Original Article

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Pharmacology Section

Restricted Parenteral Antibiotics Usage Policy in a Tertiary Care Teaching Hospital in India

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ABSTRACT

Introduction: The indoor hospital use of antibiotic irrationally has been a growing concern in the recent past. For the patients and providers of health care services this kind of drug consumption account for a major chunk of the budget.

Aim: To assess the outcome of restriction on the use of parenteral antibiotics with respect to their utilization and monetary benefits, in a tertiary care hospital in India.

Materials and Methods: Data details were collected regarding drug utilization two months before and after restriction respectively. A total 1605 patient records assessed. Drug utilization was expressed as DDD/100 patient bed days. Use of Carbapenems were restricted to culture positive cases only. Antibiotics started for patients as per clinical judgment were issued for only five days. Culture sensitivity reports verified physically on a special indent form, before every antibiotic issued thereafter.

Results: Piperacillin-tazobactum (DDD/100 BD 1.72 before and 1.29 after restrictions) was the commonly used antibiotic. Considering values expressed in DDD/100 BD before and after restriction respectively, substantial decrease in consumption of antibiotics like Imipenem- Cilastin (0.22 to 0.16), meropenem (0.30 to 0.09), piperacillin-tazobactum (1.72 to 1.29), teicoplanin (0.24 to 0.05) and vancomycin (0.69 to 0.40) was observed. An increase in consumption of amoxicillin-clavulanic acid (0.90 to 1.04) and clarithromycin (0.44 to 0.55) noted, pointing to a shift in antibiotic use. Restriction decreased expenditure burden on these antibiotics by INR 1,45,911 (17.31%).

Conclusion: Restriction of antibiotics cuts down consumption and benefits hospital budget immensely.

Keywords: Drug audit, Drug consumption, Injectable antimicrobials, Pharmacoeconomics

INTRODUCTION

Drug utilization research is defined as research on "the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences" and has the principal aim of facilitating the rational use of drugs [1]. Research regarding the pattern of antibiotic use imparts important knowledge and helps in designing sound strategies to deal with the perils of multiple antibiotics use. [2] The pattern and extent of use of antibiotics for indoor patients has been an important aspect since the recent past due to certain reasons. One of them is that major budget allocated for health-care is consumed by the hospital drug purchases; of which antibiotics form a major and essential expense [3]. Drug utilization research therefore also provides necessary information about the efficiency of drug use thus helping to set priorities for the rational allocation of health care budgets. Analytical studies try to link data on drug utilization to figures on morbidity, outcome of treatment, and quality of care, with the ultimate goal to assess whether drug therapy is rational or not. Development of resistance to antibiotics is a continuous process in nature. Surveillance on routine basis is important for designing novel and effective approaches for curbing resistance to some extent. Studying drug utilization in different settings like corporate and government hospitals will help refine the approaches in a tailor-made way.

The aims of the study were:

(a) To restrict the use of parenteral antibiotics, in a tertiary care government hospital in India.

(b) To study the impact of restriction on the use of parenteral antibiotics with respect to their utilization.

(c) To assess the monetary impact of such restriction on drug-store budget of the hospital.

MATERIALS AND METHODS

A cross-sectional retrospective drug utilization study was conducted in different surgical and medical wards (excluding pediatric wards) of a 1200 bedded tertiary care teaching hospital. The study was approved by the ethics committee (ethical app no: BJMC/IEC/Pharmac/1210115-17, dt:23-12-2010).

The data collection for this study was for four months.

Data details for the – 'before restriction period' were collected retrospectively for the month of January 2012 and March 2012 wherein the demand for selected parentral or injectable antibiotics by various wards was fulfilled by the drug store without inquiring details about the patient culture and sensitivity report, dose and duration for which the patient had been receiving antibiotic. Only total amount of antibiotic consumed patient-wise and ward-wise was noted. Data for the month February 2012 was intentionally not considered due to missing data (due to technical limitations) which would have affected the study outcome. Hence, the next month i.e., March 2012 was included in the study period. Thus the before restriction analysis data was collected for two month.

The study site being a government setup required permission from various concerned authorities, before implementation of restriction. Therefore in January 2013 there was introduction of the restriction indent form. There was a transition period of around six months wherein the restriction indent form was implemented gradually till smooth acceptance in the hospital. Therefore, the data for the second part of the study i.e., 'after restriction' implementation was collected six months later i.e data was collected for July 2013 and August 2013. In this period of two months there was complete implementation of an 'Antibiotic Restriction Indent Form'. This was the main study tool which consisted of a simple form in which certain details like patient details had to be provided, e.g., hospital registration number, provisional diagnosis, whether culture sensitivity sample was sent or not, before beginning definitive therapy, details of the culture sensitivity reports (latest culture-sensitivity details were verified with the Hospital Information Management System Software, where routine patient related information is uploaded regularly), date of first dose of the parentral antibiotic, past number of days for which the patient had been receiving the indented injectable antibiotic, etc., The antibiotics were strictly issued when the form was complete in all manner and signed by the treating physician (Assistant/Associate Professor). Some antibiotics (i.e., meropenem and colistin) were issued only after the form was signed by the head of the concerned clinical department.

