



ISSN (E): 2277- 7695  
ISSN (P): 2349-8242  
NAAS Rating: 5.03  
TPI 2019; 8(7): 80-85  
© 2019 TPI  
www.thepharmajournal.com  
Received: 14-05-2019  
Accepted: 18-06-2019

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## Study on drug utilization of anti-platelets and anti-coagulants in patients with coronary artery disease

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### Abstract

**Background:** Coronary artery disease is also described as ischemic heart disease it is a condition in which vascular supply to the heart is impeded by atheroma, thrombosis or spasm of coronary arteries. Atheromatous plaques decrease the lumen diameter and reduce the ability of the coronary artery to dilate in response to increased oxygen demand. Coronary artery disease is a group of disease which include acute coronary syndrome and stable angina. Drug utilization research provide insights into the many aspects of drug use and drug prescribing such as pattern, quality, determinants and outcomes of drug use.

**Objectives:** The main objective of the study was to find the drug utilization review for Anti-platelets and Anti-coagulants in patients with coronary artery disease. To find ADR associated with drug therapy and cost analysis among different brands of Anti-platelets and Anti-coagulants drugs were also included in the study using DDD. The purpose of ATC/DDD was to serve as a tool for drug utilization monitoring and research in order to improve quality of drug use.

**Methodology:** A noninvasive descriptive observational study was conducted in Coronary Care Unit and in Department of Medicine, Rajah Muthiah Medical College and Hospital, Annamalai University, Annamalai Nagar, Tamil Nadu. Our hospital is multi-speciality tertiary care university teaching hospital with 1400 beds. The study period was six months i.e., November 2017 to April 2018. The study was approved by Institutional Human Ethics Committee. This study described the drug utilization of Anti-Platelets and Anti-coagulants in a group of 78 Coronary artery patients (CAD) patients in Coronary Care Unit (CCU) and Medicine ward.

**Results:** This study enrolled and completed with total number of 78 patients. In there, 46.15% were male and 53.85% were female. Anti-platelets and Anti-coagulants had been prescribed for age ranging 40-80 years with more number of patients within 70-80 age groups. Clopidogrel was prescribed to more number of patients out of 78 patient in our study. Among Anti-coagulants, LMWH was prescribed to 30 patients and UFH was prescribed to 12 patients. In our hospital, Streptokinase is the most used fibrinolytics to break the formed clot.

**Conclusion:** This descriptive study expressed the total exposure to the drugs like Clopidogrel, UFH and LMWH according to the defined study period. Drug Utilization study of Anti-platelets and Anti-coagulants in DDD gave a rough estimate of consumption of these drugs and not the exact picture of the actual drug use. It doesn't imply any judgements about efficacy or relative efficacy of drugs. Our study concluded the trends in drug use of Anti-platelets and Anti-coagulants. In future, comparative studies will be done between population groups within country or region.

**Keywords:** drug utilization, anti-platelets, anti-coagulants, patients

### Introduction

Coronary Artery Disease also called as Ischemic Heart Disease, a condition which blocks the blood supply to heart. Formation of atheromatous plaques occurs as a result of high blood pressure which damages the coronary artery especially and deposition of lipids. Spasm of coronary arteries and rupture of plaques forms thrombus results in blockage of cerebral artery (Cerebral ischemia).

### Types of cardiovascular diseases

The four main types of CVD are,

1. Coronary artery disease
2. Peripheral arterial disease
3. Aortic disease
4. Stroke

Atheromatous plaques decrease the lumen diameter and reduce the ability of the coronary artery to dilate in response to increased oxygen demand. Coronary artery disease is a group of disease which include A cute coronary syndrome and Stable Angina.

### Epidemiology in India

In developing and developed urban and rural areas, the most important cause of death in men and women was found to CVD. Indian government evaluated and reported death of more than 1, 20,000 death reports from a 6 million nationally represented sample from 661 districts. In India, more than 10.5 million deaths occur annually, and it was reported that CVD led to 20.3% of these deaths in men and 16.9% of all deaths in women. With the total number of 10.5 million death in a year, 20.3 % and 16.9% were found to be male and female with CVD. Compared to rural, mortality rates were greater than 37 % in urban areas.

