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A Prospective Observational Study on Determining the Utilization of Restricted Antibiotics Using Defined Daily Dose Calculations in A Quaternary Care Hospital

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ABSTRACT

Restricted antimicrobials are those that fit the hospital's restriction regulations for limiting their usage, as specified by the DTC in cooperation with the AMS committee. The use of these restricted antimicrobials necessitates rigorous monitoring and adherence to the hospital's antimicrobial prescribing policy. The overuse of antibiotics globally has accelerated the global public health problem of antimicrobial resistance. The cause of serious infections, complications, extended hospital stays, and higher mortality has been increasing antibiotic resistance. It may be agreed that they can only be prescribed with the approval of an infectious disease specialist, a clinical microbiologist, or the AMS team. Colistimethate sodium, Vancomycin, Fosfomycin, Minocycline, Levofloxacin, Tigecycline, Teicoplanin, Linezolid, Daptomycin, Imipenem, Meropenem, Doripenem and Ceftazidime / Avibactam are the antibiotics included in the restricted list based on the hospital protocols. The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults. This prospective observational study on determining the utilization of restricted antibiotics using the Defined Daily Dose (DDD) calculations was conducted in a quaternary care hospital in Chennai. Among the total 149 restricted antibiotics prescribed, the most frequently prescribed was Meropenem, which was prescribed 87 (59.6%) times with a DDD of 514.917 (7.413 DDD/100 bed days). The least prescribed are Fosfomycin and Imipenem, each prescribed to one patient, which accounts for about 0.7% each respectively. The DDD of Restricted Antibiotics prescribed for patients of different wards/departments during the study period was 828.503 DDD.

Keywords: Restricted antibiotics, DDD, Drug utilization, infectious diseases

INTRODUCTION

According to CDC, Antibiotics are medicines that fight infections caused by bacteria in humans and animals by either killing the bacteria or making it difficult for the bacteria to grow and multiply.(1) Antibiotics may be classified as bacteriostatic and bactericidal based on their action. Infections can be treated with antibiotics, which have also saved countless lives, but whenever antibiotics are administered, they have negative side effects and antibiotic resistance, one of the biggest risks to the general public. The advantage of using antibiotics typically outweigh the dangers of adverse reactions or antibiotic resistance. However, excessive antibiotic prescriptions and overuse endanger the effectiveness of these vital medications.(2)

Restricted antimicrobials are those that fit the hospital's restriction regulations for limiting their usage, as specified by the DTC in cooperation with the AMS committee. The use of these restricted antimicrobials necessitates rigorous monitoring and adherence to the hospital's antimicrobial prescribing policy. It may be agreed that they can only be prescribed with the approval of an infectious disease specialist, a clinical microbiologist, or the AMS team. These antimicrobials can only be recommended and supplied with a consultant microbiologist's permission before administering restricted antibiotics, the pharmacist must verify microbiology approval or formulary indication. Certain medications may be subject to restrictions depending on:

- Antimicrobial activity spectrum (last-line agent)
- The antimicrobial's cost
- Potential for toxicity

The restriction policy may state that the drug can only be used by a specific hospital specialty or unit,

- for a specific pathogen or condition
- when the organism's resistance profile precludes the use of other options
- when other options are contraindicated (allergic reactions, drug intolerance, drug interactions, etc.)
- when treatment failure with alternative options has been proven.

Authorized prescribers inside the hospital should be encouraged to only write prescriptions for antibiotics in accordance with the AMS policy, which has been approved by the executive. This should encourage the wise and proper use of antibiotics and guarantee that they are prescribed in accordance with any national or local prescribing guidelines, recommending the use of the required narrowest-spectrum agent. A way to implement these is through an approval system. A way to carry out these regulations and direct prescribers to always use the best antibiotic is through an approval system.[3]

The list of restricted antibiotics in our hospital includes Colistimethate sodium, Vancomycin, Fosfomycin, Minocycline, Levofloxacin, Tigecycline, Teicoplanin, Linezolid, Daptomycin, Imipenem, Meropenem, Doripenem and Ceftazidime / Avibactam.

