Point Prevalence Study of Use and Consumption of Antibiotics by using Anatomical and Therapeutic Chemical Classification and Defined Daily Dose Methodology in Tertiary Care Hospital

Amit Kumar[1,*], VN Vamsi Krishna[2], P Sindusha[2], M Susritha[2]

[1]Department of Pharmacy Practice, Aditya College of Pharmacy, Surampalem, Andhra Pradesh, INDIA.
[2]Aditya College of Pharmacy, Surampalem, Andhra Pradesh, INDIA.

ABSTRACT

Objectives: The aim of this study is to identify the use and consumption of antibiotics in tertiary care hospital by using Anatomical and therapeutic chemical classification and Defined daily dose index. **Material and Methods:** A point prevalence study was conducted at tertiary care hospital. A total of 640 patients were included in this study and taken from different medical departments. Patient's demographic and biological data was collected from the medical records. Antibacterial drugs were classified according to ATC/ DDD index and antibiotic consumption was measured by DDD/ 100 Patient days. **Results:** The mean age of 640 patients was 44 (sd 13.53). About 78% of the antibiotics are prescribed from the NLEM (2018-2019). The consumption of antibiotics is higher in departments like surgery (92.18%), Orthopaedics (87.5%) and General medicine (81.25%) followed by Gynaecology (78.13%) and Pulmonology (50.2%). The DDD/ 100 Patient days in Gynaecology were 19.4, in Pulmonology unit 45.2, in surgical unit 24.82, in General medicine unit 33.6 and in Orthopaedics 30.23. **Discussion:** In our study the rate of utilisation of antibiotics was found to be 78%. Broad spectrum antibiotics like cephalosporin's and aminoglycosides are prescribed frequently in the hospital which leads to increase in the microbial resistance. The DDD of ceftriaxone (1250) and cefixime (400) is higher when compared to aminoglycosides i.e. amikacin (700). **Conclusion:** The DDD of cephalosporins is higher when compared to other antibiotics. Inappropriate use of antibiotics leads to increase in the microbial resistance. Prescribers are forced to use broad spectrum antibiotics when other antibiotic therapy options are not available.

Key words: DDD/100 Patient days, ATC classification, NLEM, Antibacterial drugs, Medical units and microbial resistance.

INTRODUCTION

Anti-infective drugs which are available in the market are most frequently prescribed for treating the infectious diseases.[1] Inappropriate use of antibiotics often precede to many difficulties such as adverse effects, antibiotic resistance, drug interactions, super infections and increased hospital stay of patients.[2,3] Moreover, improper use of anti-infective agents has destructive impact on the hospital environment. As a result, infections caused by super bugs increases gradually and anti-microbial drugs used for treating infections are decreasing rapidly.[4,5] International health organizations instructed all countries to reduce the use of antibiotics in humans.[6] Use of antibiotics is important in medical interventions for prevention of infectious diseases. Unnecessary use of antibiotics is a leading problem throughout the world and several health care programs exist to monitor the use of antibiotics.[7,8] Standard method should be used in the evaluation of antibiotic use because each antibiotic has different unit of defined daily dose (DDD). The ATC/DDD index is the prominent method and universal parameter suggested by the WHO. Measurement of antibiotic consumption by DDD/100 patient days allows hospital to compare their antibiotic use with other hospitals. The use of antibiotics specifically measured by using defined daily dose. The increase in

DOI: 10.5530/ijopp.13.2.23

Address for correspondence:
Dr. Amit Kumar
Associate Professor, HOD, Department of Pharmacy Practice, Aditya College of Pharmacy, Surampalem-533437, East Godavari District, Andhra Pradesh, INDIA.
Phone no: +91 8790592977
Email Id: amit.britind@gmail.com

www.ijopp.org

antibacterial consumption can be explained by increase in their use for prophylactic therapy and also increase in tertiary care services.[9,10] The connection between antibiotic resistance and use of antibiotics is well documented. Many studies about antibiotic consumption reported that burden of infectious diseases in India reflects antibiotic sales in the pharmaceutical market. The purpose of this study was to measure the consumption of antibiotics and calculate the defined daily doses of antibiotics prescribed in different medical departments.

