Research article

Adherence to Anti-coagulant therapy in elderly patients with Atrial fibrillation in the Kyrgyzstan

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ABSTRACT

Introduction: Anticoagulant therapy can prevent adverse outcomes of Atrial fibrillation (AF), reducing the risk of stroke by 64% and death by 25%. The present study aimed to assess treatment adherence in elderly patients with non-valvular atrial fibrillation (NVAF) who were prescribed the vitamin K antagonist warfarin.

Materials and methods: In the present retrospective study, we analyzed the medical records of 202 elderly outpatients with NVAF aged between 65 and 74 years (mean ± SD: 68.7 ± 10.2 years).

Results: Problems associated with warfarin arose throughout the follow-up period. After 1 month of treatment, the number of patients taking warfarin had decreased to 71.3% of all patients; less than half of the patients (46%) were still taking the drug. In subsequent periods, the number continued to decrease; of all patients who had been prescribed warfarin with periodic international normalized ratio (INR) control, only 19 (9.4%) remained after 1 year. Our study revealed inadequate anticoagulation therapy in elderly patients, probably because most patients refused warfarin therapy because they could not control their INR. Moreover, significantly more rural residents than urban residents refused therapy (48 vs. 22; $p < 0.05$). Doctors underprescribed anticoagulants because they feared hemorrhagic complications in their patients.

Conclusion: The results of the present study showed that anticoagulants were underprescribed at the outpatient stage in centers of family medicine in our country. The main drug of choice for specialists remains warfarin, which only provides adequate therapy in a small number of patients (9.4%).

Keywords: Adherence, Anticoagulant therapy, Atrial fibrillation, Warfarin, International normalized ratio

INTRODUCTION

Atrial fibrillation (AF) is one of the most common types of cardiac arrhythmias, affecting 2%–5% of the population and increasing in frequency with age. Specifically, the incidence of AF is 6% among individuals aged 60–69 years, while it is 9%–14% in those aged 70–89 years and 22% in those aged ≥ 90 years (1–4). Prevention of stroke in patients with AF remains a particularly important public health problem worldwide, as 70%–80% of patients die or develop disabilities after suffering a stroke (5).

Anticoagulant therapy can prevent adverse outcomes of AF, reducing the risk of stroke by 64% and death by 25% (6). However, antithrombotic therapy is often ineffective over a long period of time, even when prescribed early. In this regard, patients must maintain high adherence to treatment to ensure successful therapy and effective secondary prevention of cardiovascular complications (7).

In our country, anticoagulant therapy remains underprescribed in patients with AF or other indications. One recent study in the south of the country showed that preventive treatment of stroke and systemic embolism is only carried out in 11.8% of all patients with AF (387 people in the study), even though such treatment is indicated by clinical guidelines (8). Furthermore, clinicians often only have access to a narrow range of anticoagulant drugs, namely vitamin K antagonists. Therefore, it is crucial that an objective assessment of adherence to anticoagulant treatment be carried out in our country.

The present study aimed to assess treatment adherence in elderly patients with non-valvular AF who were prescribed the vitamin K antagonist warfarin.

MATERIALS AND METHODS

In the present retrospective study, we analyzed the medical records of 202 elderly outpatients with non-valvular AF aged between 65 and 74 years (mean ± SD: 68.7 ± 10.2 years; Table 1). Confidentiality was maintained concerning the data collected from the patients, who provided their informed consent. This study was approved by the I.K. Akhunbaev Kyrgyz

State Medical Academy Bioethics Committee (Protocol No. 5 dated December 11, 2017). The characteristics of patients who received warfarin are shown in Table 1.

Table 1: The characteristics of patients who received warfarin

Indicators/factors	Value
Total patients, n	202
Average age (years), range	68.7 (65-74)
Men, n (%)	37 (18.3%)
Women, n (%)	165 (81.7%)
City residents, n (%)	104 (51.5%)
Rural residents, n (%)	98 (48.5%)
Arterial hypertension, n (%)	141 (69.8%)
Coronary heart disease, n (%) With history of myocardial infarction, n (%)	95 (47.0%) 33 (16.3%)
Congestive heart failure, n (%)	29 (14.3%)
Diabetes mellitus type 1 and 2, n (%)	51 (25.2%)
History of acute cerebrovascular accident, n (%)	28 (13.9%)
Chronic kidney disease, n (%)	7 (3.5%)

Patients were excluded if their charts contained no information about treatment adherence. In all patients taking warfarin, we determined how long the international normalized ratio (INR) remained in the therapeutic window (2.0–3.0). All patients had a high risk of thromboembolic complications on the CHA2DS2Vasc0 scale (≥ 2) and a low risk of hemorrhagic complications on the HAS-BLED scale (mean: 1.45 ± 0.03); therefore, all patients had been correctly prescribed warfarin.

