Antiplatelet Agents Utilization Pattern and Assessment of Patient Specific Drug use Problems among Cardiac Patient

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Authors' contributions

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ABSTRACT

Background: Antiplatelet agents reduce the occurrence of the cardiovascular issue in people with established cardiovascular disease.
Objective: To understand the pattern of Antiplatelet drug utilization among cardiovascular disease patients. To evaluate the prevalence of polypharmacy and responsible factors like age, gender, co-morbid condition, and patient-related drug use problems.
Methodology: A cross-sectional observational study. Patients with cardiovascular disease above 18 years of age were prescribed antiplatelet agents from the department of cardiology and ICCU were enrolled in the study.

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Result: A total of 150 patients were enrolled of which male 79% (N=119) and female 21% (N=31). Most patients belong to 51-60 years of age groups. The patients diagnosed with IWMI (inferior wall myocardial infarction) 43.3% (N=65) have highly prescribed antiplatelet agents. Smoking 54.7% (N=82) followed by Alcohol 26.7% (N=40) found to be the most dominant risk factors.60.7% (N=91) patients had no comorbidity followed by 31.3% (N=47) had a comorbid cardiac condition. Most prescribed antiplatelet agents were monotherapy of Aspirin 28.8% (N=43), Clopidogrel 16.7% (N=25), and combination therapy of both 51.2% (N=82).

Conclusion: The study concluded that increases in the number of co-morbidities can significantly increase the Utilization of drugs which can further lead to drug use problems. The clinical pharmacist can help to alleviate the problems of polypharmacy and its consequence.

1. INTRODUCTION

Cardiovascular disease is one of the major causes of mortality in India. There are two highly predominant conditions; ischemic heart disease and stroke are responsible for >80%of CVD deaths. According to the Global Burden of Disease study, it is estimated that nearly one-fourth of all the death in India occurs because of CVD in 2010. Premature mortality ratio in terms of years of life lost because of CVD. In India ratio of mortality increased by 59% from 23.2 million (1990) to 37 million (2010). [1] CVD, acute coronary syndrome is considered one of the leading causes of mortality and morbidity worldwide [2]. Acute coronary syndrome is consisting of ST-Elevation Myocardial Infarction, Non-ST Elevation Myocardial Infraction, Or Unstable Angina [3]. Drug utilization evaluation studies using collected data or health facility indicators may indicate that there is more or less consumption of medicines, and qualitative studies may indicate why certain health staff and patients act the way they do. Such studies do not give detail about the exact nature of irrational use. Such features may concern in appropriate medicine choices, wrong doses, prescribing drugs that may lead to ADRs or drug interactions, and the use of expensive drugs when cheaper ones would do [4]. Antiplatelets are the most efficacious and preventable medication for blood clotting. The formation of blood clots is a major risk factor for developing cardiac abnormality. It may include coronary artery disease (CAD), Heart attack, Angina (chest pain), Stroke, Peripheral artery disease, ischemic heart disease (IHD). Antiplatelets reduced the risk of blood clotting and they are also known as "blood thinners". Aspirin and Clopidogrel are powerful agents and are used as initial therapy. There are limited studies from India which describe the utilization pattern of Antiplatelets in all conditions. People with cardiac abnormality have a higher risk of mortality in comparison with the general population. This part reflects intrinsic factors or associated comorbidities, but poor DRP to antiplatelet drugs has also been shown to contribute to increased risk of death and increased utilization of unscheduled care. We had observed that very few studies had been carried out on this topic in the Gujarat state of India, where antiplatelet drug utilization is very high in a different population of various age groups (above 18 years) and also with comorbid conditions. Along with this, we found out patients' specific drug-related problems in Cardiac patients, as very few such studies have been carried out in cardiac patients. This study aimed to perform antiplatelet drug utilization evaluation and to study patient-related drug use problems among cardiology patients.

2. METHODOLOGY

It wasa cross-sectional observational study conducted for a period of 6 months (October-2019 to March- 2020) at the Department of Cardiology and Intensive Critical CareUnit (ICCU) of the Dhiraj General Hospital, Vadodara. All the relevant data (patient demographics, detailed history, general physical examination, cutaneous examination, lab tests, and details of prescribed medications) was obtained from the patients' medical records and through counseling the patients who visited the Out- Patient Department (OPD) or In-Patient Department (IPD) of Cardiology of Dhiraj General Hospital. All inpatients and outpatients of cardiovascular disease above 18 years of age who were prescribed antiplatelet agents were enrolled in the study. However, patients who are unable to communicate such as severely ill patients and psychiatric patients were excluded from the study. All the relevant data collected and recorded electronically. Descriptive statistics

used for the analysis of the data. After the data collection, all the data were exported to statistical software for statisticalanalysis. All the quantitative data were represented in percentage (%) and mean ± standard deviation. Comparative statistical differences were calculated using appropriate parametric tests. The categorical data were represented in the median and comparative statistical differences were calculated by using appropriate non-parametric statistical tests. (Chi-square test and independent t-test). The graphical representative was used for a better understanding ofdata. A p-value of ≤0.05 was considered a significant.

