Utilization Patterns of Anticoagulants at Medical Ward of Hiwot Fana Specialized University Hospital, Harar, Ethiopia

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ABSTRACT

Background: Anticoagulants are drugs used to prevent thrombus extension and embolic complications by reducing the rate of fibrin formation. In a hospital setting anticoagulants are mainly used for the different indications; however, both under-anticoagulation and over-anticoagulation may expose the patient to different problems. The objective of this study was to assess the utilization patterns of anticoagulants at medical ward of Hiwot Fana Specialized University Hospital (HFSUH). **Methods:** A retrospective study was conducted at Medical Ward of HFSUH from Medical record of patients' who take anticoagulants from March 30, 2014 to March 30, 2016. The study was conducted from April 1 to May 10, 2016. **Results:** A total of 87 patients over a period of 2 years were on anticoagulant and laboratory monitoring done in HFSUH. More females were on anticoagulant and monitoring. The anticoagulants used were unfractionated heparin, low-molecular weight heparins and warfarin. The most common clinical indications for anticoagulant therapy were lower leg deep vein thrombosis (45.98%), followed by pulmonary embolism (22.98%) and stroke (18.39%). Target INR was achieved in 39.1%, desired clinical outcome was achieved in 37.9%, and minor bleeding complications were seen in 11.5%. **Conclusion:**

The results of this study revealed that the most common clinical indications for anticoagulant therapy were lower leg deep vein thrombosis and the most commonly prescribed anticoagulant drugs was warfarin alone or in combination with other anticoagulants.

Key words: Anticoagulants, utilization patterns, HFSUH

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INTRODUCTION

Anticoagulants are drugs used to prevent extension of thrombus and embolic complications by reducing the rate of fibrin formation. Thrombi can form in the veins, artery, or intra-cardium and cause complication through local obstruction, distant embolism in the distal microcirculation and consumption of hemostatic material. Anticoagulants do not directly dissolve already formed clot but prevent recurrences and devastating medical complications by allowing the natural fibrinolytic system to precede normally.[1]

The coagulation pathway plays a pivotal role in the formation and progression of both arterial and venous thrombi. Therefore, drugs aimed at inhibiting this pathway are a major stratagem for the development of novel antithrombotic agents.[2] In a hospital setting anticoagulants are mainly used for disease conditions including deep vein thrombosis (DVT), pulmonary embolism (PE), myocardial infarction (MI), unstable angina, rheumatic heart disease, vascular surgery, prosthetic heart valve, retinal vessel thrombosis, extra corpuscular circulation, hemodialysis and fibrination syndrome.[3]

However, there are two major issues associated with its use: one that is related to under-anticoagulation with attendant clinical thromboembolism and the other over-anticoagulation with complications, particularly bleeding. The use of anticoagulants must follow recommended guidelines; otherwise, it is fraught with increased morbidity and mortality. When anticoagulation is used appropriately, it is an effective and safe practice.[4] This study was aimed to assess the utilization pattern of anticoagulants at the medical ward of Hiwot Fana specialized University Hospital (HFSUH).

METHODS

Study setting and period

The study was conducted at medical ward of HFSUH, Harar, Ethiopia. The medical ward has female and male wing and intensive care unit. The study period was from April 1st to May 10th, 2016.

Study design

A hospital based retrospective study was used to assess utilization patterns of anticoagulants by using patient medical record cards.

Populations

The source populations of the study were patient medical record cards found in HFSUH and the study populations were patient medical record cards from March 30, 2014 to March 30, 2016 which contain anticoagulants. Selection criteria: medical record cards of patients received anticoagulants were included in the study and incomplete medical record cards were excluded from the study.

Sampling technique and sample size

Since only 87 patient medical cards were fulfilled the inclusion criteria, all cards were included in the study.

Study variables

Socio-demographic characteristics, co-morbidty, concomitant drug, dosage regimen and duration of anticoagulant therapy were the independent variables and drug interaction, complications, INR/aPTT values and indication of the anticoagulant were dependent variables.

Data collection

Data were collected from patients' medical record card by using pretested data collection abstraction format by two graduating pharmacy students having basic knowledge of research methodology, pharmacology and pharmacotherapy.

Data quality control

Pre testing of the data collection format was undertaken at surgical ward of HFSUH before the actual data collection and completeness of collected data was checked each time.

Data analysis

The collected data was clean and checked for its completeness, categorized, and analyzed using SPSS version 16.0 software then the result was presented using tables and charts.