Among patients with poor AF monitoring, we conducted a survey to determine the reasons for their irregular doctor visits and poor INR monitoring. In addition, we devised a questionnaire to determine doctors' awareness of when antithrombotic therapy should be prescribed and their knowledge about the CHA2DS2Vasc0 and HAS-BLED scales. We then delivered this questionnaire to 57 doctors from family medicine centers.

Statistical data analysis and mathematical processing were carried out using Microsoft Excel, Statistica Excel application package, and Statistica 8.0 application package. The Mann–Whitney U-test was used to assess the statistical significance of the differences. Differences were considered statistically significant at p-values < 0.05.

RESULTS

The main risk factors for thromboembolic complications were concomitant diseases. As shown in Table 1, the most common of these were arterial hypertension (69.8%), coronary heart disease (47.0%), history of myocardial infarction (16.3%), chronic heart failure (14.3%), diabetes mellitus types 1 and 2 (25.2%), and acute cerebrovascular accident (13.9%). In addition, a small number of patients (3.5%) had chronic kidney disease with a significant decrease in the glomerular filtration rate.

Problems associated with warfarin arose throughout the follow-up period (Figure 1). After 1 month of treatment, the number of patients taking warfarin had decreased to 71.3% of all patients; less than half of the patients (46%) were still taking the drug.

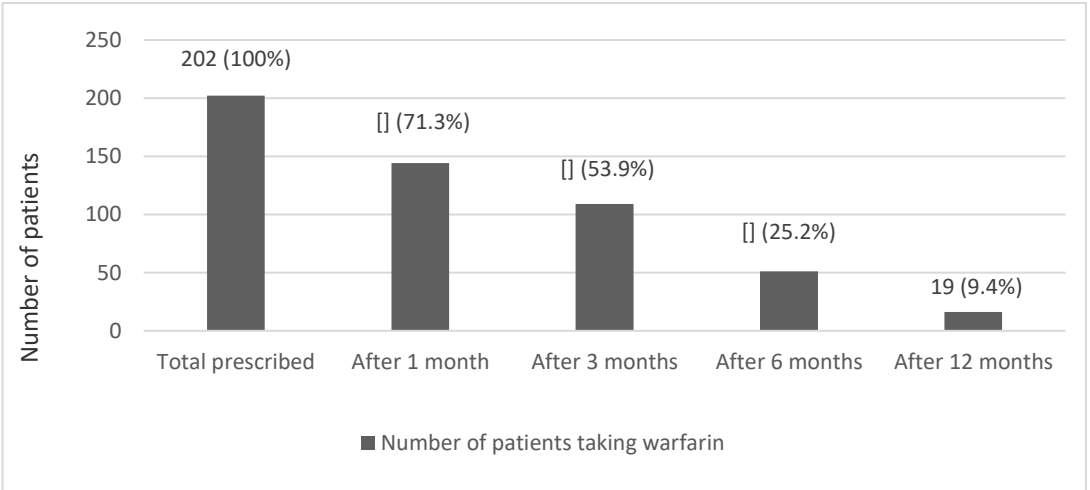

Figure 1: Dynamics of a decrease in the number of patients with atrial fibrillation taking warfarin (analysis within 12 months).

In subsequent periods, the number continued to decrease; of all patients who had been prescribed warfarin with periodic INR control, only 19 (9.4%) remained after 1 year, (Fig. 1). This is the real

number of patients who were regularly observed during the year and followed the recommendations of the doctors at the family medicine center.