### Risk factors

Risk factors for coronary artery disease include:

- Age
- Sex
- Family history
- Smoking
- High blood pressure
- High blood cholesterol levels
- Diabetes
- Overweight or obesity
- Physical inactivity
- High stress

Risk factors frequently occur in clusters and build on one another, such as obesity leading to type 2 diabetes and high blood pressure. When grouped together, certain risk factors put us at an even greater risk of coronary artery disease. Sometimes coronary artery disease develops without any classic risk factors. Researchers are studying other possible factors, including:

- **Sleep apnea**
- **High sensitivity C-reactive protein**
- **High triglycerides**
- **Homocysteine:** Homocysteine is an amino acid, high levels of homocysteine may increase your risk of coronary artery disease.

### Complication

Coronary artery disease can lead to

- **Chest pain (Angina)** – Mostly during physical activity, coronary arteries narrow, heart may not receive enough blood when demand is greatest can cause chest pain (Angina) or shortness of breath.
- **Heart attack** -- If a cholesterol plaque ruptures and a blood clot forms, complete block of blood flow on coronary artery damage the heart muscle.
- **Heart failure** – Heart fails to pump the enough blood because of weaken heart muscle.
- **Abnormal heart rhythm (Arrhythmia)** - Irregular origin of heart's electrical impulses, causing abnormal heart rhythms results in inadequate blood supply.

**Drug utilization review study - drug utilization research** was defined by WHO in 1977 as “the marketing, distribution,

prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences”.

### Types of drug utilization study

Drug utilization studies can be targeted towards any of the following links in the drug-use chain:

- The *systems and structures* surrounding drug use,
- The *processes* of drug and
  1. The *outcomes* of drug use.

### Act Classification

The ATC classification system divides the drugs into different groups according to the organ or system on which they act and according to their chemical, pharmacological and therapeutic properties. Drugs are classified in groups at five different levels. The drugs are divided into 14 main groups (first level), with two therapeutic/pharmacological subgroups (second and third levels). The fourth level is a therapeutic/pharmacological/chemical subgroup and the fifth level is the chemical substance. Drug Utilization figures should ideally be presented using a relevant denominator for the health context such as numbers of,

- DDD per 1000 inhabitants per day
- DDD per 100 bed days
- DDD/patient
- DDDs per inhabitant per year

### Aim

To study the drug utilization of Anti-platelets and Anti-coagulants in patients with coronary artery disease.

### Objectives

1. To study the drug utilization of Anti-platelets and Anti-coagulants in coronary artery disease.
2. To calculate Number of Defined Daily Dose for Anti-platelets and Anti-coagulants.
3. To find ADR associated with drug therapy.
4. Cost analysis among different brands of Anti-platelets and Anti-coagulants drugs.

### Study site

This descriptive study will be conducted in Coronary Care Unit and in Department of Medicine, Rajah Muthiah Medical College and Hospital, Annamalai University, Annamalai Nagar, Tamil Nadu. Our hospital is multi-speciality tertiary care university teaching hospital with 1400 beds.

### Study design

A Noninvasive descriptive observational study.

### Study period

The study period was six months i.e., November 2017 to April 2018.

**Study recruitment procedure:** Patients with coronary artery disease condition admitted in Department of Medicine and coronary Care Unit who met the selection criteria.

### Selection criteria

#### Inclusion criteria

- Patients of both gender of 30 years and above admitted with coronary artery disease.

**Exclusion criteria**

- Liver disorder patients.
- Pregnancy / Breast feedings females.

**Sources of data**

The only resource for data collection is patient’s case sheets available in wards of department of Medicine and Coronary Care Unit.

**Designing data collection form**

The first step in the study is to design data collection form and prescription analysis form. It includes like inpatient number, patient name, age, sex, date of discharge, chief complaints, history of present illness, past medication history, laboratory, diagnosis and therapeutic management.

**Study procedure**

- Patients satisfying the selection criteria were enrolled in the study, obtained the required information consent.
- The required information was collected from prescriptions of patients with coronary artery diseases in Medicine department and CCU.
- The prescriptions were assessed for the possible adverse drug reactions associated with the treatment and the drug prescribed.

**Drug utilization study**

**Defined daily dose (DDD)**

Defined Daily Dose is the assumed average maintenance dose

per day for a drug used to its main indication in adults

$$DDD = \frac{\text{Items issued} \times \text{Amount of drug per Item}}{DDD}$$

**Items Issued:** Total No. of tablets taken over certain span of time (i.e., Days)

**Amount of drug**

Standard dose or strength prescribed

**Steps to calculate DDD calculation**

- Find out amount of medicines used or procured in study in terms of the number of units (tablets, capsules, injection) and strength (mg, g, IU).
- Calculate the total quantity consumed in study in terms of mg/g/UI by multiply in the numbers of units by strength of dose.
- Divide the total quantity by assigned DDD for that medicine.
- Divide the total quantity by the number of patients or by the population.

