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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Outpatient oral anticoagulation in Poland in 2012: a single centre experience

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Abstract

Background: Oral anticoagulants reduce embolic complications in patients with atrial fibrillation (AF) and are used in the treatment and prevention of venous thromboembolism. In Poland, chronic oral anticoagulation is usually managed by primary care physicians, and the most commonly used drugs are vitamin K antagonists (VKA).

Aim: To evaluate effectiveness of oral anticoagulation in 104 patients receiving chronic VKA treatment in primary care from Jan 01, 2011 to Dec 31, 2011.

Methods: We performed a retrospective analysis of data of 104 patients receiving chronic VKA treatment in a primary care practice (Niepubliczny Zakład Opieki Zdowotnej ESCULAP Gniewkowo) from Jan 01, 2011 to Dec 31, 2011. These patients comprised 1.1% of the population remaining under care of this primary care practice. We determined minimum, maximum and mean values of the international normalised ratio (INR), the proportion of results within the therapeutic range, the number of INR measurements, and indications for anticoagulant treatment. In patients with AF, we determined the risks of bleeding complications and thrombotic events.

Results: Among patients receiving chronic VKA treatment, 56.84% of INR measurements were within the therapeutic range. Only 29.8% of patients had more than 70% of INR measurements within the therapeutic range. We found no association between the number of INR measurements and treatment effectiveness.

Conclusions: The effectiveness of anticoagulation in primary care is unsatisfactory. In our study population, an acceptable time in the therapeutic range was achieved in only just below 30% of patients.

Key words: anticoagulant treatment, bleeding risk, thrombotic risk, treatment effectiveness, primary care

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INTRODUCTION

Treatment with oral anticoagulants reduces thromboembolic complications in patients with atrial fibrillation (AF). Oral anticoagulation is also used for the prevention and treatment of venous thromboembolism (VTE) and in patients with prosthetic valves.

Based on data regarding the incidence and prevalence of AF and VTE, it may be estimated that chronic oral anticoagulant treatment is used in more than 400,000 patients in Poland.

Most of these patients are treated by primary care physicians, and the most commonly used drugs are vitamin K antagonists (VKA). In Western Europe and the United States, several approaches to monitoring of VKA treatment are used, including surveillance by hospital outpatient clinics, primary care physicians, dedicated anticoagulation teams, and patient self-monitoring. Regardless of the monitoring strategy used, however, many treated patients continue to remain for a long time outside the recommended target range of the international normalised ratio (INR). In a metaanalysis of 67 clinical studies that included 50,208 patients (57,155 patient-years of follow-up), the mean proportion of INR values within the therapeutic range was 64%, with the highest proportion for patient self-monitoring (72%) and the lowest proportion for monitoring by primary care physicians (57%) [1].

The aim of the present study was to evaluate the effectiveness of oral anticoagulation in a population of primary care patients. The criteria of oral anticoagulation effectiveness

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were INR values and time in the therapeutic range (TTR), with effective treatment defined as at least 70% of the INR values within the therapeutic range.

METHODS

We retrospectively analysed data on 104 patients receiving chronic VKA treatment in a primary care practice (Niepubliczny Zakład Opieki Zdowotnej ESCULAP Gniewkowo) from Jan 01, 2011 to Dec 31, 2011. These patients comprised 1.1% of the population remaining under care of this primary care practice. In all patients, the effectiveness of oral anticoagulation was monitored using INR which allows standardised comparisons of the prothrombin time measurement results regardless of the reagents used. We determined minimum, maximum and mean INR values, the proportion of results within the therapeutic range, the number of INR measurements, and indications for anticoagulant treatment. In patients with non-valvular AF, we determined the risk of bleeding complications using the HAS-BLED score and the risk of thromboembolic events using the CHA_2DS_2-VASc score.

Study population characteristics

Indications for chronic VKA treatment are shown in Figure 1. Patients were informed about the need for regular INR monitoring and appropriate long-term orders were given. The study group consisted of 104 patients, including 52 women and 52 men. The mean age was 67.89 ± 12.08 years. Duration of chronic VKA treatment in the study group was 4.36 ± 4.08 years. Hypertension was diagnosed in 75 (71.4%) patients, diabetes in 27 (25.7%) patients, heart failure in 43 (40.9%) patients, previous stroke in 9 (8.57%) patients, previous myocardial infarction in 9 (8.57%) patients, and pulmonary embolism in 4 (3.8%) patients. No concomitant chronic conditions were found in only 6 (5.7%) patients.

Statistical analysis

Descriptive statistics included absolute and relative numbers and percentages. For quantitative variables, we calculated average values and measures of dispersion. The Student *t* test was used to evaluate differences between two groups with equal variances.

