JPHSR Journal of Pharmaceutical Health Services Research

ROYAL PHARMACEUTICAL SOCIETY

Short Communication

JPHS 2020, 11; 411–414

Received July 12, 2020
Accepted July 30, 2020
DOI 10.1111/jphs.12382
ISSN 1759-8885

Anticoagulant drug utilization pattern and their cost analysis: a retrospective study from Saudi Arabia

Mohammad Daud Ali[a], Ayaz Ahmad[a], Nuzhat Banu[a], Munfis Patel[b], Sherihan Ahmad Ghosn[a] and Zainab Eltrafi[a]

[a]Department of Pharmacy, Mohammed Al-Mana College for Medical Sciences, Dammam and [b]Foundation Year Department, Mohammed Al-Mana College for Medical Sciences, Dammam, Saudi Arabia

Abstract

Objective The study was aimed to evaluate the cost and drug utilization pattern of anticoagulant drugs in a clinical setting in Saudi Arabia.

Method A cross-sectional retrospective study was conducted in a private hospital in Saudi Arabia. World Health Organization, defined daily dose, and American Society of Hematology methods were used to compute the daily price of each anticoagulant agent.

Key findings Consumption of oral anticoagulants was very less as compared to the parenteral. Apixaban was the most prescribed oral drug, while enoxaparin sodium was the drug of choice among the parenteral. In oral anticoagulants, the unit-wise cost was found to be highest for Rivaroxaban (12.60 SR (3.36 USD) and less for Warfarin (0.82 SR (0.22 USD)). Heparin sodium cost (51.62 SR (13.76 USD) was found to be the most expensive parenteral agent while the least expensive was Phytomenadione (3.76 SR (1.00 USD)).

Conclusion Apixaban was the preferred oral anticoagulant among all the studied anticoagulants, although Warfarin is the cheapest. Therapeutic drug monitoring was recommended for Warfarin. The study highlights the importance of more studies to measure the advantages and disadvantages of all types of anticoagulants.

Keywords anticoagulant; defined daily dose; drug utilization pattern; Saudi Arabia

Introduction

The anticoagulant used to avert the formation or progress of thrombi in the venous blood flow. Depending on the administration route, parenteral and oral anticoagulants are available. Anticoagulants are the mainstay therapy in the treatment and preventing the recurrence of thrombotic events concomitant to pulmonary embolism, deep vein thrombosis, myocardial infarction, unstable angina, rheumatic heart disease, vascular surgery, prosthetic heart valve, retinal vessel thrombosis, extra corpuscular circulation, hemodialysis, defibrination syndrome and infection-induced thrombosis.[1,2]

Thrombosis is a multifactorial disorder that could incur many disabilities, life-threatening complications and even death.[3]

In Saudi Arabia, more than 250 000 persons are yearly affected by venous thromboembolism and 43.8 per 100 000 are affected by stroke.[4,5]

Traditionally, Warfarin stood the merely available anticoagulants.[6,7] Many studies have reported the widespread use of direct oral anticoagulants (DOACs) like Apixaban is growing worldwide, while the Warfarin use has revealed a continual and adamant drop.[8,9] Following the previous readings, the Saudi clinical practice Guidelines prefer the usage of novel anticoagulants as an alternative to the dual therapy of parenteral anticoagulants with vitamin K antagonists.[4]

A cost-effectiveness study has depicted Apixaban as the recommended medicine for preventing stroke as per Saudi Anticoagulants for nonvalvular atrial fibrillation guideline.[10]

The Medical cost for atrial fibrillation in Saudi Arabia is high and estimated to be $3000 per patient.[10] Consequently, anticoagulant selection is not only centred on their benefits and safety but also on their costs, which will influence patient adherence and clinical therapeutic benefits.[9]

The study was aimed to evaluate the cost and Drug utilization pattern of anticoagulant drugs in a clinical setting in Saudi Arabia.

Correspondence: Mohammad Daud Ali, Department of Pharmacy, Mohammed Al-Mana College for Medical Sciences, Abdulrazaq Bin Hammam Street, Al Safa, Dammam 34222, Saudi Arabia.
E-mail: dali.niper@gmail.com

Methodology

The study was designed as a single centred, cross-sectional retrospective pharmacy database study of utilization of anticoagulation therapy and their cost analysis. Data for the period from 1 January 2019 to 31 December 2019 were retrieved from the inpatients and outpatient electronic pharmacy records along with the unit dose prices of anticoagulant drugs in Al-Mana Group of Hospital- Al-Khobar, Saudi Arabia. The daily price of each drug was computed based on the World Health Organization (WHO) defined daily dose (DDD) and American Society of Hematology (ASH). Patients who were not prescribed and dispensed any medications for anticoagulation therapy were excluded from the study.

