Drug Utilisation Study in a Tertiary Care Center: Recommendations for Improving Hospital Drug Dispensing Policies

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Drug therapy accounts for a major portion of health expenditure. A useful strategy for achieving cost efficient healthcare is drug utilisation research as it forms the basis for making amendments in drug policies and helps in rational drug use. The present observational study was conducted to generate data on drug utilization in inpatients of our tertiary care hospital to identify potential targets for improving drug prescribing patterns. Data was collected retrospectively from randomly selected 231 medical records of patients admitted in various wards of the hospital. WHO Anatomical Therapeutic Chemical/Defined Daily Dose methodology was used to assess drug utilisation data and drug prescriptions were analysed by WHO core drug indicators. Antibiotics were prescribed most frequently and also accounted for majority of drug costs. The prescribed daily dose for most of the antibiotics corresponded to defined daily dose reflecting adherence to international recommendations. Brand name prescribing and polypharmacy was very common.78% of the total drugs prescribed were from the National List of Essential Medicines 2003. Restricting the use of newer and costlier antibiotics, branded drugs and number of drugs per prescription could be considered as targets to cut down the cost of drug therapysignificantly.

Key words: Drug utilisation, Defined daily dose, Prescribed daily dose, Polypharmacy, Essential medicines

Drug utilisation research holds a crucial place in clinical practice as it forms the basis for making amendments in the drug dispensing policies at local and national levels. The ultimate goal of such research is to facilitate rational drug use. Also, since it helps in developing strategies to utilize health resources in the most efficient manner, it is particularly needed in a developing economy like India where 72% of all health care burden is borne by the patients[1].

The reference standard for drug utilisation is WHO ATC/DDD (Anatomical Therapeutic Chemical/Defined daily dose)methodology[2]. Foreach drug and route of administration, defined daily dose (DDD) is defined by the WHO Collaborating Centre for Drug Statistics andMethodology as the assumed averagemaintenance adult dose per day for its main indication. The DDD therefore is an international unit serving for international or regional comparisons. However, DDD does not necessarily reflect the recommendedor prescribed daily dose (PDD). In fact, several studies have reported discrepancies between DDD and PDD for different groups of drugs[3-6].

A number of studies have reported drug usage patterns in different health care sectors in India[7-16]. The aim of the present study was to generate data on drug utilisation in patients admitted in various wards ofour hospital with a focus to analyse drug prescriptions for WHO core indicators and comparison of average PDD with WHO DDD. The study results would be taken as basis for identifying potential targets to make improvements in prescribing patterns and drug dispensing policies of the hospital.

MATERIALS AND METHODS

This inpatient drug utilisation study was conducted at the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh. Ours is a tertiary care referral centre. In a calendar year about 2 lakh and

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about 18 thousand patients in a month are admitted in various wards of the hospital. Drug prescriptions are written by the treating physicians while the drugs are procured by the patients themselves.

Data was collected by evaluating treatment charts of inpatients stored at the medical records department of the hospital. 231 treatment charts from the month of July 2008 were randomly selected. The data was extracted by two investigators independently. Data collection was done using a predesigned proforma which included patient characteristics such as age, gender, diagnosis, duration of hospitalisation and prescription characteristics such as name of the drug, strength and dosage form, number of units dispensed, whether prescribed in generic name or not. We also evaluated the WHO core drug prescribing indicators including (a) average number of drugs per encounter, (b) percentage of drugs prescribed by generic names, (c) percentage of encounters with an antibiotic, (d) percentage of encounters with an injection, and (e) percentage of drugs prescribed from the essential drugs list or formulary.

All drugs were coded as per the WHO Anatomical Therapeutic and Chemical Classification (ATC) coding system. National List of Essential Medicines 2003 of India[17] was used for assessing the number of drugs prescribed from the essential list. From the prescription data of commonly prescribed groups of drugs, the amounts of drugs consumed were converted into the number of DDD as per the 2010 version of ATC/DDD index. DDD was calculated as items issued × amount of drug per item/WHO DDD measure. The number of DDDs per 100 bed days was calculated. Finally, for anti-infectives, estimated PDD was calculated in grams by multiplying DDD with the ratio of number of DDDs to the number of treatment days.

