STUDY OF DRUG UTILIZATION PATTERNS WITH ASSOCIATED DRUG THERAPY PROBLEMS IN CARDIOVASCULAR PATIENTS AT A TERTIARY CARE TEACHING HOSPITAL - AN OBSERVATIONAL STUDY

Section A-Research paper

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ABSTRACT:

Background: The appropriate use of cardiovascular drugs in patients had been shown to decrease the risk associated with cardiovascular morbidity and mortality. To evaluate the prescribing patterns according to essential drug list and identify any potential drug interactions in the prescriptions. A total of 850 prescriptions were analysed for drug utilisation for a period of 6 months. Socio demographic details of the subjects, disease patterns in the study population, drug utilisation patterns according to essential drug list, distribution of adverse drug interactions, drug therapy problems, average number of drug interactions per prescription were evaluated. **Results:** A total number of 5152 drugs were prescribed, at 6.06 drugs per patient. The mean age of the study population is 54.27 years. A total of 4194 drugs were prescribed for cardiovascular problems out of which 3837 drugs are from the essential drug list. Drug therapy problems were uunnecessary drug use (6.8%), need for an extra drug (17.1%), non-compliance (14.3%). **Conclusions:** The average number of cardiovascular drugs prescribed per patient is 4.93, 772 moderate drug interactions were observed from the 850 prescriptions studied. Average drug interactions per prescription are 0.90. Antiplatelets, lipid lowering agents had been prescribed more when compared to other classes of drugs. Drug therapy problems should be addressed with the help of clinical pharmacists. The cardiologist should be encouraged to write drugs by generic name. Majority of the drugs prescribed are from the essential drug list which indicates the knowledge of the cardiologist.

Key words: prescribing patterns, cardiovascular drugs, rational drug use, adverse drug reactions, drug therapy problems

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5210

Eur. Chem. Bull. 2023,12(10), 5210-5216

STUDY OF DRUG UTILIZATION PATTERNS WITH ASSOCIATED DRUG THERAPY PROBLEMS IN CARDIOVASCULAR PATIENTS AT A TERTIARY CARE TEACHING HOSPITAL - AN OBSERVATIONAL STUDY

Section A-Research paper

INTRODUCTION

Cardiovascular diseases (CVD) are the still leading cause of death globally. The projected number of cardiovascular resulted deaths were 12.3 million (25.8%) in 1990, that has been increased to 17.9 (32.1%) million deaths in 2015. It has been proved that cardiovascular diseases are the most frequent cause of morbidity and mortality worldwide (1, 2). CVD death rate have been increasing in developing world while death rates were declined in developed world at a given age since 1970 coronary artery disease and stroke accounts for 80% in male and 75% in females [3, 4]. For the evaluation of present trend of drug use and appropriateness, drug utilization review can be employed. It is a method of collection, quantification, understanding and evaluation of prescriptions and is a powerful investigative tool. It is the process of collection and analysis of the data for the present treatment options for better outcomes in the areas of prescribing and prognosis of the patient. It provides the accuracy of prescription, prescribing practice, concomitant medication evaluation, and implementation of medical standards, monitoring and supervision of drug behaviour. Drug utilisation review services are practically appreciated in various clinical settings and health care management services, considering therapeutic drug class and disease conditions to assess the fundamental patient care system which can overcome the inappropriate drug use and also determine patient's effectiveness and safety of drug utilisation. Identification of prescribing problems, irrational medication patterns and informing patient well about therapy provides an effective drug treatment [5].

Drug utilisation review studies evaluate the drug use at a patient population level as per age, sex, social, economic class, morbidity among other characteristics. They also provide feedback to health providers and acts as indicators to modify or alter treatment strategies and thus result in providing a rational and cost-effective therapy to patients [6, 7]. Rational prescription is essential for better patient care and the initial step in any intervention program need to improve drug utilization in order to assess the degree of the existing problem in prescribing. The present study is an attempt to evaluate the pattern of prescriptions of the patients in out-patients in a government set-up tertiary care teaching hospital.

METHODS

The present study was a questionnaire-based observational study. The study was conducted in the outpatient cardiology department, for a period of 6 months from September 2018 to February, 2019 (Approval number: No. IEC/Pharm. D 09/05-11-2018) which is a tertiary care teaching hospital. The study details were explained to the patients who had attended to the cardiology outpatient unit and informed consent was obtained for collection of the information.

A profile form was used to collect the patient demographics and drugs prescribed. Prescription pattern data of the study participants includes (according to WHO guidelines) a) Average number of drugs per prescription b) Average number of cardiovascular drugs per prescription c) Number of drugs received by the patient d) Percentage of drugs from the national essential drug list of INDIA (2016-18). Drugs were classified into different groups according to the ATC classification of WHO, collaborating Centre for Drugs Statistics methodology for the prescription pattern analysis.

