

# Anticoagulants: The Need for Austere Monitoring: Utilization and Evaluation Pattern from Tertiary Care Referral Hospital, Kerala

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## ABSTRACT

**Background:** Drug utilization evaluation is a systematic quality improvement process that is designed to assess the rational use of medicines in the populations. This study is designed to analyze the utilization pattern of anticoagulants in a tertiary care hospital. **Aim:** The objective of the study is to assess the utilization and prescribing patterns of anticoagulants in various departments of the hospital. **Methods:** A prospective observational study was conducted for 4 months from 1<sup>st</sup> September 2019 to 31<sup>st</sup> December 2019 to evaluate the utilization of anticoagulants among the 75 patients selected from 3 departments (cardiology, neurology and general medicine) and their respective intensive care units of a tertiary care referral hospital. **Results:** During the study period, among the anticoagulants prescribed, injection enoxaparin was most the commonly prescribed followed by injection heparin in the cardiology and neurology departments. Oral anticoagulants were prescribed in small number of patients and the most commonly administered drugs were warfarin and acenocoumarol. From the 75 cases analyzed, the monitoring parameters Prothrombin Time (PT), International Normalized Ratio (INR), APTT were monitored in 50 cases and were not analyzed in 25 cases. Target INR was achieved in 45 patients. The remaining 5 cases showed abnormal values in whom the drug therapy was withheld. **Conclusion:** Anticoagulants are the class of drug that are most commonly prescribed in the hospitals and should follow appropriate guidelines to ensure the rational use of drugs. Injection enoxaparin was preferred over other anticoagulants in all the selected departments. The pattern of potential drug-drug interactions with enoxaparin was found to be moderate and mild. Medication errors, mostly prescription-centered, were reported. Monitoring parameters for anticoagulant therapy has to be evaluated as per the ACCP guidelines (revised 2016), in order to ensure the rational use of drug but was performed only in some patients. Maintenance of normal INR level through the evaluation of monitoring parameters is thereby inevitable.

**Key words:** APTT, Anticoagulants, Enoxaparin, INR, PT.

## INTRODUCTION

Anticoagulants are the drugs which are commonly known as blood thinners.<sup>1</sup> These belongs to a class of high risk medicines and are used both as prophylactic and therapeutic regimen for many indications.<sup>1</sup> Anticoagulation is mainly indicated for arterial, venous and intra-cardiac thromboembolism. The two major problems associated with its use are one that is related to under-dose of anticoagulants, leading to clinical thromboembolism and the over-use of anticoagulants causing bleeding and hemorrhagic disorders. Anticoagulant therapy therefore must follow recommended guidelines to ensure better therapeutic outcomes.<sup>2</sup> The continuous and

repeated monitoring of utilization pattern of anticoagulants is essential to ensure the therapeutic effectiveness. It also helps to identify any drug interactions or ADR associated with anticoagulant therapy. It could be an efficient approach to guarantee proper prescription and administration of anticoagulants.<sup>1</sup> Ensuring drug utilization study is essential to evaluate the prescription patterns, rational drug use and to develop interventions for proper, scientific and prudent use of drugs that will enhance the quality of life of a patient. Emergence of OTC drugs, lack of essential drug policy, irrational prescribing of drugs can all culminate in poor access to healthcare.

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Inappropriate utilization of drugs and lack of knowledge on prescriptions are the factors that negatively affect evaluation of therapeutic value, cost effectiveness and ADR occurrences.<sup>3</sup> In India, socio-economically backward classes, illiterate people, utilizing of multiple health care systems, availability of prescription drugs as over the counter drugs, competition in pharmaceutical field and lack of drug information are the main factors hindering in achieving optimal health care.<sup>4</sup> Rational drug use in patient care is one of the most important factors to be considered for achieving optimal benefit from drug therapy.<sup>5</sup> Rational drug use and formulary management can be done using drug utilization analysis. It also assists the health care providers in recognizing various prescribing patterns and also to achieve better clinical outcomes. Drug Utilization Evaluation (DUE) plays an important role in preventing medication errors, adverse drug reactions (ADRs), drug-drug interactions, drug-toxicity and therapeutic duplications.<sup>6</sup> The clinical areas requiring further investigations can be identified and additional information for better patient care can be achieved by the healthcare professionals using drug utilization studies.<sup>7</sup>

Focusing on the importance of anticoagulant therapy, the study was conducted prioritizing on the utilization evaluation of anticoagulants commonly prescribed and administered in the tertiary care hospital and with the objective to assess the prescribing pattern and rationality of prescriptions containing anticoagulants.

