

A Study of Using Anticoagulants in a Tertiary Care Hospital in Bangalore: A Prospective Study

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Abstract

Background: drug utilization studies are necessary to evaluate the rational use and associated risks of anticoagulants. This study aimed to identify drug utilization pattern and possible drug interactions with the use of anticoagulants in a tertiary care hospital in Bangalore.

Methods: This prospective, observational study was conducted on 100 patients and anticoagulants utilization was assessed from Medicine ward of Bannerghatta Apollo hospital in Bangalore, India, during six months.

Results: The most common indication for anticoagulants administration was ischemic heart disease (IHD)+acute coronary syndrome (ACS) with 47% and IHD alone with 22%. Most of the patients received single drug therapy, and parenteral drugs were more preferred than oral ones (91% vs. 6%). Among the medications, heparin (49%) followed by enoxaparin (29%) and fondaparinux (13%) were the most commonly prescribed drugs. Regarding laboratory tests, 29% of the patients were evaluated for the international normalized ratio (INR) and prothrombin time(PT). The finding showed that anticoagulants might interact with corticosteroids, some antibiotics such as piperacillin, azithromycin or other drugs such as tirofiban and losartan.

Conclusion: Anticoagulant drug utilization pattern followed very commonly American College of Clinical Pharmacy (ACCP) guidelines. The inappropriate utilization patterns of anticoagulants may compromise the patient's safety.

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Introduction

The principal aim of drug utilization researches is to facilitate the rational use of drugs in population.¹ Studies on the process of drug utilization focus on the factors related to prescribing, dispensing, administering, and taking of medication, and its associated events, covering the medical and non-medical determinants of drug utilization, the effects of drug utilization, as well as studies of how drug utilization relates to the effects of drug use, beneficial and adverse effects to improve the patient's therapeutic outcomes.²

Thromboembolic events are major causes of morbidity and mortality. Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), is the main cause of mortality with an estimated prevalence of over 1,000,000 per year and 100,000 deaths in USA which is 5–10% of all deaths among hospitalized patients. The health care costs associated with VTE are considerable, exceeding \$1.5 billion annually in the US and it has become an economic burden for health care.^{3,4} The incidence of VTE in India is also reported to be 17.46 per 10,000 admissions.⁵ Anticoagulants

are the drugs used to prevent thrombus extension and embolic complications by reducing the rate of fiber formation.⁶ In a hospital setting, anticoagulants are mainly used for the indications like DVT, PE, unstable angina, myocardial infarction (MI), vascular surgery, rheumatic heart disease, retinal vessel thrombosis, prosthetic heart valve, and extra corporcular circulation.⁷ Low molecular weight heparin, unfractionated heparin, fondaparinux, and oral vitamin K antagonists (warfarin) are parenteral anticoagulants used historically. There are several oral anticoagulants which have been developed in the last few years such as direct thrombin inhibitor dabigatran and anti-Xa inhibitors apixaban, edoxaban, and rivaroxaban.^{3, 7}

Because anticoagulants act by different modes of action and have a narrow window for therapeutic dosing and may interact with a broad range of drugs, the administration of which requires special attention.^{8, 9} Studies on utilization of anticoagulants prescribed routinely along with the study of drug interaction is essential to improve quality of treatment. Hence, the aim of this study was to assess the drug utilization pattern of anticoagulants and to identify possible drug interactions with the use of anticoagulants in a tertiary care hospital in Bangalore, India. The most commonly prescribed anticoagulants were also reported.

Methods

This is a prospective observational study conducted at the tertiary care hospital (Bannerghatta Apollo hospital), Bangalore, India. Anticoagulants utilization was assessed in 100 patients receiving anticoagulant therapy from Medicine ward, with a variety of underlying diseases who were admitted during six months (December 2019 to May 2020). Patients of either gender and those above 18 years old who had undergone anticoagulant therapy were included in the study. Pregnant women, death cases, patients below 18 years and patient who are unwilling to participate were excluded from the study. All the patients who met the above inclusion criteria were enrolled, and full details of the case including gender, age, diagnosis, drug therapy and anticoagulant therapy monitoring (prothrombin time [PT] and international normalized ratio [INR]) were recorded to the data collection form. All the patients were monitored until discharge. The source of data included patient profile and laboratory reports. Patient's medication chart was also monitored during the study for any drug-drug interactions. The drug-drug interactions were analyzed using www.drugs.com as the resource. The study was approved by the Institutional Ethics committee – Bio Medical Research (“IEC-BMR”) of Apollo hospital.