Statistical analysis:

Data was expressed as mean±SD, median (IQR), numbers and percentages. All data was entered into Microsoft Access 2007 version database and subsequently statistically analyzed using the same. No statistical hypothesis was tested.

RESULTS AND DISCUSSION

A total of 231 treatment charts were reviewed during the study period. The patients included were admitted for various diagnosis most common being sepsis, multiple organ failure and for surgical procedures. The distribution of various inpatients was similar for males (50.2%) and females (48.9%). The mean±SD age of the patients was 40.5±17.6 years. The median duration of hospital stay was 6 days (range 1-28 days).

Antiinfective agents followed by drugs acting on gastrointestinal system, nutritional supplements and antiinflammatory agents were the most common class of drugs prescribed to the inpatients (Table 1). Eighty percent prescriptions included injectables, most commonly antibiotics. Insulin (11%), H_2 blockers (3%) and inotropes (1.5%) were other frequently used injectables.

The mean±SD [median (range)] number of drugs prescribed per prescription was 3.6±1.6 [3 (2-12)]. The percentage of prescriptions with ≥3, ≥5 and ≥10 drugs prescribed were 78, 53.6 and 16.5 percent, respectively. Antibiotics were prescribed in more than 60% prescriptions (154/231). Of these, 70 (45.7%) were single antibiotic prescriptions, while 56 (36.3%) and 28 (18%) had two and three or more antibiotics prescribed respectively.

The major classes of drugs prescribed in various speciality wards are shown in fig. 1. The percentage of drugs prescribed from different classes varied in different wards due to variable patient profiles and indications. More than three-fourth prescriptions were by trade names [648/826 (78.45%)] (fig. 2).

The drug prescriptions were analysed for WHO core indicators (Table 2). Overall, 78% of the total drugs

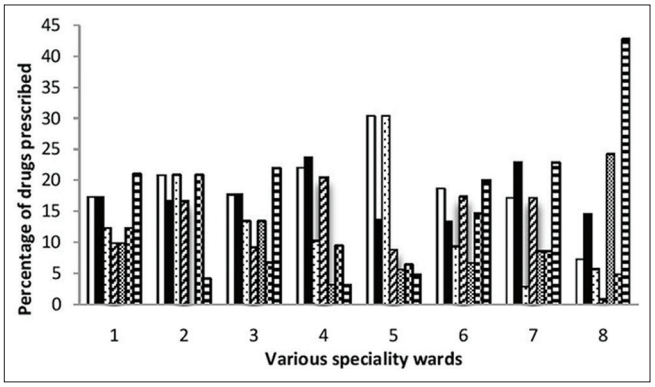

Fig. 1: Drug usage pattern in various speciality wards.
1: Emergency medicine ward, 2: emergency surgery ward, 3: medical ward, 4: surgical ward, 5: gynecology/maternityward, 6: private ward, 7: radiotherapy ward, 8: intensive/coronary care unit, □ antiinfectives, ■ GIT, ⊡ nutritional, ▨ antiinflammatory, ▩ CVS, ◘ CNS and ▤ others.