## METHODOLOGY

This prospective observational study was carried out in a tertiary care hospital and presented the data on drug utilization and prescribing pattern of anticoagulants in different departments of the hospital. Prior ethical clearance was obtained from the institutional ethical committee of the hospital before commencing the study, as per the letter no: KAS/IEC/M.pharm/2019-10. The study was carried out for a period of 4 months commencing from September 2019 to December 2019 among the in-patients of selected departments like general medicine, cardiology, neurology and their respective intensive care units. All patients prescribed with anticoagulants on inpatient basis were screened and 75 cases were included in the study. Among the 75 cases, 4 deaths were reported. The study included patients of either sex or aged more than 18 years. Out-patients, pediatric and psychiatric patients, pregnant and lactating women, patients on hemodialysis were excluded from the study. Predesigned data collection forms were used to collect and record patient data, which describe patient demographics, past medical history, past medication history, the laboratory values, medications

prescribed (anticoagulants and other drugs), the final diagnosis, discharge medications etc. The patient details were obtained from the case files and also directly from the patients/bystanders during the ward rounds. The assessment of DUE processes was done in two phases. The first one is investigational which include defining the drug use, identifying drug related problems and developing new interventions. In the second phase problem solving, consensus building and implementation of activity towards improving drug use were done. All the cases were reviewed prospectively and monitored extensively. The pattern of anticoagulants 'utilization, their brand name, generic name, indication, dose, dosage form, administration site and numbers of drugs in prescription were studied. The prescribing factors were assessed using the hospital formulary and suitable guidelines like ASH VTE guidelines. Drug interaction of anticoagulants were categorized as major, moderate and minor according to their severity and were investigated using MEDSCAPE, LEXICOMP, DRUG.COM, INTERACTION CHECKER. The prescription of the anticoagulants were also reviewed for medication errors that may occur during the course of treatment regimen and the observed errors were classified as dispensing centered, prescription-centered or administration-centered medication errors.

Statistical analysis was done using collected data, which were analyzed using the SPSS 20 of the Microsoft Windows version. Numerical data were expressed as mean and standard deviation. For the categorical variables, frequencies and percentage were computed with the Pearson Chi square test. For quantitative variables, paired *t*-test was used. Results were interpreted with *p*-value which is probability of accepting null hypothesis. Significant level was set at < 0.05

## RESULTS

From September 2019 to December 2019, 75 patients were enrolled in the study. Among which majority of the patients 62% (*n*=46) were males, while the remaining 38% (*n*=29) were females. Patients were categorized into 7 age groups (below 30, 30-40, 41-50, 51-60, 61-70, 71-80 and above 80) and majority 25.3% (*n*=12 males and *n*=7 females) of the patients were under the age of 71-80 years which inferred that males were dominating over females in the disease incidence, followed by 24% (*n*=10) males and *n*=8 females within the age of 61-70 yrs. During the study period, majority of the anticoagulants were prescribed in Neurology ICU department followed by 32% (*n*= 24) in Cardiac ICU, 10% (*n*=8) in Neurology, 8% (*n*=6) in Cardiology, 7% (*n*=5) in medical ICU and 7% (*n*=5) in general medicine department. From the patients data, comorbidities were identified which included hypertension,

diabetes mellitus, CVA and others. Out of the enrolled subjects, 40 patients had a history of hypertension, 28 patients with diabetes and 17 patients with CVA. 26 patients had history of other co-morbidities like asthma. The most common indication for anticoagulation is CVA 45% ( $n=33$ ), followed by ACS 27% ( $n=20$ ), arrhythmia 16% ( $n=12$ ) and 14% ( $n=10$ ) other conditions. Majority of the patients were administered with parenteral anticoagulants, 45 patients (60%); 19 patients (25.3%) with oral anticoagulants and 15 patients (20.0%) with both oral and parenteral anticoagulants. As shown in Figures 1 and 2, in the study for monitoring parameters, Prothrombin Time (PT), International Normalized Ratio (INR), APTT were monitored in 50 cases and omitted in 25 cases. In monitoring the patients' anticoagulant therapy, it was unveiled that not every patient achieved target INR. 88% ( $n=45$ ) achieved target INR and 12% ( $n=5$ ) did not achieve the target. When the type of anticoagulants prescribed was analyzed, it was noticed that 4 major types of anticoagulants were used in the sample size namely heparin, enoxaparin, warfarin and acenocoumarol. 44 patients were on enoxaparin therapy among which 38 patients were prescribed with inj. clexane and 6 with inj. lupenox in neurology ICU (59%) followed by Cardiac ICU 17.3% ( $n=6$  and 7) (Figure 3). From the Figure 4, it was observed that injection heparin was prescribed most commonly in cardiac ICU ( $n=14$ ) (19%). Oral anticoagulants were prescribed in limited number of patients. From the Figure 5 and 6, it