Statistical Analysis

The data were analyzed using SPSS version 16.0.

and Microsoft excel. The results are expressed in terms of percentages and numbers.

Results

From December 2019 to May 2020, 100 patients receiving anticoagulants were enrolled in the study. Among patients, 67 were male and 33 female; this showed that males were more frequently administered anticoagulants than females. Most of the patients were in the age group of 61-70 years (29%) followed by 71-80 years (21%). The remaining patients were in age group of 51-60 (17%), 41-50(16%), 81-90 (8%), 31-40 (4%), 91-100 (4%), and 20-30 (1%) (Figure 1).

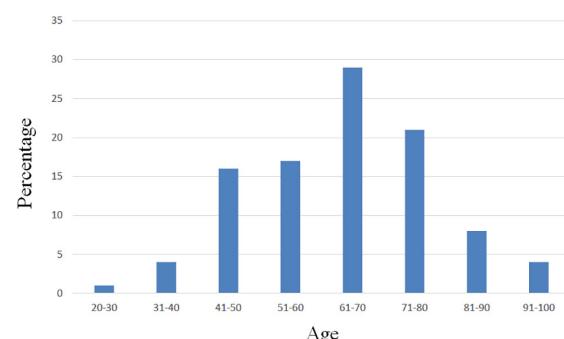


Figure 1: Distribution of patients according to age(N=100).

The most common indication for anticoagulants administration was IHD+ACS with 47% and IHD alone with 22%. The rest of indications were ACS (9%), arterial fibrillation (AF) (8%), AF+ACS (6%), PE (3%), AF+IHD (2%) and DVT, DVT+PE and CVT, each one comprising 1% of the total (Figure 2).

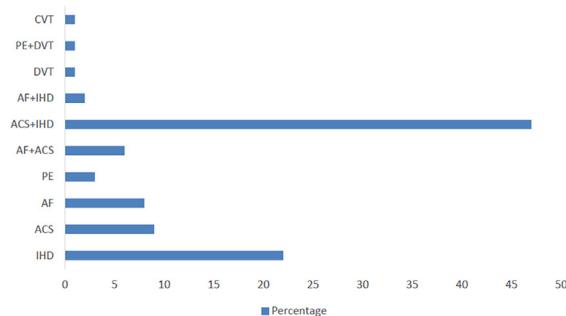
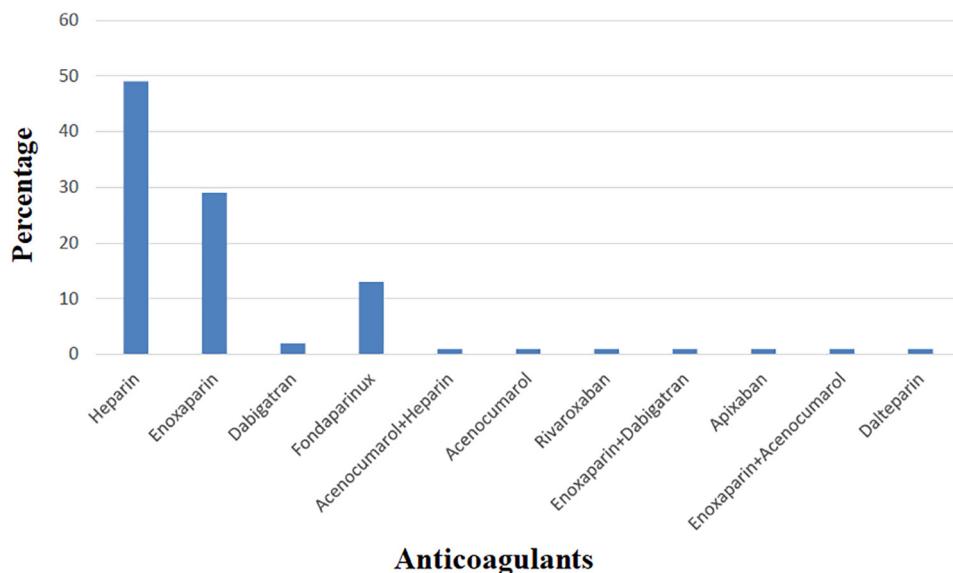


Figure 2: Indications for anticoagulants administration. CVT: cerebral venous thrombosis, PE: pulmonary embolism, DVT: deep vein thrombosis, AF: atrial fibrillation, IHD: ischemic heart disease, ACS: acute coronary syndrome.