Ethical consideration

Before beginning data collection, official permission letter was obtained from school of pharmacy, Haramaya University. Then the letter was submitted to hospital administrative and all the responsible officials are informed about purpose and aim of the study and permission was obtained. After getting consent from the responsible bodies, patients chart were accessed using their card numbers and the confidentiality of data collected was maintained. Name and address of the patient and prescriber is omitted from the data collection format.

RESULTS

Socio-demographic characteristics

In the two year period (2014-2016) only ninety three patients were taking anticoagulant therapy and from these the medical records of six patients were excluded from the study due to incompleteness of the required data and eighty seven medical records were assessed. From these 54.0% were females and most of them (53%) were in the age group of 26-50 years [Table 1].

Clinical characteristics of the patients and distribution of anticoagulant drug therapy

In this study, the most common clinical indications for anticoagulant therapy were lower leg DVT (45.9%) and PE (22.9%). Seventy two patients had co morbidities and the most common co morbid disease was anemia (13%) [Table 2]. During their hospital stay most patients were treated by warfarin and enoxaparin in combination (39.1%) followed by warfarin, enoxaparin and heparin together (26.4%) as shown in Figure 1.

Duration of anticoagulant therapy

The duration of therapy of the study patients on anticoagulant were 26(55.32%) of them were on heparin for 5-10 days. On the other hand, the duration of therapies on warfarin greater than 30 days were 46(58.23%). In the case of enoxaparin 43(66.15%) patients had less than 5 days duration of therapy [Table 3].

Drugs co-administered with warfarin and their potential drug interaction with warfarin

A total of 236 drugs were prescribed with warfarin and from these Injectable anticoagulants (20.8%) were the most common [Table 4]. Out of 236 drugs co-administer with warfarin, 140 drugs have a potential drug-drug interaction with warfarin and the most common drug was unfractionated heparin (35%) followed by enoxaparin and aspirin both accounts 10.7% [Table 5].

Coagulation profiles of study participants

Table 1: Socio-demographic characteristic of patient who received anticoagulant therapy at medical wards of HFSU Hospital, from March 30, 2014 to March 30, 2016, Harar, Ethiopia

Age (years)	Sex	Number (%)
15-25	Female	15 (17.24)
	Male	13 (14.94)
26-50	Female	28 (32.2)
	Male	18 (20.69)
51-75	Female	3 (3.45)
	Male	9 (10.34)
76-100	Female	1 (1.15)
Total		87 (100)

Table 2: Clinical characteristic of patients on anticoagulant therapy in medical ward of HFSUH from March 30, 2014 to March 30, 2016

	Clinical characteristics	Number (%)
Indication of anticoagulant therapy	Lower leg DVT	40 (45.98)
	Pulmonary Embolism	20 (22.98)
	Stroke	16 (18.39)
	Congestive Heart failure, secondary to MVHD, VHD, AF, PE	8 (9.20)
	DVT plus 1st TMP, 3rd TMP	3 (3.45)
Co-Morbidity	Yes	72 (82.72)
	No	15 (17.24)
Co-morbid disease	Anemia	13 (13.13)
	Epilepsy	11 (11.11)
	Diabetes Mellitus	10 (10.10)
	Myocardial infarction	9 (9.09)
	Cellulites	8 (8.08)
	UTI	7 (7.07)
	HIV	7 (7.07)
	Congestive Heart Failure	7 (7.07)
	Tuberculosis	6 (6.06)
	Community acquired pneumonia	6 (6.06)
	Hypertension	4 (4.04)
	Others	11 (11.11)

Table 3: Duration of anticoagulant therapy at medical wards of HFSUH, Harar, Ethiopia from March 30, 2014 to March 30, 2016

Anti-coagulant	Duration of treatment	Number (%)
Heparin	<5 days	21 (44.68)
	5-10 days	26 (55.32)
Warfarin	less than 5 days	7 (8.86)
	5-10 days	4 (5.06)
	10-30 days	22 (27.85)
	greater than 30 days	46 (58.23)
Enoxaparin	less than 5 days	43 (66.15)
	5-10 days	22 (33.85)

Note: the duration of therapy given above includes bridge therapies like heparin and warfarin and enoxaparin.

All study participants had coagulation profile such as INR and aPTT and these tests were repeated during their stay in the hospital in order to monitor the efficacy of the anticoagulant therapy. As recorded on the medical records 252 INRs and 239 aPTT tests were performed. Among the INR values only 39.28% were within the therapeutic range and most of aPTT values (36.8%) were less than ≤ 26 [Table 6].

