the clinical pharmacist with the surgeon, with ideal suggestions for further action and sought corrective measures. The identified DRPs were categorized as per the Hepler and Strand classification. The problems other than those in Hepler and Strand classification were identified and categorized based on medical literature and clinical practice evidence. The remedial action required for the identified DRP was formulated based on the information available on various relevant, updated drug information. Each DRP was assessed for clinical significance based on Alderman's classification of clinical pharmacy interventions [10].

2.5 Data analysis and interpretation

A computerized format of the data collection form was created using Google forms, and Microsoft Excel 2016 was used for easy data entry, accessibility, storage, retrieval, and analysis of data. The predictors associated with the DRPs were identified at a P-value of < 0.05. Using SPSS version 21.0, bivariate logistic regression analysis was done to obtain the P-value for categorical variables.

3 Results and Discussion

Among the 614 patients enrolled in this study, 396 (64.49%) were male, and 218 (35.51 %) were female. The majority of the patients belonged to the age group of 40-59 years (35.99 %). A total of 331(53.9%) patients presented with at least one co-morbid condition. The WHO - ICD 10 classification was used to code patients' diagnoses. Most of the patients presented with diseases of the digestive system (51.21%), followed by diseases of the skin and subcutaneous tissue (29.7%). A total of 58.96% of patients had undergone surgery. Patient demographics and clinical characteristics of the study population are depicted in Table 1.

A total of 1085 antibiotics were prescribed for the patients in surgery wards during this period. The most common use for which patients were prescribed antibiotics was for prophylaxis (47%), followed by empirical therapy (44%), as most cases had undergone surgical intervention. The findings were similar to studies conducted in India and Nigeria [3,11]. Of the 1085 antibiotics prescribed, 96.13% were injectables, which was found to be higher when compared to a study in Nigeria, where only 58.7% of antibiotics were injectables. This difference might be due to the following study design, i.e., point prevalence survey [11]. The characteristics of antibiotic prescriptions in the study population are depicted in Table 2.

During the study period, 441 DRPs were identified in 414 patients. Per patient, the average number of DRPs identified was 1.41 ± 0.6 (range: 1–4), which was similar to studies conducted in the past [8,12]. It was found that the prevalence of DRPs among the study population was 71.8%, which was similar to a study in Ethiopia, probably as DRPs associated with antibiotic use were prevalent in developing countries [8]. It was observed that the majority (39%) of DRPs were observed in patients who had a LOS of 6–10 days, received only one antibiotic (43.96%), and had one co-morbid condition (68.28%). The presence of a co-morbid condition, antibiotic use, and increased LOS can increase the risk of developing DRPs.

Table 1. Patient Demographics & Clinical characteristics of the study population

Patient Demographics & Clinical characteristics	No. of patients (%) n = 614
Gender	
Male	396 (64.49)
Female	218 (35.51)
Age	
<18	35 (5.7)
≥18-39	207 (33.71)
≥40-59	221 (35.99)
≥60-79	139 (22.63)
≥ 80-99	12 (1.97)
Comorbid condition(s)	
Yes	331 (53.9)
No	283 (46.1)
Surgical procedure performed	
Yes	362
No	252
Patient Diagnoses	
Diseases of the digestive system	338 (51.21)
Diseases of skin and subcutaneous tissue	196 (29.7)
Diseases of the blood and blood forming organs and certain disorders involving the immune mechanism	11 (1.67)
Endocrine, nutritional and metabolic diseases	14 (2.12)
Diseases of the genitourinary system	26 (3.94)
Diseases of the circulatory system	58 (8.79)
Neoplasm	8 (1.21)
Diseases of the respiratory system	7 (1.06)
Symptoms, signs and abnormal laboratory findings not elsewhere classified	2 (0.3)

Table 2. Characteristics of antibiotic prescriptions in the study population

Type of formulations	Category of Antibiotic use			
	Prophylaxis (n=508)	**Empirical (n=481)**	**Definitive (n=96)**	**Total (n=1085)**
Injectables	495 (45.62)	457 (42.12)	91 (8.39)	1043 (96.13)
Tablets	13 (1.20)	24 (2.21)	4 (0.37)	41 (3.78)
Capsule	-	-	1 (0.09)	1 (0.09)

In the majority [n=391, (94.44%)] of cases, a single DRP was identified, whereas, in the remaining cases, > 2 DRPs were identified [n=23, (5.56%)]. The most common DRPs identified, among the ones not enlisted in the Hepler and Strand classification, were inappropriate duration of drug use (20.86%) followed by partially untreated indication (14.06%), while it was improper drug selection (14.29%) followed by drug use without indication (13.15%) as per Hepler and Strand classification. These results contradict the study's findings in Ethiopia, where 'dose too low' (28.9%) was the most common DRP associated with antibiotic use [8]. Whereas in Malaysia, a study had shown that inappropriate duration of treatment topped the list; however, compared with the present study, it had a higher rate of inappropriate duration of treatment (47.4%) [13]. This may be explained by certain factors such as the surgeon's choice of antibiotic therapy, personal experience, lack of proper prophylactic protocols, etc.