RESULTS

We analysed data obtained from 104 patients aged 21 to 91 years (mean age 67.89 ± 12.08 years) receiving chronic VKA treatment, including 52 women and 52 men. The most common indication for chronic anticoagulation was AF, followed by VTE, valve prosthesis, and echogenic blood in the left ventricular cavity (Fig. 1). During the study period, the number of INR measurements per patient ranged from 1 to 28 (mean 9.27 ± 6.16) despite the fact that a permanent order for INR measurements was issued in all patients. INR values ranged from 1.2 to 12.8 (mean 2.42 ± 0.53). Overall, we analysed 964 INR measurements, with 548 (56.84%) of them in the therapeutic range. More than 70% of INR measurements in the therapeutic range were found in only 31 (29.8%) patients, 30–70% of measurements in 52 (50%) patients, and less than 30% of measurements in 21 (20.19%) patients (Fig. 2). INR below 1.5 was noted in 58 (6.01%) measurements, and above 4.0 in 50 (5.18%) measurements. In patients with AF, who comprised 68.26% of the study population, the risk of thromboembolic events was determined using the CHA_2DS_2-VASc score (Fig. 3), and the risk of bleeding complications using the HAS-BLED score (Fig. 4).

We did not find a relationship between the number of INR measurements and treatment effectiveness. Mean INR value was 2.49 ± 0.39 in patients with 12 or more measurements compared to 2.35 ± 0.59 in patients with 3–8 measurements. Among AF patients with 3 or more points

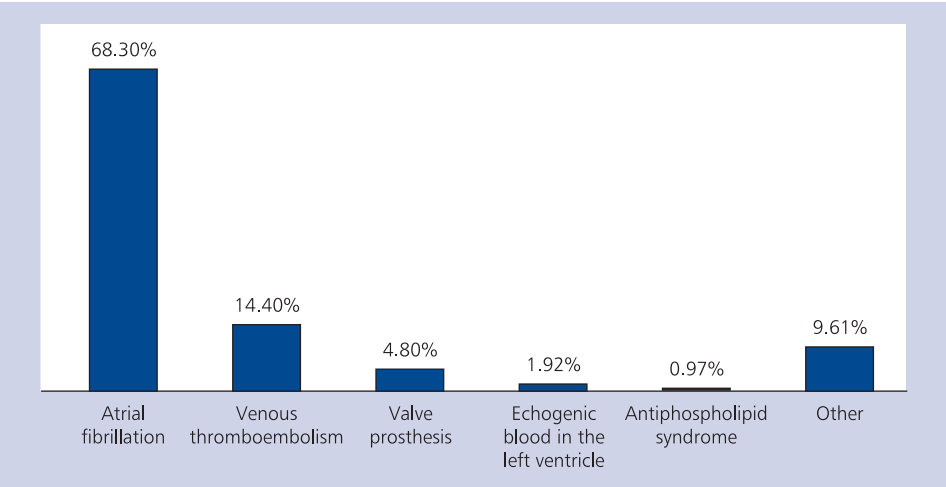

Figure 1. Indications for anticoagulant therapy

in the HAS-BLED score, an INR result above 4.0 was noted in 11 of 24 (45.83%) patients. In these patients 39.91% of INR values were within the therapeutic range (mean INR value 2.47), compared to 56.29% of INR values within the therapeutic range (mean INR value 2.47) among those with 0–2 points in the HAS-BLED score (p = 0.1). No significant differences were found when INR values were analysed in patient groups with the risk of thromboembolic complications categorised using the CHA_2DS_2-VASc score. In 2 patients in the study group, the risk of thromboembolic complications was 0 points by the CHA_2DS_2-VASc score, and thus these patients had no indications for chronic VKA treatment according to the current guidelines.

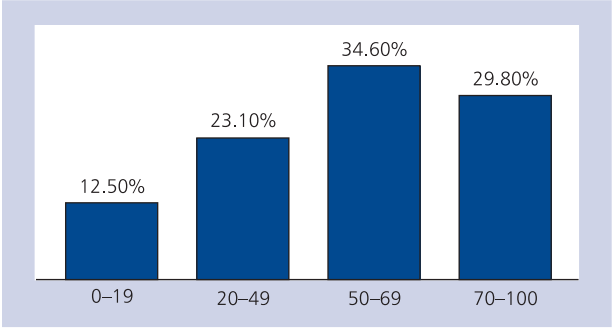

Figure 2. Time in the therapeutic range

DISCUSSION

No systematic large-scale research to evaluate the effectiveness of chronic anticoagulation has been performed in Poland. In the literature data, the proportion of INR values in the therapeutic range is estimated at 50–70%. The importance of strict INR monitoring was shown in patients with nonvalvular AF in whom INR < 2.0 was associated with an increased risk of stroke, and INR > 3.0 was associated with an increased