Clinical outcome and complication of anticoagulant therapy

In this study target INR was achieved in 39.09% of the study participants and desired clinical outcome was achieved in 37.93% study participants. Minor bleeding complications as gingival and genitourinary bleedings were seen in 11.6% of study participants and major bleeding and life threatening as GI bleedings and incidental nasal bleeding were reported in 4.6% of the study participants [Figure 2].

DISCUSSION

The present study was aimed to assess the utilization patterns of anticoagulants at medical ward of HFSUH**.** In this study, the most common indications of anticoagulant therapy were lower leg DVT

Table 4: Drugs that are co-administered with warfarin in HFSUH at MW from March 30, 2014 to March 30, 2016

Class of drugs	Administered drugs	Number (%)
Antibiotics	Cloxacillin 500 mg I.V. QID	8 (3.39)
	Ceftriaxone 1 g I.V. BID	14 (5.93)
	Augmentin 625 mg P.O.TID	3 (1.27)
	Metronidazole 500 mg I.V TID	4 (1.69)
	B.pencilline 1.2 million IU	3 (1.27)
	Ciprofloxacin 500 mg, P.O. BID	8 (3.39)
	Norfloxacin 400 mg P.O. BID	5 (2.12)
	Azithromycin P.O. 500 mg QD	6 (2.54)
	Cephalexin P.O 500 mg B.I.D	6 (2.54)
Non-Steroidal Anti-inflammatory Drugs	Diclofenac 75 mg IM Injection	10 (4.24)
	Aspirin 81 mg PO QD	15 (6.35)
	Tramadol 100 mg IM	5 (2.12)
Injectable anticoagulants	UFH 5000 IU iv stat, SC	49 (20.76)
	Enoxaparin 60 mg SC bid	15 (6.35)
Diuretics	Hydrochlorothiazide 25 mg P.O.Q.D	10 (4.24)
	Furosemide 40 mg P.O. daily	4 (1.69)
	Furosemide 40 mg iv	8 (3.39)
Cardiovascular	Digoxin 0.25 mg	7 (2.97)
	Atenolol 50 mg P.O. Q.D	5 (2.12)
	Enalapril 2.5 mg P.O B.I.D	4 (1.69)
Anti-tuberculosis	2EHRZ (400, 150, 75, 400) mg	6 (2.54)
Anti-diabetic	Metformin 500 mg P.O. B.I.D	10 (4.24)
Anti-Retroviral drugs	TDF, 3TC, EFV (300, 300, 600) mg	7 (2.97)
Antiepileptic Drugs	Phenobarbital 100 mg	11 (4.66)
Iron product	Ferrous Salts PO 200 mg TID	13 (5.51)
	Total	236

UFH - Unfractionated Heparin; EHRZ - Ethambutol, Isoniazid Pyrazinamide and Rifampicin, Anti-Retroviral (ART), Tenofovir, Lamivudine and Efavirenz (TDF, 3TC, EFV)

Table 5: Drugs that have potential drug-drug interaction with warfarin in HFSUH at medical ward from March 30, 2014 to March 30, 2016

Potentially Interacting drugs	Frequency	Percentage (%)
UFH 17,500 IU S.C BID	49	35
LMWHs (enoxaparin) 60 mg S.C TID	15	10.71
Aspirin 81 mg P.O. daily	15	10.71
Ceftriaxone 1 g I.V. BID	14	10
Phenobarbital 100 mg	11	7.87
Diclofenac 75 mg I.M. Injection	10	7.14
Ciprofloxacin 500 mg, P.O. BID	8	5.71
Rifampicin (anti Tb)	6	4.29
Tramadol 100 mg I.M Injection	5	3.57
Metronidazole 500 mg iv TID	4	2.86
Augmentin 625 mg P.O. TID	3	2.14
Total	140	100%

