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A Prospective Study on Prescribing Pattern of Anticoagulants in Cardiovascular Disease

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ABSTRACT

Introduction: Protection against Atrial Fibrillation and Thromboembolism is central to the management of patients with cardiovascular disease. Anticoagulants are well recognized as blood thinners for their beneficial impact that inhibits thrombus formation by preventing fibrin clot. **Objectives:** To assess the prescription pattern of anticoagulant drugs in cardiovascular disease. **Methodology**: This was a Prospective Observational study carried out for a period of 6 months at Apollo Multi-Speciality Hospital, Bengaluru. Patients were included from Cardiology and Medicine department was based on the criteria. Data was analyzed with suitable statistical tool. **Results:** Out of 300 patients enrolled, 208 were male (69.33%) and 92 were female (30.65%) patients. Age distribution showed that patients of age group 60 years and more were predominantly using anticoagulants than others. Based on the distribution of therapy, 251 patients were prescribed with monotherapy, 44 patients with dual therapy and 05 patients with triple therapy. Low Molecular Weight Heparin was the most commonly used anticoagulant class. **Conclusion:** Enoxaparin sodium is the most commonly used anticoagulant drug due to its reduced risk of bleeding and low molecular weight heparin being the most commonly utilized anticoagulant class. Maximum people were exposed to moderate drug-drug interactions. Most of the patients had well controlled PT/INR and PTT values and hence the therapy was found to be effective.

INTRODUCTION

Cardiovascular diseases are the number one cause of death globally, more people die annually from CVDs than from any other cause.[1]Cardiovascular diseases contributed 28·1% of the total deaths and 14·1% of the total disability adjusted life year in India in 2016, compared with 15·2% and 6·9% respectively, in 1990.[2]Non pharmacological management of coronary artery disease includes lifestyle recommendations like quitting smoke, eating a healthy diet, and exercise regularly. Medications includes Statins, antiplatelets, beta blockers, ACE inhibitors, calcium channel blockers, anticoagulants and nitrates, cardiac glycosides and antiarrhythmic drugs). Surgery can open or replace blocked arteries include Coronary bypass grafting, angioplasty, stent placement and laser surgery[3]. Clotting is a complex cascade of enzymatic reactions in which clotting factors activates another factor in a fixed sequence till a fibrin clot is formed. The clotting involves several enzymes and chemical factors known coagulating factors which includes factor I fibrinogen, II prothrombin, III tissue thromboplastin or tissue factor, IV calcium, V proaccelerin, VII proconvertin, VIII antihemophilic factor-A, IX Christmas factor, X Stuart factor, XI plasma thromboplastin antecedent, XII Hageman factor, XIII fibrinase.[4]

Anticoagulants: The anticoagulant drugs inhibit the action of the coagulation factors or interfere with the synthesis of coagulation factor. These drugs reduces the coagulability of the blood.

Classification of Anticoagulants

1.Parentral Anticoagulants:

a) Indirect thrombin inhibitors- Heparin, Enoxaparin

b) Direct thrombin inhibitors- Argatroban, Lepirudin

2.Oral Anticoagulants:

a) Coumarin derivatives- Warfarin, Acenocoumarol

b) Direct factor Xa inhibitor- Rivaroxaban

c) Oral direct thrombin inhibitor- Dabigatran[5]

The study of prescribing pattern is a component of medical audit that does monitoring and evaluation of the prescribing pattern of the prescriber as well as recommends necessary modification to achieve effective medical care and it helps to evaluate and suggest modifications in prescribing practices of medical practitioners so as to make medical care rational. A prescription based survey is the most effective method to assess and evaluate prescribing attitude of physician. Rational drug prescribing is defined as the use of the least number of the drug to obtain the best possible effect in the shortest period and at a reasonable cost. Use of multiple cardiovascular agents leads to Polypharmacy and chances to drug related problems in prescription. Drug interaction is said among the major drug related problem. A drug interaction is said to occur when the effect of one drug is changed by the presence of other drug, food or by some environmental chemical agent. A potential drug interaction is an event that is likely to develop if pharmacist do not make any appropriate interventions. Drug-drug interaction pose significant challenge to health care providers and may affect morbidity, mortality and patient's quality of life[6]. The study of the efficacy of the drug determines that ability of a drug to elicit a response when it interacts with the receptor and maximum effect that a drug can produce regardless of dose[7].