3. RESULT

In our study, 150 patients were enrolled according to the proposed inclusion and exclusion criteria. Out of 150 patients, inpatients were 57% (N=85) while OPD patients were 43% (N=43). Comparing the gender popularity, males represent 79% (N=119) and females represent 21% (N=31) of the total population. In our study, the age of patients varies from 18 to 80 years with a mean age of 25 ± 18.6 years. The maximum number of patients from the age group 51-60 years 37% (N=55), 41-50, 22% (N=33),61-70, 21%(N=32), 31-40, 10% (N=15), 71-80, 6% (N=15) and followed age group of 21-30, 4% (N=6) as mentioned in (Table 1).

In the study, the majority of our patients suffered acute coronary syndrome. Among them, IWMI patients 43.3% (N=65) have the highest number of antiplatelet agents was prescribed followed by AWMI 30% (N=45). Patients with NSTEMI 20% (N=30) and Unstable Angina 6.7% (N=10) also used antiplatelet therapy (Table 2).

Among the study population, 54.7% (N=82) of patients prescribed antiplatelet agents are having the habit of smoking followed by 26.7% (N=40) alcohol consumption and 18.7% (N=28) habit of tobacco use. Out of 150 patients, a total of 39.1% (N=59) patients were enrolled with co-morbiditieswhereas 60.7% (N=91) were enrolled without any co-morbidities. The most common co-morbid condition found were hypertension, diabetes, hyperthyroidism, anemia, etc. Patients were also categorized as many co-morbidities present and all 59 patients were divided into four groups. Group-A patients60.7% (N=91) had no co-morbidity. Group-B patients 31.3% (N=47) had at least 1 co-morbidity with a cardiac condition. Followed by Group-C 7.3% (N=11) where the patient had 2 comorbid conditions and the least number of patients there in Group-D 0.7% (N=1)] having 3 comorbidities with a cardiac condition. A total of 494 medications were prescribed among 150 cardiac patients. The majority of the patient was prescribed with the highest number of drugs that were 56% (N=84) in group 5-8, followed by 1-5 group with 32% (N=49) and least number of populations found in >8with 11.3% (N=17). Polypharmacy, for this study, is defined as the concurrent use of 5 or more drugs after excluding all the vitamin and dietary supplements. Polypharmacy was seen in 101 (67.3%) patients out of 150 patients. Analytical results of polypharmacy show that majority of the patients took 5-8 drugs which constitute 56% followed by >8 drugs which were taken by 11.3% of patients.In the tertiary care hospital among the study population Aspirin and Clopidogrel were widely used antiplatelet agent where monotherapy of aspirin was prescribed for 28.8% (N=43) of the study population and Clopidogrel was prescribed for 16.7% (N=25) in combination therapy with Aspirin and Clopidogrel provide benefits over monotherapy 51.2% (N=82) and least prescribed was Prasugrel 3.3% (N=5) (Table 3).

Table 1. Distribution of study population according to age

Age Groups	Total no of Patient	Percentage
21-30	06	04
31-40	15	10
41-50	33	22
51-60	55	37
61-70	32	21
71-80	09	06
Total	150	100
Mean	25	
SD	18.6	

Table 2. Indication based segregation

Type	No of Patients	Percentage
UA	10	6.7
NSTEMI	30	20
IWMI(STEMI)	65	43.3
AWMI(STEMI)	45	30

UA-Unstable Angina, NSTEMI-Non-ST-elevation myocardial infraction, STEMI-ST Elevation Myocardial Infraction, IWMI-Inferior wall myocardial infraction, AWMI-Anterior wall myocardial infraction

Table 3. Number of Antiplatelet Prescribed

Drug	No of Patient	Percentage
Aspirin	43	28.7
Clopidogrel	25	16.7
Prasugrel	05	3.3
Dual therapy Aspirin +Clopidogrel	82	51.2

Table 4. Types of the combination given to the patient

Therapy Type	APDS	Number(Percentage)
Single APD	Aspirin	43(28.7)
	Clopidogrel	25(16.7)
	Prasugel	05(3.3)
Two APD	Aspirin+Clopidogrel	82(51.1)
Three APD	Aspirin+Clopidogrel+Prasugrel	01(0.6)

Out of a total of 494 drugs prescribed,150 antiplatelet were prescribed over the study period. Amongst all the patients who received APDs (Anti-platelets agents),51.2% of the prescribed with Dual therapy APDs followed by single APDs prescribed to 46.8%, the least number of patients 2% prescribed with three APDs. Among APDs, Combination therapy was mostly prescribed, Aspirin+Clopidogrel 51.1%. Among single drugs, aspirin was mostly prescribed 28.7% followed by Clopidogrel16.7%, and Prasugrel 3.3% where the least prescribed APDs were polytherapy.