The cost analysis of each studied drug was calculated in terms of the average price of each unit dose of each prescription. Lastly, the prescribing pattern was evaluated based on the adherence of guidelines and protocols of the ASH, which are the followed guidelines at the study centre (hospital) used for the treatment of various diseases with anticoagulants. All the anticoagulant drugs were categorized into two different groups as oral anticoagulants and parenteral anticoagulants also coded in WHO anatomical therapeutic chemical classification code/ATC.[11] These included the oral anticoagulants (four drugs), for example Apixaban (B01AF02), Dabigatran Etexilate (B01AE07), Rivaroxaban (B01AF01) and Warfarin (B01AA03) and parenteral anticoagulant (three drugs), for example Enoxaparin Sodium (B01AB05), Heparin Sodium (C05BA03) and Phytomenadione (B02BA01). Details of ATC code and dosing schedules are described in Table 1.

Data analysis

Demographic characteristics were demonstrated as frequencies and percentages (with Wilson 95% confidence intervals for proportions). The chi-square (for *P*-value calculation) was used as appropriate to compare the utilization rates of anticoagulant medicines for the treatment of various diseases. All statistical analyses were conducted using SPSS version 26 (SPSS Institute Inc., Cary, NC, USA) and Microsoft Excel 2013. *P*-value ≤ 0.05 considered as statistically significant.

Table 1 Anticoagulants approved by SFDA for marketing in Saudi Arabia

Drug	ATC	DDD	Dose (ASH)
Oral anticoagulant			
Apixaban	B01AF02	10 mg	5 mg BD
Dabigatran Etexilate	B01AE07	300 mg	150 mg BD
Rivaroxaban	B01AF01	20 mg	15 mg BD/20 mg OD
Warfarin	B01AA03	7.5 mg	2–10 mg daily
Parenteral anticoagulant			
Enoxaparin sodium	B01AB05	2 TU	1 mg/kg body wt.
Heparin sodium	C05BA03	10 TU	200 units every 4 h
Phytomenadione	B02BA01	20 mg	5–20 mg daily

ATC, anatomical therapeutic chemical; Dose, As per American Society of Hematology (ASH); DDD, defined daily dose; SFDA, Saudi Food and Drug Authority.

Results

Table 2 shows the study on 10 036 patients clarifies that the use of anticoagulants was more amongst female patients compared with male patients.

Figure 1 shows that the overall utilization percentage of oral anticoagulants is very less compared with the parenteral anticoagulants.

Table 3 shows the division of anticoagulant drugs into two categories oral and parenteral with all *P*-value findings ≤ 0.5 except Dabigatran Etexilate with *P*-value 0.05.

Apixaban (4.71%) was the most prescribed drug among the oral category and Enoxaparin Sodium (61.48%) amongst the parenteral drug category.

For men, Warfarin (2.72%) and, for women, Apixaban (2.77%) were the most prescribed oral anticoagulant drugs and Enoxaparin Sodium was preferred drug from parenteral category for both.

Table 4 shows that for oral anticoagulants, the duration of therapy was highest for Rivaroxaban and lowest for Apixaban. The unit-wise cost was highest for Rivaroxaban (12.60 SR (3.36 USD)) making Warfarin as the cheapest drug (0.82 SR (0.22 USD)).

For parenteral anticoagulants, the duration of therapy was highest for Enoxaparin Sodium and lowest for Phytomenadione with Heparin Sodium being the most expensive (51.62 SR (13.76 USD) and the cheapest being Phytomenadione (3.76 SR (1.00 USD)).

Discussion and Conclusion

In the present study, there is a high prevalence of the use of parenterally administered anticoagulants (86.69%) compared with oral (13.31%).

In comparison between genders, our findings are in line with research conducted in Asian people for treating atrial fibrillation that reveals that Warfarin was prescribed more commonly in men and novel oral anticoagulants (NOACs) were prescribed frequently in women.[12] Among orally administered anticoagulants, Apixaban NOACs were firstly used contributing to 4.61% then secondly by Warfarin (3.56%). This study is further confirmed by another study

Table 2 Baseline demographic characteristics of the studied patient's

Characteristics	Total 10 036% (95% CI) (*n*)
Gender	
Male	35.16% (34.23–36.10) (3529)
Female	64.83% (63.90–65.77) (6507)
Age (years)	
≤30	30.07% (29.14–30.93) (3014)
≥31	69.93% (69.07–70.86) (7022)
Nationality	
Saudi	66.69% (65.72–67.57) (6689)
Non–Saudi	33.31% (32.43–34.28) (3347)

