Pharmacy Education (2024) 24(3) 286 - 291
https://doi.org/10.46542/pe.2024.243.286291

IGSCPS SPECIAL EDITION

RESEARCH ARTICLE

Use of anticoagulant drugs for hospitalised patients: A multicentre study

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Keywords
Anticoagulant use
Inpatient
Multicentre study

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Abstract

Background: Anticoagulants are indicated for several types of diseases with progression related to coagulation. Patients who are administered this drug need to be evaluated by the pharmacist regarding its effectiveness and possible side effects. **Objective:** This research aimed to analyse the profile of the use of anticoagulants among patients at Yogyakarta Hospital. **Method:** This research was a multicentre study conducted retrospectively using the medical records of inpatients who received anticoagulants. **Result:** Among 486 respondents, the majority were male (63.58%), and the adult age category (18-59 years) was 55.76%. Most anticoagulants were used in cases of cardiovascular disease, diagnosed with NSTEMI as much as 20.21%. The most used anticoagulant drug was heparin (48.9%), followed by fondaparinux (34.3%) and enoxaparin (16.8%). The most common duration of anticoagulant use was one to four days (73.02%), with the dose range being 200-1000 units/day. **Conclusion**: Heparin was the anticoagulant widely used in patients with NSTEMI. Although the elderly were the group most at risk of ADR due to anticoagulants, most of these drugs were precisely taken by adults, who also required serious attention. Further research is needed to provide a more comprehensive approach to anticoagulant therapy.

Introduction

Anticoagulants are indicated to prevent thrombotic events in various diseases, disorders and conditions. The development of anticoagulant drugs has increased in the last ten years in line with the increasing use of these drugs (DeWald *et al.*, 2018). In Indonesia, anticoagulants are included in the national formulary, which can be claimed for several diagnoses and certain conditions (Kemenkes, 2022). Anticoagulant use is frequently linked to a risk of adverse effects, according to earlier studies. Thus, it is essential to assess how these medications are taken (Alquwaizani *et al.*, 2013). Several studies on anticoagulant use have been conducted, but only involved specific population characteristics in elderly patients with atrial fibrillation and did not examine the dosage range of anticoagulant drugs used to control the chronic disease (Shah *et al.*, 2019; Ko *et al.*, 2022; Ding *et al.*, 2024).

This study aimed to determine the profile of anticoagulant drug use in Yogyakarta as a step in evaluating their use. It could ensure optimal anticoagulant therapy and meet treatment standards, including criteria according to diagnosis/indication, duration of anticoagulant use, and dosage (World Health Organisation, 2021).

Methods

Design

This research was conducted descriptively with a purposive sampling method in several hospitals in Yogyakarta. This includes the PKU Muhammadiyah Yogyakarta Hospital, PKU Muhammadiyah Gamping Hospital, and Sleman General Hospital. Data was collected retrospectively from the medical records of

inpatients who received anticoagulant drug therapies in 2019-2020.

Ethical approval

This research was ethically feasible based on the ethical committee approval letter issued by the Health Research Ethics Committee Yogyakarta City Hospital No.12/KEP/RSUD/IV/20.

Inclusion and exclusion criteria

The inclusion criteria in this study include age (≥ 18 years old) and receiving anticoagulant drugs with complete medical record data (name of anticoagulant drug, dose, duration of use). The exclusion criteria were patients undergoing haemodialysis.

Assessment

This study used statistical analysis, a univariate analysis on SPSS version 25, to determine patient characteristics, such as gender, age, diagnosis, and the profile of anticoagulant use, including type of anticoagulants, duration of use, and dosage.

Results

The study involved 486 respondents; 309 patients (63.58%) were male. The age range of the respondents was dominated by "*Adults*" (18-59 years), with 271 respondents (55.76%), while 215 respondents (44.24%) were the "*Elderly*" (≥ 60 years). The average patient age in this study was 57.25 ± 12.8 (Table I).