Our study revealed inadequate anticoagulation therapy in elderly patients, probably because most patients refused warfarin therapy because they could not control their INR. Moreover, significantly more rural residents than urban residents refused therapy (48 vs. 22; $p < 0.05$). Seventeen of the patients had medical contraindications to the drug, such as anemia, impaired renal function, exacerbation of gastric ulcer, drug intolerance, etc. In seven patients, warfarin was discontinued due to alcohol abuse. Thirty-three patients independently switched to taking aspirin-based drugs, which do not prevent cardiogenic embolism.

Doctors underprescribed anticoagulants because they feared hemorrhagic complications in their patients. Specifically, outpatient doctors did not prescribe warfarin to 39 patients (19.3%) because they feared serious bleeding, while in 17 patients (8.4%), warfarin therapy was discontinued after hemorrhagic syndrome manifested as nosebleeds and bruises, even though these are easily stopped.

Among urban residents, the main reason for irregular doctor visits and poor monitoring of INR indicators was long queues at family medicine centers. Rural residents mainly responded that they had insufficient finances for the journey—to monitor INR, patients had to travel 10–25 km to a district center with a laboratory.

The survey showed that 42 physicians (73.9%) replied that warfarin as their main anticoagulant drug of choice for preventing antithrombotic complications; 11 (19.2%) named antiplatelet agents. The existence of new oral anticoagulants was noted in the questionnaire by 21 (36.8%) doctors. When asked about whether they used the CHA2DS2-VASc and HAS-BLED scales in practice, 14 (24.6%) doctors answered in the positive.

With regards to how long the INR remained in the therapeutic window, of 2709 INR measurements conducted in 181 patients during 1 year of follow-up, only 284 (10.5%) were within the target range (2.0–3.0). Concerning the complications of warfarin, hemorrhagic syndrome manifested as subcutaneous hematomas and bleeding of varying degrees (gingival, nasal, and microhematuria) in 16.3% of cases.

DISCUSSION

Effective prevention of thromboembolic complications depends on adherence to anticoagulant therapy, which can significantly improve long-term clinical outcomes. In patients who are advised to take cardiovascular medications indefinitely, poor adherence to treatment is usually independent of the type of therapy or population (9, 10). In a study by Russian authors observing 244 patients with non-valvular AF, the patients were divided into two groups: Group 1, 124 patients who received the primary options for acute care; Group 2, 120 people who were administered warfarin and observed using the centralized monitoring system of the INR. One year after drug prescription, only 22.6% of patients in the Group 1 were still complying with the doctor's recommendations; in Group 2, none of the patients had stopped taking warfarin, indicating higher adherence to therapy (11). In the present study, the patients took warfarin and were only under the supervision of a family medicine doctor. With this approach to observation, only 9.4% of patients continued to take warfarin and maintained their INR within the target range.

The patients in the present study refused to continue anticoagulant treatment mainly because they could not control their INR or because they feared bleeding. In fact, doctors were also concerned that patients would experience bleeding complications. According to the results of a systematic review by Pugh, doctors feel a sense of responsibility for when patients show serious bleeding, and this concern outweighs their fears of stroke risk (12). In the present study, doctors discontinued warfarin in 17 patients after minor and isolated manifestations of hemorrhagic syndrome.

A study using the US insurance database and involving 64,661 patients with AF found that, in patients with an initially low risk of stroke, low adherence to anticoagulant treatment did not increase the risk, as measured using the CHA2DS2-VASc 0–1 (13). In other cases, the relative risk (RR) of stroke was higher with poor adherence, higher CHA2DS2-VASc scores, and longer interruptions in anticoagulant intake. Thus, in patients with a CHA2DS2-VASc score of ≥ 2, the risk of stroke more than doubled when anticoagulant therapy was discontinued for 6 months or more compared with when it was interrupted for less than 1 week (RR: 2.73, 95% confidence interval: 1.76–4.23). For this reason, doctors should strive to achieve the highest possible adherence to therapy in patients with AF, rather than simply prescribing anticoagulants in a formal sense.

Nonetheless, no comprehensive study of the problem of adherence, considering the quality of the prescribed treatment, has yet been carried out. Of course, all methods available in the arsenal of modern medicine should be used to improve adherence and increase patient compliance with all medical prescriptions.

CONCLUSION

The results of the present study showed that anticoagulants were underprescribed at the outpatient stage in centers of family medicine in our country. The main drug of choice for specialists remains

warfarin, which only provides adequate therapy in a small number of patients (9.4%).