**Observation and Results**

The study comprises 78 patients prescribed with Anti-platelets and Anti-coagulants in Coronary artery disease who were enrolled into the study based on the selection criteria after obtaining their consent.

**Table 1:** Gender-wise distribution of patients included in present study

Gender	No of patients	Percentage
Male	36	46.15 %
Female	42	53.85 %
Total	78	100 %

Among the study population female patients were found to be higher than the male patients.

**Table 2:** Age-wise distribution

Age	No Of Patients	Percentages (%)
40 – 50	11	14.10 %
50 – 60	10	12.82 %
60 – 70	19	24.35 %
70 – 80	38	48.71 %
Total	78	100 %

The age-wise distribution of the study shows that the maximum number of patients being in 70-80 years, accounting 48.71% of the total.

**Table 3:** Co-Morbidities with CAD patients

Co-Morbidities with CAD	Males		Females		Total	
	Number	%	Number	%	Number	%
Cva (hemiparesis)	3	8.3	2	4.7	5	6.4
Systemic hypertension	10	27	17	40	27	34.6
Hypertensive emergency	1	2.7	6	14.2	7	8.9
Pulmonary edema	1	2.7	2	4.7	3	3.8
Type 2 dm	4	11	4	9.7	8	10.2
Diabetic retinopathy	3	8.3	1	2.3	4	5.1
Atrial fibrillation	1	2.7	6	14.2	7	8.9
Hyperlipoproteinemia	10	27	3	6.9	13	16.6
Chronic kidney disease	3	8.3	1	2.3	4	5.1
Total	36	100	42	100	78	100

**Table 4:** Anti-platelets, Anti-coagulants and Fibrinolytics prescribed in study population

Drugs	Total number of patients
Clopidogrel	78
Aspirin	56

Statins	65
Heparin	42
Streptokinase	29

**Table 5:** Difference among prescribing Anti - platelets.

Anti-platelets	No of patients	Percentage
Aspirin	56	71 %
Clopidogrel	78	100 %

**Table 6:** Patients prescribed with Un fractioned heparin and Low molecular weight heparin.

Heparin therapy	No of patients	Percentage
UFH	12	15%
Lmwh	30	38%

**Table 7:** Daily defined dose of anti-platelets and anti-coagulants - drug utilization evaluation

Drugs	Atc code	Ddd [atc]	Amt of drug/item	Items issued	Ddd/78 pts
Clopidogrel	B01AC04	75 mg	75 mg	7	0.089
LMWH	B01AB05	2 TU	40 mg	3	2.051
UFH	B01AB01	10 TU	5000 U	4	57.69

Drug utilization figures should ideally be presented using a relevant denominator for the health context such as numbers

of DDD per 1000 inhabitants, DDD per inhabitant per year, DDD per 100 bed days and DDD/patients.

**Table 8:** Cost minimization analysis for high and low cost brands.

Drug	Brands	Mfg company	Cost (rs. Paise) per tablet	Cost difference ( % )
Aspirin	Delisprin optaz	Genetica Shreya	0.260 0.847	69 %
Clopidogrel	ClopiKin stromix	Mankind Abbott	2.6 15.3	83 %
Aspirin + clopidogrel	Pragril-a ceruvin-a	Dr. Reddy's Ranbaxy	2.8 5.7	50 %
Heparin (UFH)	Heparin troyhep	Abbott Troikkaa	91.88 234.00	64.6 %
Enoxaparin (LMWH)	Grefac lmwx	Dr. Reddy's Abbott	381.00 556.00	31.47 %