Table I: Characteristics of patients

Characteristics	Frequency (%)	Mean ± SD
Gender		
Male	309 (63.58)	-
Female	177 (36.42)	
Age		
Adult (18-59 years)	271 (55.76)	57.25 ± 12.83
Elderly (≥ 60 years)	215 (44.24)	

The five most common diagnoses among respondents were NSTEMI (20.22%), STEMI (16.94%), Unstable Angina Pectoris (UAP) (14.39%), Coronary Artery Disease (CAD) (12.93%), Congestive Heart Failure (CHF), and COVID (10.75%) (Table II).

Table II: Diagnosis of patients receiving anticoagulant therapy

Diagnosis	Frequency (%)
NSTEMI	111 (20.22)
STEMI	93 (16.94)
Unstable Angina Pectoris (UAP)	79 (14.39)
Coronary Artery Disease (CAD)	71 (12.93)
CHF (Congestive Heart Failure)	59 (10.75)
COVID-19	59 (10.75)
Ischemic Heart Disease (IHD)	24 (4.37)
Stroke non-haemorrhagic (SNH)	21 (3.83)
Deep Vein Thrombosis (DVT)	12 (2.19)
VT (ventricular tachycardia)	7 (1.28)
Extra systole ventricles	5 (0.91
Hypertensive Heart Disease (HHD)	4 (0.73)
Atrial Fibrillation	4 (0.73)

Anticoagulants used were heparin (48.9%), fondaparinux (34.3%), and enoxaparin (16.8%). Anticoagulants were taken for one to four days by 360 respondents (73.03%), 114 respondents (23.12%) for five to seven days, and greater or equal to eight days by 19 respondents (3.85%) (Tables III). The most common dose of fondaparinux was 2.5 mg/day for 167 respondents (98.82%), heparin was 200-1000 units/day in 157 respondents (65.15%), and enoxaparin was 12.000 units in 44 respondents (53.01%) as shown in Table IV.

Table III: Anticoagulant use profile

Drug	Frequency (%)	Mean ±SD
Anticoagulant		-
Heparin	241 (48.9)	
Fondaparinux	169 (34.3)	
Enoxaparin	83 (16.8)	
Duration of anticoagulant use		
1-4 days	360 (73.03)	3.42 ±1.90
5-7 days	114 (23.12)	
≥ 8 days	19 (3.85)	

Table IV: Profile of anticoagulant dosage

Drug	Frequency (%)	Mean ± SD
Fondaparinux (n=169)		
2.5 mg	167 (98.82)	2.53 ± 0.27
5 mg	2 (1.18)	
Heparin (n=241)		
200-1000 Unit	157 (65.15)	1811.21 ± 2507.43
>1000-2000 Unit	39 (16.18)	
>2000-3000Unit	9 (3.73)	
>3000 Unit	36 (14.94)	
Enoxaparin (n=83)		
4000 unit	10 (12.05)	9421.69 ± 2988.27
6000 unit	9 (10.84)	
8000 unit	20 (24.10)	
12000 unit	44 (53.01)	

Discussion

Characteristics of respondents

In this study, male respondents predominated with 309 patients (63.58%), while female respondents were 177 (36.42%). This aligns with the disease diagnoses dominated by cardiovascular disease and adult patients. Previous research found that the percentage of cardiovascular disease incidence was higher in the male group at an older age and increased in the female group at an advanced age (George *et al*., 2015).

This study found that the adult age group with ages ranging from 18 to 59 dominated with 271 respondents (55.76%), while the older age group (≥ 60 years) was 215 respondents (44.24%). The average age of patients was 57.25± 12.8, which showed that the average age of the respondents belonged to the late adult category. A previous study has suggested that the incidence of cardiovascular disease increases with age (George *et al*., 2015).

Anticoagulants prevent blood clots and are given to people who are at high risk of developing blood clots to reduce their chances of developing severe conditions such as strokes and heart attacks. Anticoagulant treatment may be recommended if the patient has a higher risk of developing blood clots. Indications for giving anticoagulants are based on the D-dimer value in COVID-19 cases, while in patients with cardiovascular disease and Deep Vein Thrombosis (DVT), D-dimer is the monitoring of anticoagulant use (Bradbury & McQuilten, 2022). Anticoagulants have multiple roles in the treatment of cardiovascular disease, including in the management of acute myocardial infarction, during percutaneous coronary intervention as stroke prevention in patients with atrial arrhythmias (Onwordi *et al*., 2018; Larson *et al*., 2019).