Aspirin+Clopidogrel+Prasugrel 0.6%. (Table 4)

Many other drugs were prescribed with antiplatelet agents and they were also further classified into the basic classes that were Anti-hypertensive, Anti-Diabetic, Anti-hyperlipidemic, etc. Highest number of drugs prescribed were from Anti-hyperlipidemic 21.7% (N=107), followed by Antacid 21.1% (N=104), Anti-hypertensive 19.8% (N=98), Antibiotic 13% (N=64) class (Table 5).

The highest number of drugs prescribed other than antiplatelet include anti-hyperlipidemic like Rosuvastatin (N=100) and Atorvastatin. Anti-hypertensive like Metoprolol (N=60), Telmisartan. Amlodipine, Antianginal like nitroglycerine (N=40), Isosorbide Dinitrate (n=6). (Table: 6)

Table 5. Prescribing Pattern of Drugs other than antiplatelet agents

Drugs	No of Patient	Percentage
Antibiotic	64	13.0
Anticoagulant	56	11.3
Anti-hyperlipidemic	107	21.7
Anti-Hypertensive	98	19.8
Anti –diabetic	12	2.4
Antacid	104	21.1
Diuretic	28	5.7
Inotropic agent	03	0.6
Anti-thyroid	01	0.2
Other	21	4.3
Antianginal	56	10.2
Anxiety	11	2.0

Table 6. Highly prescribed drug other than Antiplatelets

Group of Drug	Name of Drug	No of Patient
Antihyperlipidemic	Rosuvastatin	100
	Atorvastatin	07
Antihypertensive	Metoprolol	60
	Telmisartan	20
	Amlodipine	07
	Ramipril	07
	Carvedilol	02
	Bisoprolol	02
Antianginal	Nitroglycerine	40
	Isosorbide dinitrate	06
	Isosorbide mononitrate	06
	Nicorandil	04
Antacid	Pantoprazole	90
	Ranitidine	14

Table 7. Drug –related problems related questionnaire

Drug Use Problem	Percentage(%)	Patient with DRP (N=150)
Patient unable to understand instruction properly	12.3%	89
Inappropriate timing or dosing intervals	15.4%	10
Administers/uses the drug in a wrong way	7.7%	05

A total of 10 drug use problems were asked to patients who participated in our study including IPD and OPD. Amongst the most common drug use problem was, unable to understand instruction properly (N=89) 12.3%. The second most common problem was inappropriate timing or dosing intervals (N=10) 15.4%. Another drug used problem was administered the drug in the wrong way(N=5)7.7% found in OPD patients (N=65). IPD patients found zero drugs used problems. (Table 7).

4. DISCUSSION

Cardiovascular diseases are the first leading cause of mortality worldwide. By, 2030 almost a 23.6million people are estimated to die from CVDs. The present study evaluates drug utilization and specific drug used problems in cardiovascular patients at a tertiary care teaching hospital. We studied 150 patients out of which 43 were OPD and 85 IPD patients. Comparing gender proportionality, Male patients (N=119) encountered were more than female (N=31). It was observed that the highest number of patients were of 51-60 (37%) age group which was similar to the study carried out previously36.62% in the age group of 51-60. [5] In a previous study,

Indication-based segregation revealed that the majority of patients had Myocardial infarction (IWMI-43.3%,AWMI-30%), followed by Unstable Angina (6.7%), which was similar to the study carried out in Tamilnadu [4]. An attempt to study the social history of the patient revealed that the majority of the patients were smokers (54.7%), followed by alcoholics (26.7%) and tobacco users (18.7%) which was in concordance with the study carried out in Tirupati among cardiovascular patient were smokers (26%) while alcoholics (22%) [6]. In our study, it is reported that it is reported the number of patients having comorbidities considerably lower (39.3%)as compared to the patient without comorbidities (60.7%). In our study most common comorbid condition like Hypertension, Anemia, Diabetes, Hyperlipidemia. This result was not supported by the study conducted in Guwahati which reported that patients present with comorbid condition (68.15) higher number than without comorbid condition (31.85%) where there was the highest occurrence of Diabetes, Asthma, Anemia, followed by Hypertension and thyroid [7]. Out of 150, comorbidities were found in 59 patients. It was further divided into four group, a patient without comorbidities was classified in Group – A(60%) whereas with one comorbidity were

