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INCREASING PRESCRIPTON OF NEW NON VITAMIN K DEPENDENTS ANTICOAGULANTS FOLLOWING THEIR INTRODUCTION

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ABSTRACT

Objectives: To study and analyse the increase in prescripng the new Non vitamin K dependents anticoagulants in two main hospitals of the Royal Medical Services of Jordan from the date of their first introduction in May 2016. **Method:** A retrospective study to measure the dispensed quantities of both old oral anticoagulants and new non vitamin K dependents anticoagulants and calculating number of patients started using anticoagulants depending on the records of out patient pharmacies in King Hussein hospital and Queen Alia center for cardiology within the period between May 2016 to January 2019. **Results:** the results showed a significant increase in number of patients using newly introduced non vitamin K dependent oral anticoagulants associated with decrease in the use of old oral anticoagulants. **Conclusion:** The increased proportions of the number of patients converted from old oral anticoagulants to newly introduced oral non vitamin K dependents anticoagulants reflects an increase in tendency toward using these types of oral anticoagulants in Royal medical services of Jordan although this may increase the direct cost of anticoagulation therapy.

KEYWORDS: Warfarin, Dapigatran, Revaroxaban, non-vitamin K dependents oral anticoagulants.

INTRODUCTION

Stroke and venous thromboembolism with other thrombotic disorders are associated with very high morbidity and mortality worldwide. Stroke is the second cause of death associated with 10.2% of death in 2016 and major cause of disability.[1] Atrial fibrillation is important cause of stroke and contributes to five times increase in stroke risk.[2] Around 30% of venous thromboembolism admissions come as pulmonary embolism and the remainder comes as deep vein thrombosis, both types associated with 11% of hospitals death cases.[3]

Warfarin is widely used oral anticoagulants worldwide. It is well known as very effective medicine reducing the risk of stroke for patients with atrial fibrillation. Unfortunately warfarin needs monitoring because of its high degree of food-drug interactions and its interactions with other medicines. Also it cause major bleeding for patients which may contributes to hospital admissions. on other hand it may cause under treatment for other patients. For previous causes newly discovered non vitamin K dependents oral anticoagulants were introduced in royal medical services of Jordan and all other well-known medical centers worldwide. It is well known nowadays newly used non vitamin K dependents anticoagulants (NVKDA) have many benefits over warfarin that includes there high efficacy and they don't need continuous drug monitoring as warfarin. However they have higher prices than warfarin which should be taken in consideration before changing therapy for patients already use warfarin or those newly diagnosed patients.

AIM OF STUDY: to measure distribution of newly introduced non vitamin K dependents oral anticoagulants and their effect on anticoagulation therapy.

MATERIALS AND METHODS

Before starting our study an ethical agreement to start our study was obtained from Directorate of Royal Medical Services (DRMS).

This study took place in two main medical centers of royal medical services of Jordan located in Amman, King Hussein hospital and Queen Alia center for cardiology. First one has variety of medical specialties including internal medicine; the second is mainly for cardiology. Both cover the medical needs of all area of Jordan.

Our study used data collected from both hospitals during period from May 2016 till January 2019. The data was reviewed by research team and collected from the medical records in both medical centers and from the pharmacists in both hospitals too. We measured quantities of dispensed old oral anticoagulants represented by warfarin and newly introduced oral non vitamin K dependents anticoagulants

represented by revaroxaban and dabigatran in monthly bases as viewed in **(table 1)**. from that point we could estimate number of patients according to recommended daily dose of each medicine which is 30 tablet per month for eachpatient.

Population of the study

The data of our study was collected using the medical records in pharmacies of both medical centers of our study. The age of most patients included in our study is well known to be elder than 60 years as it be the age of starting anticoagulation therapy for most of Jordan population. At the beginning of the study most of them were using warfarin, and they were divided equally as males and females.

RESULTS

According to our study there was a significant increase in quantities of non vitamin K dependent oral anticoagulants prescribed during the period from May 2016 to Jan 2019. These quantities when converted to number of patients according to monthly dose bases (30 tablets monthly) showed an increase in number of patients using newly introduced non vitamin K dependent oral anticoagulants during all period of our study. During May 2016, the starting time of the study, the number of patients using all types of oral anticoagulants was around 1551 patients, the ratio of patients using warfarin between them could be around 98.8% of our study populations. in January 2019 the estimated number of patients using all types of oral anticoagulants increased to 1496 patients but at this time the ratio of patients using warfarin between them decreased to 72%. During period of our study there was increase in number of patients using revaroxaban 15mg tablets. The value of increase was from 0.43% at May 2016 to 10% at January 2019. Also revaroxaban 20mg tablets use increased on the same period from 0.2% to 14%. on other hand there was increase in number of patients using dabigatran 75mg tablets in the period of our study from 0.3% to 10%. Dabigatran 110mg use also increased to lower extent from 0.3% to 6.4% on the same period. Our data shown on Fig (1) for warfarin and Fig (2) for non-vitamin K dependents oral anticoagulants.