Antibiotics were not issued if:

1. The form was incomplete in any manner and not been signed by the treating physician;
2. Appropriate sample not sent for Culture sensitivity;
3. Recent culture sensitivity reports were showing no growth in the appropriate samples yet antibiotic indented;
4. Antibiotic demand does not match as per the culture sensitivity report.

All the data details were collected retrospectively from inpatients medical files. Each drug prescribed was recorded including its frequency of administration, indications for use, and duration of therapy. The drug utilization was calculated in DDD/100 bed–days [4-6]. The data was evaluated by Microsoft Excel software for analysis.

$$\text{DDD/100 bed–days} = \frac{\text{(Drug consumption in the study period (mg)} \times 100)}{\text{(Assigned DDD (mg)} \times \text{Period of study} \times \text{Bed strength} \times \text{Average occupancy)}}$$

Anatomical Therapeutic Chemical (ATC) classification system was prescribed by WHO and the ATC codes for each antibiotic were obtained from WHO Guidelines for ATC classification. Aggregate data were analysed according to the ATC/DDD methodology guidelines for ATC classification [7].

The expenditure on antibiotics was calculated according to the purchase rate of antibiotics available on the Government rate-contract (which remains constant for 3 three years, here 2012-2015) as it was teaching government hospital.

It was calculated as:

Cost Difference = A - B

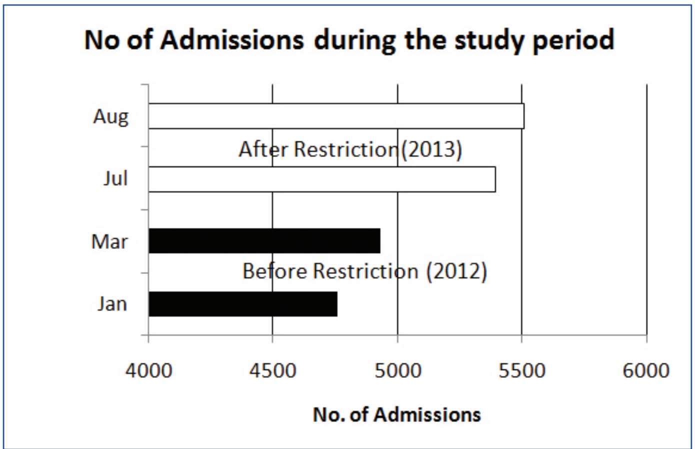
Where- A (before restriction) = ∑(total vials consumed of injectable antibiotic per antibiotic under study x price per unit/vial)

B (after restriction) = ∑ (total vials consumed of injectable antibiotic per antibiotic under study x price per unit/vial)

RESULTS

A total of 20,587 patients (4760 for the month January 2012, 4930 for the month of March 2012, 5390 month of July 2013 and 5507 for the month of August 2013) were admitted during study [Table/Fig-1]. Average treatment period was rounded off and found to be five days in all the study months. These parameters were used for calculating bed occupancy. Out of which 1605 patient record were accessed and used for the study as these patients were on the injectable antibiotics which were restricted. Piperacillin-tazobactum (DDD 800 g) was the most commonly used antibiotic followed by amoxicillin-clavulanic acid (DDD 418 g) and vancomycin (DDD 320.3 g) in 2012 when no restriction was imposed, while the use of drugs such as colistin and linezolid (DDD 0 g) was nil as these antibiotics were not purchased by hospital drug store in 2012. In the months of 2013 after implementation of the restriction; piperacillin-tazobactum (DDD 703.4 g) and amoxicillin-clavulanic acid (DDD 567.3 g) were still most commonly used antibiotics but clarithomycin (DDD 299.5 g) was replaced by vancomycin (DDD 222 g) as regards to the third most commonly used antibiotic [Table/Fig-2].

Considering values expressed in DDD/100 BD before and after restriction respectively, substantial decrease in consumption of antibiotics like Imipenem- Cilastin (0.22 to 0.16), Meropenem (0.30 to 0.09), Piperacillin-Tazobactum (1.72 to 1.29), Teicoplanin (0.24 to 0.05) and Vancomycin (0.69 to 0.40) was observed. An increase in consumption of Amoxicillin-Clavulanic acid (0.90 to 1.04) and Clarithromycin (0.44 to 0.55) noted, pointing to a shift in antibiotic use [Table/Fig-3].