TABLE 1: VARIOUS CLASSES OF DRUGS PRESCRIBED

Major group	Classes of drugs	Number prescribed (%)*
Antiinfectives		167 (72.3)
	β-lactams	68 (29.4)
	Quinolones	39 (16.9)
	Aminoglycosides	37 (16)
	Antiprotozoal and antihelminthic drugs	35 (15)
	Antifungals	11 (0.05)
	Antitubercular drugs	10 (0.04)
	Macrolides	9 (0.04)
	Others	8 (0.03)
	Tetracyclines	5 (0.02)
	Antivirals	1 (0.004)
Drugs acting on gastrointestinal system		151 (65.4)
	Proton pump inhibitors	68 (29.4)
	Antiemetics	46 (19.9)
	Laxatives	33 (14.3)
	H2 blockers	28 (12.1)
	Others	2 (0.008)
	Nutritional supplements	120 (51.9)
Antiinflammatory		104 (45)
	Nonsteroidal antiinflammatory drugs	72 (31.2)
	Corticosteroids	30 (13)
Immunosuppressants		8 (0.03)
Cardiovascular drugs		96 (41.6)
	Beta blockers	36 (15.6)
	Diuretics	35 (15)
	Calcium channel blockers	31 (13.4)
	ACE inhibitors	29 (12.5)
	Vasodilators	15 (0.06)
	Inotropes	13 (0.05)
	Alpha blockers	1 (0.04)
Drugs acting on central nervous system		45 (19.5)
	Opioid analgesics	31 (13.4)
	Sedatives and hypnotics	25 (10.8)
	Antiepileptics	17 (0.07)
	Antipsychotics	3 (0.01)
	Antidepressants	3 (0.01)
Hypolipidemic drugs		35 (15)
Antiplatelet drugs		31 (13.4)
	Aspirin	28 (12.1)
	Clopidogrel	18 (0.08)
Hormonal agents		30 (13)
	Insulin	20 (0.08)
	Thyroid hormones	8 (0.03)
	Growth hormone	1 (0.004)
	Erythropoetin	1 (0.004)
Drugs acting on respiratory system		19 (0.08)
	Bronchodilators	15 (0.06)
	Antihistamines	4 (0.02)
Anticoagulant drugs		16 (6.9)
	Heparin	15 (0.06)
	Warfarin	1 (0.004)
Oral hypoglycaemic agents		12 (0.05)
Total no of prescriptions		826

*Number (percent) of patients prescribed a particular drug (total number of patients=231)

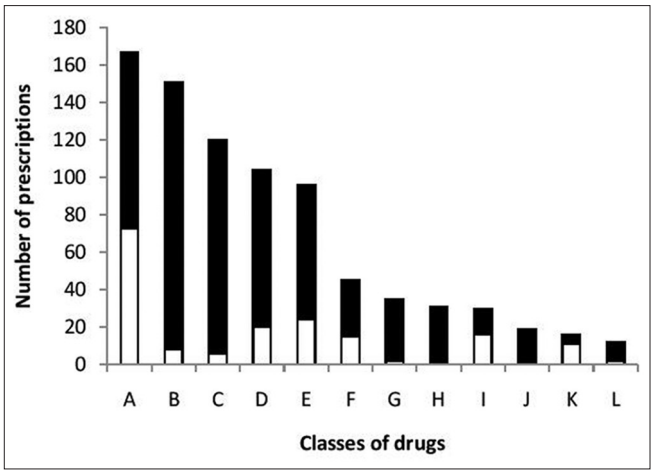

Fig. 2: Generic and trade name drug prescription pattern.
A: Antiinfectives, B: gastrointestinal tract drugs, C: nutritional agents, D: antiinflammatory, E: cardiovascular drugs, F: central nervous system drugs, G: hypolipidemics, H: antiplatelets, I: hormones, J: respiratory drugs, K: anticoagulants, L: oral hypoglycaemic agents, ■ trade, □ generic.