MATERIALS AND METHODS

Study site: The study was conducted in cardiology and medicine department of Apollo multi-speciality hospital and research centre, Bengaluru.

Study design: This was a Prospective and Observational study. It was performed in 300 patients to assess the current prescribing pattern of anticoagulants in cardiovascular diseases.

Study period: The study was conducted over a period of six months starting from September 2018 to February 2018.

Ethical approval: Ethical committee clearance has been obtained by the institutional Ethical Committee of Apollo Multi-Speciality Hospital and Research Centre, Bengaluru.

Study Criteria:

Inclusion Criteria:

- Cardiac patients prescribed with anticoagulants.

- Patients with cardiovascular diseases and other comorbidities.
- Include all the geriatric, pediatric and pregnant patients.
- Treatment chart which includes anticoagulants.

Exclusion criteria:

- Patient who are not prescribed with any anticoagulant during the study period.
- Patient who stays less than 48hrs in hospital.
- Patient who have no recorded diagnosis of cardiovascular disease.

Source of data: Patients demographic, laboratory and therapeutic data were collected from patients admitted and the main sources for collection of data were:

- Patient's case note
- Treatment chart/ medication chart
- Lab data reports

Study procedure

- **Patient Enrollment-** A hospital based prospective observational study was conducted in the Apollo Multi Speciality Hospital & Research Centre. The study was conducted in 300 patients who had undergone treatment with anticoagulant drugs.

- **Methods of Data Collection -**All the patients admitted to the General medicine and Cardiology department of the Apollo Multi-Speciality Hospital Bengaluru during the study period was screened for use of anticoagulants. Those who met the inclusion criteria was enrolled for the study. Necessary information such as patient's age, date of admission, past medical, medication history and details on visit of treatment was obtained from patient's case notes. Therapeutic data such as name of drugs, doses, route of administration, duration of treatment laboratory data were collected in a suitably designed data collection form.

- **Determination of Prescription Patterns-** After the diagnosis was confirmed the entire relevant and necessary baseline information such as demographic details of patient, past

medical, medication history, date of admission, occupation were collected. Therapeutic data such as name of drugs, doses, route of administration, duration and laboratory data were collected and documented in suitably designed documentation form. The changes in prescribing drugs or their doses and duration was also documented.

- **Statistical Method-** This model was Descriptive statistical analysis has been carried out in present study. Chi-Square test has been used to find the significance of study parameters on categorical findings among different groups.

Significant Figures

*Strongly significant if P value is =0.01.

*Moderately significant if P value is 0.01-0.05.

*Significant if P value is >0.05 to 0.1.

* Non-significant if P value is > 0.1.

Statistical Software- The statistical software called SPSS (IBM) version 25.0 was used for the analysis.

Microsoft Word and Excel are used to generate tables and graphs respectively.

RESULTS

Study design: Prospective and observational

Table No. 01 - Gender distribution of study population

Gender	No .of patients	Percentage
Male	208	69.33
Female	92	30.67
Total	300	100

As shown in the table no: 01, Out of 300 patients 208 were males (69.33%) and 92(30.65%) were female.

Table No. 02 – Age distribution of study population

Age (years)	Male	Female	Total	Percentage
21-30	4	1	5	1.66
31-40	28	5	33	11
41-50	35	8	43	14.33
51-60	38	16	54	18
> 60	103	62	165	55
Total	208	92	300	100

In table 02, the age distribution in the given population showed that, 1.66% of patients belonged to the age group of 21-30 years, 11% from 31-40 years, 14.33% from 41-50 years, 18% from 51-60 years and 55% of the total population are from the age group of >60 years.

