Brief Communication

Retrospective Analysis of Drug Prescription Statistics in a Tertiary Care Center in India: Recommendations for Promoting Prudent Utilization of Drugs

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Abstract

Objective: Drug utilization studies provide information regarding the drug usage pattern in hospital settings, which can be used to promote cost-efficient uses of drugs. The present observational retrospective study was conducted to evaluate the drug utilization pattern in a tertiary care center in India and create a baseline consumption data for the drugs, simultaneously identifying targets for improving drug prescribing pattern. **Methods:** The current retrospective cross-sectional study was conducted at All India Institute of Medical Sciences Raipur, wherein the 217 medical records of different departments for August 2019 were chosen randomly (using systematic random sampling) for evaluation. The information was extracted from medical records regarding the basic demographic details, drug strength, route, and total amount, and eventually, the World Health Organization (WHO) core indicators were estimated. Drug utilization data were assessed using the WHO Anatomical Therapeutic Chemical/Defined Daily Dose (ATC-DDD) methodology. Potential drug–drug interactions were also analyzed. **Findings:** Most of the records analyzed were of male patients (56.2%). Drugs prescribed by their generic name were 50%. Prescriptions containing injection and antimicrobials were 68.1% and 83.6%, respectively. 49.3% of the patients had received a fixed-dose combination, and 60.9% of drugs belonged to the National List of Essential Medicines 2015. A total of 15 potential drug interactions were found. **Conclusion:** Calculated prescribed daily dose of most of the antimicrobials and other groups of drugs was close to the WHO-DDD. Trade name prescription and polypharmacy were very common. Antibiotics accounted for the majority of drug costs.

Keywords: *Antimicrobial consumption index, defined daily dose, essential medicines, prescribed daily dose, World Health Organization prescribing indicators*

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Introduction

Drug utilization studies serve as a tool for assessment of the quality of therapeutic care and evaluation of drug usage. These studies play a significant role in improving drug-dispensing policies at every level of health care, promoting their rational use. These studies may prove beneficial for developing countries like India, where drugs constitute the major cost of health care and are borne by patients themselves.[1] The World Health Organization (WHO) recommends the Anatomical Therapeutic Chemical Classification/Defined Daily Dose (ATC/DDD) for drug utilization studies, which was developed for the same.[2] This method certainly helps us in improving health care and comparison of drug consumption statistics at various levels of health care

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and analyzing trends in drug use in a different timeline. The DDD is the "average maintenance dose per day for a drug used for its main indication in adults and is a unit of measurement."[3] For an ATC code and route of administration, only one DDD is being assigned. Drug utilization statistic expressed in DDDs is reported in units which are independent of population size. The prescribed daily dose (PDD) is defined as "the actual average dose prescribed, which can be determined by analyzing prescriptions and can be different from DDD." The DDDs per 100 bed days can be applied when drug utilization in inpatients is considered. A bed day is a day during which a person is admitted to the hospital overnight and is restricted to bed. Few studies which reported drug utilization pattern in India have been mentioned.[4-6] The present retrospective observational study was aimed to evaluate the drug usage pattern in indoor patients along with the WHO core prescribing indicators in All India Institute of Medical Sciences (AIIMS), Raipur, Chhattisgarh, India. Further, the study was done to analyze potential drug–drug interactions and areas of improvement in drug prescription.

Methods

The current inpatient drug utilization study was conducted in 2019 at AIIMS Raipur, Chhattisgarh, India. Our institution is a relatively new institution with a continuously increasing number of inpatients, i.e., 13,417 in the 2018 calendar year which increased to 21,387 in 2019.[7] The present study was conducted after approval from the institutional ethics committee vide letter no. AIIMSRPR/IEC/2019/311.This study is the first drug utilization study of our institute. As per the WHO guidelines, a minimum of 600 prescriptions needs to be considered over the year. As we wanted to analyze the drug utilization pattern for a particular month, we needed at least 50 prescriptions. After reviewing the literature and based on convenience sampling, a minimum of 200 medical records were analyzed (10% of total admission in August 2019).[8] With the pilot study of 5 medical records, a standard operating procedure was formulated:

1. Verify the completeness of the medical records
2. Case records of pediatric patients were not included
3. Drugs for which DDD was not available or was prescribed SOS (as and when required), and vaccines and fluids were excluded
4. Patients should have been admitted and discharged in the same month
5. The day of discharge was not included in the duration of hospitalization.