MATERIALS AND METHODS

This study was conducted at GSL General Hospital for a period of one month, November 2019. A total of 640 patients were taken from the departments of General medicine, Surgery, Pulmonology, Orthopaedics and Gynaecology. All the demographic details of the patients and prescribed antibacterial drugs were collected from the medical records. The pharmacy unit provided net quantity dispensed for one month. Antibacterial drugs were classified according to ATC/ DDD index and consumption of antibiotics was measured by DDD/ 100 patient days. National List of Essential Medicines (NLEM 2018-2019) of India was used for evaluating the number of drugs prescribed from the essential list.

Defined Daily Dose

It is defined as the assumed average maintenance dose per day for a drug used for its main indication for adults and is assigned by the WHO collaborating centre using established principles.[11] It is a technical unit of measurement assigned for different drug formulations. DDD's only specifies medicines given in ATC codes. Only one DDD is assigned per ATC code and route of administration (oral and parenteral formulations).[12,13] It is sometimes rarely or never prescribed because it is an average of two or more doses. By applying DDD, it is possible to examine changes in drug utilization and evaluate the effects of interactions on prescribing pattern.[14,15] (Table 1)

Classification Of A.T.C System

Anatomical and therapeutic chemical classification system is used for the classification of drugs according to organ systems.[16] It is controlled by the World Health Organisation collaborating centre for drug statistics methodology (WHOCC) at Oslo, Norway and was published in 1976.[17] The system has divided into 1st level which is anatomical main group. Each ATC main group has divided into 2nd level which could be either pharmacological or therapeutic groups. The 3rd and 4th levels are pharmacology and chemical subgroups and 5th level is the chemical substance.[18] (Table 2)

ATC/DDD Methodology

ATC/DDD acts as a tool for monitoring of drug utilization and research. It is essential that a tool for drug utilization monitoring and research is able to convert most medicines available in the market.[19,20] Each pharmaceutical product has to be linked to appropriate ATC code and DDD. It is important that correct ATC code is assigned to each pharmaceutical product package. The number of DDD's per package should be calculated for each product package and this information should be added to the pharmaceutical products.[21,22] The methodology should include medicinal product name, pharmaceutical form, strength, pack size, ATC code, active pharmaceutical ingredient, defined daily dose and route of administration.[23,24]

DDD = Net quantity administered / WHO DDD.

RESULTS

The study was conducted in November 2019 at G.S.L General Hospital, Rajahmundry. Total 640 patients were included in this study; mean± SD age of the patients was

Table 1: DDD's of drugs in A.T.C classification.

A.T.C drugs	A.T.C codes	WHO D.D.D
Azithromycin	J01FA10	0.3 gm (O), 0.5 gm (P)
Ciprofloxacin	J01MA02	1 gm (O), 0.8 gm (P)
Cefixime	J01DD08	0.4 gm (O)
Piperacillin+ b-lactum inhibitor	J01CR05	14 gm (P)
Amikacin	J01GB06	1 gm (P)
Clindamycin	J01FF01	1.2 gm (O), 1.8 gm (P)
Ampicillin	J01CA01	2 gm (O), 6 gm (P)
Amoxicillin	J01CA04	1.5 gm (O), 3 gm (P)
Amoxicillin+ clavulanate potassium	J01CR02	1.5 gm (O), 3 gm (P)
Vancomycin	J01XA01	2 gm (P)

Table 2: ATC classification of Ceftriaxone antibiotic.

A.T.C codes	A.T.C. Category	Description
J	Anti-infective for systemic use	1ST level, anatomical main group
J01	Anti-bacterial for systemic use	2nd level, therapeutic main group
J01D	B-lactum anti-bacterial other than penicillin	3rd level, therapeutic/ pharmacology subgroup
J01DD	3rd Generation Cephalosporins	4th level, chemical subgroup
J01DD04	Ceftriaxone	5th level, chemical substance

Table 3: Analysis of monthly report.