Most of the DRPs in the study were related to the inappropriate duration of drug use followed by improper drug selection. Instances of the inappropriate duration of drug use can be explained with an example from the study population wherein the majority of the patients were diagnosed with gastrointestinal and skin and soft tissue-related diseases for which antibiotics were used for surgical prophylaxis but continued post-surgically to prevent the occurrence of surgical site infections (SSIs)

and readmissions to the hospital. Considering the case of improper drug selection, it was observed that few of the surgeons were not ready to change the antibiotic according to the available culture and sensitivity report as they occasionally observed clinical improvement with empirical therapy itself. Sometimes, it was even observed that patients were reluctant to purchase antibiotics as per the report due to cost issues. Another instance noted under improper drug selection commonly as an example was the prescription of cephalosporins instead of fluoroquinolones for disease conditions related to the genito-urinary system as these has more penetration into the genito-urinary system and urine. In partially untreated indications, cephalosporins alone were prescribed for polymicrobial infections such as necrotizing fasciitis, assuming that these have excellent coverage for both aerobes and anaerobes, despite the fact that these only have moderate coverage for anaerobes. Cephalosporins were the most commonly implicated antibiotic class in DRPs (27.67%), followed by nitroimidazoles (25.63%). This was consistent with the findings of a few Ethiopian studies[1–8]. This is quite understood as cephalosporins and nitroimidazoles play a major role in surgical prophylaxis. Details of the DRPs identified in the study population are represented in Table 3.

Table 3. Details of the Drug Related Problems identified in the study population

DRPs per patient	
Number of DRPs	**Number of patients (%) (n=414)**
One	391 (94.44)
Two	20 (4.83)
Three	2 (0.48)
Four	1 (0.24)
Types of DRPs	
Categories of DRPs	**Number (%)**
DRPs as per Hepler and Strand classification	
Improper drug selection	63 (14.29)
Drug use without indication	58 (13.15)
Sub therapeutic dose	32 (7.25)
ADR	21 (4.76)
Overdose	14 (3.18)
Failure to receive drugs	1 (0.23)
DRPs other than Hepler and Strand classification	
Inappropriate duration of drug use	92 (20.86)
Partially untreated indication	62 (14.06)
Inappropriate multiple drug use	51 (11.56)
Lack of Monitoring	26 (5.9)
Alternative dosage form	21 (4.76)
Classes of antibiotics implicated in DRPs	
Classes of antibiotics	**No. of DRPs (%) (n=441)**
Cephalosporins	122 (27.67)
Nitroimidazoles	113 (25.63)
Carbapenems	55 (12.57)
Penicillins	46 (10.46)
Lincosamides	26 (5.92)
Quinolones	25 (5.58)
Polymyxins	25 (5.58)
Oxazolidinediones	21 (4.77)
Aminoglycosides	7 (1.59)
Glycopeptide	1 (0.23)

A total of 441 suggestions for the identified DRPs. The most frequent suggestion for the identified DRPs was drug withdrawal [n=222, (50.34%)]. This was in contrast to the top suggestion provided most in the study done in Ethiopia, which was a need for an additional drug[8]. The acceptance rate of pharmacist interventions was 99%, and as a result, there was a change in

drug therapy as per pharmacist recommendations. This acceptance rate was higher than in previous studies in China, Ethiopia, Japan, and Turkey[1,14–16]. This might be due to a well-established clinical pharmacy facility with a full-time clinical pharmacist exclusively dedicated to the Surgery ward to provide clinical pharmacy services at the bedside as tailored recommendations in real-time by considering the patient's condition and closely associating and understanding the various concerns of surgeons. Various studies have shown that clinical pharmacists, recommendations that aid in resolving and preventing DRPs are accepted widely[17]. Suggestions provided by the intervening pharmacist during the study are depicted in Table 4.

Table 4. Suggestions provided by the intervening pharmacist

Suggestion made	No. of interventions (%) (n = 441)
Drug withdrawal	222 (50.34)
Change of therapy	64 (14.51)
Addition of a drug	62 (14.06)
Dosage adjustment	46 (10.44)
Monitoring	26 (5.89)
IV to oral conversion	21 (4.76)

This study shows that, out of 441 DRPs identified, 49% (n = 215) were 'major', 46% (n = 205) 'moderate' and 5% (n=21) 'minor' level of significance. Pharmacist interventions that fell in the category of 'major' significance level were mainly related to overdose. This study mostly had gastrointestinal disorders followed by skin and soft tissue-related disorders. Patients sometimes presented with co-morbid conditions like diabetes mellitus, even with complications like acute kidney injury, etc. In such cases, patients have been prescribed an antibiotic without adjusting the dosage and frequency of administration irrespective of the serum creatinine levels and creatinine clearance. Cases of moderate significance were mostly associated with antibiotic conversion from IV to oral. The significance of pharmacist interventions in the study is depicted in Figure 1 .