A questionnaire administered to doctors demonstrated low awareness of the need for anticoagulant therapy in AF, with low adherence to the recommendations. It should always be remembered that good adherence to anticoagulant therapy is crucial to the effective prevention of thromboembolic complications in AF.

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CONFLICTS OF INTEREST

Authors declare no conflict of interest.

AVAILABILITY OF DATA AND MATERIAL

Data are available from the corresponding author upon reasonable request.

AUTHOR CONTRIBUTIONS

Conception, design of the work, manuscript preparation, and data acquisition Kanat kyzy Bazira, Nazgul Kinderbaeva, Gulnora Karataeva, Sabira Mamatova, Ulan Kundashev, and Sagynali Mamatov. Clinical management: Kanat kyzy Bazira, Nazgul Kinderbaeva, Gulnora Karataeva, and Sabira Mamatova. Manuscript preparation and data acquisition: Ulan Kundashev, and Sagynali Mamatov.

REFERENCES

1. January, C. T., Wann, L. S., Alpert, J. S., Calkins, H., Cigarroa, J. E., Cleveland, J. C., *et al.,* 2014 AHA/ACC/HRS 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; 130(23): e199–e267.
2. Turakhia, M. P., Solomon, M. D., Jhaveri, M., Davis, P., Eber, M. R., Conrad, R., *et al.,* Burden, timing, and relationship of cardiovascular hospitalization to mortality among Medicare beneficiaries with newly diagnosed atrial fibrillation. Am heart J. 2013; 166(3): 573-580.
3. Kirchhof, P., Auricchio, A., Bax, J., Crijns, H., Camm, J., Diener, H. C., *et al.,* Outcome parameters for trials in atrial fibrillation: executive summary. Eur Heart J. 2007; 28(22): 2803-2817.
4. Kakkar, A. K., Mueller, I., Bassand, J. P., Fitzmaurice, D. A., Goldhaber, S. Z., Goto, S., *et al.,* Risk profiles and antithrombotic treatment of patients newly diagnosed with atrial fibrillation at risk of stroke: perspectives from the international, observational, prospective GARFIELD registry. PloS one. 2013; 8(5): e63479.
5. Gladstone, D. J., Bui, E., Fang, J., Laupacis, A., Lindsay, M. P., Tu, J. V., *et al.,* Potentially preventable strokes in high-risk patients with atrial fibrillation who are not adequately anticoagulated. Stroke. 2009; 40(1): 235-240.
6. Hart, R. G., Pearce, L. A., Aguilar, M. I. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med. 2007; 146(12): 857-67.
7. Frishman, W. H. Importance of medication adherence in cardiovascular disease and the value of once-daily treatment regimens. Cardiol Rev. 2007; 15(5): 257-63.
8. Bazira, K., Musakeev, A. O., Mamatov, S. M., Kinderbaeva, N. K., Kundashev, U. K. Anticoagulant therapy in elderly people in the clinical practice of family medical centers in the Kyrgyz Republic. Clinical gerontology. 2020; 26(9-10): 3-8.
9. McClellan, M., Brown, N., Califf, R. M., Warner, J. J. Call to Action: Urgent Challenges in Cardiovascular Disease: A Presidential Advisory From the American Heart Association. Circulation. 2019; 139(9): e44-e54.
10. Ten, Cate. H. New oral anticoagulants: discussion on monitoring and adherence should start now!. Thromb J. 2013; 11(1): 8.
11. Garkina, S. V., Vavilova, T. V., Lebedev, D. S., Mikhaylov, E. N. Compliance and adherence to oral anticoagulation therapy in elderly patients with atrial fibrillation in the era of direct oral anticoagulants. JGC. 2016; 13(9): 807-10.
12. Pugh, D., Pugh, J., Mead, G. E. Attitudes of physicians regarding anticoagulation for atrial fibrillation: a systematic review. Age Ageing. 2011; 40(6): 675-83.
13. Yao, X., Abraham, N. S., Alexander, G. C., Crown, W., Montori, V. M., Sangaralingham, L. R., et al. Effect of Adherence to Oral Anticoagulants on Risk of Stroke and Major Bleeding Among Patients With Atrial Fibrillation. J Am Heart Assoc. 2016; 5(2): e003074.