## Discussion

This study describes the drug utilization of Anti-Platelets and Anti-coagulants in a group of 78 Coronary artery patients (CAD) patients in Coronary artery unit (CCU) and Medicine ward. The aim of this study is to study the drug utilization of Anti-platelets & Anti-coagulants in patients with CAD. This study done in a period of short time to give an overview of utilization of above mentioned category of drugs in our hospital. This study enrolled and completed with total number of 78 patients. In there, 46.15% were male and 53.85% were female. Our study has generated data on optimal use of Anti-platelets and Anti-coagulants. We found that Anti-platelets and Anti-coagulants had been prescribed for age ranging 40-80 years with more number of patients within 70-80 age groups. Prescribing these lifesaving drugs shows a gradual increase with increase in age of patients. Among Anti-platelets, Clopidogrel was prescribed to more number of patients out of 78 patient in our study. Based on physician interest and experience, patients were prescribed with combination of clopidogrel with aspirin and some are with aspirin alone. Among Anti-coagulants, LMWH was prescribed to 30 patients and UFH was prescribed to 12 patients. This is similar to conducted on in our study, we found that LMWH was prescribed with dose of 40mg subcutaneous BD and UFH was prescribed with dose of 5000 IU intra-venous TDS based on physician interest and off-label use. Out of 78 patients enrolled in the study, 29 experienced anterior wall and inferior wall myocardial infarction. Anterior wall myocardial infarction further divides into antero-septal and antero-lateral myocardial infarction. In our hospital, Streptokinase is the most used fibrinolytics to break the formed clot. Patients are then managed with anti-platelets and anti-coagulants. Among anti-platelets, clopidogrel was

prescribed to more number of patients than the combination of aspirin plus clopidogrel. Among anti-coagulants, LMWH is prescribed most than UFH. The most common co-morbid disease associated with CAD is systemic hypertension. In our study, we observed CAD with 27 patients who had systemic hypertension. In those female patients are in more number compared to male patients. The second most common co-morbid condition is Hyperlipoproteinemia. In our study population, we observed CAD with 13 patients who had hyperlipoproteinemia. In those male patients are in more number than female. Type 2 Diabetes Mellitus is the third most common co-morbid condition along with CAD. In this male patients and female patients are equal in number.

## Defined daily dose

World Health Organization (WHO) recommends Defined Daily Dose (DDD) method of measuring drug use. The purpose of ATC/DDD is to serve as a tool for drug utilization monitoring and research in order to improve quality of drug use. The classification of a substance in the ATC/DDD system is therefore not a recommendation for use and it does not imply any judgements about efficacy or relative efficacy of drugs and groups of drugs. WHO given DDD for Aspirin - 75mg, UFH - 10 TU and LMWH (Enoxaparin) - 2 TU, are the only DDD used in this study. DDD/patient expresses the total exposure to the drug according to the defined study period. For drugs like Clopidogrel, if the actual dose is equivalent to the DDD, the DDD/patient would also express number of treatment days in a specific period. Drug utilization in data presented in DDDs gives a rough estimate of consumption of drugs and not the exact picture of the actual drug use. The estimates prescribed above are only true if there is good agreement between the actual prescribed dose and the DDD.

During this short period of study, there is no incidence of any ADR for these drugs reported/notified by physicians. In this study we compared the most commonly prescribed drugs under the category of anti-platelets and anti-coagulants. Drugs like Aspirin, Clopidogrel, and Combination of Aspirin with clopidogrel, UFH and LMWH under different brands are compared. The cost difference between the brands of lowest price and highest price are compared and results are reported in percentage (%) difference.

### Conclusion

Our present study shows that female patients are more in number to male patients. Anti-platelets and Anti-coagulants had been prescribed for age groups ranging from 40 – 80 years. The age group 70-80 contains more number of patients. Co-morbid conditions associated with CAD has the ranking from Hypertension (34.6%), Hyperlipoproteinemia (16.6%) and Diabetes mellitus (10.2%). Clopidogrel tops the lists of commonly prescribed drug followed by Aspirin, Statin and Heparin. Among Anti-platelets, Clopidogrel was prescribed more than Aspirin. Among Anti-coagulants, LMWH was prescribed more than UFH. Statins always have a role in lipid reductions in CAD, which are commonest among prescribed drugs. Streptokinase, the most used first line fibrinolytics in emergency conditions. No ADR was reported by physician for anti-platelets and anti-coagulants category of drugs during this short period of study. The result of cost comparison study states that practice of prescribing “Generic drug” will be cost effective for the patients, since the drugs like anti-platelets are meant for long term treatment. This descriptive study expresses the total exposure to the drugs like Clopidogrel, UFH and LMWH according to the defined study period. Drug Utilization study of Anti-platelets and Anti-coagulants in DDD gives a rough estimate of consumption of these drugs and not the exact picture of the actual drug use. It doesn't imply any judgements about efficacy or relative efficacy of drugs. Our study concluded the trends in drug use of Anti-platelets and Anti-coagulants. In future, comparative studies will be done between population groups within country or region.

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