The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults. The DDD is a unit of measurement and should not be confused with the PDD (recommended or Prescribed Daily Dose). Patients' individual characteristics (such age and weight) and pharmacokinetic variables must be taken into account when determining doses for individuals and patient groups, therefore they frequently differ from the DDD. The DDD can often be a compromise reached after reviewing information on doses used in various countries. The DDD, which is an average of two or more commonly used dose sizes, may even be a dose that is rarely recommended. Data on drug utilization should ideally be given as DDDs per 1000 inhabitants per day or, when inpatient drug use is taken into account, as DDDs per 100 bed-days.

For each antibiotic, DDD was calculated by dividing the total dose of antibiotic prescribed by the standard DDD for that antibiotic as provided by the ATC/DDD index.

$$\text{DDD} = \frac{\text{Number of items (Antibiotic) issued x Amount of drug per item (mg)}}{\text{WHO recommended DDD of the Antibiotic}}$$

DDDs per 1000 inhabitants per day

Sales or prescription data presented in DDDs per 1000 inhabitants per day may provide a rough estimate of the proportion of the study population treated daily with a particular drug or group of drugs. The general utilization is often assessed for the total population across all age categories, but some drug classes are only very rarely used by those under the age of 45. Simple age adjustments can be made by using the number of inhabitants in the relevant age group as the denominator to account for utilization differences resulting from different age structures between countries.

DDD per 1000 inhabitants per day was calculated by the formula

$$\text{DDD/ 1000 inhabitants/ day} = \frac{\text{Total consumption in DDD x 1000}}{\text{Number of inhabitants x study period (Days) in the study period}}$$

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DDDs per 100 bed-days:

When considering inpatient drug use, the DDDs per 100 bed-days may be applied. A bed-day should be adjusted for occupancy rate because bed-day definitions can vary between hospitals and countries. As an example, 70 DDDs per 100 bed-days of hypnotics provide an estimate of the therapeutic intensity and suggest that 70% of the inpatients might receive a DDD of a hypnotic every day.

DDD per 100 bed days was calculated using the formula;

$$\text{DDD/100 bed days} = \frac{\text{Total dose in mg during study period X 100}}{\text{DDD of drug x Study duration x bed strength x Avg. bed occupancy rate}}$$

DDDs per inhabitant per year:

The DDDs per inhabitant per year can be used to estimate the average annual number of days spent in treatment for each inhabitant. For instance, an estimate of five DDDs per inhabitant every year means that the utilization is equal to treating every inhabitant with a five-day course during the course of that year.[4]

Objective

1. To calculate the DDD of restricted antibiotics prescribed.

2. To determine the prescription pattern of restricted antibiotics across different departments.

MATERIALS AND METHODOLOGY

This prospective observational study on determining the utilization of restricted antibiotics using the Defined Daily Dose (DDD) calculations was conducted in a quaternary care hospital in Chennai during the period of 6 months from February 2023 to July 2023. We have included all those patients who received restricted antibiotics during their course in our hospital, patients above 18 years of age belonging to both genders. Patients who are pregnant and lactating are excluded from the study. The estimated sample size of the total study population was calculated as 110 patients who have been prescribed restricted antibiotics during the study period with a CI = 95%, and a Margin of error of 5%. An antimicrobial audit and measuring antibiotic consumption are the basic area of an antimicrobial stewardship program. Considering the importance of Restricted antibiotics and utilization pattern of restricted antibiotics, we decided to carry out a study to determine the utilization of restricted antibiotics using DDD calculation in a quaternary care hospital, located in Chennai-Tamil Nadu. We have designed a data collection form which included data such as department name, patient diagnosis, name of restricted antibiotics, doses of restricted antibiotics prescribed and duration of restricted antibiotic therapy. We calculated the Defined Daily Dose (DDD) of the restricted antibiotics using the Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) index published by the World Health Organization (WHO) collaborating Centre for Drug Statistics Methodology.