Most of the patients received single drug therapy. It was also shown that parenteral drugs were more preferred than oral drugs. 91% of the patients received parenteral drugs, 6% oral drug and only 3% received combination of parenteral and oral drugs (Table 1). The study results showed that totally 7 anticoagulants were administered. Among the medications, heparin (49%) followed by enoxaparin (29%) and fondaparinux (13%) were the most commonly prescribed drugs. Dabigatran was prescribed to 2% of the population and Dalteparin,

Table 1: Distribution of patients according to the route of drugs administrations

| Rout of administration | Parenteral | Oral | Combination | Total |
|------------------------|------------|--------|-------------|------------|
| Frequency(percentage) | 91 (91%) | 6 (6%) | 3 (3%) | 100 (100%) |

**Figure 3:** Different anticoagulants administered to patients**Table 2:** Possible drug interactions with anti-coagulants in the involved prescription

| Interaction | Effect |
|---------------------------|--|
| Enoxaparin+Piperacillin | Increase anticoagulants effect of enoxaparin |
| Enoxaparin+Budesonide | Decrease anticoagulants effect by increasing blood coagulability |
| Enoxaparin+Hydrocortisone | Decrease anticoagulants effect by increasing blood coagulability |
| Enoxaparin+Prednisolone | Decrease anticoagulants effect by increasing blood coagulability |
| Enoxaparin+Azithromycin | Increasing effect of enoxaparin by decreasing metabolism |
| Enoxaparin+Tirofiban | Increase effect of each other |
| Heparin+Budesonide | Decrease anticoagulants effect by increasing blood coagulability |
| Heparin+Tirofiban | Increase effect of each other |
| Heparin+Thyronorm | Increase effect of heparin |
| Heparin+Losartan | Increase toxicity of losartan |
| Heparin+Prednisolone | Decrease anticoagulants effect by increasing blood coagulability |
| Heparin+Azithromycin | Increase effect of heparin by decreasing metabolism |
| Dalteparin+Cefuroxime | Increase effect of dalteparin |

Apixaban, Rivaroxaban, Enoxaparin+Acenocumarol, Enoxaparin, Dabigatran and Acenocumarol+Heparin each one comprised only 1% of the total population (Figure 3).

Regarding laboratory tests, 29% of the patients were evaluated for the INR and PT and for the remaining 71% these tests were not performed. Study finding showed that anticoagulants might interact with corticosteroids, some antibiotics such as piperacillin and azithromycin or other drugs such as tirofiban, losartan (Table 2).

Discussion

Thromboembolic events are life-threatening conditions, and anticoagulants are the drugs used to prevent thrombus extension and embolic complications; thus, it is

necessary to raise knowledge about them.¹⁰ The principal aim of drug utilization studies is to facilitate the rational use of drugs in population. Without a knowledge of how drugs are being prescribed and used, it is difficult to initiate a discussion on rational drug use or to suggest measures to improve the prescribing habits.^{11, 12} This study aimed to assess utilization of anticoagulants at a tertiary care hospital in order to increase knowledge about anticoagulants prescription and administration.

The study described utilization of anticoagulants among 100 patients who met the inclusion criteria; 67% of them were male and 33% female. It was found that males more frequently administered anticoagulants than females; this is in the same line with Jokandan *et al.*'s results. Data indicated that patients were in the range of 20 to 100 years of age. Most of the patients were in the age group of 61-70 years (29%) followed

by 71-80 years (21%), which is comparable with the study done by Jonathan Arland *et al.* They reported that anti-coagulants had been administered for 40-80 year old age groups with most of the patients within 70-80 year age groups.¹³ Based on other reports, it seems that people aged over 60 years old are more susceptible to coagulation disorders.¹³⁻¹⁵ Although in our study men were more frequently administered with anticoagulants, there are some studies with the same and some studies with opposite results.¹³ The main reason of this difference is not clear.

The current study showed that the most common indications for anticoagulants administration were IHD+ACS with 47% and IHD alone with 22%. These results are comparable with the findings of previous studies.^{15, 16} Acute myocardial infarction and acute coronary syndrome were the two main indications for heparin therapy in the study of Namazi *et al.*¹⁵

In our study, DVT and PE were not common indications; however, some other studies found DVT as the most common indication for anticoagulant therapy.¹⁷ The distribution of coagulation disorders is not same in different areas. Some studies have indicated that DVT and PE are the main reasons of anticoagulant prescription; however, some other studies reported different results.^{17, 18} Based on Anakwue *et al.*'s results,¹⁷ the most common indications for anticoagulant therapy included DVT, PE, congestive heart failure with atrial fibrillation and mitral valve disease with atrial fibrillation. Mengistu *et al.*¹⁸ reported that DVT, PE and stroke were among the most common indications for anticoagulant administration. There are conflicting results regarding the indication of anticoagulant therapy and more studies are needed to clarify the most common reasons of anticoagulant therapy.

