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Original Research Article

Intake of Anti-Microbials in Subjects Admitted to ICU at Trauma Units in India

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Abstract

Background: Increasing incidence of resistance to antibiotics is a global concern in the healthcare sector including India. AMPS (antimicrobial stewardship programs) have been recommended to mitigate antimicrobial resistance which is rapidly rising.

Aim: The present study aimed to assess the intake of anti-microbials in subjects admitted to ICU at trauma units in India by both DOT (Days of Therapy) and DDD (Defined Daily Dosage) methods.

Methods: The present prospective clinical study was done at an Indian center in subjects admitted to ICU (intensive care units) with polytrauma and in subjects admitted to neurosurgical ICUs. Antibiotic intake was gathered manually on daily basis by the practitioners performing the infection controls concerning DDD and DOT.

Results: During the study duration, antibiotic intake at ICU for both culture-based therapy and empirical therapy were 460.5 and 531.6 DDD/1000 subjects. The intake of antimicrobials at the ICU for both culture-based therapy and empirical therapy were 426.02 and 489.7 DOT/1000 subjects.

Conclusions: The data gathered from the Indian ICU set-up concerning the intake of antimicrobials is helpful in monitoring, evaluating, and establishing the functions of antimicrobial stewardship programs in Indian healthcare settings.

Keywords: Antibiotics, Antimicrobials, DDD (Defined Daily Dosage), DOT (Days of Therapy), ICU.

Introduction

In Indian acute care settings hospitals, it has been reported that nearly 20% to 50% of the antimicrobials used are injudiciously used. Owing to the inappropriate and unnecessary use of antimicrobials, a negative impact is being posed in the community and subject level [1]. Inappropriate use of antibiotics can directly lead to antibiotic resistance. An

increase in the cost of healthcare is also reported owing to antibiotic misuse that further leads to antibiotic resistance [2].

Also, the Indian healthcare sector is facing a high burden secondary to increased bacterial resistance with a marked decrease in antibiotic discovery. Indian healthcare sectors have reported high antibiotic resistance, mainly to carbapenems and quinolones. It has also been noted that the use of polymyxin and other last-resort antibiotics has increased in India resulting in increased antibiotic resistance in India. Hence, the focus is increasingly on developing the AMSP (antimicrobial stewardship programs) to ensure proper antibiotic use [3].

There is an increased need to assess antimicrobial consumption in healthcare settings to assess the relationship between resistance emergence and antimicrobial use. It is also vital to effectively apply AMSP tools to the healthcare sector. WHO (World Health Organization) recommends the DDD (defined daily dose) as a metric and tool to assess antibiotic consumption. An alternative assessment tool can be DOT (days of therapy). Previous literature data recommend a direct measurement method to evaluate antibiotic intake. It is governed by the days of the therapy and the number of subjects' days [4].

Hence, the DOT tool is independent of the dose. The classification of WHO can be used to prepare a plan that is globally accepted which is ATC drug classification [5]. Various methods have been documented that help in monitoring the use of drugs including decentralized pharmacists, practice audits, and prospective/retrospective drug utilization reviews. Inappropriate and injudicious use of antibiotics can significantly increase pathogen resistance rates [6].

Hence, it is vital to implement a policy to measure the consumption of antibiotics and compare the DDD and DOT in the Indian healthcare sector.

Materials and Methods

The present prospective clinical study aimed to assess the intake of anti-microbials in subjects admitted to ICU at trauma units in India by both DOT (Days of Therapy) and DDD (Defined Daily Dosage) methods. The study was done at ACSR Government Medical College, Nellore, Andhra Pradesh , from June 2021 to February 2022 after the clearance was given by the concerned Institutional Ethical committee. Before the commencement of the study, informed consent was taken from all the subjects in both written and verbal format. The study was done at the Department of Microbiology of the Institute.

The study was aimed at improving the antimicrobial use at a polytrauma center ICU of the institute and involved pharmacists, infection control personnel, nurses, and microbiologists. The tools and metrics used in the study were DDD as recommended by WHO. The defined daily dose/DDD is the average assumed to maintain per day dose of a drug as indicated for use in the adult subjects. The consumption of antimicrobials was assessed using the ATC codes (Anatomical Therapeutic Chemical codes) by WHO recommended DDD of a particular antimicrobial.