Table No. 03: Distribution of anticoagulants prescribed in the study population, according to respective classes

Class of anticoagulants	Drug prescribed	Gender		Total	Percentage
		Male	Female		
Low molecular weight heparin	Fondaparinux	27	18	226	52.56
	Enoxaparin Sodium	122	58		
	Dalteparin	0	1		
Coumarin Derivatives	Acenocoumarol	19	12	36	8.37
	Warfarin	1	4		
Indirect Thrombin Inhibitors	Heparin	106	44	150	34.89
Oral Direct Thrombin Inhibitors	Dabigatran	13	4	17	3.95
Direct Factor Xa Inhibitors	Rivaroxaban	0	1	1	0.23

P=0.32, Non-Significant, Chi-Square test

According to the table 03, the distribution of anticoagulants with respect to class showed the order of usage as Low molecular weight heparin (52.56%) > Indirect thrombin inhibitors (34.89%) >Coumarin derivatives (8.37%) > oral direct thrombin inhibitors (3.95%) > Direct factor Xa inhibitors (0.23%).The order of usage of drugs irrespective of class is – Enoxaparin

sodium (180) > Heparin (150) >Fondaparinux (45) >Acenocoumarol (31) >Dabigatran (17) > Warfarin (5) >Rivaroxaban (1) = Dalteparin (1).

Table No. 04: Distribution of therapy in the given population

Therapy	Drugs prescribed	Gender		Subtotal	Total	Percentage
		Male	Female			
Monotherapy	Fondaparinux	16	12	28	251	83.67
	Acenocoumarol	13	6	19		
	Enoxaparin sodium	68	25	93		
	Dabigatran	5	0	5		
	Heparin	75	28	103		
	Dalteparin	0	1	1		
	Warfarin	1	1	2		
Dual Therapy	Acenocoumal & Heparin	1	1	2	44	14.67
	Dabigatran& Heparin	2	0	2		
	Enoxaparin sodium & Acenocoumarol	4	3	7		
	Enoxaparin sodium & Fondaparinux	4	1	5		
	Enoxaparin sodium & Heparin	6	4	10		
	Heparin & Fondaparinux	11	2	13		
	Acenocoumarol & Fondaparinux	0	1	1		
	Dabigatran & Fondaparinux	0	1	1		
	Enoxaparin sodium & Warfarin	0	1	1		
	Heparin & Rivaroxaban	0	1	1		
	Warfarin & Fondaparinux	0	1	1		
Triple Therapy	Acenocoumarol, Dabigatran, Heparin	2	0	2	5	1.66
	Heparin, Warfarin, Enoxaparin sodium	0	1	1		
	Dabigatran, Heparin, Enoxaparin sodium	0	2	2		
Total		208	92	300	300	100

P=0.56, Non-Significant, Chi-Square test

Table 04 shows the distribution of therapy in total study population in which, 83.67% of patients were receiving monotherapy and Heparin (103) was the highly prescribed anticoagulant followed by, Enoxaparin sodium (93) and Fondaparinux (28). 14.67% of patients were receiving dual therapy, in which, Heparin & Fondaparinux (13), Enoxaparin sodium & Heparin (10), Enoxaparin sodium & Acenocoumarol (7) and Enoxaparin sodium & Fondaparinux (5) were highly prescribed. Remaining 1.66% of patients were receiving triple therapy of anticoagulants, in which, Dabigatran, Heparin, Enoxaparin sodium were prescribed to 2 patients, Acenocoumarol, Dabigatran, Heparin to 2 patients and Heparin, Warfarin, Enoxaparin sodium to 1 patient.

Reference: out of 300 patients, 251 were on monotherapy. Therefore, single anticoagulant drug is producing necessary anticoagulation and preventing the risk of clot in 83.67% of patients.

Efficacy of anticoagulants based on laboratory parameters in the study population

Table No.05: Distribution based on average PT/INR and PTT values

PT (11-13.5 sec) / INR (0.8-1.1)	Average	PTT (25-35 sec)	Average	Outcome
At Admission	6.59/1	At Admission	16.73	Increased
At Discharge	11.96/2.1	At Discharge	29.83	

From the above table 05, the evaluation of efficacy of anticoagulants based on PT/INR and PTT values showed that there was significant rise in the average values of both PT/INR and PTT, which means the time taken to form a clot is increased in the study population. Therefore, the prophylactic and therapeutic anticoagulant treatment was found to be effective.