(45.98%) and PE (22.98%). Similarly studies from Nigeria and Kenya also reported the major indication for anticoagulants were DVT and PE.[5,6] But a population-based retrospective cohort study in Minnesota, USA showed that the major indications for anticoagulants were VTE (39%) and transient ischemic attack (21%).[7] The presence of more DVT indications in this study might be correlated with the incidence of thromboembolic complications. The achievement of desired anticoagulation is low in Africa, ranging from 7% to 30% in Kenya (40); 39% in Nigeria[6] and 32-58% in South Africa[8] which is comparable to the result of this study (39.1%). Reaching optimal target in anticoagulation is directly related to the infrastructure of anticoagulation services available. Studies from USA, China and
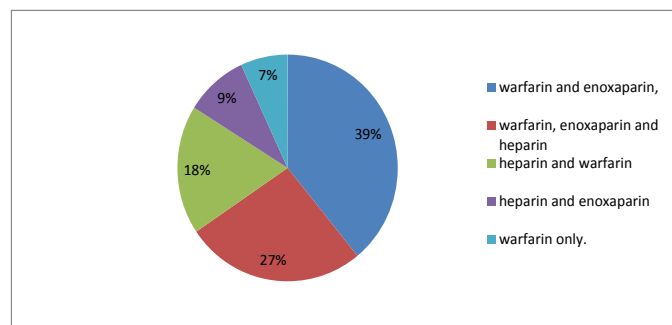

Figure 1: Frequencies of anticoagulant drug use at medical wards of HFSUH, Harar, Ethiopia, from March 30, 2014 to March 30, 2016
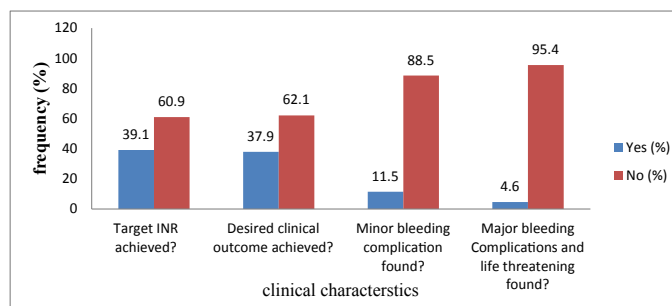

Figure 2: Clinical outcome and complications of study participants during anticoagulant therapy at medical wards of HFSUH from March 30, 2014 to March 30, 2016, Harar, Ethiopia

Canada showed a higher level of achievement of desired anticoagulation compared to data from African centers.[4]

This study also revealed that 82.7% of the study participants had a co morbid condition and the most common co morbid disease was anemia. The most commonly used anticoagulant used in this study were warfarin and enoxaparin in combination and around 91% of the study participant used warfarin alone or in combination with other anticoagulants. Since most patients had a co morbid condition they used additional drugs to treat the co morbidities and the most commonly drugs concomitantly used with warfarin were Injectable anticoagulants. These drugs had a potential to interact with warfarin and might lead to bleeding which is a cause of anemia (most common co morbid condition in this study).

In the present study, the incidence of bleeding complications was 16.1% which is comparable with study done by Wehinger *et al.* which was 14.6%.[9] Another study done in USA[7] showed the three months cumulative incidence of bleeding were 20.8%. Different researches show a difference in risk of bleeding complication which might be due to difference in the set-up, drugs used and other factors.

The incidence of complication may be related with the presence of concomitant drugs, the use of more than one anticoagulant and co morbid conditions but in this study none of them showed significant association with bleeding. Desired clinical outcome and adequate dosing was achieved only in 37.93% of the patients [Table 6]. Anticoagulation service in HFSUH is still evolving, and there are challenges associated with it. There is a need for dedicated anticoagulation services with defined roles and mission.

CONCLUSION

The present study revealed that the most common clinical indications for anticoagulant therapy were lower leg deep vein thrombosis and the most commonly prescribed anticoagulant drugs was warfarin alone or in combination with other drugs. Above half of the co-administered drugs had potential drug interaction with warfarin. The most INR values were not in the therapeutic range and this may lead to low

Table 6: Number of study participants on laboratory monitoring at medical wards of HFSUH from March 30, 2014 to March 30, 2016, Harar, Ethiopia.

	Coagulation profile	Frequency	Percent (%)
INR range	≤ 1.2	33	13.09
	1.2-1.5	39	15.47
	1.5-2.0	49	19.45
	2.0-3.0	99	39.28
	3.0-4.5	22	8.72
	4.5-9.0	7	2.78
	9.0-10.0	3	1.19
aPTT Range	≤ 26	88	36.82
	26-30	63	26.36
	30-40	38	15.89
	40-50	34	14.24
	50-100	8	3.35
	≥ 100	8	3.35
INR values	Below therapeutic range	121	48.01
	Within therapeutic range	99	39.28
	Above therapeutic range	32	12.69

Note: aPTT: Activated partial Prothrombin time, INR: International Normalized Ration, INR range (0.73-9.2), aPTT range (14.5-153)

desired clinical outcome. The inappropriate utilization patterns of anticoagulants may also compromise patient safety.

Conflict of interest

The authors declare that there is no conflict of interest

Acknowledgements

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