[Table/Fig-1]: Patient admissions during the study period (2012 and 2013).

Sr. No	Drug	DDD used (before restriction 2012)	DDD used (after restriction 2013)
1	Amoxicillin + Clavulanic acid	418**	567.3**
2	Imipenem+ Cilastin	102.5	87.8
3	Clarithromycin	208.5	299.5***
4	Colistin	0	66.7
5	Linezolid	0	36
6	Meropenem	140.5	50.5
7	Piperacillin + Tazobactum	800*	703.4*
8	Teicoplanin	114.5	28.5
9	Vancomycin	320.8***	222

[Table/Fig-2]: Comparative DDD of parentral antibiotics used before and after restriction.
*First most commonly used,** Second most commonly used,*** Third most commonly used.

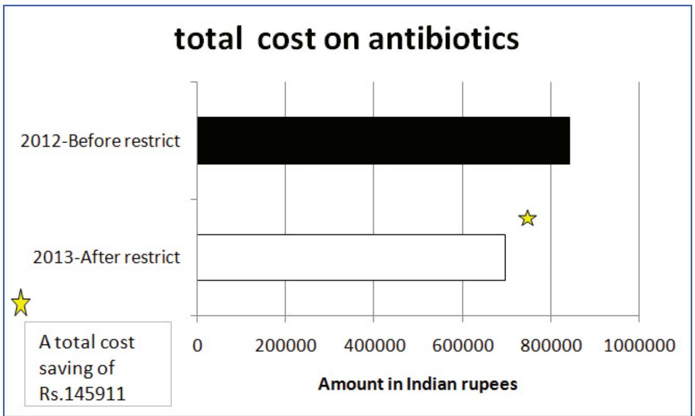
Although apparently Colistin and Linezolid show increase but these drug were available in the hospital drug store only in 2013. Restriction decreased expenditure burden on these antibiotics by INR 1,45,911 (17.31%) [Table/Fig-4,5].

DISCUSSION

Drug utilization studies though appear apparently simple yet are equally tedious to carry on as they deal with compilation of vast data at times. In a limited resource setting as in government hospitals, where the budget on healthcare is limited and fixed for a certain financial year; a pharmaco-economic analysis proves to be an effect tool in optimizing healthcare needs of patients without compromising quality. Such studies conducted all over the world express a common concern regarding the extensive indiscriminate use of antibiotics leading to antibiotic resistance globally [8-12]. Therefore, drug utilization studies are important as they invariably bridge the gap between public health, rational pharmacotherapy, pharmaco-vigilance and pharmaco-economics [13]. The indiscriminate use of broad-spectrum antibiotics is much emphasized in various studies [14-16]. The studies dealing with prescription audits are invariably form a subset of the antimicrobial stewardship programme that is designed to overcome the problem of antibiotic resistance. Antimicrobial resistance substantially raises

Sr. No	Drug	Dose/unit	ATC Codes (WHO)	Standard DDD (WHO)	DDD/100 BD (before restriction 2012)	DDD/100 BD (after restriction 2013)
1	Amoxicillin + Clavulanic acid	1200 mg	JO1CR02	3 gm	0.901	1.042#
2	Imipenem+ Cilastin	500 mg	JO1DH51	2 gm	0.221	0.161
3	Clarithromycin	500 mg	JO1FA09	1 gm	0.449	0.55#
4	Colistin	10lac units	JO1XBO1	3 MU	0	0.122#
5	Linezolid	600 mg	JO1XXAO8	1.2 gm	0	0.066
6	Meropenem	500 mg	JO1DH02	2 gm	0.303	0.093
7	Piperacillin + Tazobactum	4.5 gm	JO1CRO5	14 gm	1.725	1.292
8	Teicoplanin	200 mg	JO1XAO2	0.4 gm	0.247	0.052
9	Vancomycin	500mg	JO1XAO1	2 gm	0.691	0.408

[Table/Fig-3]: Comparative DDD/100 bed-days of parentral antibiotic use before and after restriction with ATC codes.
#Increase in consumption despite of restriction.



[Table/Fig-4]: Total expenditure on antibiotic during the study period (2012-2013).

already-rising health care costs and ultimately increases patient morbidity and mortality [11]. The current study was done to assess the effects of antibiotic restriction randomly in two months when no restrictions were imposed as compared to random two months when restriction were imposed.