Drug name	Dose conversion	Net quantity dispensed	WHO D.D.D	D.D.D	D.D.D/ 100 Patient days
Inj. Sulbactum+cefoperazone 1.5gm	1.5gm	800	4gm	200	31.25
Inj. Cefixime 1gm	1gm	1600	4gm	400	62.5
Inj. Amikacin 500mg	0.5gm	400	1gm	400	62.5
Tab. Metronidazole 400mg	0.4gm	1500	1.5gm	1000	156.25
Tab. Ciprofloxacin 500mg	0.5gm	600	1gm	750	117.18
Inj. Ceftriaxone 1 gm	1 gm	2500	2 gm	1250	195.3
Inj. Clindamycin 600 mg	0.6 gm	60	1.8gm	33.33	5.2
Tab. Levofloxacin 500 mg	0.5 gm	500	0.5gm	1000	156.25
Inj. Linezolid 600 mg	0.6gm	40	1.2gm	33.33	5.2
Tab. Amoxicillin+ Clavulanate Potassium 625 mg	0.625 gm	1500	1.25 gm	1200	187.5

Table 4: Utilisation of antibiotics in medical units.

Antibiotics	Gynaecology	Pulmonology	Surgery	General medicine	Orthopaedics	D.D.D
Inj. Cefixime 1gm	31.25%	10.9%	10.1%	18.75%	9.3%	400
Inj. Ceftriaxone 1gm	12.1%	32.3%	17.1%	20.2%	23.43%	1250
Inj. Amikacin 750mg	10.2%	29.6%	9.37%	8.6%	10.3%	700
Inj. Gentamicin 500mg	10.9%	8.6%	6.35	9.3%	5.3%	416
Tab. Amoxicillin+ Potassium clavulanate 625 mg	22.1%	8.9%	7.81%	10.15%	14.84%	1200
Tab. Ciprofloxacin 500mg	9.2%	5.3%	3.13%	9.8%	10.15%	750

44±13.53. Among them 338 were male (52.8%) and 302 were female (47.2%). Antibiotics are the most commonly prescribed drugs in medical units of our hospital. To calculate antibiotic consumption in a hospital, the net quantity administered or dispensed in grams for a period of one month are summed and divided by the WHO defined daily dose of a particular antibiotic (Table 3).

Patients using antibiotics were determined according to the suitable dose, indication and administration. Among these cephalosporin's (ceftriaxone, cefixime, cefuroxime and cefpodoxime) constitutes maximum number of defined daily doses, followed by amino-glycosides (amikacin and gentamicin), β-lactamase inhibitors (tazobactum, clavulanate potassium and sulbactum) and quinolones (Levofloxacin and ciprofloxacin). (Table 4)

All the patients were using combinations containing more than one drug. In similar studies, no errors were seen in the prophylaxis and main problem was with unnecessary extension of therapy. In our study 85% of prescriptions had injectable antibiotics because of chronic illnesses. The rate of antibiotic use in the departments is Gynaecology 78.13%, Pulmonology 50%, Surgery 92.18%, General Medicine 81.25% and Orthopaedics 87.5%. The highest rate of antibiotic use was in Surgery unit and lowest rate of antibiotic use was found in Pulmonology unit. The mean period of surgical prophylaxis was 7 days. The duration of prophylaxis according to departments is Orthopaedics 6 days, General Medicine 8 days, Pulmonology 10 days and Gynaecology 7 days. Total days of use was calculated to be 19.4 in Gynaecology unit, 45.2 in Pulmonology unit, 24.82 in Surgery unit, 33.6 in General Medicine unit and 30 DDD/100 patient days in Orthopaedic units. (Table 5)

DISCUSSION

Measurement of antibiotic consumption is a first step in increasing the awareness and importance of

Table 5: Total consumption of antibiotics in several medical units.