Using this information, the data were collected by three different investigators for August 2019. Two hundred and seventeen medical records were chosen randomly using systematic random sampling, which fulfilled the desired criteria. The collected data were patients' demographical characteristics, i.e., patients' record number, age, sex, diagnosis, and duration of hospitalization.Prescription parameters, i.e., name of the drug, strength and dosage form, amount, and duration of drug prescribed, whether prescribed in a generic name or not, were evaluated. We evaluated the WHO core drug prescribing indicators, i.e., average number of drugs per encounter, percentage of drugs prescribed by generic names, percentage of encounters with an antibiotic, percentage of encounters with an injection, and percentage of drugs prescribed from the essential drug list.[8] All drugs were mentioned as per the WHO Anatomical Therapeutic and Chemical Classification (ATC) coding system. The National List of Essential Medicines (NLEM) 2015 of India was used for assessing whether the drug was prescribed from the essential list.[9] Those drugs which were prescribed in at least 5% of patients were evaluated. From the prescription data, the amounts of drugs prescribed were converted into the number of DDD as per the 2019 version of the ATC/DDD index.[10] DDDs, PDD, and DDDs per 100 bed days were calculated using standard formulae.[4,5] A list of possible drug–drug interactions and their severity was prepared by analyzing the literature.[11-13] The severity of the drug interaction was assessed using standard severity grading scale, in which designation A indicates no known interaction, B indicates minor interaction and no action needed, C stands for moderate interaction, and monitoring of therapy is required, D indicates major interaction and therapy modification is required, and X stands for contraindication, i.e., the combination should be avoided.[14] All the data obtained were presented using suitable statistical parameters, i.e., mean ± standard deviation, median, and percentage.

Results

The study was conducted with the help of the medical record department during September–December 2019. For August 2019, a total of 2047 patients were admitted, and the number of functional beds was 700, with a 65.29% occupancy rate. A total of 217 medical records were examined. Various causes for which the admission was made were surgical procedures, exacerbation of preexisting diseases, and sepsis. Out of the total medical records analyzed, 56.2% belonged to males. The mean age of the patients was 44.6 years. The mean duration of hospital stay was 5.5 days (1–16 days). The mean and median number of drugs prescribed per prescription was 4.8 and 5, respectively. The percentage of prescriptions with ≥5 drugs prescribed was 26.5%. Half of the

drugs (50%) were prescribed by their generic name. And the number of prescriptions with injectable and antibiotic was 68.1% and 83.6%, respectively. In our study, we found that a total of 115 drugs were prescribed, and 60.9% of drugs were from NLEM-2015 [Table 1]. Among the drugs prescribed, 22.6% were drugs acting on the cardiovascular system, followed by antimicrobials 20%. Out of 115 drugs prescribed, 31 drugs (28.2%) were found to be prescribed in at least 5% of patients, and their detailed evaluation was done.

Table 2 represents the detailed evaluation of antimicrobial agents. Among the antibiotics, the PDD was found to be very much similar to DDD, except for the PDD of amoxicillin-clavulanic acid (oral), cefuroxime (oral), and metronidazole. Table 3 represents the detailed evaluation of drugs acting on the cardiovascular system. Most of the drugs prescribed were have PDD similar to DDD, except for metoprolol, amlodipine, and atorvastatin. Table 4 represents the list of potential drug–drug interactions. A total of 15 potential drug–drug interactions were observed, and most of the interactions (53.3%) belonged to category B (mild), which did not require any action. Only two interactions (13.3%) belonged to category D (major interaction), where therapy modification was necessary. The majority of drug cost was because of antimicrobials (approximately 90%). Amoxicillin + clavulanic acid and piperacillin + tazobactam were responsible for the majority of cost among the antimicrobials (approximately 70%).