In this study, the five most common diagnoses in patients were NSTEMI (20.22%), STEMI (16.94%), unstable angina pectoris (14.39%), coronary artery disease (12.93%), congestive heart failure and COVID-19 (10.75%). Anticoagulants can be used in acute coronary syndromes, and they can effectively reduce recurrent ischemic events, including myocardial infarction and stent thrombosis and the risk of death (Onwordi *et al*., 2018). Vascular inflammation, endothelial dysfunction, and platelet activation are characteristics of acute coronary syndrome, followed by the production of a thrombus. Uncontrolled thrombosis can result in total vascular blockage and ST-segment elevation MI (STEMI) in the most severe condition (Onwordi *et al*., 2018).

The 2014 American Heart Association (AHA)/ American College of Cardiology (ACC) guidelines recommend anticoagulants to treat NSTEMI. Intravenous anticoagulants with shorter half-lives, e.g., unfractionated heparin (UFH), are recommended for patients with an early invasive strategy. The European Society of Cardiology (ESC) recommends the additional use of parenteral anticoagulation both before and after fibrinolysis in ST-elevation ACS (STE-ACS) for at least 48 hours (Zeitler & Eapen, 2015; Onwordi *et al*., 2018; Larson *et al*., 2019; Rodriguez & Harrington, 2021).

The use of anticoagulants in angina can prevent the development of a sub-occlusive coronary thrombus to coronary artery occlusion, thereby preventing myocardial infarction and death. Precisely 59 (10.75%) COVID-19 patients were included in this study. Anticoagulants for COVID-19 are used to treat frequent thrombotic (arterial and venous) complications that occur in hospital inpatients and are an independent predictor of poor outcomes. Based on a systematic review and meta-analysis study, COVID-19 patients have a thrombotic risk and bleeding that occurs earlier after admission to the hospital, so it is advisable to give anticoagulants in therapeutic doses as soon as possible (Tsigkas *et al*., 2021; Bradbury & McQuilten, 2022).

Use of anticoagulants

Anticoagulants work by interfering with the processes involved in blood clot formation. Blood clots can block blood flow through blood vessels, and the affected body part becomes deprived of oxygen and stops working properly (Onwordi *et al*., 2018; Larson *et al*., 2019). This study's most widely used anticoagulant was heparin (48.9%). Since its discovery in 1916, UFH has been commonly used in modern cardiology practice because of its flexibility, rapid effect, reversibility, and safety in renal disease. Administration of UFH during

PCI intervention reduced the risk of acute stent thrombosis and decreased catheter-associated thrombosis compared with fondaparinux in the OASIS-6 trial (Mukherjee, 2022; Tan *et al*., 2022). The percentage of respondents who used fondaparinux in this study was 34.3%. According to the European Society of Cardiology (ESC) guidelines, the prevalence of side-effect bleeding in patients with fondaparinux is small, but the effectiveness of therapy to prevent thrombotic events is small in patients with PCI catheter insertion (Larson *et al*., 2019; Tan *et al*., 2022).

A further anticoagulant with an anti-IIa drug (such as UFH) should be administered to fondaparinux-treated patients who undergo angiography. But fondaparinux might be preferred to alternative anticoagulants for patients who aren't getting angiography (Larson *et al*., 2019). Fondaparinux enhances haemostasis and has no impact on fibrinolytic activity or bleeding time compared to LMWHs like enoxaparin and UFH. Fondaparinux also has a decreased rate of life-threatening haemorrhage. No other plasma proteins or cellular components, such as platelets or platelet factor 4, can be bound to or interacted with by fondaparinux. Unlike enoxaparin and UFH, Fondaparinux can cause a syndrome such as heparin-induced thrombocytopenia (Szummer *et al*., 2015; Han & Jin, 2020; Khan *et al*., 2022).