Table No. 06: Severity of drug interactions in the study population

Severity of drug interactions	Males	Females	Total	Percentage
Mild	12	23	35	11.67
Moderate	98	39	137	45.67
Severe	4	9	13	4.33
None	58	21	79	26.33
Total	208	92	300	100

P=0.82, Non-Significant, Chi-Square test

Table 06 shows the distribution of drug interactions in the study population and it is found that 45.67% of patients were exposed to moderate drug interactions, 11.67% of patients were exposed to mild interactions, 4.33% of patients were exposed to severe drug interactions and 26.33% of patients were not exposed to drug interactions. Therefore the severity of drug interactions is in the order of moderate interactions > mild interactions > severe interactions.

DISCUSSION

Selection of anticoagulants in patients with cardiovascular disease is complex and equivocal in nature, owing majorly to the non-adherence to standard clinical guidelines. Moreover, there is a scarcity of data on utilisation pattern of anticoagulants in Indian population. Our primary objective was to analyse the prescribing pattern of anticoagulants among all the patients with cardiovascular disease. The secondary objective was to evaluate the efficacy and find out all possible drug-drug interactions in the prescriptions.

Table No.1 represents the total number of male and female patients, there were more number of male patients with cardiovascular diseases enrolled in the study. Similar findings were found in the study conducted by **Jonas O**[8]*et al*. in which 61.3% were males and 43% were females indicating that anticoagulants are more prescribed in males over females. As shown in Table No.2, patients ranging from age group 21 years to >60 years were enrolled in the study. The maximum number of patients were seen in the age group of >60 years with 165 patients (55%). The lowest number was seen in the age group of 21-30 years. Similar findings were found in the study conducted by **Torn M**[9]*et al* in which out of 4202 patients, 842 patients younger than 60 years; 1200 patients aged between 60 and 70 years; 1464

patients aged between 71 and 80 years; and 696 patients older than 80 years, indicating that anticoagulants are more prescribed in age above 60 years. As shown in Table No.3 the patients were prescribed with various class of anticoagulant drugs. In this study, it was found that Low molecular weight heparin class are more prescribed over other class. It is also found that Enoxaparin sodium is the most commonly used drug. Similar results were observed in a study conducted by **Harold P**[10]*et al*. in which they compared LMWH with other classes and found that LMWH have the advantage of a more predictable dose-response curve and incidence of bleeding is less as compared to others, indicating that LMWH are more prescribed class as compared to others. Table No.4 shows the prescribing pattern based on Mono, Dual and triple therapy of anticoagulant drugs. Distribution of therapy in study population is found to be 251(83.67%) patients were receiving monotherapy and Heparin (103) was the highly prescribed anticoagulant. Number of patients receiving dual therapy were 44(14.67%). Remaining 5(1.66%) patients were receiving triple therapy of anticoagulants. Similar findings were observed in the study conducted by **C Seth**[11]*et al* in which anticoagulants prescribed as monotherapy (87%) is compared with dual therapy (34%) and triple therapy (2.3%) indicating that anticoagulants are mostly prescribed as monotherapy.PT/INR and PTT is the most commonly used parameters to assess the efficacy of anticoagulants. From the above Table No.5, the evaluation of efficacy based on PT/INR and PTT values showed that there is significant rise in the average values of both PT/INR and PTT, which means the time taken to form a clot is increased in the study population. Therefore, the prophylactic and therapeutic anticoagulant treatment is found to be effective. Similar findings were observed in the study conducted by **Adam Cuker**[12]*et al* in which laboratory measurement of anticoagulant activity is studied. In this study, they found that there is significant rise in the average values of PT, INR, PTT and other parameters in a successful anticoagulant therapy. Table No.6 represents the drug-drug interactions occurring within the anticoagulant class of drugs or the interaction between anticoagulants and any other class of drugs observed. Out of 300 prescriptions, distribution of drug interactions in the study population was found that 45.67% of patients were exposed to moderate drug interactions, 11.67% of patients were exposed to mild interactions, 4.33% of patients were exposed to severe drug interactions and 26.33% of patients were not exposed to drug interactions. Most common interacting effect was found to be increased risk of bleeding. Similar findings were observed in the study conducted by **Joseph A.D**[13]*et al* in which out of the 4028 cases studied severity of the interactions are found out to be, 73% of the interaction

are moderate, 23% are mild and 11% are severe indicating that severity of the interactions are in order of moderate interactions > mild interactions > severe interactions.