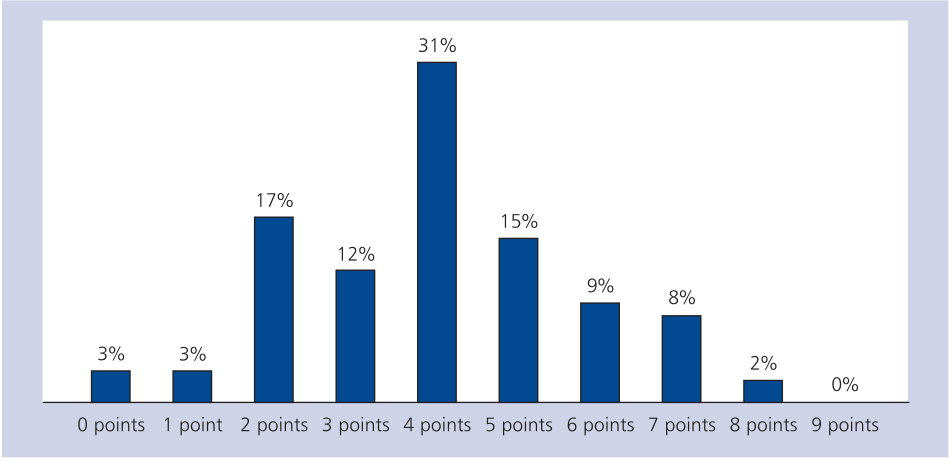

Figure 3. Thromboembolic risk as determined using the CHA_2DS_2-VASc score

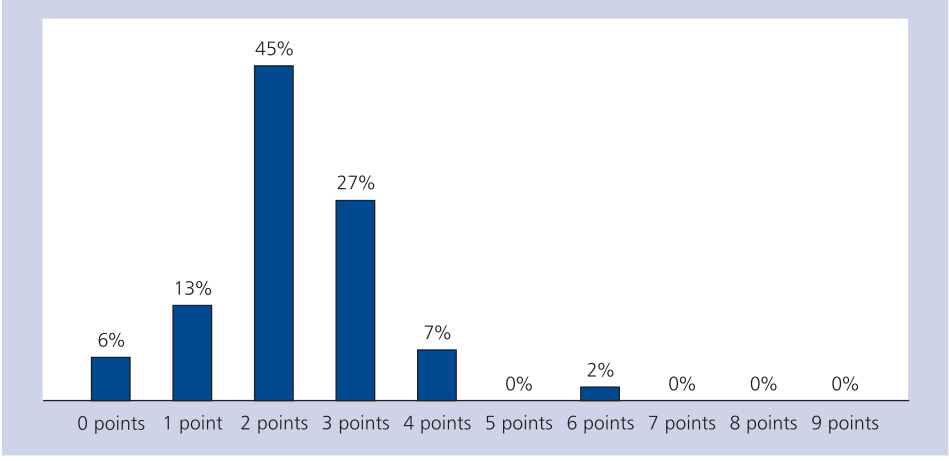

Figure 4. Bleeding risk as determined using the HAS-BLED score

bleeding risk [2–4]. Multiple studies showed that the optimal therapeutic range associated with the lowest risk of bleeding and thrombotic complications is 2.0–3.0 [5]. INR values are affected by numerous factors including treatment, concomitant conditions, patient compliance, other medications, dietary factors associated with daily vitamin K intake, INR decision thresholds calling for dose adjustment, and patient education regarding VKA therapy.

Oral anticoagulation has been discussed in multiple guidelines, including Polish recommendations on VTE prevention and treatment, and guidelines on the management of patients with AF. The most commonly used drugs are VKA including acenocoumarol and warfarin. In our primary care population, anticoagulant drugs other than VKA were used in 6 patients, including apixaban in 4 patients participating in a open clinical trial, and rivaroxaban in 2 patients (these patients were not included in the present analysis). In most cases, oral anticoagulation is managed by primary care physicians. For VKA therapy, monthly cost of medications and blood tests is approximately 9–15 Polish zlotys, compared to at least 150 Polish zlotys in case of novel oral anticoagulants. Despite unlimited access to INR monitoring, only 34 (32.69%) patients had these tests performed more frequently than once in 4 weeks, and only 1–3 measurements were performed in 27 (25.96%) patients. Overall, 56.84% of INR measurements were within the therapeutic range, similarly to data reported by van Walerven [1], and more than 70% of INR measurements were within the therapeutic range in only 31 patients (according to the literature data, TTR above 70% is considered an indicator of effective anticoagulant treatment).

In a retrospective study evaluating two groups of patients managed in dedicated anticoagulation clinics (one group was consulted over the phone and the other during direct visits to physicians), no significant differences were found between the two groups in regard to INR control, bleeding and embolic events, visits to emergency departments, and admissions related to warfarin treatment [6]. Portable INR monitors that allow patient self-management are already available in some countries. When combined with appropriate training and quality control, these devices allow effective home-based treatment and appropriate VKA dosing in most patients [7, 8].