Table (1): Dispensed anticoagulants by month within the period (May 2016-Jan 2019).

month/year	warfarin 5mg	revaroxaban 15mg	revaroxaban 20mg	Dabigatran 75mg	Dabigatran 110mg	Total quantity of NVKDA
Jun-16	42500	240	190	250	280	960
Jul-16	45541	350	288	340	300	1278
Aug-16	39700	460	304	360	240	1364
Sep-16	40460	400	440	450	440	1730
Oct-16	36795	510	1050	400	490	2450
Nov-16	41000	520	1090	480	520	2610
Dec-16	54465	600	1250	495	500	2845
Jan-17	45800	1220	1330	540	630	3720
Feb-17	46400	1260	1660	510	620	4050
Mar-17	44280	1340	960	690	600	3590
Apr-17	44000	1290	1590	720	710	4310
May-17	40000	1360	1690	900	820	4770
Jun-17	41000	1420	1880	1030	800	5310
Jul-17	45800	1660	1800	1320	1100	5880
Aug-17	41110	1890	1930	1560	1330	6710
Sep-17	43040	2150	2140	1860	1410	7560
Oct-17	43000	1980	2756	1490	1600	7826
Nov-17	45110	2200	1840	1930	1980	7950
Dec-17	46410	2170	2670	2140	1800	8780
Jan-18	42660	2440	2450	2120	2300	9310
Feb-18	41150	2350	2890	2390	1300	8930
Mar-18	35300	2450	3020	2400	1600	9470
Apr-18	35540	2400	3450	2560	1450	9860
May-18	36600	2630	3310	2860	2200	11000
Jun-18	37800	2580	2968	2480	1990	10018
Jul-18	38760	2610	3410	2600	1950	10570
Aug-18	35420	2390	4100	2690	2240	11420
Sep-18	40635	2642	4620	2990	1960	12212
Oct-18	38520	3160	4660	3060	2160	13040
Nov-18	36170	3210	4630	3360	1970	13170
Dec-18	33300	3120	4714	3310	2200	13344
Jan-19	31600	3200	4690	3330	2050	13270

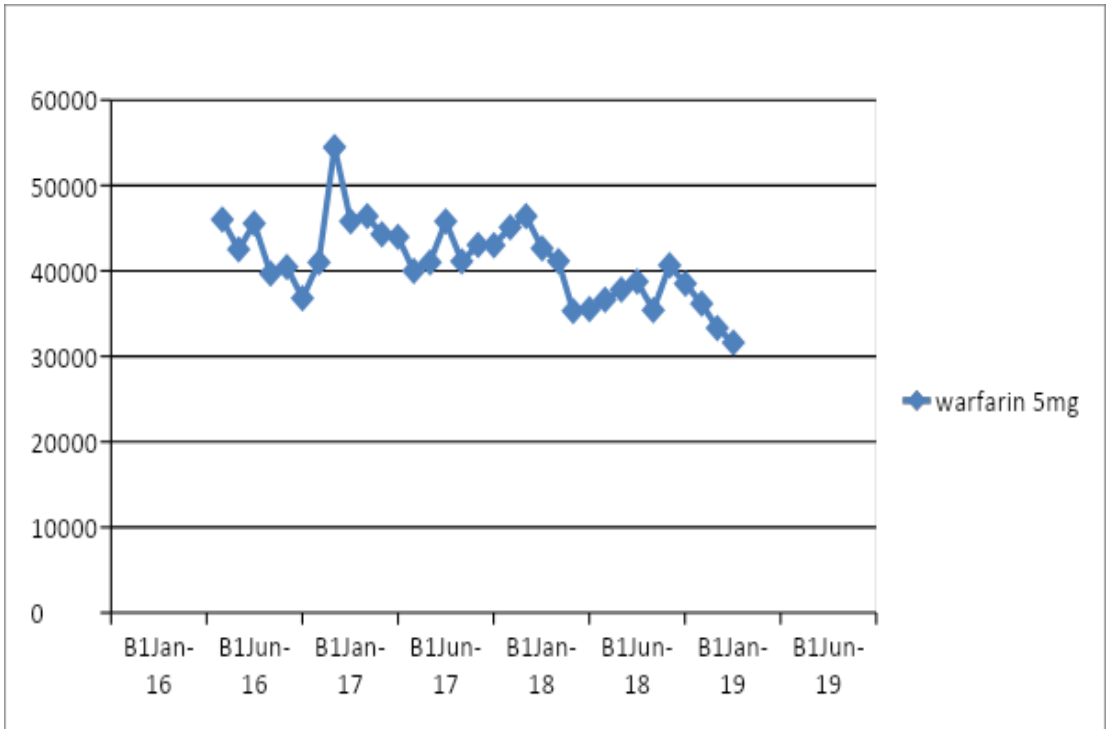

Fig (1): warfarin quantities dispensed within the period (May 2016-Jan 2019).