The study assessed only systemic antifungals with an ATC code of J02 and antibacterials with an ATC code of J01 which include antibacterial agents based on their chemistry and mode of action excluding the antimycobacterial agents and combination drugs. Another tool used in the study is DOT which directly measures the consumption of antibiotics and represents single agent administration on a day irrespective of dose strength or number. Days of therapy/DOT were assessed following Momattin H *et al* in 2018 [7] On a preformed structured proforma, the data gathered were antibiotic use following the culture sensitivity reports, samples or culture reports, diagnosis, an antibiotic given at the time of admission, death/discharge date,

data collection date, admission date, and demographic data. The study included daily patient surveillance and antibiotic use with culture sample details that were sent to a microbiologist for sensitivity or culture testing. The therapy given was divided into two parts culture-based therapy based on the microbiology report of the subjects and empirical therapy considering the condition of the subject. The infection control personnel monthly reviewed the antimicrobial use and data. The study assessed 251 males and 40 females for 6 months within the age of 19-74 years. Based on age, the subjects were divided into 3 groups of age 19-35, 36-55, and >55 in groups I, II, and III respectively. The inclusion criteria for the study were the age of 19 or more and subjects that consumed a minimum of one parenteral antibiotic from the mentioned WHO ATC code. The exclusion criteria were subjects of age <18 years, terminally ill, immunocompromised subjects, pediatric subjects, and subjects that did not take any antibiotics. The subjects were followed till they died, were discharged, or shifted from ICU. In culture-based and empirical therapy, the doses were divided into DOT/1000 and DDD/1000 patient days.

Empirical therapy was started within 24 hours of admission and antibiotics given were Amikacin, Sulbactum/Cefoperazone, and metronidazole. The culture-based therapy was started after 48 hours of admission and the antibiotics given were Tigecycline, Colistin, and Meropenem. Caspofungin and fluconazole antimycotics were used commonly in both groups. In DDD and DOT, the subjects were counted more than once if subjects were discharged many times during the study with 24 hours difference between readmission to ICU and discharge date. When a subject received a minimum of one antimicrobial dose on a certain day, this was considered one day of antimicrobial therapy.

DOT and DDD were assessed as per 1000 subject days. DDD/1000 subject days will be equal to the total grams of antibiotics taken by the number of subject days. DOT per 1000 subject days was equal to the total antibiotic therapy days by several subject days. The data gathered were assessed statistically using SPSS software Version 23.0 (Armonk, NY, IBM Corp.) where data were expressed in percentage and number, and consumption was represented as DDD/1000 patient days and DOT/1000 subject days.

Results

Table 1: Demographic data of study participants

S. No	Characteristics	Frequency (n=291)	Percentage (%)
1.	Mean age (years)	42.6±5.24	
2.	Age range (years)	19-74	
3.	Group I	19-35	
4.	Group II	36-55	
5.	Group III	>55	
6.	Gender		
7.	Males	251	86.25
8.	Females	40	13.74

Table 2: Overall and 6 months DDD/1000 and DOT/1000 in empirical and culture-based therapy

S. No	Parameter	Culture-based	Empirical
1.	Overall DDD/1000	460.5	531.6
2.	Overall DOT/1000	426.02	489.7

3.	DDD/1000		
a)	1st month	483.43	534.16
b)	2nd month	591.81	532.52
c)	3rd month	441.04	530.92
d)	4th month	437.6	563.54
e)	5th month	467.45	538.49
f)	6th month	339.39	487.94
4.	DOT/1000		
a)	1st month	413.16	496.70
b)	2nd month	581.2	480.53
c)	3rd month	369.51	499.96
d)	4th month	424.60	521.2
e)	5th month	444.1	500.5
f)	6th month	323.23	440.3

Table 3: Frequently use antimicrobials in ICU following empirical therapy

S. No		Frequency (n=291)	Percentage (%)
1.	Antimycotics		
a)	1st highest (Fluconazole)	20	6.87
b)	2nd highest (Caspofungin)	8	2.74
2.	Antibacterials		
a)	1st highest (Metronidazole)	125	42.95
b)	2nd highest (Cefoperazone)	107	36.76
c)	3rd highest (Amikacin)	101	34.70

Table 4: Frequently use antimicrobials in ICU following culture-based therapy

S. No		Frequency (n=291)	Percentage (%)
3.	Antimycotics		
c)	1st highest (Fluconazole)	8	2.74
d)	2nd highest (Caspofungin)	4	1.37
4.	Antibacterials		
d)	1st highest (Colistin)	7	2.40
e)	2nd highest (Meropenem)	27	9.27
f)	3rd highest (Tigecycline)	18	6.18

The present prospective clinical study aimed to assess the intake of anti-microbials in subjects admitted to ICU at trauma units in India by both DOT (Days of Therapy) and DDD (Defined Daily Dosage) methods. The study included 86.25% (n=251) males and 13.74% (n=40) females. The mean age of the study subjects was 42.6±5.24 years. The age range was 19-74 years. The 291 study subjects were divided into 3 groups where the group I included subjects from 19-35 years, group II had subjects of 36-55 years, and Group III included subjects of age >55 years as summarized in Table 1.