was found that tablet warfarin and acenocoumarol were prescribed commonly in the cardiology, general medicine and cardiac ICU departments, while assessing the cost of fast moving drugs, injection enoxaparin (single unit = 387 INR) was found to be expensive. As shown in Figure 7, 10 prescription-centered and 1 administration-centered errors were reported. 24 drug interactions were identified from various departments in which most of them occurred in the neurology ICU ( $n=10$ ), followed by cardiac ICU ( $n=6$ ), neurology ( $n=5$ ) and cardiology ( $n=3$ ). Majority of the drug interactions can be attributed to enoxaparin (Figure 8). 74 prescriptions were rational and 1 was irrational as per the ACCP guidelines.

### DISCUSSION

The data were prospectively collected from 75 subjects

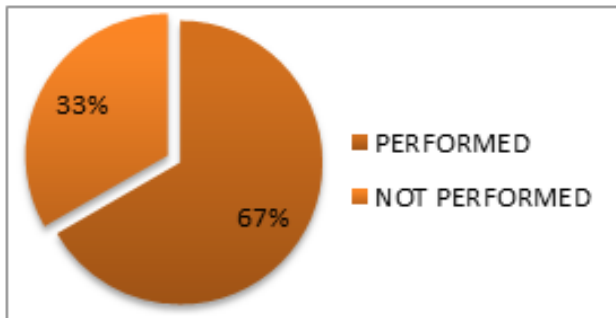


Figure 1: Monitoring parameters.

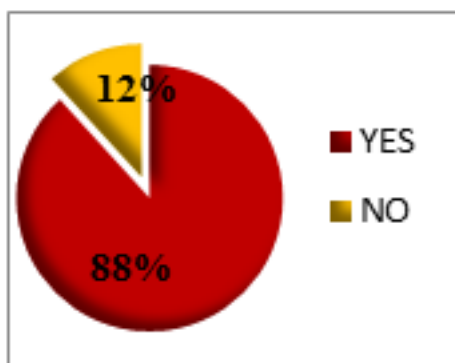


Figure 2: Is target INR achieved?.

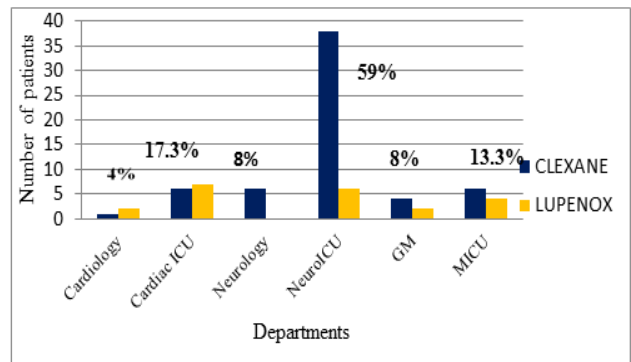


Figure 3: Department wise distribution of injection enoxaparin.

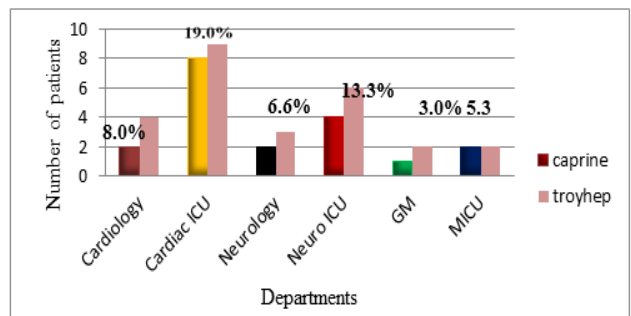


Figure 4: Department wise distribution of injection heparin.