The percentage of patients who used enoxaparin in this study was 16.8%. During the acute phase of care of patients with unstable angina or non-ST elevation myocardial infarction, enoxaparin medication can reduce clinical events by 20%. Enoxaparin was better than UFH in reducing mortality and the risk of bleeding during PCI intervention, especially in patients undergoing primary PCI intervention for ST-elevation myocardial infarction. Compared with UFH, enoxaparin is associated with a 32% relative risk reduction and a 2.01% absolute risk reduction in death or myocardial infarction. The use of enoxaparin is also associated with a 20% relative risk reduction and a 1.20% absolute risk reduction of bleeding (Antman *et al*., 2002; Silvain *et al*., 2012; Weerasaksanti *et al*., 2023). The length of treatment with anticoagulants after the acute period has been traditionally debated and depends on the severity, history of previous cardiovascular disorders and the patient's risk factors.

Anticoagulants as prophylaxis in COVID-19 patients can be used for up to 14 days. This study found that the duration of anticoagulant use was predominantly one to four days. This is in line with Albani's 2020 research, which showed that the duration of anticoagulant use was mainly two to four days (49.2%). Enoxaparin for a maximum of seven days can significantly reduce the rate of recurrent ischemic events in the hospital. The use of the same dose of enoxaparin during prehospital in the ASSENT-3 PLUS trial is for intracranial haemorrhage in elderly patients (Onwordi *et al*., 2018; Larson *et al*., 2019; Albani *et al*., 2020; Alexander *et al*., 2021). This study revealed that anticoagulants are commonly prescribed for different medical conditions. Physicians may replace one anticoagulant drug with another during treatment, making it challenging to analyse the duration of use of each anticoagulant drug for a particular condition.

Several options for anticoagulant medication are available for patients with NSTE-ACS, according to the 2014 AHA/ACC recommendations. Enoxaparin can be given a loading dose of 30 mg (3000 IU) and 1 mg/kg (100 IU/kg) every 12 hours. The daily dose of enoxaparin in patients with renal impairment can be adjusted to the recommended initial daily dose of 1 mg/kg every 12 hours for patients with creatinine (CrCl) clearance ≥ 30 mL/minute and 1 mg/kg every 24 hours for patients with CrCl < 30 mL/minute (16). UFH can be given as a maintenance dose of 60 IU/kg (max 4000 IU), followed by 12 IU/kg/hour (max 1000 IU/hour). The dose of IV UFH is weight dependent according to current ESC guidelines, which recommend an initial bolus of 60–70 IU/kg up to a maximum of 5000 IU, followed by an infusion of 12–15 IU/kg/hour up to a maximum of 1000 IU/hour. The recommended daily dose of fondaparinux is 2.5 mg daily (Larson *et al*., 2019). According to Larson and colleagues in 2019, fondaparinux should be taken twice daily at a dose of 2.5 mg. When treating DVT or PE for the first time, fondaparinux, a parenteral selective factor Xa inhibitor, may be administered instead of UFH or LMWH. Under these conditions, it is administered in a fixed dose of 7.5 mg subcutaneously once daily (10 mg for patients > 100 kg, 5 mg for patients < 50 kg). A dose of 2.5 mg dominated the use of fondaparinux in this study. The use of 2.5 mg fondaparinux has the same efficacy as enoxaparin (1 mg/kg body weight twice daily) in reducing the risk of ischemic events at nine days (Onwordi *et al*., 2018; Douketis, 2022). Differences in body weight, D-Dimer values, and patient diagnoses can cause heparin and enoxaparin dose variations.

Limitations

This research's limitation is that the data was taken only from medical records, considering that it was conducted retrospectively.

Conclusion

Anticoagulant drugs were mainly used in cases of cardiovascular disease, although they were also

indicated for other diagnoses with a risk of thrombosis. Heparin was the most widely used anticoagulant, with various doses. The duration of use of anticoagulant drugs was usually less than seven days.

Acknowledgement

The authors thank the Department of Pharmacy, Universitas Islam Indonesia, for funding this research through a Collaborative Research Grant.

Source of funding

This research was funded by the Department of Pharmacy, Universitas Islam Indonesia.

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