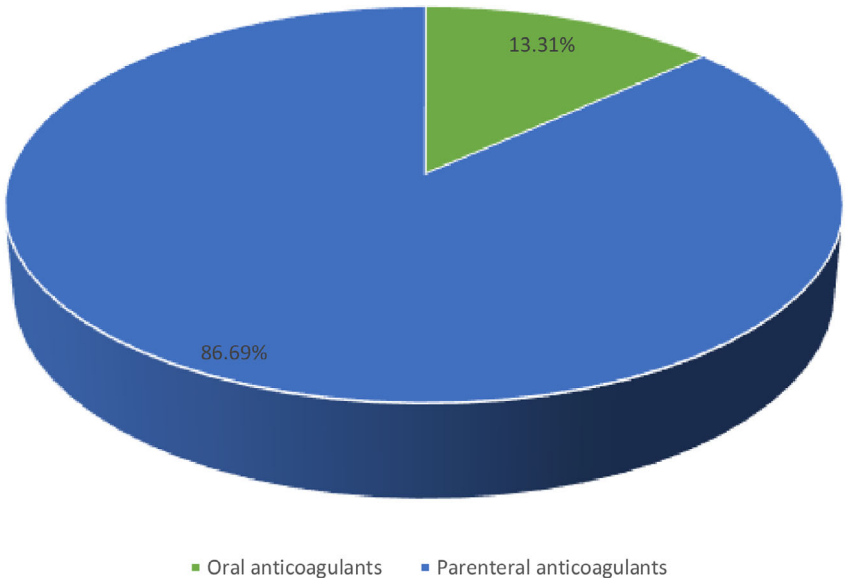

Figure 1 Overall utilization percentage of oral and parenteral anticoagulants among studied patients.

Table 3 Adherence of prescribing pattern of Anticoagulant drug as per American Society of Hematology (ASH)

Drug category (ATC code)	Total 10 036% (95% CI) (*n*)	Male % (95% CI) (*n*)	Female % (95% CI) (*n*)	*P*-value
Oral anticoagulant				
Apixaban (B01AF02)	4.71% (4.31–5.14) (473)	1.93% (1.68–2.22) (194)	2.77% (2.48–3.12) (279)	≤0.5
Dabigatran Etexilate (B01AE07)	1.78% (1.54–2.06) (179)	1% (0.84–1.24) (102)	0.78% (0.62–0.96) (77)	0.05
Rivaroxaban (B01AF01)	2.98% (2.67–3.34) (300)	1.87% (1.62–2.15) (188)	1.11% (0.93–1.35) (112)	≤0.5
Warfarin (B01AA03)	3.56% (3.22–3.95) (358)	2.72% (2.42–3.06) (273)	0.84% (0.69–1.05) (85)	≤0.5
Parenteral anticoagulant				
Enoxaparin Sodium (B01AB05)	61.48% (60.77–62.68) (6195)	21.48% (20.91) (2179)	40% (39.07–40.98) (4016)	≤0.5
Heparin Sodium (C05BA03)	7.58% (7.08–8.11) (761)	5.24% (4.82–5.69) (526)	2.34% (2.06–2.65) (235)	≤0.5
Phytomenadione (B02BA01)	17.63% (16.91–18.40) (1770)	0.66% (0.53–0.85) (67)	19.96% (16.25–17.72) (1703)	≤0.5

Table 4 Cost analysis of anticoagulants used among studied patients

Drug category (ATC code)	Average therapy of duration in days	Average cost unit wise in SR (USD)
Oral anticoagulant		
Apixaban (B01AF02)	31.33	6.41 (1.71)
Dabigatran Etexilate (B01AE07)	31.70	7.41 (1.97)
Rivaroxaban (B01AF01)	41.18	12.60 (3.36)
Warfarin (B01AA03)	32.22	0.82 (0.22)
Parenteral anticoagulant		
Enoxaparin sodium (B01AB05)	9.55	21.62 (5.76)
Heparin sodium (C05BA03)	2.32	51.62 (13.76)
Phytomenadione (B02BA01)	1.03	3.76 (1.00)

that states that Direct oral anticoagulants over a few years had become more convenient and safer drugs of choice in VTE treatment.[13] Bleeding is the major side effect of Warfarin, which is in contrast to NOACs like Apixaban that shows anticoagulant action without bleeding.[14]

In parenteral therapy, Enoxaparin Sodium was the drug of choice and Heparin Sodium was the least. This finding was in contrast to a research conducted in 2018; where Heparin was the preferred drug of choice and the least preferred was Enoxaparin.[15]

Overall, Heparin Sodium is the most expensive anticoagulant drug. In oral therapy, Warfarin is the cheapest and Rivaroxaban expensive of all with highest duration of therapy. In parenteral therapy, Heparin is the costliest and Phytomenadione is the cheapest one.

Although NOACs are expensive they offer various benefits over Warfarin which requires INR levels of monitoring that puts an economic burden on the patient.