Similar conclusions were arrived from the THINRS study [9], in which 2922 patients treated with warfarin due to a mechanical valve prosthesis or AF were randomised to weekly INR self-monitoring or monthly evaluation in a specialised unit. After 8730 patient-years of follow-up, no significant difference was found in the rate of a primary combined endpoint that included stroke, major bleeding, and death. In the self-monitoring group, a small but significant improvement in TTR (by 3.8%) and a lower rate of minor bleedings was found.

An example of study with high quality of INR monitoring is the Leiden Thrombophilia Study [10] with TTR of 84% (target INR range was 2.5–3.0). On the other hand, only 50% of INR values were within the therapeutic range in the Connecticut study [11].

The importance of strict INR control was primarily shown in patients with nonvalvular AF (70% of patients in our study group), in whom INR < 2.0 were associated with a substantially increased stroke risk, and INR > 3.0 were associated with a large increase in the bleeding risk [2, 3, 12].

Similar results were obtained in a metaanalysis of 19 studies of oral anticoagulant therapy for various indications, including nonvalvular AF [13].

Three novel oral anticoagulants introduced in the clinical practice in the recent years, dabigatran, rivaroxaban and apixaban, hold promise for a safer and more effective therapy in the future. Candidates for this treatment are primarily those patients who do not achieve therapeutic targets during conventional VKA therapy. In our study population, as many as 70% of patients were found to belong to this group.

Our findings were obtained in a single community population. No evidence is available to suggest that these findings may be extrapolated to other patients groups. A small number of subjects also limited statistical power of the data obtained. We believe, however, that this study calls for further research regarding anticoagulation in Poland to develop effective and safe approaches to this therapy. Large multicentre studies are needed to evaluate the effectiveness of anticoagulant therapy in Poland.

CONCLUSIONS

When we analysed the effectiveness of chronic VKA treatment, only 56.84% of INR values were within the therapeutic range. An acceptable TTR (≥ 70%) was obtained in only just below 30% of patients. In the remaining 70% of patients, therapeutic targets were not met despite treatment and appropriate opportunities for its monitoring.

Conflict of interest: *TD and BW conducted medical trials for BMS and Pfizer.*

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Doustne leczenie przeciwkrzepliwe w warunkach ambulatoryjnych w Polsce: stan na rok 2012 na podstawie doświadczenia jednego ośrodka

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Streszczenie

Wstęp: Doustne leki przeciwkrzepliwe zmniejszają liczbę powikłań zatorowych u pacjentów z migotaniem przedsionków, są także stosowane w leczeniu i profilaktyce żylnej choroby zatorowo-zakrzepowej. W warunkach polskich długotrwała terapia lekami przeciwkrzepliwymi pozostaje w większości przypadków w gestii lekarzy podstawowej opieki zdrowotnej, a preparatami najczęściej stosowanymi są antagoniści witaminy K (VKA).

Cel: Celem badania było określenie skuteczności terapii lekami przeciwkrzepliwymi w grupie 104 pacjentów otrzymujących przewlekle VKA, leczonych w warunkach podstawowej opieki zdrowotnej w okresie od 01.01.2011 do 31.12.2011 r.

Metody: Retrospektywną analizą objęto dane 104 pacjentów przyjmujących przewlekle VKA w okresie od 01.01.2011 do 31.12.2012 r., leczonych w Niepublicznym Zakładzie Opieki Zdrowotnej „ESCULAP" w Gniewkowie. Grupa ta stanowiła 1,1% populacji osób objętych opieką tego ośrodka. Określono minimalne, maksymalne i średnie wartości międzynarodowego wskaźnika znormalizowanego (INR), odsetek wyników znajdujących się w okienku terapeutycznym, liczbę wykonanych badań INR, wskazania do leczenia przeciwkrzepliwego. W przypadku pacjentów z migotaniem przedsionków określono ryzyko powikłań krwotocznych i ryzyko wystąpienia incydentów zakrzepowych.

Wyniki: W grupie chorych otrzymujących przewlekle VKA 56,84% oznaczeń INR mieściło się w oczekiwanym przedziale wartości. Tylko 29,8% osób miało więcej niż 70% oznaczeń INR w przedziale terapeutycznym. Nie wykazano zależności między liczbą wykonywanych oznaczeń INR a skutecznością leczenia.

Wnioski: Skuteczność terapii przeciwkrzepliwej prowadzonej w warunkach podstawowej opieki zdrowotnej jest niezadowalająca. W obserwowanej populacji zakładany efekt leczenia udało się osiągnąć u niespełna 30% pacjentów.

Słowa kluczowe: leczenie przeciwkrzepliwe, ryzyko krwawień, ryzyko powikłań zakrzepowych, skuteczność terapii, podstawowa opieka zdrowotna.

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