Discussion

The study was conducted to improve patient care positively. Drugs acting on the cardiovascular system constituted the maximum number among the total drugs prescribed (slightly higher than antimicrobials), which is not similar to the previous studies.[5,15] The observed results of WHO indicators in our study were substantially different from the optimal value.[16] The two important indicators, i.e., the number of drugs prescribed by generic names and the number of drugs from the essential medicine list, should always be close to the optimal value, whereas for the other indicators, the value may vary depending on the clinical need of patients. The PDD of metronidazole, cefuroxime (oral), amoxicillin-clavulanic acid (oral), metoprolol, and amlodipine was not similar to DDD, probably due to the variable dose range, and multiple indications.[12,13] Overall, most of the drugs were having PDD similar to the DDD and were prescribed within the recommended therapeutic dose correspondence reflecting adherence to international guidelines.

Two major potential drug–drug interactions noted were of ramipril with telmisartan and ramipril with spironolactone. Spironolactone can cause dangerous hyperkalemia in patients who are also taking ramipril.[17] However, ramipril with telmisartan may lead to a steep fall in blood pressure, especially in patients with salt depletion and congestive heart failure.[13] Antimicrobials were responsible for the majority of drug cost (90%), and among them, amoxicillin + clavulanic acid and piperacillin + tazobactam were found to be mainly responsible for the most of the cost which is in accordance with previous studies.[5,18] In our study, we observed certain deficiencies in clinical practice. The substantial differences among WHO indicators, and the potential drug–drug interactions observed, could be corrected by organizing continuous medical education, which will make the physicians not only aware about the practicing guidelines but also sensitize them toward it.[19] To curb the frequent and inappropriate prescription of antimicrobials, especially the costlier agents, restricted use of antimicrobials is recommended. As per the Centers for Disease Control and Prevention, nearly 30% of all antimicrobials prescribed for acute care were inappropriate.[20] Optimizing the use of antimicrobials by formulating and implementing hospital antimicrobial policy and hospital antimicrobial stewardship programs (ASPs) will reduce drug resistance, adverse drug effects, and cost of treatment with improved patient outcome. Hospital ASPs include the core elements, i.e., hospital leadership commitment; accountability; pharmacy expertise (previously, drug expertise); action; tracking; reporting; and education.[21] The authors recommend the incorporation of these updated core elements in implementing the hospital ASPs. To avoid potential drug–drug interactions in indoor patients, the use of software for predicting drug interactions can be useful.

Table 1: Demographics of the study patients and the frequency of the WHO core indicators in the evaluated prescriptions

Patients' demographic characteristics	
Age (years, mean±SD)	44.6±15.3
Gender distribution ration (male: female)	122:95
Total number of medical records	217
Total number of treatment charts	1192
The average duration of stay	5.5±2.7
Total number of drugs prescribed	110
WHO core indicators (%)	
The average number of drugs per encounter	4.8
Percentage of drugs prescribed by generic names	50
Percentage of encounters with an antibiotic	83.6
Percentage of encounters with an injection	68.1
Percentage of drugs prescribed from the essential drugs list	60.9

SD=Standard deviation; WHO: world health organization

Table 2: Number of defined daily doses and prescribed daily doses for antimicrobial agents

Drugs	ATC code	WHO-DDD (g)	Number of DDDs	DDDs/100 bed days (ACI)	PDD (g)
Amoxicillin + clavulanic acid (oral)	J01CR02	1	67.5	0.55	1.41
Amoxicillin + clavulanic acid (parenteral)	J01CR02	3	269.2	2.21	3.10
Piperacillin + tazobactam	J01CR05	14	94.5	0.77	11.8
Ceftriaxone	J01DD04	2	196.5	1.61	1.99
Cefixime	J01DD08	0.4	97	0.79	0.39
Cefuroxime (oral)	J01DC02	0.5	64	0.53	1
Cefuroxime (parenteral)	J01DC02	3	76.7	0.63	3.03
Azithromycin	J01FA10	0.5	62	0.51	0.5
Ciprofloxacin (oral)	J01MA02	1	74.5	0.61	0.99
Amikacin	J01GB06	1	112.5	0.92	0.97
Metronidazole	J01XD01	2	152	1.25	1.52