The overall DDD/1000 was 460.5 and 531.6 respectively for culture-based and empirical studies. The overall DOT/1000 was 426.02 and 489.7 respectively for culture-based and empirical therapy. DDD/1000 at 1st, 2nd, 3rd, 4th, 5th, and 6th month was 483.43, 591.81, 441.04, 437.6, 467.45, and 339.39 for culture-based and 534.16, 532.52, 530.92, 563.54,

538.49, and 487.94 respectively for empirical therapy. The DOT at 1st, 2nd, 3rd, 4th, 5th, and 6th month was 413.16, 581.2, 369.51, 424.60, 444.1, 323.23 for culture-based and 496.70, 480.53, 499.96, 521.2, 500.5, and 440.3 respectively for empirical therapy as shown in Table 2.

Concerning the empirical therapy, the most commonly used antimycotics were fluconazole used in 6.87 (n=20) study subjects followed by Caspofungin in 2.74% (n=8) study subjects. The most commonly used antibacterial was metronidazole followed by cefoperazone, and amikacin in 42.95% (n=125), 36.76% (n=107), and 34.70% (n=101) subjects respectively (Table 3).

For the culture-based antibiotic use in subjects admitted to ICU, the most commonly used antimycotics were fluconazole followed by caspofungin used in 2.745 (n=8) and 1.37% (n=4) study subjects respectively. The antimicrobials used were colistin followed by meropenem and Tigecycline used in 2.40% (n=7), 9.27% (n=270, and 6.18% (n=18) study subjects respectively as depicted in Table 4.

Discussion

The present prospective clinical study aimed to assess the intake of anti-microbials in subjects admitted to ICU at trauma units in India by both DOT (Days of Therapy) and DDD (Defined Daily Dosage) methods. The demographic data of the study showed that the study included 86.25% (n=251) males and 13.74% (n=40) females. The mean age of the study subjects was 42.6±5.24 years.

The age range was 19-74 years. The 291 study subjects were divided into 3 groups where the group I included subjects from 19-35 years, group II had subjects of 36-55 years, and Group III included subjects of age >55 years. These demographics were comparable to the studies of Dellit *et al* [8] in 2007 and Lesch CA [9] in 2001 where authors assessed subjects with demographic data comparable to the present study.

The study results showed that the overall DDD/1000 was 460.5 and 531.6 respectively for culture-based and empirical studies. The overall DOT/1000 was 426.02 and 489.7 respectively for culture-based and empirical therapy. DDD/1000 at 1st, 2nd, 3rd, 4th, 5th, and 6th month was 483.43, 591.81, 441.04, 437.6, 467.45, and 339.39 for culture-based and 534.16, 532.52, 530.92, 563.54, 538.49, and 487.94 respectively for empirical therapy. The DOT at 1st, 2nd, 3rd, 4th, 5th, and 6th month was 413.16, 581.2, 369.51, 424.60, 444.1, 323.23 for culture-based and 496.70, 480.53, 499.96, 521.2, 500.5, and 440.3 respectively for empirical therapy. These results were consistent with the previous studies of Mandy B *et al* [10]. in 2004 and Kern VW *et al* [11]. in 2005 where authors suggested the DDD/1000 and DOT/1000 were comparable to the used reported in the present study.

On following the empirical therapy, the most commonly used antimycotics were fluconazole used in 6.87 (n=20) study subjects followed by Caspofungin in 2.74% (n=8) study subjects. The most commonly used antibacterial was metronidazole followed by cefoperazone, and amikacin in 42.95% (n=125), 36.76% (n=107), and 34.70% (n=101) subjects respectively. These results were in agreement with the findings of Pate PG *et al* [12]. in 2012 and Meyer E *et al* [13]. in 2006 where authors suggested fluconazole and metronidazole as the most commonly used antibiotics in ICU empirical therapy.

The study results showed that for the culture-based antibiotic use in subjects admitted to ICU, the most commonly used antimycotics were fluconazole followed by caspofungin used in 2.745 (n=8) and 1.37% (n=4) study subjects respectively. The antimicrobials used were colistin followed by meropenem and Tigecycline used in 2.40% (n=7), 9.27% (n=270, and 6.18% (n=18) study subjects respectively. These results were in line with the findings of Walia K *et al* [14]. in 2015 and Polk Ronald E *et al* [15] in 2007 where fluconazole and colistin were the most

commonly used antibiotics in culture-based therapy.

Conclusion

Considering its limitations, the study results conclude that data gathered from the Indian ICU set-up concerning the intake of antimicrobials is helpful in monitoring, evaluating, and establishing the functions of antimicrobial stewardship programs in Indian healthcare settings.

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