RESULTS

In our study, we have enrolled 110 patients who have received restricted antibiotic during the hospital stay period. Of the total 110 patients, about 28 patients (25.5%) were from the Nephrology department who had been prescribed restricted antibiotics, followed by 19 patients (17.3%) from the Pulmonology department receiving restricted antibiotics, 16 patients (14.5%) each from General Medicine and Internal medicine were administered with restricted antibiotics. Among the total 149 restricted antibiotics prescribed, the most frequently prescribed was Meropenem, which was prescribed 87 (59.6%) times, followed by Linezolid which was prescribed 27 (18.5%) times, Levofloxacin which was prescribed 8 times (5.5%). The least prescribed are Fosfomycin and Imipenem, each prescribed to one patient, which accounts for about 0.7% each respectively. The DDD of Restricted Antibiotics prescribed for patients of different wards/departments during the study period was 828.503 DDD. Among all, Meropenem has the highest DDD of 514.917 (7.413 DDD/100 bed days). This is followed by Linezolid with a DDD of 117 (1.685 DDD/100 bed days), followed by Levofloxacin with DDD of 39 (0.561 DDD/100 bed days). Drugs with the least DDD were Minocycline and Vancomycin with DDD of 14.5 (0.209 DDD/100 bed days) each respectively.

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Table 1: Restricted antibiotics distribution across departments

DEPARTMENT	NUMBER OF PATIENTS	PERCENTAGE
CARDIOLOGY	10	9.1
GASTROENTEROLOGY	4	3.6
GENERAL MEDICINE	16	14.5
GENERAL SURGERY	1	0.9
HEPATOLOGY	8	7.3
INTERNAL MEDICINE	16	14.5
NEPHROLOGY	28	25.5
NEUROLOGY	4	3.6
ORTHO SURGERY	4	3.6
PULMONOLOGY	19	17.3
Total	110	100.0

Table 2: Categorization based on count of each restricted antibiotics prescribed

RESTRICTED ANTIBIOTICS PRESCRIBED	NUMBER OF PRESCRIPTIONS	PERCENTAGE
MEROPENEM	87	59.6
LINEZOLID	27	18.5
LEVOFLOXACIN	8	5.5
TIGECYCLINE	7	4.8
VANCOMYCIN	4	2.7
CEFTAZIDIME/AVIBACTAM	3	2.1
COLISTIMETHATE SODIUM	3	2.1
TEICOPLANIN	3	2.1
MINOCYCLINE	2	1.4
FOSFOMYCIN	1	0.7
IMIPENEM	1	0.7
TOTAL	146	100.0

Table 3: Categorization of patients according to the number of restricted antibiotics prescribed per patient

NUMBER OF RESTRICTED ANTIBIOTICS PRESCRIBED PER PATIENT	NUMBER OF PATIENTS	PERCENTAGE
1 Restricted Antibiotic	81	73.6
2 Restricted Antibiotics	26	23.6
≥3 Restricted Antibiotics	3	2.8
Total	110	100.0

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Table 4: Calculation of DDD for the restricted antibiotics

SL.NO	NAME OF THE ANTIBIOTIC	DDD (WHO)	DDD	DDD/100 bed days	ROA	ATC Code
1)	Meropenem	3.0 g	514.917	7.413	IV	J01DH02
2)	Linezolid	1.2 g	67.0	0.965	PO	J01XX08
		1.2 g	50.0	0.720	IV	J01XX08
3)	Levofloxacin	0.5 g	36.0	0.518	PO	J01MA12
		0.5 g	3.0	0.043	IV	J01MA12
4)	Tigecycline	0.1 g	61.500	0.885	IV	J01AA12
5)	Teicoplanin	0.4 g	11	0.158	IV	J01XA02
6)	Imipenem/Cilastatin	2.0 g	6.00	0.086	IV	J01DH51
7)	Fosfomycin	8.0 g	0.003	0.000043	IV	J01XX01
8)	Ceftazidime/Avibactam	6.0 g	27.083	0.390	IV	J01DD52
9)	Colistimethate sodium	9 MU	23	0.331	IV	J01XB01
10)	Minocycline	0.2 g	14.500	0.209	IV	J01AA08
11)	Vancomycin	2.0 g	14.500	0.209	IV	J01XA01