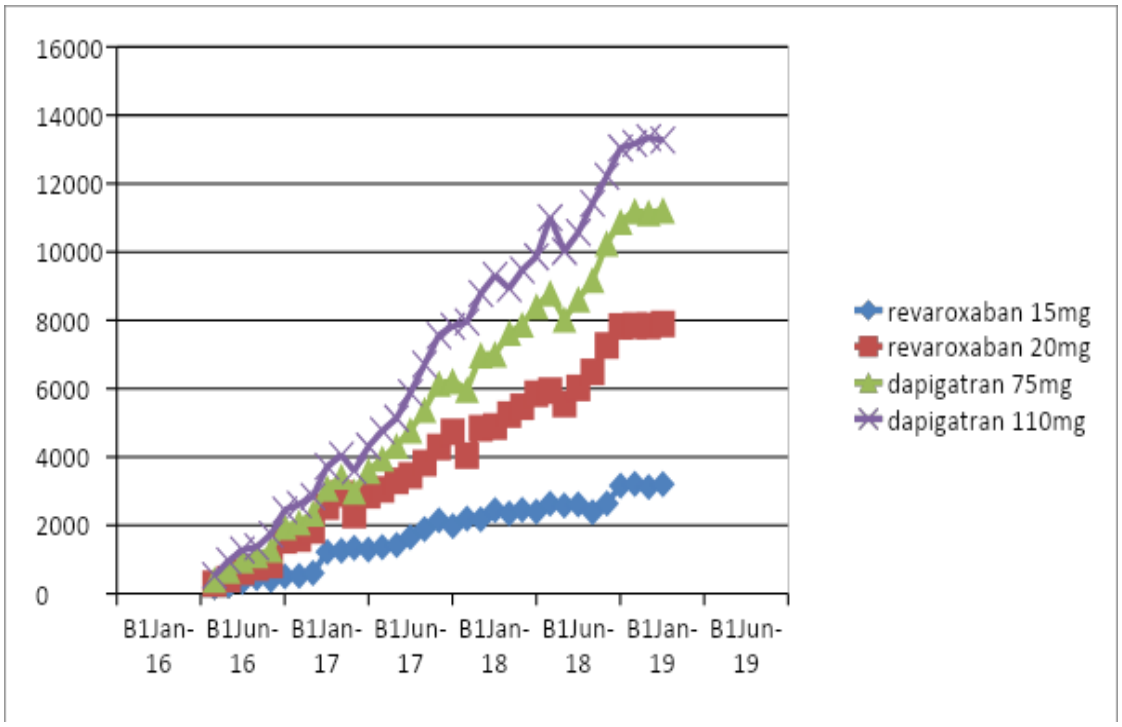

Fig (2): non vitamin K dependent anticoagulants (revaroxaban, dapigatran) dispensed within the period (May 2016-Jan 2019)

Statistical analysis

We compared and analyzed the data mentioned in Table (1) using the statistical package for the social sciences (SPSS program version 21.0) and Microsoft Excel software especially between warfarin use and total quantities of non-vitamin K dependents anticoagulants and we got results illustrated in Fig(3), Fig(4) (p value < 0.05 for significant results).

