Original Article

Mahidol Univ J Pharm Sci 2016; 43 (2), 85-90

Evaluation of pharmacists' role in rational use of antithrombotic drugs in patients with non-valvular atrial fibrillation

T.T.P. Mai[1], H.T. Dung[1], P.T.T. Hien[1], N.D. Cong[1], B.T.H. Quynh[2]*
[1] Thong Nhat Hospital, Ho Chi Minh City, Vietnam.
[2] Department of Clinical Pharmacy, Faculty of Pharmacy, University of Medicine and Pharmacy, Ho Chi Minh City, Vietnam.

Abstract

CHA_2DS_2VASc is the most widely used scheme to help improve rational indication of antithrombotic drugs for stroke prevention in patients with non-valvular atrial fibrillation. The objective of this study was to evaluate pharmacists' role in rational use of antithrombotic drugs in patients with non-valvular atrial fibrillation. We conducted a retrospective cohort study comparing the rate of appropriate antithrombotic treatment between conventional practice and new practice with pharmacist intervention. Medical records of patients diagnosed with non-valvular atrial fibrillation and hospitalized from January to June 2013 (phase I without pharmacist intervention) and from December 2013 to May 2014 (phase II with pharmacist intervention) were included in this study to check the rational use of antithrombotic drugs based on CHA_2DS_2VASc scores. A total of 126 patients in the phase I and 106 patients in phase II were included. There was no statistically significant difference in CHA_2DS_2VASc scores between two phases. The proportion of patients who were appropriately prescribed antithrombotic drugs based on CHA_2DS_2VASc scores was significantly higher in phase II, compared to that in phase I (47.2% vs 22.2%, p=0.032). The intervention of the pharmacists could improve rational use of antithrombotic drugs in patients with non-valvular atrial fibrillation.

Keyword: CHA_2DS_2VASc scores, non-valvular atrial fibrillation, antithrombotic drugs, stroke

1. INTRODUCTION

Atrial fibrillation is one of the most common arrhythmia. It can cause serious complications that lead to disablement and even death. Atrial fibrillation causes about 5% of stroke annually.[1] In Vietnam, prevalence of recorded atrial fibrillation among adults in Hue city was 0.44%, and among over-60-year-old people in the North was 1.1%. Unsubstantiated atrial fibrillation accounted for 6% of total cases in cardiology department of Bach Mai hospital, and atrial fibrillation accounted for 28.7% of total arrhythmia cases in Hue hospital.[2]

Thromboembolism is a complication of atrial fibrillation. Hence, evaluating risk of thromboembolism and using antithrombotic drugs to prevent stoke are essential. CHA_2DS_2VASc is widely used to help doctors with rational indication for antithrombotic drugs in order to prevent patients with non-valvular atrial fibrillation from stroke.[1,3,4] Collaboration with pharmacists in prescribing can increase rational use of drugs in clinical practice. The aim of this study was to evaluate pharmacists' role in rational use of antithrombotic drugs in patients with non-valvular atrial fibrillation.

2. MATERIALS AND METHODS:

Study settings

We conducted a retrospective cohort study comparing the rate of appropriate antithrombotic treatment between conventional practice and new practice with pharmacist intervention. The protocol of this study was approved by the Institutional Review Board of the Thong Nhat hospital (Project Number: 136 IRB/ QD-BVTN 13062013).

***Corresponding author:** huongquynhtn@gmail.com

We included medical records of all patients diagnosed with non-valvular atrial fibrillation hospitalized from January to June 2013 (phase I) and from December 2013 to May 2014 (phase II) in this study.

Study process

Phase I: Without pharmacist intervention

The patients' data were recorded, including age, sex, history of congestive heart failure, hypertension, stroke or transient ischemic accident (TIA) or thromboembolism, vascular diseases, diabetes mellitus; antithrombotic drugs used, baseline INR, INR during treatment courses, and bleeding related to antithrombotic drugs.