Medical units	Total consumption of antibiotics	D.D.D/ 100 patient days
Surgery	92.18%	24.82
Orthopaedics	87.5%	30.23
General medicine	81.25%	33.6
Gynaecology	78.13%	19.4
Pulmonology	50.2%	45.2

antibiotic use. The data was obtained from the usual wards within our hospital (surgery, orthopaedics, gynaecology, pulmonology and general medicine).[25,26] The consumption of antibiotics in hospital is counted by the number of patient days (admission day and discharge day are both counted as full days).[26] High rate of antibiotic use is adequate because one of the pharmacological therapies used in treatment of infectious diseases are antibiotics. Many reports have represented serious misuse of antibiotics and rational antibiotic practices.[27,28] There are more antibacterial drugs available in the market, with a large spectrum of activities and they are better tolerated.[28] In our study the rate of utilization of antibiotics was found to be 78%. While in the department of Gynaecology the rate of consumption was 78.13%, in Pulmonology the rate was 50.2%, in Surgery 92.18%, in General medicine 81.25% and in Orthopaedics 87.5% respectively. The duration of prophylaxis in surgical unit was 7 days. Surgical prophylaxis was most regularly used in orthopaedics unit approximately 6 days. The increase in the antibacterial consumption can be explained by the increase in their use for prophylactic therapy.[29,30] It may not increases the DDD but shows impact on the hospital stay of patients.[31,32] Broad spectrum antibiotics like cephalosporins, aminoglycosides and β-lactamase inhibitors are prescribed frequently in surgical units to prevent post-operative infections.[33,34] Ceftriaxone, cefixime and cefuroxime are prescribed as empirical therapy due to their broad spectrum activities leads to increase in the microbial resistance.[35] Our study includes both I.V and Oral doses of antibacterial agents. The percentage of antibiotics prescribed is varied in different wards due to varying in patient biological data. 78% of the antibiotics prescribed were from the NLEM-2015. Cefixime (31.25%) and Metronidazole (23.43%) are frequently prescribed antibiotics in Gynaecology Unit. Ceftriaxone (32%) and Amikacin (29.6%) in Pulmonology unit. Ceftriaxone (17.1%), Metronidazole (15.6%) and Sulbactum+ Cefperazone (10.2%) in Surgical unit, Cefixime (18.75%), Piperacillin+ Tazobactum (15.6%) and Cefuroxime (13.28%) in General medicine unit and Ceftriaxone (23.43%), Ampicillin (14.3%) and Levofloxacin (10.15%) in Orthopaedic units, DDD/ 100 patient days were calculated and the value is more in Pulmonology unit (45.2 DDD/ 100 patient days), 33.6 DDD/100 Patient days in General medicine, 30.23 DDD/ 100 Patient days in Orthopaedics, 24.82 DDD/ 100 Patient days in Surgical units and 19.4 DDD/ 100 patient days in Gynaecology unit. β-lactam antibiotics along with the β- lactamase inhibitors were prescribed frequently as compared to β-lactam inhibitors alone. Among the antibiotics given in combinational form DDD/ 100 patient days of Amoxicillin+ Clavulanate Potassium are 187.5 in surgical unit, 185.6 in Orthopaedic unit and 125.4 in Gynaecology unit. Inappropriate use of antibiotics increases the risk of adverse reactions to medications. The more antibiotics prescribed, the higher is the risk of microbial resistance.

CONCLUSION

The use of ATC/DDD index improves the evaluation of antimicrobial treatment. This study will be helpful for prescribers to make them aware of their own prescribing practices and better management of infectious diseases. In-appropriate use of antibiotics is causative for increase incidence of microbial resistance and execution of antimicrobial education to prescribers is required to reduce the resistance of antibiotics. When first and second line antibiotic therapy options are unavailable, prescribers are forced to use antibiotics that show more toxic effects and increase the hospital stay of patients. Global policies need to be established to reduce the overuse of antibiotics.

ACKNOWLEDGEMENT

The authors would like to thank all the staff of GSL General Hospital and Medical College, Rajahmundry for clinical support and help in the creation and presentation of this article. Written consent was obtained from the patient.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

A.T.C: Anatomical Therapeutic and Chemical Classification; **D.D.D:** Defined Daily Dose; **N.L.E.M:** National List of Essential Medicines; **W.H.O:** World Health Organisation; **W.H.O.C.C:** World Health Organisation Collaborating Centre.