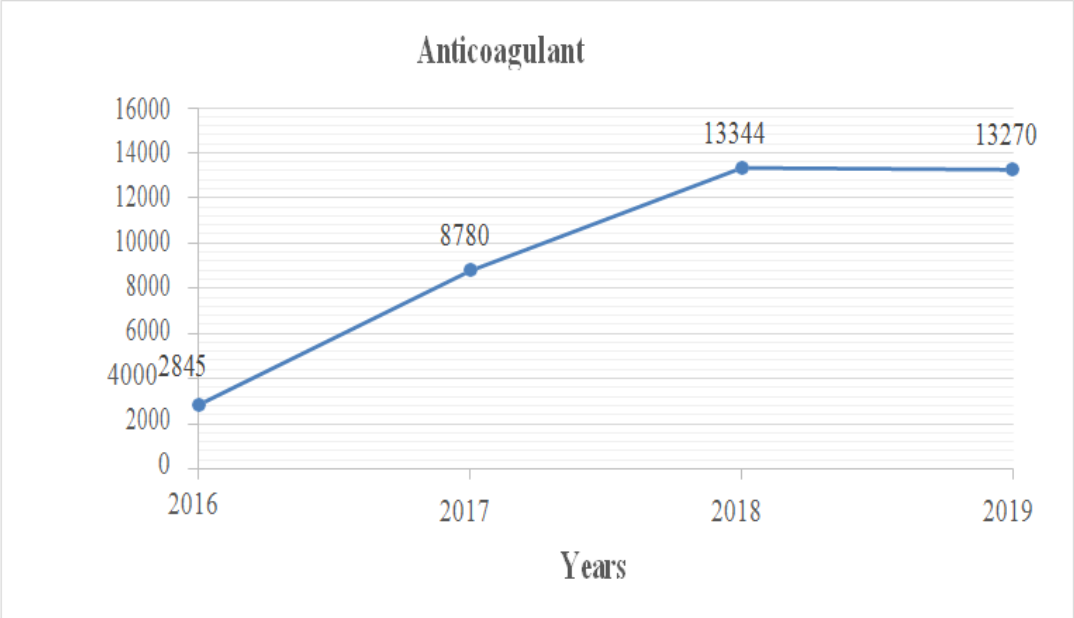

Fig (3): total quantities of non vitamin K dependent anticoagulants dispensed within the period (May 2016-Jan 2019).

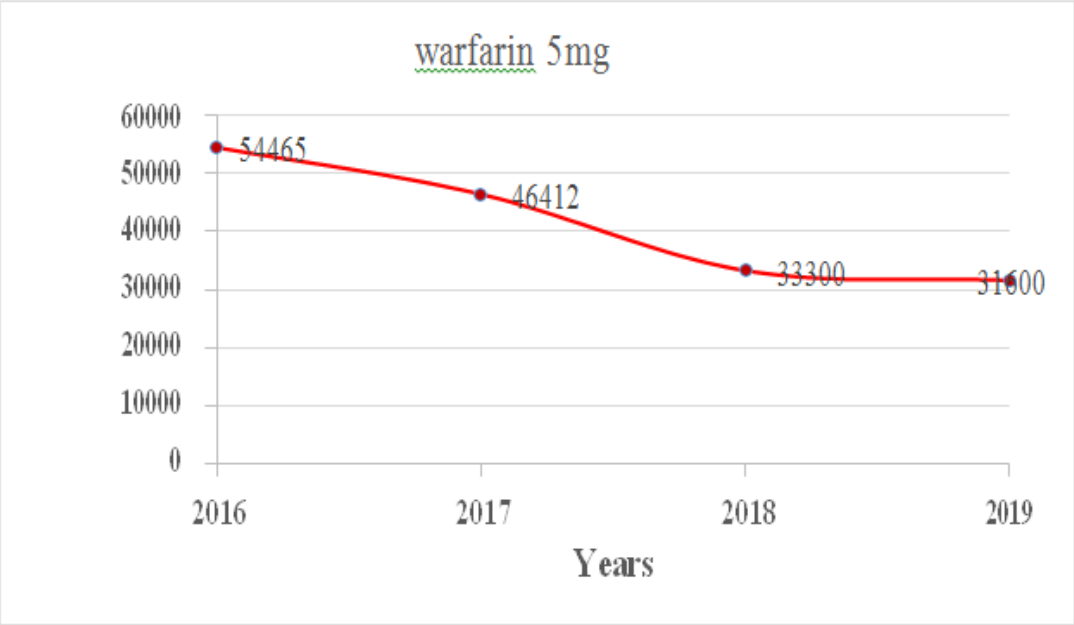

Fig (4): warfarin quantities dispensed within the period (May 2016-Jan 2019)

DISCUSSION

According to our study a real expansion in use of non-vitamin k dependents oral anticoagulants was noticed. Also it was noticed that the rate of increase in use of non-vitamin k dependents anticoagulants was faster than the decrease in warfarin use, these parameters indicate an increase in number of patients using these drugs as first line therapy for anticoagulation regardless of their cost, this may related to the advantages of the non-vitamin k dependents oral anticoagulants over warfarin. However, It should be taken in consideration the impact of this expansion in use of these newly introduced drugs on total cost of anticoagulation therapy because they are more expensive.

CONCLUSION

There is an increase in tendency toward prescribing Non-vitamin k dependents oral anticoagulants as first line therapy over warfarin because of its preferred features. Also we should keep in mind the cost of these drugs compared to warfarin, however, more studies should be carried out to measure the health benefits and the cost saving associated with using these newly introduced anticoagulants.

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