Phase II: With pharmacist intervention

Intervention methods:

- Pharmacists took part in drug and treatment association, and updated their expertise in the use of antithrombic drugs to prevent patients with atrial fibrillation from stroke through professional related activities in hospital.
- Pharmacists suggested clinical staff about:
  - Evaluating risk factors of patients with non-valvular atrial fibrillation based on CHA_2DS_2VASc scheme.
  - Evaluating risk of bleeding based on HAS-BLED scheme.
  - Adjusting antithrombotic drug dose based on INR.
  - Monitoring INR at least once a week after initiation of antithrombotic drugs, and once a month during stable condition.
- INR was evaluated, and the target INR must be in the range from 2.0 to 3.0 before discharge.
- Pharmacists evaluated CHA_2DS_2VASc and HASBLED scores for patients with non-valvular atrial fibrillation and communicated with doctors about prescription and rational dose for patients.

Definitions

Oral anticoagulant drug used to prevent stroke in Thong Nhat is Sintrom (acenocoumarol).

In this study, we defined treatment as following:

- "Appropriate treatment" if a patient who had CHA_2DS_2VASc score ≥ 2 was treated with acenocoumarol; OR if a male patient who had $CHA_2DS_2VASc = 1$ was treated with acenocoumarol; OR if a female patient who had $CHA_2DS_2VASc = 1$ was not treated with acenocoumarol; OR if a patient who had $CHA_2DS_2VASc = 0$ was not treated with acenocoumarol.
- "Under treatment" if a patient who had $CHA_2DS_2VASc \geq 2$ was not treated with acenocoumarol.
- "Over treatment" if a patient who had $CHA_2DS_2VASc = 0$ was treated with acenocoumarol.[1]

Study outcomes

Effectiveness of pharmacist intervention in rational use of antithrombotic drugs was assessed by comparing the following parameters before and after pharmacist intervention:

- Proportion of appropriate treatment based on CHA_2DS_2VASc score (primary outcome)
- Proportion of patients with target INR (2.0-3.0) before discharge and proportion of patients with controlled time of target INR (2.0-3.0) more than 60% of total monitoring period (secondary outcome).

Statistical analysis

Data were analyzed using Statistical Package for Social Sciences (SPSS) Program, version 20.0. Patient's data were presented as mean ± S.D. or percentage. Comparison of the proportion of patients with appropriate treatment, the proportion of patients achieved target INR before discharge and proportion of patients with controlled time of target INR more than 60% of total monitoring period between phase I and phase II were assessed using Chi-square test or Fisher's exact test. The level of statistical significance was specified at $p < 0.05$.

3. RESULTS

Baseline characteristics of patients in two phases

A number of 126 patients in phase I

and 106 patients in phase II were included in this study. Patients' characteristics were not statistically significant different between two phases, including sex, age, CHA_2DS_2VASc score, related diseases (hypertension, heart failure, diabetes) ($p<0.05$). There was a statistically significant difference in proportion of vascular diseases and previous stroke between two phases, but this had no effect on antithrombotic indication which was mainly based on CHA_2DS_2VASc score.

Data of patients' characteristics in two phases were shown in table 1.

Table 1. Baseline characteristics of patients in the two phases

Patient characteristic	Phase I (N = 126)	Phase II (N = 106)	p value
Sex.%			
Male	56.3%	54.7%	0.090
Female	43.7%	45.3%	
Age. years			
< 65	12.7%	10.4%	
65- 74	18.3%	24.5%	0.478
≥ 75	69%	65.1%	
Average age	77.2 ± 11	76.6 ± 11.6	0.717
Risk factors			
Hypertension	79.4%	80.2%	0.876
Heart failure	34.9%	40.6%	0.376
Diabetes	22.2%	17.9%	0.900
Previous stroke	15.9%	6.6%	0.028
Vascular disease	6.4%	15.1%	0.029
CHA2DS2VASc score			
0	2.4%	1.9%	
1	4%	5.7%	0.822
≥2	93.6%	92.4%	
Mean ± SD	3.7 ± 1.5	2.17 ± 1.08	0.828
Median	4	4	