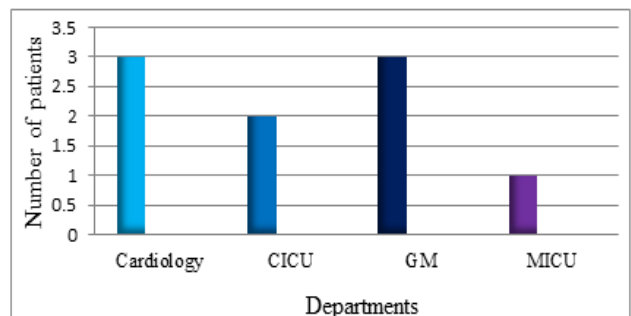


Figure 5: Department wise prescription of tablet warfarin.

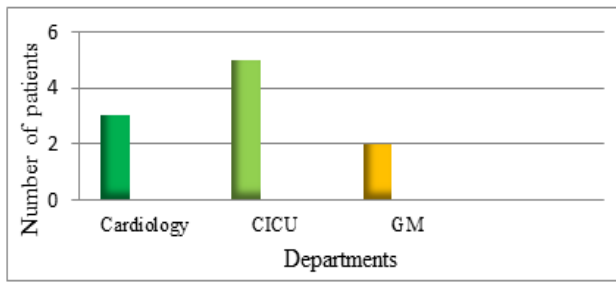


Figure 6: Department wise distribution of tablet acenocoumarol.

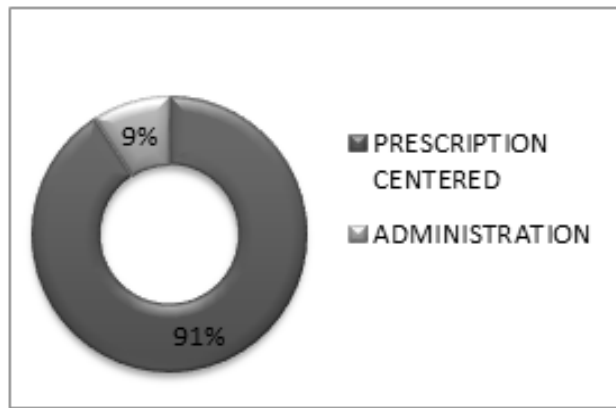


Figure 7: Medication errors.

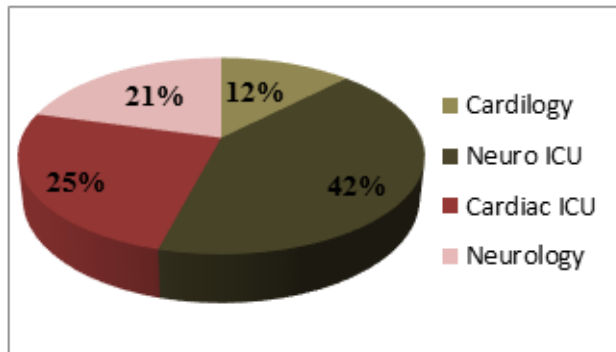


Figure 8: Drug interactions.

enrolled as per inclusion and exclusion criteria. In total, 75 patients were involved in the study which included both males and females. Majority of the patients 62% ( $n=42$ ) were males, while the remaining 38% ( $n=26$ ) were females. Similar data were shown in study conducted by Soha Namazi *et al.* (2011) and Shazia Alam *et al.* (2015).<sup>8,9</sup> It was recognized that the male population is more prone to diseases. When the age was categorized, most of the subjects were above 70 years (“old” as per the WHO Classification of the geriatric population) with male patients dominating the female subjects. Only few subjects belonged to the age group below 30 years old. It was inferred that the geriatric population was more prescribed with the anticoagulants. A study conducted by Vineela Chadalavada *et al.* (2018) reported majority of patients belongs to the age group of 70 years (old