CONCLUSION

Both male and female patients were enrolled in this study and it was found that there were more number of male patients in the study. The age distribution of patients were studied from 21 years and above, the maximum distribution was seen in patients of 60 years and above.

In this study, low molecular weight heparin class were more prescribed over other class. The mostly prescribed anticoagulant drug was enoxaparin. Based on the distribution of therapy, most of the patients were on monotherapy.

In severity of drug-drug interactions occurring within the anticoagulant class of drugs or the interaction between anticoagulants and any other class of drugs**,** maximum patients were exposed to moderate drug-drug interactions.

Treatment was based on the PT/INR and PTT levels of the patient which were monitored frequently by using anti-coagulants monotherapy and/or combination therapy. The efficacy of the anticoagulant therapy was observed based on the PTT and PT/ INR during the time of admission and discharge. PT/INR and PTT values showed that there is significant rise in the average values of both PT/INR and PTT indicating that the time taken to form a clot is increased in the study population.

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REFERENCES

1. Cardiovascular diseases. 2017 May 17[cited 2017 May 20]; Available from: https ://www.who.int/news.room/pack sheets/details/cardiovascular diseases-(Cvds).
2. Dr.Prabhakaran. The changing pattern of cardiovascular diseases and their risk factors in the states of India: the global burden of disease study 1996-2016, 2018 Dec 1;6(12), PE1339-E1351. Available from : https//www.the lancet .com
3. Management and treatment of cardiovascular disease. 2014 January 15[cited on 2017 November9;https://jeanhailes.org.au/health-a-z/cardiovascular-health/management-treatment.
4. HL Sharma, KK Sharma. Coagulation pathway: Principles of pharmacology; 2nd ed:671-673.
5. KD Tripathi. Pharmacological classification of drugs with doses and preparations; 5th ed. p. 111.
6. Manjusha S, Amit M, Ronak S. A study on prescribing pattern and potiential drug-drug inteactions. IJPP 2014 Jan-Mar; 7(1): 7-11.
7. Muhammad A. A study on efficacy of the drugs. 2016 Apr08[cited on 2016 April 12]: https://www.slideshare.net/mobile/muhammadasad397948/efficacy-and-potency-of-drug.
8. Jonas O, Lars W, John H.A, Stefan J, Gabriel S, Johan S. New oral anticoagulants in addition to single or dual antiplatelet therapy after an acute coronary syndrome. Eurheartj. 2013 June 7;34(22):1670-80.
9. Torn M, Bollen WLEM, van der Meer FJM, van der Wall EE, Rosendaal FR. Risks of Oral Anticoagulant Therapy With Increasing Age. Intern Med. 2005;165(13):1527–32.
10. Harold P. Emergent Use of Anticoagulation for Treatment of Patients With Ischemic Stroke.Stroke.AHA. 2018 April 7;33(3):856-61.
11. C Seth, Rebecca j. Anticoagulant related bleeding: clinical epidemiology, prediction and prevention. Am J Med. 1993 Sept 9,5(3):315-28.
12. Adam C, Deborah MS, Mark AC, David AG. Laboratory Measurement of the Anticoagulant Activity of the Target-specific Oral Anticoagulant Agents: A Systematic Review. J Am CollCardiol. 2014 Sep 16; 64(11): 1128–1139.
13. Joseph A.D, Lucie O, James M.B and Samy S. Drug-drug interactions between antithrombic medications and risks of gastrointestinal bleeding. CMAJ. 2007 Aug 14;177(4):347-51.

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