Drug therapy problems (DTP) were identified and classified by using the Cipolle's and Strand's method 9, 21 and with talks held by clinical pharmacists and cardiologist on the confirmation of DTP [8,9]. The pharmacists further refined DTP identification and classification method to the study setting based on review of patients' medical records assessment of lab investigations, and patient's interview about medication use and adherence. Information about medication therapies, such as the recommended drug of choice, recommended dosages, regarding administration schedule, therapy duration, drug interactions, and adverse drug reactions were classified based on the standard pharmacotherapeutics textbooks, and guidelines for hypertension and heart failure management [10-13].

STATISTICAL ANALYSIS

The data was collected, complied in MS-Excel and analysed for percentages and counts. The mean and standard deviation was calculated for continuous variables.

5211

Eur. Chem. Bull. 2023,12(10), 5210-5216

STUDY OF DRUG UTILIZATION PATTERNS WITH ASSOCIATED DRUG THERAPY PROBLEMS IN CARDIOVASCULAR PATIENTS AT A TERTIARY CARE TEACHING HOSPITAL - AN OBSERVATIONAL STUDY

Section A-Research paper

RESULTS

Table: 1. Socio-demographic profile of total subjects of all CVD's (N=850)

S.no.	Socio-demographic factors	No. of subjects	Percentage of subjects
1	Males	450	52.94
2	Females	400	47.05
3	Diabetic	243	28.58
4	Non-Diabetic	607	71.41
5	Smoker	136	16
6	Non-smoker	714	84
7	Alcoholic	112	13.17
8	Non-Alcoholic	738	86.82
9	Literate	332	39.05
10	Illiterate	518	60.94
11	Urban	493	58
12	Rural	336	39.52
13	Tribal	21	2.47

Among the 850 subjects 451 (53.05%) were males and 399 (46.94%) were females indicating that cardiovascular diseases are slightly more prevalent in the male gender. 243 (28.58%) were diabetic and 607 (71.41) were non-diabetic, 136 (16%) were smokers and 714 (84%) were non-smokers, 112 (13.17%) were alcoholic 738 (86.82%) were non-alcoholic. 332 (39.05%) were literate and 518 (60.94%) were illiterate. patients 493 (58%) were urban, 336 (39.52%) were rural and 21 (2.47%) were tribal.

Table 2: Disease pattern distribution in the study subjects

S.no	Clinical conditions	No. of subjects	Percentage of subjects
1	STEMI	438	51.52
2	CAD	162	19.06
3	Unstable angina	60	7.06
4	Left ventricular dysfunction	50	5.88
5	Chronic Rheumatoid heart disease	33	3.88
6	NSTEMI	31	3.65
7	Chest pain	27	3.18
8	Cardiomyopathy	24	2.82
9	CABG	21	2.47
10	Stable angina	19	2.24
11	Hypertension	12	1.41
12	Total	850	100

Out of 850 patients 438 (48.35%) had STEMI, 162(19.06%) had CAD, 60(7.06%) had Unstable angina, 50(5.88%) had LVD, 33 (3.88%) had CRHD, 31(3.65%) had NSTEMI, 27(3.18%) had Chest pain, 24(2.82%) had cardiomyopathy, 21(2.47%) had CABG, 19(2.24%) had Stable angina and 12(1.41%) had Hypertension.

Table 3 Distribution pattern of overall cardiovascular drug therapy

S. No	Drugs category	No. of drugs	Percentage of drugs
1	Anticoagulant and Antiplatelets	768	18.31
2	LLA's	745	17.76
3	β- blockers	655	15.61
4	ACE inhibitors	467	11.13
5	Nitrates	367	8.75
6	ARB'S	298	7.10
7	Diuretics	248	5.91
8	CCBs	163	3.88
9	Cardiac glycosides	18	0.42

A total number of 4194 drugs used for cardiovascular disease were prescribed of which 768 (18.31 %) were antiplatelet

5212

Eur. Chem. Bull. 2023,12(10), 5210-5216

STUDY OF DRUG UTILIZATION PATTERNS WITH ASSOCIATED DRUG THERAPY PROBLEMS IN CARDIOVASCULAR PATIENTS AT A TERTIARY CARE TEACHING HOSPITAL - AN OBSERVATIONAL STUDY

Section A-Research paper

and anticoagulants followed by 745(17.76 %), dyslipidemia agents, 655(15.61 %), β-blockers, 467(11.13 %), angiotensin converting enzyme inhibitors, 367(8.75%), anti-angina drugs, 298(7.10 %), angiotensin-receptor blockers 467(11.13) and 248 (5.91%) were diuretics. We also observed the remaining drugs in less percentage of Calcium channel blockers (3.88%) and 0.42% were cardiac glycosides.