and elderly).<sup>1</sup> The study observed that most of the patients presented with multiple co-morbidities namely hypertension followed by diabetes mellitus, CVA and others including asthma, hyperlipidemia etc. A study conducted by Arathi R *et al.* (2018) showed predominance of hypertension as the co-morbid condition.<sup>10</sup> When the number of patients’ distribution among the selected departments was calculated, most of the patients were prescribed with anticoagulants predominantly in neurology ICU followed by cardiac ICU, neurology, cardiology, MICU and general medicine departments. A study conducted by Vineela chadalavada *et al.* (2018) observed differently.<sup>1</sup> While analyzing the disease treated with anticoagulants, majority of patients had CVA (45%), followed by ACS in 27% of patients. A study conducted Gonela Sai Meda Sree *et al.* (2018) observed differently.<sup>1</sup> When analyzing the type of anticoagulant prescription, it was noticed that 4 types of anticoagulants were used in the sample size namely heparin, enoxaparin, warfarin and acenocoumarol. Our study showed that enoxaparin was the most commonly prescribed anticoagulant enoxaparin (CLEXANE®) in the neuro-ICU followed by inj.heparin. A study conducted by Binu Mathew *et al.* (2017) *et al.* produce similar findings.<sup>11</sup> In India, a study conducted by Vijay *et al.* (2015) had reported acenocoumarol was the mostly preferred anticoagulant followed by enoxaparin.<sup>12</sup> Warfarin and acenocoumarol were the only 2 oral anticoagulants prescribed among the patient. Similar results were shown by Alzubaidi *et al.* (2019) in his study.<sup>3</sup> From the data collected, 24 drug interactions have been observed with majority of occurrence in the neurology ICU then in the cardiac ICU. Out of 75 cases collected, 45 patients (60%) were administered with parenteral, 19 patients (25.3%) with oral anticoagulants and 15 patients (20.0%) with both oral and parenteral anticoagulants. Monitoring parameters for anticoagulant therapy include prothrombin time (PT), International Normalized Ratio (INR), APTT and were monitored in 50 cases and not done in 25 cases with target INR achieved in 88% of patients. Similar results were shown by study conducted by Vineela Chadalavada *et al.* (2018) and Reshma Elisa Jeny.<sup>1,13</sup> The monitoring parameters were done in some of the patients and it is advised to carry out the test for better therapeutic outcomes. Low molecular weight heparin, enoxaparin, was the most commonly prescribed drug and it found to be more expensive compared to other anticoagulants. Results shown by Vineela Chadalavda *et al.* (2018) while assessing the cost of drugs, enoxaparin and dalteparin (single unit= 387 INR) were expensive followed by rivaroxaban and heparin. Acenocoumarol and warfarin are least expensive drugs.<sup>1</sup> According to the ACCP guidelines, from 75 prescriptions analyzed, 74 were rational and 1 was irrationally prescribed. Arathi R *et al.* (2018) showed similar findings.<sup>11</sup> No Adverse Drug



Reactions (ADRs) occurred during the study period. The study assessed the monitoring parameters of the anticoagulants, which is the major strength of the study. Since this was a prospective observational study, complete and timely documentation was possible. All categories of anticoagulants, both enteral and parenteral, used in the hospitals were evaluated.

The study has certain limitations too. The study was carried out for short duration and had small sample size. Therefore the statistical power of this survey is quite limited and chance of error may not be ignorable. It was a single centered study. It is only by extending a study to different settings, the prescribing practices of that population can be revealed. This study only addresses information from selected departments.

## CONCLUSION

The study revealed that the most cost-effective anticoagulant therapy was achieved by prescribing injection enoxaparin (CLEXANE®) in the selected departments. The predominance of male gender and age above 80 years were identified among the enrolled patients that indirectly implies on the senility induced coagulation and cardiac health issues. The pattern of potential drug-drug interactions with enoxaparin was found to be moderate and mild. Medication errors, mostly prescription-centered, were reported which included omission of the dose, route and frequency of administration of the drugs. Monitoring parameters for anticoagulant therapy has to be evaluated as per the ACCP guidelines (revised 2016), in order to ensure the rational use of drug but was performed only in some patients. The major failure to evaluate monitoring parameters can be attributed to improper patient-follow up, death/ atresia of the patients and irrational drug prescribing. This may lead to serious medical complications like embolisms and internal hemorrhagic disorders. Maintenance of normal INR level through the evaluation of monitoring parameters is thereby inevitable for the effective management of bleeding-embolic disorders, as being recommended by the ASH-VTE guidelines. More stringent assessments are therefore required by both the patients and the healthcare professionals to maintain rationality of the anticoagulant therapy.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ABBREVIATIONS

**DUE:** Drug Utilization Evaluation; **PT:** Prothrombin Time; **INR:** International Normalized Ratio; **APTT:** Activated Partial Thromboplastin TIME; **ACCP:** American College of Chest **Physician;** **ASH VTE:** American Society of Hematology Venous Thromboembolism; **SPSS:** Statistical Package for Social Sciences; **OTC:** Over The Counter; **ADR:** Adverse Drug Reaction.

## SUMMARY

This prospective observational study was carried out among the inpatients of three selected departments of a tertiary care hospital. The study evaluated the utilization pattern of anticoagulants and identified the prominent use of injection enoxaparin.

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