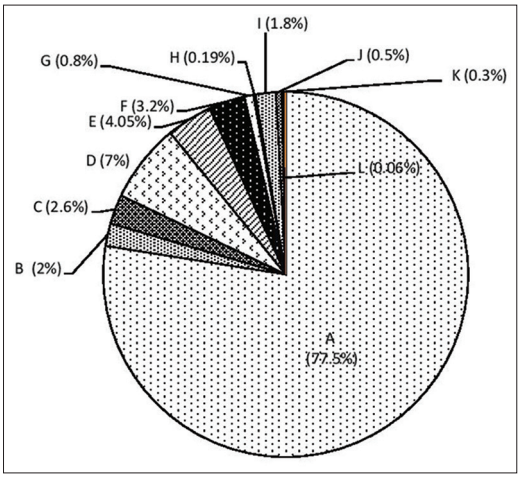

Fig. 3: Percent cost of various drug classes.
GIT: Gastrointestinal tract drugs, CVS: cardiovascular drugs, CNS: central nervous system drugs, A: antiinfectives, B: GIT, C: nutritional, D: antiinflammatory, E: CVS, F: CNS, G: hypolipidemics, H: antiplatelets, I: hormones, J: respiratory, K: anticoagulants, L: oral hypoglycemics.

prescribed were from the National List of Essential Medicines 2003. Adherence to the list was most commonly seen with nutritional agents (iron, folic acid, vitamin and calcium preparations) (82%) and least with gastrointestinal drugs (40%).

The percentage cost of various groups of drugs is shown in fig. 3. Antiinfective agents comprised the major cost of all prescribed drugs (77.5%). Among these, newer agents like piperacillin-tazobactam, vancomycin and amoxicillin-clavulanic acid accounted for majority of the cost. The median (IQR) cost per prescription in various speciality wards is shown in Table 3.

TABLE 2: WHO CORE INDICATORS ASSESSING DRUG PRESCRIPTION

WHO core indicators	*N* (%)
Encounters with injectables*	185 (80.1)
Encounters with antibiotics*	154 (66.7)
No. of prescriptions with drugs from EML	648/826 (78.4)
Average number of drugs per prescription	3.6
No. of prescriptions with generic drugs	178/826 (21.5%)

*Number (percent) of patients having encounters with injectables and antibiotics. (EML: Essential medicine list)

TABLE 3: MEDIAN (IQR) COST PER PRESCRIPTION IN VARIOUS WARDS

Ward	Median (IQR) Cost (in INR)
Female medical ward	108 (74-225)
Radiotherapy ward	146 (126-455)
Gynaecology ward	299 (165-1863)
Maternity ward	1065 (128-1320.5)
Cardiothoracic ward	1413 (333-3212)
Female surgical ward	1938 (1587.5-3494)
Male surgical ward	1982.5 (1554-2431.5)
Emergency ward	2110 (1707-7600)
Male medical ward	2373.5 (1488-9263)
Private ward	3758.5 (1087-4805.5)

INR: Indian National Rupee

The total number of DDDs consumed were maximum for antibacterials followed by proton pump inhibitors, ACE inhibitors and diuretics while the number of DDDs per 100 bed days was higher for sedatives and hypnotics and ACE inhibitors (Table 4). The comparison of number of PDDs and DDDs of various antibacterials is shown in Table 5.

Our study reports the drug usage pattern among inpatients at a tertiary care level in India. Antibiotics were the most commonly prescribed class of drugs, a finding similar to a previous study conducted in emergency medicine department of our hospital[18]. Among these, β-lactams comprised maximum number of defined daily doses consumed followed by quinolones and aminoglycosides. Piperacillin-tazobactam was the commonly prescribed penicillin-enzyme inhibitor, in contrast to amoxicillin-clavulanate acid reported previously[19], which might be due to its broader spectrum of action and changing resistance patterns and prescription habits.

For β-lactams, the average PDD was similar to or higher than DDD while for aminoglycosides, PDD was lower than DDD, which might be due to different safety profiles of these two groups. Overall, correspondence was observed between PDD and