Table 4: Details of drug therapy in cardiovascular disease patients

S.no	Details of drug therapy	Number
1	Total no of prescriptions analyzed	850
2	Total no of drugs prescribed	5159
3	Average no of drugs per patient	6.06
4	Total no of cardiovascular drugs prescribed	4194
5	Average no of cardiovascular drugs per patient	4.93
6	Cardiovascular drugs from the essential drug list	3827
7	Cardiovascular drugs out of the essential drug list	367
8	Average no of drug-drug interactions per prescription	0.90

Total number of drugs prescribed ware 5159. The average number of drugs per patient was 6.05. Out of the total number of 5159 drugs prescribed, 81.29 % (5159) were cardiovascular drugs. The average number of cardiovascular drugs during hospitalization was 4.93. 91.24 % (3827) were from essential drug list of INDIA (2011) and 8.75% (367) were out of essential drug list.

Table 5: Distribution of potential drug-drug interactions

S. No	Drug pair	Level of severity	Mechanism	Frequency
1	ACE-inhibitor-Aspirin	Moderate	Pharmacodynamics	401
2	Atorvastatin-Clopidogrel	Moderate	Pharmacodynamics	338
3	Digoxin-Furosemide	Moderate	Pharmacokinetic	18
4	Digoxin-Atorvastatin	Moderate	Unknown	15

Moderate Drug – drug interactions identified from the Prescriptions were listed in the above table. The most frequently occurred were those with Atorvastatin - Clopidogrel (338) with moderate severity and pharmacokinetic Mechanism, Angiotensin converting enzyme inhibitors (ACE) - Aspirin (401) with moderate severity and pharmacodynamic mechanism, Digoxin-Furosemide (18) with moderate severity and Pharmacokinetic mechanism and Digoxin-Atorvastatin (15) with moderate severity and Unknown mechanism.

Table 6: Drug therapy problems among patients with cardiovascular diseases

Categories of Variables		N (%)
Types of DTP	Unnecessary drug therapy	58(6.8)
	Need for an extra drug	146(17.1)
	Ineffective drug products	5(0.5)
	ADR	0
	Noncompliance	122(14.3)

Drug therapy problems among patients were presented in table 6. Unnecessary drug use (6.8%), need for an extra drug (17.1%), non-compliance (14.3%)

DISCUSSION

Total 850, subjects' data was collected and analysed, males 52.94% with early onset of cardiovascular diseases than female 47.05% %. Heart diseases progresses with the advancing age, there is a greater prevalence, which increases with the higher age, 36% were from the age group 51-60 years, followed by 25.41 % in 61-70 age group, 24.94% in 41-50 age group. There were significantly lower number of patients in the younger ages, 8.33 % in the age group 31-40 and 0.58 % in the age group <30 which is comparable to studies by Cheah Whye Lian et al., and Mitu Baskota et al ., which shows (38.6 %) in more than 60 years and (45 %) in 46-65 years [14, 15].

Anti-platelets, lipid lowering agents, beta-blockers, angiotensin converting enzyme inhibitors, and nitrates were frequently prescribed, which certainly improve the treatment outcomes. Majority of the subjects received anti-platelets similar to other centres in Southern India [16, 17]. In our study among the Antiplatelets 41.32 % of the patients received dual Antiplatelets therapy (Aspirin and clopidogrel) which shows similarity with Kamath A et al., study 90 % of the dual Antiplatelets therapy [18]. The association of physicians of India recommends that all patients with MI, including those with STEMI, should receive dual anti-platelets therapy. Aspirin inhibits platelet activation through TxA2 pathway, clopidogrel inhibits platelet activation by a different mechanism different from aspirin and the

5213

Eur. Chem. Bull. 2023,12(10), 5210-5216

STUDY OF DRUG UTILIZATION PATTERNS WITH ASSOCIATED DRUG THERAPY PROBLEMS IN CARDIOVASCULAR PATIENTS AT A TERTIARY CARE TEACHING HOSPITAL - AN OBSERVATIONAL STUDY