Group B(31.13) followed by Group C (7.3) in which patient had 2 comorbid condition in the last patient with 3 comorbid condition were classified in Group D. Increase in the number of cases of MI in the age group of 50-60 is mainly due to sedentary lifestyle and comorbidities, which reduces blood supply to the heart, and because of deposition cholesterol in arteries supplying blood to the heart leading to cardiac arrest. Hyperlipidemia is a key risk factor for coronary heart disease. [2] In our study total medication prescribed was 494, the highest number of drugs prescribed was 5-8(56%), followed by 1-5 (32.7%). The least number of patients were prescribed >8(11.3%) drugs. Dual therapy with Aspirin and Clopidogrel has shown more benefits over monotherapy with Aspirin or Clopidogrel. The highest number of monotherapies prescribed were Aspirin (28.7%), Clopidogrel (16.7%), and Prasugrel (3.3%). This result wassimilar to a study conducted in Manipal super specialty hospital where Aspirin alone (16%) [8] Dual therapy of Antiplatelet agent like Aspirin+Clopidogrel shown more than 80% of prescription. These study results are supported by the study conducted in Chennai where dual therapy was highly prescribed (80%) as compared to monotherapy (20%). Aspirin occupied a significant portion among the Antiplatelet (due to its less cost, more effectivity, wide availability with two doses 75 mg and 150 mg. Clopidogrel was a commonly utilized antiplatelet drug in our study. The use of clopidogrel is beneficial in HTN and CAD patients with aspirin intolerance or contraindication to aspirin. Prasugrel was the least utilized agent in our study. [9] Polypharmacy, for this study, is defined as the concurrent use of 5 or more drugs after excluding all the vitamin and dietary supplements. Polypharmacy was experienced by 101(67.3%) patients of 150 patients this was concordance with the study done in Vishva Bharti Medical College, Kurnool on the incidence of polypharmacy in a cardiovascular patient where 75.6% of the patient received >5 drugs while 24.4% of the patient received <5 drugs. [10] In our study, many other drugs were prescribed with antiplatelet and they were also further classified into the basic classes that were Anti-hypertensive, Anti-Diabetic, Anti-hyperlipidemic, etc. The highest number of drugs prescribed was from Anti-hyperlipidemic 21.7%, followed by Antacid 21.1%, Anti-hypertensive 19.8%, Antibiotic 13% class. Rosuvastatin was prescribed in 66.66, patients and Atorvastatin in 4.66%, as Anti-hyperlipidemic. This is comparable with the study conducted in

Ahmedabad. Anti-hypertensive agents like Metoprolol (40%), Telmisartan (13.33), Beta-blocker therapy with Metoprolol reduce the mortality in patients. In our study 50% of patients using beta-blockers mostly Metoprolol. other were using alpha+beta-blocker Carvedilol (5%) patients didn't use any beta-blockers due to certain contraindication like second or third heart block without cardiac peacemaker. A result was similar to the study conducted in Tamilnadu where Metoprolol was most commonly prescribed. Other widely used agents like Antacid like Pantoprazole (60%), Ranitidine (9.33%) [10] We also studied drug-related problems occurring among the study population using PACNE classification. A total of 10 drugs used problems were asked patients who participated in the study including IPD and OPD. Amongst them majorly drug use problem was seen in both the patients like, unable to understand instruction properly (N=89) followed by inappropriate timing (N=10), dosing intervals, and at least administration the drug in the wrong way (N=5). which was similar to the study conducted in Switzerland where they found a lack of certain items for in-patients and the most common drug use problem was an inappropriate or wrong drug and inappropriate time of administration of the drug [11]. ADRs with Antiplatelets were theoretically possible like Aspirin-induced epigastric pain, aspirin-induced nephrotoxicity, GI irritation, and aspirin-induced epistaxis. Aspirin-induced nephrotoxicity occurred due to chronic use of aspirin and other contributing factors such as alcoholism, smoking, and high blood pressure. Responders are recruited in tertiary care hospitals where more than half of the population have low education, poor –economic status providing improper answers, showing less interest thus leading to bias. Thus, the validity of findings is questionable as there are chances of overestimation or underestimation.

5. CONCLUSION

To conclude, an increase in the number of co-morbidities can significantly increase the Utilization of drugs which can further lead to drug use problems. The clinical pharmacist can help to alleviate the problems of polypharmacy and its consequence.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely

no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT AND ETHICAL APPROVAL

The study obtained ethical approval from the Sumandeep Vidyapeeth Institutional Ethics Committee (Ref no: SVIEC/ON/Phar/BNPG18/D19039). Patients who were fulfilled the inclusion criteria were enrolled in the study after explaining to the patients the details of the study, the Informed consent form was taken.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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