TABLE 4: COMPARISON OF THE NUMBER OF DEFINED DAILY DOSES PER 100 BED DAYS OF MAJOR GROUPS OF DRUGS PRESCRIBED

Major group	Class	ATC code	Number of DDDs	Number of bed days	DDDs per 100 bed days
Antibacterials					
	Beta lactams	J01C	1506.34	661	228
	Aminoglycosides	J01G	153.11	208	73
	Macrolides	J01F	34.5	33	104
	Quinolones	J01M	315.3	222	142
	Total		2009.25	1124	547
Drugs acting on gastrointestinal system					
	Proton pump inhibitors	A02BC	836.33	651	128
	H2 blockers	A02BA	74.23	121	61
	Total		910.56	772	189
Non steroidal antiinflammatory drugs		M01A	195.3	171	114
Cardiovascular drugs					
	Beta-blockers	C07A	89.58	185	48
	Diuretics	C03	439.9	152	289
	Calcium channel blockers	C08	415.25	211	197
	ACE inhibitors	C09	449.5	141	318
	Total		1394.23	689	852
Central nervous system drugs					
	Opioid analgesics	N02A	48.7	104	47
	Sedatives and hypnotics	N05C	272.33	36	756
	Antiepileptics	N03A	146.11	174	84
	Total		467.14	314	887

DDDS: Defined daily doses, ATC: anatomical therapeutic and chemical classification, ACE: angiotensin-converting enzyme

DDD for most antibiotics reflecting adherence to international recommendations in contrast to findings in few other studies demonstrating marked deviations between PDD and DDD for most antibiotics[4,20].

Antibiotics also comprised the highest percentage costs (77.5%) of all groups of drugs similar to a studyin the emergency unit of our hospital in which antibiotics accounted for more than 50% of drug cost expenditure[14]. Agents like piperacillin-tazobactam, amoxicillin-clavulanate and vancomycin mainly accounted for such high costs. Inappropriate use of antibiotics is also responsible for rising incidence of microbial resistance[21]. Such a scenario demands changes in the hospital antibiotic policy to limit the frequent and inappropriate prescription

TABLE 5: COMPARISON OF ESTIMATED PRESCRIBED DAILY DOSES AND DEFINED DAILY DOSES OF VARIOUS ANTI-BACTERIALS

Class	Individual drugs	ATC code	Number of DDDs	Number of bed days	DDDs per 100 bed days	WHO DDD	PDD
Beta lactams							
	Ceftriaxone	J01DD04	520.5	153	340	2	6.8
	Imipenem	J01DH51	16	16	100	2	2
	Piperacillin-tazobactam	J01CR05	139.87	173	81	14	11.34
	Ampicillin	J01CA01	83.75	93	90	2	1.8
	Amoxicillin	J01CA04	109	74	147	1	1.47
	Cefixime	J01DD08	352.25	57	618	0.4	2.47
	Ceftizoxime	J01DD07	7.75	10	77	4	3.08
	Cefuroxime	J01DC02					
	Oral		22.33	16	139	0.5	0.69
	Injectable		11	6	183	3	5.49
	Amoxicillin-clavulanate	J01CR02					
	Oral		42.23	38	111	1	1.11
	Injectable		74.5	46	162	3	4.86
	Cefazolin	J01DB04	1.75	3	58	3	1.74
	Cefepime	J01DE01	22	11	200	2	4
	Cloxacillin	J01CF02	25	16	156	2	3.12
	Ceftazidime	J01DD02	3	3	100	4	4
	Meropenem	J01DH02	12	8	150	2	3
	Cefoperazone	J01DD12	13.75	12	114	4	4.56
	Cefadroxil	J01DB05	4.5	2	225	2	4.5
Aminoglycosides							
	Amikacin	J01GB06	82.09	96	85	1	0.85
	Streptomycin	J01GA01	5.11	6	85	1	0.85
	Kanamycin	J01GB04	7.28	8	91	1	0.91
	Gentamicin	J01GB03	53.2	68	78	0.24	0.18
Macrolides							
	Azithromycin	J01FA10	22.9	22	104	0.5	0.52
	Clindamycin	J01FF01					
	Oral		4.85	4	121	1.2	1.45
	Injectable		6.75	7	96	1.8	1.73
Quinolones							
	Ciprofloxacin	J01MA02					
	Oral		145.2	115	126	1	1.26
	Injectable		118.7	67	177	0.5	0.88
	Ofloxacin	J01MA01	23.5	19	123	0.4	0.49
	Levofloxacin	J01MA12	30.8	24	128	0.5	0.64