Our study indicated that the most of patients received single drug therapy. It was found that parenteral drugs were more preferred than oral drugs, 91% received parenteral drugs, 6% received oral drug, and only 3% received combination of parenteral and oral drugs. Oral drugs are the most widely used anticoagulants. However, the parenteral anticoagulants are used when rapid anticoagulation is required, because the oral forms take several days before achieving optimal antithrombotic effect. This study assessed drug usage in a tertiary care unit where the patients need rapid treatment and it can explain why the parenteral drugs are used more than oral drugs.¹⁷ In a study by Alzubaidi *et al.*¹⁴ conducted on 50 patients from 4 wards of a tertiary care teaching hospital, 36 (72%) patients were on single drug therapy and 14 (28%) were on drug combination therapy. The combination therapy included oral and parenteral drugs. The mostly used combination therapies were Warfarin+Enoxaparin (50%) and

Acenocoumarol+Enoxaparin (21%).

The study results showed that heparin was the first common prescribed drug (49%), and the second one was enoxaparin (29%) which is near to Alzubaidi *et al.*'s results, reporting that Enoxaparin (31%) and Heparin (28%) were the most common used drugs.¹⁴ Although the education and market in the country can also affect the prescription of heparin, studies have shown that it is one of the mostly prescribed drugs for treating coagulation disorders.¹⁶ Vijay Singh *et al.*'s¹⁶ results indicated that Heparin, Enoxaparin and Acenocoumarol were the most commonly used drugs in a tertiary care teaching hospital in Bengaluru city. In the present study, Dabigatran was given to 2% of the population and Dalteparin, Apixaban, Rivaroxaban, Enoxaparin+Acenocumarol, Enoxaparin and Acenocumarol+Heparin each one comprised the only 1% of total population.

This study revealed that Enoxaparin was the most widely prescribed low molecular weight Heparin (LMWH) among other available alternatives; this is consistent with Alam *et al.*'s results.¹⁹ They reported that Enoxaparin was the most widely prescribed low molecular weight Heparin (LMWH) among other available drugs.¹⁹

Twenty-nine percent of patients were evaluated for the INR and PT, showing that these tests were not performed for the majority of patients. Contrary, Alzubaidi *et al.* found that 56% of patients were evaluated for INR and PT.¹⁴ Since these tests are essential for evaluation of the coagulation process in the body,²⁰ it would be better to be ordered for all patients who receive the anticoagulant drugs.

All 100 patient's prescriptions were evaluated for any possible serious drug interaction; it was shown that anticoagulants administration along with corticosteroids could increase blood coagulability, thus decreasing the anticoagulants' effect. Such combinations were Enoxaparin+Prednisolone, Enoxaparin+Hydrocortisone, Enoxaparin+Budesonide, Heparin prednisolone, and Heparin+Budesonide. Enoxaparin with Piperacillin and Azithromycin can lead to increased effect of Enoxaparin and increased risk of hemorrhage. Enoxaparin with Tirofiban can increase the effect of both drug and increase the risk of bleeding. Heparin along with Azithromycin or Levothyroxine may increase the effect of anticoagulation. Heparin along with Losartan can increase the risk of toxicity of Losartan, and co administration of Heparin and Tirofiban can act synergistically.²¹ All the above prescriptions should be monitored closely during the treatment course.

The present study had some limitations. The study was conducted for a short period of time, i.e. 6 months. Data were collected from patients' case sheet which

were the secondary source introducing possible bias in the study. Also, the study was conducted on a small sample. Result of demographic and pattern of illness may be changing from one period of time to another, and we were unable to see the trend of this conditions. However, the present study reveals the anticoagulant prescription pattern in different age groups and explains anticoagulant usage based on type of drugs, possible drug interactions and main reasons of anticoagulant prescription in different age and sex groups.

Conclusion

Anticoagulant drug utilization pattern followed very commonly American College of Clinical Pharmacy (ACCP) guidelines. Adherence to anticoagulant therapy plays a major role in improving the outcomes and reducing the risk of bleeding; frequent monitoring of the parameters helps to evaluate the safety of anticoagulant drug use. The inappropriate utilization patterns of anticoagulants may also compromise the patients' safety.

Conflicts of interest: None declared.

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