Effectiveness of pharmacist intervention in rational use of antithrombotic drugs

According to recommendation of American College of Cardiology (AHA) 2014 and European Society of Cardiology (ESC) 2012 for rational use of antithrombotic in order to prevent patients with non-valvular atrial fibrillation from stroke[1,3], if CHA_2DS_2VASc score = 0, there is no indication of antithrombotic drug and/or use of antiplatelet drug (aspirin 75-325mg/day); if CHA_2DS_2VASc score =1, indication of anticoagulant drug is considered in male, but not in female; if CHA_2DS_2VASc score ≥2, anticoagulant therapy is recommended. The result showed that, the proportion of patients with appropriate treatment was significantly higher in phase II than that in phase I (47.2%, and 22.2%, p =0.032) (Table 2).

In phase I, 21 patients who used acenocoumarol were taken INR test during hospitalization but only 18 of them were taken INR test before discharge. In phase II, 45 patients

who used acenocoumarol were taken INR test during hospitalization but only 43 of them were taken INR test before discharge. Most patients had INR lower than 2 (90.5% in phase I and 80% in phase II) at admission. The proportion of patients with target INR (2.0-3.0) at admission was similar between two phases (9.5% in phase I and 11.1% in phase II, p=0.059). The mean INR at admission was not significantly different between two phases (1.7 in phase I and 1.8 in phase II, p=0.791) (data not shown).

The proportion of patients achieved target INR (2.0-3.0) before discharge was higher in phase II compared to phase I (32.6% and 27.8%, respectively) without statistically significant difference (p=0.920) (Table 3).

Table 2. Antithrombotic treatment based on CHA_2DS_2VASc scores in the two phases

Treatment	Phase I (N=126) n (%)	Phase II (N=106) n (%)	p value
Appropriate treatment	28 (22.2%)	50 (47.2%)	0.032
Under treatment	98 (77.8%)	56 (52.8%)	
Over treatment	0	0	

Table 3. Patients' INR before discharge

INR before discharge	Phase I (N = 18) n(%)	Phase II (N = 43) n(%)	p value
<2	11 (61.1%)	25(58.1%)	
2.0-3.0	5 (27.8%)	14(32.6%)	0.920
>3	2 (11.1%)	4 (9.3%)	

According to the guidance of INR monitoring in patients with anticoagulant, proportion of time with controlled target INR (2.0-3.0) must be more than 60% of total monitoring period. Proportion of patients with over 60% controlled time of target INR (2.0-3.0) in phase II was higher compared to phase II (13.3% and 4.8%, respectively), but the difference was not statistically significant (p=0.3) (data not shown).

No case of bleeding complications during hospitalization was recorded. Only two cases were hospitalized because of bleeding while using anticoagulant drug (once in each phase). After treatment, these two patients' INR were stable.

4. DISCUSSION

Demographics and baseline characteristics of patients in the two phases of study were generally well balanced, including CHA_2DS_2VASc score. CHA_2DS_2VASc score was the main parameter used to assess the appropriateness of antithrombotic treatment in this study.

Proportion of patients with rational indication based on CHA_2DS_2VASc in phase II was significantly higher compared to phase I (47.2% vs 22.2%, p=0.032). Proportion of under-treatment in phase II was significantly lower than those in phase I.

The proportion of under-treated patients in our study (77.8 and 52.8 in phase I and II, respectively) was much higher than in study of Brandes A et al. (2013) in Denmark[6] (22.7%), because of more frequent use of oral anticoagulants in this research. This can be explained that doctors were very careful to prescribe oral anticoagulants for patients in our research because of old age, multiple diseases, risk of

bleeding, or contraindications. In some cases of our study, doctors did not indicate acenocoumarol in patients with CHA2DS2VASc ≥ 2 because of patient's clinical condition. If indication was adequately explained, it was also considered as a right decision. We assessed every case, and the result showed that, the proportion of adequately explained decisions in phase II was statistically higher compared to phase I (58.9% and 29.6%, respectively, p=0.001). Clinical conditions for not prescribing acenocoumarol for patients with $CHA_2DS_2VASc \geq 2$ include cerebral infarction, stroke, HAS-BLED score ≥ 3, serious diseases (including serious chronic kidney disease, coma, and cancer), after surgery, using injected antithrombotic, serious chronic kidney disease, and patients without INR monitoring.