An important goal of this study was to assess the impact of such a strategy on antibiotic utilization and effect on budget in resource limited setting. Prior to restriction (i.e., in 2012) antibiotics were most frequently used for post surgical patients (21.16%), followed by pneumonitis (18.76%) and after restriction (i.e., in 2013) too, antibiotics were most frequently used for post surgical patients (28.35%) followed by pneumonitis (19.58%). In a study conducted by Deshmukh V et al., emphasizes that maximum antimicrobial utilization in surgery department was done for surgical chemoprophylaxis [17]. This indicates that there is a strong need to create awareness about the correct practices of surgical chemoprophylaxis. There is also a need to address issues related to respiratory infections at national level. The most commonly used antibiotic during the study period was piperacillin-tazobactum. Although restriction decreased its consumption yet this combination was the most commonly used one, thus indicating that piperacillin-tazobactum is the most preferred antibiotic combination amongst physicians and surgeons but it does have a liability to be used irrationally. This finding is in accordance with a study conducted by Mittal N et al., which found that piperacillin-tazobactum is most commonly used antibiotic, in contrast to earlier studies that claim the same for amoxicillin+clavulanic acid combination. The study also states that maximum drug cost-expenditure was attributed to antiinfectives especially to drugs like piperacillin-tazobactum, amoxicillin+clavulanic acid and vancomycin [18]. A study conducted by Jaykar B et al., also observed that antibiotic restriction did not alter the usage of piperacillin subatantially [19]. The next most commonly used antibiotic was the combination of amoxicillin+clavulanic acid (418 gms DDD) before restriction but after restriction the consumption of this combination increased (567.3 gm DDD) indicating an increase in preferential use of this antibiotic and a definite change in trend. Such changes in antibiotic preferences after restriction are demonstrated by various studies [19]. The least frequently prescribed antibiotics before restriction were colistin and linezolid apparently, but to be specific these were not available in the drug store of the institute in this period. Therefore actually, the least used antibiotics were teicoplanin (114.5 gm DDD) and meropenum (140.5 gm DDD). Whereas during the restriction period consumption of teicoplanin (28.5 gm DDD) and linezolid (36 gm DDD) decreased yet they were the least used antibiotic. The consumption of Teicoplanin after restriction drastically decreased to 28.5 gm which was half of the initial consumption. The possibility of this decrease can also be attributed to the availability of alternatives like linezolid. The antibiotic whose consumption increased was clarithromycin (from 208.5 gm DDD to 299.5 gm DDD). The probable

Sr. No.	Drug	Dose/unit	Rate (Rs/ vial)	No. of Vials (Before restriction-2012)	Total expense per antibiotic (Rs.) (Before restriction-2012)	No. of Vials (After restriction-2013)	Total expense per antibiotic (Rs.) (After restriction-2013)
1	Amoxicillin + Clavulanic acid	1200 mg	34	1254	42636	1702	57868
2	Imipenem+ Cilastin	500 mg	297.09	410	121806.9	351	104278.59
3	Clarithromycin	500 mg	393.96	417	164281.32	599	235982.04
4	Colistin	10lac units	447	0	0	20	8940
5	Linezolid	600 mg	72	0	0	72	5184
6	Meropenem	500 mg	197.09	562	110764.58	202	39812.18
7	Piperacillin + Tazobactum	4.5 gm	68	2802	190536	2464	167552
8	Teicoplanin	200 mg	690	229	158010	57	39330
9	Vancomycin	500mg	42.59	1283	54642.97	888	37819.92
TOTAL COST					842677.77		696766.73
Cost Difference					**Rs.1,45,911**		

[Table/Fig-5]: Details of total expenditure on antibiotic during the study period (2012-2013).

explanation for this is that the cases pneumonitis had increased from 18.76 % before restriction (in the month of January and March) to 19.58 % in the period after restriction (in the month of July and August).

LIMITATION

Limitation of this study is that the sample comprises of data of two non-consecutive months for the before restriction and consecutive months after restriction not considering the seasonal variations in occurrence of specific diseases. Hence, it should purely be considered as two months data before and after intervention. The data for the whole year was not included due to the large volume of the data; as this data is still being analysed for a further study. In these months the concurrent microbiological data should have been studied to actually assess the need for use of the antimicrobials and differentiate them from indiscriminate use. The patient outcomes on the whole should also be assessed along with restriction of antibiotics. To overcome such limitations, this study is a part of a larger ongoing study which is considering the change in microbial resistance patterns with such change in antimicrobial prescribing practices and the related morbidity and mortality outcomes in patients due to implementation of such restrictions. Another limitation of the study is that a clear utilization of important drugs like colistin and linezolid could not be commented on; which is the real need of the hour.

CONCLUSION

The present study demonstrated piperacillin-tazobactum was the most commonly used parentral antimicrobial followed by amoxicillin-clavulanic acid. Restriction on antimicrobial not only decreased expenditure burden on these antimicrobial by INR 1,45,911 (17.31%) but also showed trends in change of preferences for antimicrobial. This can be a welcome change as may causes an automatic antimicrobial recycling and indirectly help to bring down the problem of antimicrobial resistance. There is a need to continuously monitor antimicrobial utilization and also to restrict it periodically.

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