ATC=Anatomical therapeutic chemical, DDD=Defined daily dose, PDD=Prescribed daily dose, ACI=Antibiotic consumption index

Table 3: Number of defined daily doses and prescribed daily doses for drugs acting on cardiovascular system

Drugs	ATC code	WHO-DDD (g)	Number of DDDs	DDDs per 100 bed days	PDD (g)
Metoprolol	C07AB02	0.15	27.25	0.22	0.04
Amlodipine	C08CA01	0.005	193	1.58	0.008
Telmisartan	C09CA07	0.04	115.5	0.95	0.05
Ramipril	C09AA05	0.0025	68.4	0.56	0.0029
Furosemide	C03CA01	0.04	79	0.65	0.053
Nitroglycerin	C01DA02	0.005	71.6	0.59	0.005
Nicorandil	C01DX16	0.04	17.4	0.14	0.01
Clopidogrel	B01AC04	0.075	126	1.03	0.077
Atorvastatin	C10AA05	0.02	313.5	2.57	0.042

ATC=Anatomical therapeutic chemical, DDD=Defined daily dose, PDD=Prescribed daily dose

Table 4: List of potential drug-drug interactions

Concurrent prescription	Category	PK/PD	Interaction
Telmisartan + furosemide	C	PD	Symptomatic hypotension may be precipitated
Budesonide + furosemide	B	PD	May cause severe hypokalemia
Aspirin + clopidogrel	B	PD	May increase risk of bleeding
Alprazolam + tramadol	B	PD	Increased sedation and respiratory depression
Telmisartan + aspirin	B	PD	May cause hyperkalemia
Aspirin + ramipril	B	PD	May decrease the effectiveness of ramipril May cause hyperkalemia
Ciprofloxacin + metoprolol	B	PK	May increase metoprolol level
Telmisartan + diclofenac	B	PD	May increase risk of hyperkalemia and renal impairment
Ramipril + telmisartan	D	PD	May increase the risk of hypotension, renal impairment, and hyperkalemia
Aspirin + furosemide	C	PD	Decreased effectiveness of diuretics
Ramipril + spironolactone	D	PD	Serious hyperkalemia
Ciprofloxacin + metronidazole	C	PK	Increased risk of QTc prolongation and torsade de pointes
Nitroglycerin + aspirin	C	PD	Additive effect
Clopidogrel + atorvastatin	B	PK	May decrease effectiveness of clopidogrel
Furosemide + ramipril	C	PD	Vasodilation and relative intravascular volume depletion

PK=Pharmacokinetic, PD=Pharmacodynamic

Certain limitations exist in the study, i.e., analysis of only 1 month was done and diagnosis-wise drug analysis and cost per prescription analysis were not done. Drug–drug interactions were not performed by commercially available software. This study is the first of its kind in our hospital, which has helped us to create a baseline consumption data of frequently prescribed drugs in inpatients of our hospital, irrespective of the departments, and diagnosis. These data enable us to compare the consumption, particularly of antimicrobials within and outside the hospital. Further, we found that most of the parameters were within practice range,

and also, potential areas of improvement have been recognized. We expect that this study will help in the future to design and implement appropriate measures, whose output can also be assessed.

Authors' Contribution

Alok Singh, Pugazhenthan Thangaraju, and Suryaprakash Dhaneria participated in study design and concept; Ajaya Kumar Sahoo, Dhyuti Gupta, and Alok Singh participated in data collection; and Alok Singh and Dhyuti Gupta prepared the manuscript. Suryaprakash Dhaneria and Pugazhenthan Thangaraju commented and critically reviewed it and all authors approved the final manuscript.

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Conflicts of interest

There are no conflicts of interest.

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