DISCUSSION

In this study, the utilization pattern of restriction antibiotics across different antibiotics was evaluated and the utilization of restricted antibiotics prescribed to those patients was also determined based on the ATC/DDD methodology.

On evaluating the drug utilization pattern of restricted antibiotics in our study reported that Meropenem was the highly prescribed restricted antibiotic in our hospital (59.6 %). Ceftazidime/Avibactam, Teicoplanin, Colistimethate sodium are least used which found similar with the results of other studies. The same result was found by Shantanu and Shakti B Mishra in a study conducted in Eastern India where Meropenem was the most prescribed restricted antibiotics.[5]

Another study conducted by Dhakchinamoorthi Krishna Kumar et al., in Chennai showed that Meropenem (29.8%) was most commonly prescribed 29.8% followed by Imipenem (28.8%) and the least prescribed were Linezolid and Vancomycin.[6]

Among the 110 patients, the restricted antibiotics were most commonly prescribed in the Nephrology Department (25.5 %) as most of the patients were admitted for Urinary Tract Infection, and Sepsis affecting kidneys. Least usage of restricted antibiotics was recorded in General Surgery department with 0.9 %.

In our study, the pattern of restricted antibiotics usage within the hospital during study period was assessed using ATC/DDD methodology. Total DDD of Restricted antibiotics is 828.503 DDD. Meropenem was the most frequently prescribed restricted antibiotic with highest DDD of 514.917 and 7.413 DDD/100 bed days.

A similar study conducted in Karnataka showed that Cefipime was most commonly prescribed Restricted Antibiotic with 29.25 DDD /100 bed days followed by Meropenem with 8.25 DDD/100 bed days which is Higher compared to our study even being the second highest prescribed drug in that hospital and Vancomycin with 7 DDD/100 bed days and Ceftazidime with 1.56 DDD/ 100 bed days.[7] There exists a difference in Restricted Antibiotics list between the Hospitals.

Meropenem was most common restricted antibiotic used in our study (DDD/100 bed days – 7.413). This may be attributed to its wide spectrum of antibacterial activity. This is an alarm for our prescribers to reduce the use of this drug and use it only after culture and sensitivity testing.

CONCLUSION

Antimicrobials that fall within the concept of "restricted" as defined by the DTC in collaboration with the AMS committee can only be used in hospitals under certain conditions. Strenuous oversight and adherence to the hospital's antimicrobial prescribing policy are required for the use of these restricted antimicrobials. Only after proper consent from a clinical microbiologist or infectious disease specialist or the AMS committee, the restricted antimicrobials should be dispensed.

The overuse of antibiotics globally has accelerated the global public health problem of antimicrobial resistance. The cause of serious infections, complications, extended hospital stays, and higher mortality has been increasing antibiotic resistance. Antibiotic overuse is linked to a higher risk of adverse effects, more frequent re-visits, and increased medicalization of self-limiting conditions.

Restricted antibiotic consumption is also an important measure used to assess the need of AMS programs. Our study illustrates the restricted antibiotics consumption data in ten different departments during the six-month study period. We have also calculated the DDD of all the restricted antibiotics prescribed in our study period and DDD/100 bed days. The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults. The ATC/DDD system is very effective tool for comparison of drugs. The DDD calculated in our study serves as a baseline data for comparison in future studies. This will help in comparison of trends over years. These data can also be used in comparing other academic research and reports.

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