SUMMARY

Inappropriate use of antibiotics leads to the development of antibiotic resistance and increased hospital stay of patients. In this study we measured the consumption of antibiotics by using ATC and DDD methodology in tertiary care hospital. In our study cephalosporins constitutes maximum number of defined daily doses, followed by amino glycosides, β-lactamase inhibitors and quinolones. The consumption of antibiotics was more in departments like surgery, orthopaedics and general medicine when compared to gynaecology and pulmonology departments. Implementation of antimicrobial education reduces the risk of bacterial resistance.

REFERENCES

1. Shlaes DM, Gerding DN, JrJohn JF, *et al*. Society for Healthcare Epidemiology of America and Infectious Diseases, Society of America Joint Committee on the Prevention of Antimicrobial Resistance. Clin Infect Dis. 1997;25(3):584-99.
2. Shapiro M, Townsend TR, Rosner B, Kass EH. Use of antimicrobial drugs in general hospitals. II. Analysis of patterns of use. J Infect Dis. 1979;139(6):698-706.
3. Craig WA, Uman SJ, Shaw WR, Ramgopal V, Eagan LL, Leopold ET. Hospital use of antimicrobial drugs: Survey at 19 hospitals and results of antimicrobial control program. Ann Intern Med. 1978;89(5_Suppl_2):S93-5.
4. MacKenzie FM. Antibiotic consumption in European hospitals. Med Mal Infect. 2005;35(S2):S121-2.
5. Lesch CA, Itokazu GS, Danziger LH, Weinstein RA. Multi-hospital analysis of antimicrobial use and resistance trends. Diagn Microbiol Infect Dis. 2001;41(3):149-54.
6. Muller A, Monnet DL, Talon D, He´non T, Bertrand X. Discrepancies between prescribed daily doses and WHO defined daily doses of antibacterials at a university hospital. Br J Clin Pharmacol. 2006;61(5):585-91.
7. Natsch S, Hekster YA, DeJong R, et al. Application of the ATC/DDD methodology to monitor antibiotic drug use. Eur J Clin Microbiol Infect Dis. 1998;17(1):20-4.
8. Patel MK, Barvaliya MJ, Patel TK, Tripathi C. Drug utilization pattern in critical care unit in a tertiary care teaching hospital in India. Int J Crit Illn Inj Sci. 2013;3(4):250-5.
9. Balaji V, Aithal S, Geetha S, Swetha ES. Utilization pattern among geriatric patients admitted in medical Intensive Care Unit of a tertiary care teaching hospital. Asian J Pharm Clin Res. 2015;8(2):281-3.
10. Mythri H, Kashinath K. Nosocomial infections in patients admitted in Intensive Care Unit of a tertiary health center, India. Ann Med Health Sci Res. 2014;4(5):738-41.
11. Shah S, Patel J, Desai M, Dikshit R. Critical analysis of antimicrobial and respiratory fixed dose combinations available in Indian market. Int J Med Public Health. 2015;5(2):161.
12. Guillemot D, Carbon C, Vauzelle KF, *et al*. Inappropriateness and variability of antibiotic prescription among French office-based physicians. J Clin Epidemiol. 1998;51(1):61-8.
13. Birkett DJ, Mitchell AS, Godeck A, Grigson T, Cully R, Lee C. Profiles of antibacterial drug use in Australia and trends from 1987 to 1989. A report from the Drug Utilization Subcommittee of the Pharmaceutical Benefits Advisory Committee. Med J Aust. 1991;155(6):410-5.
14. Rønning M, Blix HS, Harbo BT, Strom H. Different versions of the anatomical therapeutic chemical classification system and the defined daily dose - Are drug utilisation data comparable?. Eur J Clin Pharmacol. 2000;56(9-10):723-7.
15. Sketril IS, Metge C, Blackburn J, *et al*. A Canadian Guide for Drug Utilization Studies using Administrative Claims Data: Focus on the WHO ATC System and Defined Daily Dose. Supported by the Health Transition Fund, Health Canada. 2001.