DDD: Defined daily doses, PDD: prescribed daily doses, WHO: World Health Organization, ATC: anatomical therapeutic and chemical classification

of antibiotics particularly the newer and costlier agents. An important step in this direction could be implementation of antibiotic restriction program. As per this program, hospital needs to develop a list of restricted antibiotics depending on prevailing resistance patterns and costs, dispensing and initiating course of whom necessitates prior approval from a member of the Infectious diseases team, which would be a multidisciplinary team of staff physicians and clinical/staff pharmacists. In this way, this strategy might prove useful in combating high health care costs and emergence of resistance to newer susceptible agents. The success of this program in decreasing antibiotic utilisation has been demonstrated previously[22]. Another proven useful strategy might be improvement in prescribing practices by making practice guidelines accessible to physicians while they are making clinical decisions[23]. Also, the indiscriminate use of prophylactic antibiotics needs to be curtailed. The use of biomarkers like procalcitonin (PCT) also might help to reduce antibiotic misuse. PCT has been identified as a surrogate marker for estimating the likelihood of a bacterial infection (PCT levels >0.5 μg/l: very likely chances of bacterial infection and levels <0.1 μg/l: very unlikely chances of bacterial infection)[24]. The use of PCT-guided antibiotic management has been shown to markedly reduce the overuse of antibiotic therapy without an

apparent negative impact on patient outcome in 11 randomized controlled trials including over 3500 patients from different European countries[25].

Drugs acting on gastrointestinal system and nutritional agents were among the other commonly prescribed agents. However, whether the use of these supplements was actually medically indicated needs a closer scrutiny.

In spite of various benefits like low cost of drug therapy, increased patient adherence[26,27] and equivalent therapeutic benefits as brand name alternatives[28], generic prescribing is not a common practice in India. In our study, more than 75 percent prescriptions were by brand names. Pharmaceutical step-therapy approach, whereby use of a first line agent, a generic alternative, is required prior to coverage of a second line agent, usually a branded product, can be a useful strategy in increasing drug cost savings[29].

Approximately 80 percent of prescriptions had a drug prescribed as an injectable, mostly antibiotics. The high percentage of injectables was quite explainable since this was an inpatient study with patients mostly having acute illnesses. Injectable drugs are associated with problems of administration and medication errors[30]. Hence, the need to switch over to other routes of administration as soon as possible needs to be emphasised.

Seventy eight percent of drugs prescribed were from the Indian National List of Essential Medicines, 2003[17] which is modelled on the WHO Essential Drugs List[31]. The understanding of concept of essential medicines and their availability to different sections of society needs to be tested. One step in this direction in India was the 'Delhi model' for developing a comprehensive drug policy which aimed to improve the accessibility of essential medicines to all[32]. This model implemented a pooled procurement system of medicines, whereby government obtained medicines from manufacturers in bulk at much lower price than the market price which led to an estimated saving of nearly 30% in the annual drugs bill for the government of Delhi[32].

The average number of drugs per prescription was 3.6. Similar trend has been observed in previous studies[13,33]. Polypharmacy has a number of drawbacks like high health care costs and poor patient compliance, higher incidence of adverse events[34,35] and drug-drug interactions[18]. Hence, there is a continous need to identify predictors of polypharmacy and bring amendments in prescribing practices.

The median (range) cost per prescription in various wards ranged from INR 108 (74-225) in female medical ward to INR 3758.5 (1087–4805.5) in private ward. This amounts to a substantial burden on patient's finances in a country like India where majority of population bears health expenses themselves.

Hence, there is a need to bring changes in the prescribing practices with particular emphasis on generic drug prescribing and restricting polypharmacy. Also, some amendments need to be incorporated in the hospital antibiotic policy. Besides, establishment of a system for provision of medicines at a subsidised rate to patients might prove a useful step towards decreasing costs of health care burden.

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