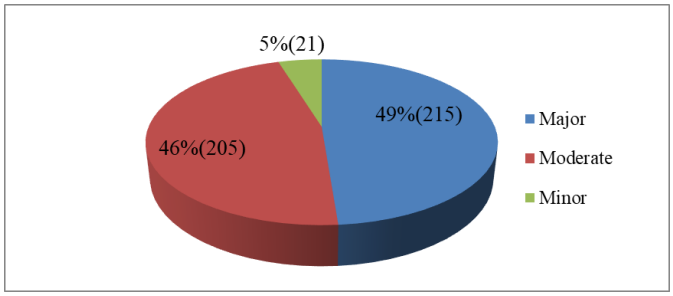

Fig 1. Level of significance of pharmacist interventions

Of the 614 patients, the DRPs were identified in 414 patients, and the remaining 200 patients who were not presented with DRPs were considered the control group. The predictors of DRPs were determined using bivariate logistic regression analysis. Age, gender, co-morbid conditions, length of stay, and the number of antibiotics were the parameters considered for assessing predictors. Age was a significant predictor associated with the DRPs. Based on the P-value, Odd's ratio, and C.I., all age groups (18; > 18-39; > 40-59; > 60) (O.R. =5.16, 3.24, 5.5 CI =2.41-11.1, 1.54-6.87, 2.5-12.09 & P=0.0001, 0.0021, 0.0001) were found to be significant. Thus, patients of all age groups were at risk of developing DRPs. The number of antibiotics (two and three) received (O.R. =1.7, 3.71 CI=1.17-2.47, 1.89-7.35 & P = 0.0051, 0.002) were found to be significant based on the P-value, Odd's ratio and CI when compared to the number of antibiotics >3 (O.R. 3.71, 2.72, 7.5, CI = 0.75-9.86, 0.41-136.94, P=0.12, 0.17). Length of stay for 6-10 days and 16-20 days (O.R. = 1.55, 2.93 CI=1.04-2.3, 1.16-7.41 & P=0.02, 0.02) were found to be significant based on the P-value, Odd's ratio, and CI when compared to LOS > 20 days (O.R.0.89, 3.9, 8.47, 5.86, CI = 0.38-2.02, 0.46-33.02, 0.47-152.49 0.31-110.44, P = 0.77, 0.21, 0.14, 0.23). The presence of two comorbid conditions (O.R. = 0.31 CI=1.16-7.41 P=0.002) was found to be significant based on the P-value, Odd's ratio, and CI when compared to co-morbid conditions >3 (O.R. 0.31, 0.89, 0.16, CI=0.15-0.66, 0.19-4.14, 0.01-1.89, P=0.002, 0.89, 0.14). Hence, two co-morbid conditions, intake of two and three antibiotics, 6–10 days, and 16–20 days of LOS were statistically significant (P <0.05) predictors of DRPs. As the length of stay at the hospital extends, the more the patients will be exposed to antibiotics and the more chances for hospital-acquired infections, which again require antibiotic therapy[8]. Predictors of DRPs associated with antibiotic use in this study are depicted in Table 5.

Table 5. Predictors of DRPs associated with antibiotic use

Predictors		With DRP (n = 414)	Without DRP (n = 200)	Odd's ratio	CI	P value
Gender	Male	274	122		-	-
	Female	140	78	0.79	0.56-1.13	0.21
Age	<18	12	23		-	-
	≥18-39	151	56	5.16	2.41-11.1	0.0001
	≥ 40-59	139	82	3.24	1.54-6.87	0.0021
	≥ 60	112	39	5.5	2.5-12.09	0.0001
No. of antibiotics	1	182	124		-	-
	2	155	62	1.7	1.17-2.47	0.0051
	3	60	11	3.71	1.89-7.35	0.0002
	4	12	3	2.72	0.75-9.86	0.12
	5	5	0	7.5	0.41-136.94	0.17
Length of stay	1-5	123	80		-	-
	6-10	172	72	1.55	1.04-2.3	0.02
	11-15	61	30	1.32	0.78-2.22	0.29
	16-20	27	6	2.93	1.16-7.41	0.02
	21-25	15	11	0.89	0.38-2.02	0.77
	26-30	6	1	3.9	0.46-33.02	0.21
	31-35	6	0	8.47	0.47-152.49	0.14
	36-40	4	0	5.86	0.31-110.44	0.23
Comorbid conditions	1	209	17		-	-
	2	62	16	0.31	0.15-0.66	0.002
	3	22	2	0.89	0.19-4.14	0.89
	4	2	1	0.16	0.01-1.89	0.14

4 Conclusion

The prevalence of DRPs associated with antibiotic use was found to be high. The most common DRP identified was the improper duration of drug use, followed by improper drug selection. The majority of DRPs were observed with antibiotics of the cephalosporin class. More DRPs were observed in male patients; the most vulnerable age group was 18–39. There was a strong association between the occurrence of DRPs and all the age groups, the presence of two co-morbid conditions, receiving two and three antibiotics, and length of stay of 6–10 and 16–20 days ($P < 0.05$). Even though antibiotics are necessary for surgical management, their vigilant use is warranted.

This study portrays how clinical pharmacist services can enormously optimize antibiotic therapy in surgical patient care. Hence, the surgery ward should not be neglected concerning clinical pharmacy services. The clinical pharmacy should not be considered an 'elective speciality' at health care facilities as it can positively influence patient care.

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