16. Laxminarayan R, Matsoso P, Pant S, Brower C, Rottingen JA, Klugman K, *et al*. Access to effective antimicrobials: A worldwide challenge. Lancet. 2016;387(10014):168-75. PMID: 26603918.
17. Wirtz VJ, Mol PG, Verdijk J, Vander SRH, Taxis K. Use of antibacterial fixed-dose combinations in the private sector in eight Latin American Countries between 1999 and 2009. Trop Med Int Health. 2013;18(4):416-25. PMID: 23379471.
18. Chandy SJ, Thomas K, Mathai E, Antonisamy B, Holloway KA, Stalsby LC. Patterns of antibiotic use in the community and challenges of antibiotic surveillance in a lower-middle-income country setting: A repeated cross-sectional study in Vellore, South India. J Antimicrob Chemother. 2013;68(1):229-36. PMID: 22945913.
19. Kotwani A, Chaudhury RR, Holloway K. Antibiotic-prescribing practices of primary care prescribers for acute diarrhea in New Delhi, India. Value Health. 2012;15 (5 Suppl 1):S116-9. PMID: 22265057.
20. Shet A SS, Forsberg BC. Pharmacy-based dispensing of antimicrobial agents without prescription in India: Appropriateness and cost burden in the private sector. Antimicrobial Resistance and Infection Control. 2015;4(1):55.
21. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections. Am J Infect Control. 1988;16(3):28-40.
22. Jones SR, Barks J, Bratton T, McRee E, Pannell J, Yanchick VA. The effect of an educational program upon hospital antibiotic use. Am J Med Sci. 1977;273(1):79-85.
23. Dellinger EP, Gross PA, Barrett TL, *et al*. Quality standart for antimicrobial prophylaxis in surgical procedures. Clin Infect Dis. 1994;18:422-7.
24. Akalin S, Caylak S, Ozen G, Turgut H. Antimicrobial consumption at a university hospital in Turkey. African J of Mic Research. 2012;6:4000-5.
25. Vlahovic-Palcevski V, Morovic M, Palcevski G. Antibiotic utilization at the university hospital after introducing an antibiotic policy. Eur J Clin Pharmacol. 2007;56(1):97-101.
26. Cizman M. The use and resistance to antibiotics in the community. Int J Antimicrob Agents. 2003;21(4):297-307.
27. Cars O. Defined daily doses of antimicrobials reflect antimicrobial prescriptions in ambulatory care. J Antimicrob Chemother. 2004;53(6):1109-11.
28. Filius PMG, Liem TBY, DerLinden PDV, *et al*. An additional measure for quantifying antibiotic use in hospitals. J Antimicrob Chemother. 2005;55(5):805-8.
29. Shenoy N. Investigation of antimicrobial use pattern in the intensive treatment unit of a teaching hospital in western Nepal. Am J Infect Control. 2003;31(7):410-4.
30. Gould IM. Antibiotic polices and control of resistance. Curr Opin Infect Dis. 2002;15(4):395-400.
31. Catrou PP. Reduction in broad-spectrum antimicrobial use associated with no improvement in hospital antibiogram. J Antimicrob Chemother. 2004;53(5):853-9.
32. Barza M. Favorable Impact of a Multidisciplinary Antibiotic Management Program conducted during 7 years. Infec Control Hosp Epidemiol. 2003;24(9):699-706.
33. Goldmann DA, Weinstein RA, Wenzel RP, *et al*. Strategies to prevent and control the emergence and spread of antimicrobial-resistant microorganisms in hospitals: A challenge to hospital leadership. JAMA. 1996;275(3):234-40.
34. Dasgupta S, Das S, Chawan NS, Hazra A. Nosocomial infections in the Intensive Care Unit: Incidence, risk factors, outcome and associated pathogens in a public tertiary teaching hospital of Eastern India. Indian J Crit Care Med. 2015;19(1):14-20.
35. Carling PC, Fung T, Coldiron JS. Parenteral antibiotic use in acute care hospitals: A standardized analysis of fourteen institutions. Clin Infect Dis. 1999;29(5):1189-96.