According to Vietnamese guideline about the use of antithrombotic drugs in patients with non valvular atrial fibrillation, target INR was from 2.0 to 3.0.[2] INR lower than 2 can lead to unavoidable thromboembolism, meanwhile INR more than 3 can increase risk of bleeding. Before treatment, doctors should evaluate patient's risk factors to determine right strategy in order to prevent stroke and bleeding complications during treatment. If antithrombotic drug is prescribed, guideline of use must be followed. In addition, INR must be routinely monitored and adjusted to achieve target level. This would help decrease complications and achieve target of treatment. Patients should have controlled INR before discharge. If INR is in target range, dose of antithrombotic drug is remained. Proportion of patients with over 60% controlled time of target INR before discharge in phase II was higher compared to phase I (32.6% and 27.8%, respectively). However, the difference was not statistically significant. Controlled time target INR proportion in this research was lower than Altmann David R. et al's research.[5] According to Altmann David R. et al's research, 52.5% of 305 patients with atrial fibrillation used antivitamin K drugs achieved target INR (2.0-3.0). Although proportion of patients with over 60% controlled time of target INR increased from 4.8% in phase I to 13.3% in phase II, the difference was not statistically significant.

Overall, comparing two phases, drugs and treatment association frequently updated specialized knowledge about the use of antithrombotic drugs in order to prevent patients with non-valvular atrial fibrillation from stroke, and direct advices of pharmacists increased the proportion of appropriate antithrombotic indication based on CHA_2DS_2VASc and patients' clinical conditions.

5. CONCLUSION

Proportion of appropriate treatment of antithrombotic drugs based on CHA_2DS_2VASc in phase II was statistically significant higher than those in phase I (47.2% vs 22.2%, p-0.032). Though proportion of patients with above 60% controlled time of INR in target increased from 4.8% (phase I) to 13.3% (phase II), the difference was not statistically significant (p=0.3). In both phases, there was no case of bleeding complications during hospitalization. Hence, pharmacist advice increased proportion of rational use of antithrombotic based on CHA_2DS_2VASc in patients with non-valvular atrial fibrillation.

6. ACKNOWLEDGEMENTS

The authors thank Thong Nhat Hospital for granting permission to access to medical records. This study was financially supported by the Faculty of Pharmacy, University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam. We would like to thank Ms Luu Thi Hoa for editing the manuscript.

REFERENCES

1. Camm AJ, Lip GY, De CR. Focused update of the ESC Guidelines for the management of atrial fibrillation: An update of the 2010 ESC Guidelines for the management of atrial fibrillation. Developed with the special contribution of the European Heart Rhythm Association. Europace. 2012;14(10):1385–413.
2. Huynh Van Minh, Phạm Gia Khai. Recommendation of Vietnam heart association in cardiovascular and metabolic diseases. Medicine. 2008;1:151-216. (in Vietnamese

3. Alpert JS, Cigarroa JE, Cleveland JC. Guideline for the management of patients with atrial fibrillation: A report of the american college of cardiology/american heart association task force on practice guidelines and the heart rhythm society. Circulation. 2014.
4. Camm AJ, Kirchhof P, Lip G. Y. Guidelines for the management of atrial fibrillation: the task force for the management of atrial fibrillation of the European Society of Cardiology (ESC). Eur Heart J. 2010; 31(19):2369-2429.
5. Altmann DR, Kühne M, Sticherling C, Osswald S, Schaer BA. Use of the $CHADS_2$ risk score to guide antithrombotic treatment in patients with atrial fibrillation – room for improvement. Swiss Med Wkly. 2010; 140(5–6):73–77.
6. Brandes A, Overgaard M, Plauborg L. Guideline adherence of antithrombotic treatment initiated by general practitioners in patients with nonvalvular atrial fibrillation: a danish survey. Clinical Cardiology. 2013;36(7):427- 432.