Section A-Research paper

combination therapy with aspirin may offer benefits over either drug used alone [19]. Enoxaparin was found effective in treating, stable and unstable angina and the utilization of anticoagulants was optimal to other Indian studies (75%–85%) [20]. The only lipid lowering used was Atorvastatin, but it was identified that the dose was not calculated according to low-density lipoprotein cholesterol levels and was lower than the recommended use. The use of angiotensin converting enzyme inhibitors and statins was optimal and similar to other studies [21, 22]. Similar to ACS-US registry, [23] females receive less heparin and ACE inhibitors, aspirin, and statins than males. Among the Diuretics therapy Aldactone was most prescribed drug 70.56 %. Among the anti-anginal drugs only nitro-glycerine was prescribed. β-blockers drug therapy in our study shows Metoprolol in 63.51 % and Atenolol 36.48%. In Angiotensin II antagonist drug therapy, our study shows 98.66 % of Losartan and 1.34 % of Telmisartan. ACE Inhibitors include enalapril in 11.13%, calcium channel blockers include Amlodipine 3.88%. Only 0.42% of patients were receiving Digoxin.

In our study the prescribing prevalence has been expressed as the total number of prescriptions for a particular drug/drug category and also as the prescribing frequency. Prescribing prevalence studies are helpful to determine the prevailing morbidity patterns. Average number of drugs per subject was 6.06, as the drug number increases it eventually leads to polypharmacy and in most cases it was unavoidable, as the age increases there will be a rise in health complications [24]. 91.24 % of the drugs prescribed from the essential drug list of the India 2016-18 and drugs out of the essential drug list was 8.75%. Minimal or no prescription errors were identified as it is a tertiary care level government hospital. Prescription errors should be reduced by usage of generic names, and polytherapy could be avoided by fixed combinations rather than single formulation which can improve patient medication adherence. We also extended our study to determine the drug - drug interactions. But the entire drug–drug interactions are moderate. All the interactions were moderate in which ACE inhibitor-Aspirin constitute 51.94%, Atorvastatin-Clopidogrel constitutes 43.78%, Digoxin- Furosemide

constitutes 2.33% and Digoxin-Atorvastatin constitute 1.94%. The average no. of drug-drug interactions per prescription was 0.90. Subjects with cardiovascular conditions are more prone for drug interactions because of their increasing age, polypharmacy and the impact of heart disease on drug kinetics. The degree of utilization of cardiovascular drugs varies from person to person, disease being treated, and the impact of other drugs being used [18]. A minimal percentage of drugs, prescribed by generic names was seen, which is a major concern. The drugs were majorly prescribed from essential drug list, which is effective in promoting rational drug use and cost effectiveness [21].

Drug-related problems are a great concern to the health care system and majority are avoidable [22-24]. From the past studies it can be understood the occurrence and inhibiting the drug therapy-related losses of life [25, 26]. Inappropriate use of medicines had been associated with emergency hospital admissions [27, 28, 29] and unwanted drug effects had adversely affected the decrease in quality of life. This has been a concern to cause high morbidity and mortality in the inpatients and outpatients of health care systems [30-32]. Considering this fact, this study was aimed to assess the incidence of DTPs among patients attending for cardiology care. The study identified different types of DTPs among outpatient clinics of cardiology department. They are unnecessary drug therapy, the need for extra drug, ineffective drug products, and patient medication adherence with the treatment. All these have severe effects on the treatment outcomes of the patients in addition to allowing them to make an extra expenditure on healthcare of the individual

CONCLUSIONS: We can clearly observe a phenomenal increase of health hazards in the present days. The rise in cardiovascular hospitalisations due to co-morbid conditions, increasing age, sedentary lifestyle, high work stress, personal habits like alcoholism and smoking providing a route to more morbidity and mortality. Antiplatelets, lipid lowering agents had been prescribed more when compared to other classes of drugs. The cardiologist should be encouraged to write drugs by generic name. Majority of the drugs prescribed are from the essential drug list which indicates the knowledge of the cardiologist. Effective strategies, regular monitoring must be

Eur. Chem. Bull. 2023,12(10), 5210-5216

5214

STUDY OF DRUG UTILIZATION PATTERNS WITH ASSOCIATED DRUG THERAPY PROBLEMS IN CARDIOVASCULAR PATIENTS AT A TERTIARY CARE TEACHING HOSPITAL - AN OBSERVATIONAL STUDY

Section A-Research paper

implemented to improve the patient compliance reducing drug therapy problems and achieve better outcomes.

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5215

Eur. Chem. Bull. 2023,12(10), 5210-5216

STUDY OF DRUG UTILIZATION PATTERNS WITH ASSOCIATED DRUG THERAPY PROBLEMS IN CARDIOVASCULAR PATIENTS AT A TERTIARY CARE TEACHING HOSPITAL - AN OBSERVATIONAL STUDY

Section A-Research paper

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5216

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