Novel oral anticoagulants are considered of the same efficacy as seen with Warfarin; in comparison, they are safer and cost-effective.[16] Although oral anticoagulants are

taken under the supervision of a treating physician, still their safety and efficacy are warranted. In the case of Warfarin therapeutic drug, monitoring should be recommended to get the complete therapeutic outcome. Anticoagulants such as Heparin Sodium and Rivaroxaban are expensive even though they are safer, much effective and have an advantage over other drugs; their cost needs to be revised to reduce the economic burden of patients.

There is a lack of comparative research on the use of Oral and parenteral anticoagulant use, more studies are required to highlight the advantages and disadvantages of one kind of drug therapy over the other.

Limitation of the study

Current study was based on retrospective data, so it was very hard to do follow-up of patients regarding their efficacy as well as adverse drug reaction and few laboratory data, and to identify exact safety and efficacy of all the anticoagulants used in the studied patients in the hospital.

Declarations

Conflict of interest

None.

Funding

Nil.

Acknowledgements

My special thanks to Madam Dr. Aisha Al-Mana, Head of Board of trustee MACHS, for giving me an opportunity for research publication, providing unpublished data, her kind support and encouragement. I would like also express my thanks to Prof. Emad AlShwaimi, Dean, MACHS to facilitate in obtaining research data.

Study ethical approval

Prior to conduction of Study, study protocol has been submitted to Scientific Research Unit (SRU) of Mohammed Al-Mana College for Medical Sciences for research protocol review and obtaining Ethical Approval Number. Study has been conducted in compliance of recent ICH-GCP guideline.

Study place

A retrospective observational study was carried out in Al-Mana General Hospital (AGH), Al-Khobar, Saudi Arabia. AGH Al-Khobar is 250 bedded teaching private hospital with 74 outpatient clinic to provide healthcare facilities to the community of Saudi Arabia.

References

1. Jackson MR *et al*. Heparinoid anticoagulation and topical fibrin sealant in heparin-induced thrombocytopenia. *Ann Thorac Surg* 1997; 64: 1815–1817.
2. Schmidt M *et al*. Acute infections and venous thromboembolism. *J Intern Med* 2012; 271: 608–618.
3. Raskob GE *et al*. Thrombosis: a major contributor to global disease burden. *Arterioscler Thromb Vasc Biol* 2014; 34: 2363–2371.
4. Al-Hameed F *et al*. The Saudi clinical practice guideline for the diagnosis of the first deep venous thrombosis of the lower extremity. *Ann Thorac Med* 2015; 10: 3–15.
5. Memon I *et al*. Point prevalence study for stroke in Saudi Arabia: a cross-sectional survey. *Saudi J Health Sci* 2019; 8: 93–97.
6. Verdecchia P *et al*. Why switch from warfarin to NOACs? *Intern Emerg Med* 2016; 11: 289–293.
7. Pol D *et al*. NOACs now mainstream for the use of anticoagulation in non-valvular atrial fibrillation in Australia. *Heart Lung Circ* 2019; 28: e40–e42.
8. Lippi G *et al*. Direct oral anticoagulants: analysis of worldwide use and popularity using Google Trends. *Ann Transl Med* 2007; 5: 332.
9. Mendoza-Sanchez J *et al*. Benefit, risk and cost of new oral anticoagulants and warfarin in atrial fibrillation; a multicriteria decision analysis. *PLoS One* 2018; 3: e0196361.
10. Hersi A *et al*. Cost-effectiveness of apixaban for stroke prevention in non-valvular atrial fibrillation in Saudi Arabia. *Ann Saudi Med* 2019; 39: 265–278.
11. ATC/DDD Index 2020 https://www.whocc.no/atc_ddd_index/ (accessed 13 June 2020).
12. Lee JM *et al*. Gender-related differences in management of nonvalvular atrial fibrillation in an Asian population. *Korean Circ J* 2018; 48: 519–528.
13. Burnett AE *et al*. Guidance for the practical management of the direct oral anticoagulants (DOACs) in VTE treatment. *J Thromb Thrombolysis* 2016; 41: 206–232.
14. Tejus A *et al*. A six year drug utilization study in a tertiary healthcare system: emergence of newer oral anticoagulants. *J Evid Based Med Healthc* 2019; 6: 676–679.
15. Ziakas PD, Mylonakis E. Web search popularity, publicity, and utilization of direct oral anticoagulants in the United States, 2008–2018: a STROBE-compliant study. *Medicine (Baltimore)* 2020; 99: e20005.
16. Crouse B, Quigley S. New oral anticoagulants: an economic analysis. *LECOM*. https://lecom.edu/content/uploads/2015/09/LECOM-Point-V4_I3.pdf (accessed 18 June 2020).