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ORIGINAL ARTICLE

COMPLICATIONS AT USAGE OF THE NEW ANTICOAGULANT THERAPY IN ELDERLY PATIENTS

KOMPLIKACIJE PRIMENE NOVE ANTIKOAGULANTNE TERAPIJE

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Abstract

Introduction: New anticoagulant therapy (DOAC) was introduced few years ago. It is an alternative therapy for antagonists of vitamin K (VKA) in prevention and therapy of diseases with different etiology. Despite their advantages, bleeding stays a major complication. The fact is that there are no significant researches on this topic.
Aim: To analyze the incidence of bleeding as a complication in patients treated with dabigatran.
Material and methods: A retrospective study was conducted including 60 patients older than 65 years with nonvalvular atrial fibrillation treated with anticoagulant therapy. Half of this number was taking dabigatran (examined group) and half was taking warfarin (control group). Apart from demographical and clinical parameters, incidence, type and localization of bleeding was also followed.
Results: In the group of patients who were taking dabigatran, in 13.3% of cases bleeding occurred as a complication of therapy. Among them, gastrointestinal bleeding was the most common (75%), but also hematomas on the body occurred (25%) and the therapy was immediately discontinued. In 45% of patients taking warfarin, bleeding was verified as a complication. From that number, 33.5% had gastrointestinal bleeding and epistaxis, 8.6% hematomas and 24.4% hematuria. By comparing these two groups, it can be concluded that incidence of bleeding in the group taking dabigatran was significantly lower than in the group taking warfarin ($p = 0.038$).
Conclusion: In the examined group of patients older than 65, who were taking dabigatran, a significantly lower percentage of bleeding as a complication was noticed, compared to the control group taking VKA.

Keywords:
new anticoagulant therapy,
bleeding,
elderly

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Sažetak

Uvod: Nova antikoagulantna terapija (NOAKT) uvedena je u upotrebu pre nekoliko godina. Predstavlja alternativu za antagoniste vitamina K (OAKT) u prevenciji i lečenju tromboza različite etiologije. I pored njihovih prednosti, krvarenje ostaje značajna komplikacija, posebno kod starijih osoba. Činjenica je da nema dovoljno istraživanja u vezi s ovim problemom.

Cilj: Analizirati učestalost krvarenja kao komplikacije primene dabigatrana.

Materijal i metode: Od ukupno 60 bolesnika starijih od 65 godina sa nevalvularnom atrijalnom fibrilacijom (AF) koji su uzimali antikoagulantnu terapiju, u ovoj retrospektivnoj studiji polovina njih je primala direktne oralne antikoagulante (dabigatran; ispitivana grupa), a druga polovina antagoniste vitamina K (varfarin; kontrolna grupa). Pored demografskih i kliničkih, praćeni su parametri krvarenja (učestalost, vrsta/lokalizacija).

Rezultati: U grupi ispitanika koji su uzimali dabigatran kod 13,3% su verifikovana krvarenja kao komplikacija uzimanja terapije – GIT krvarenja (75%) i hematomi po telu (25%). Kod 45% ispitanika koji su uzimali varfarin je verifikovano krvarenje kao terapijska komplikacija – GIT krvarenje (33,5%), epistaksa (33,5%), hematomi po koži (8,6%), a hematurija kod 24,4% bolesnika. Statistički, učestalost pojave krvarenja kao posledice terapije značajno je manja u grupi bolesnika koji su tretirani dabigatranom (p = 0,038)

Zaključak: U ispitivanoj grupi bolesnika starijih od 65 godina i atrijalnom fibrilacijom koji su koristili dabigatran registrovan je značajno manji broj krvarenja kao komplikacija u odnosu na grupu lečenu varfarinom.

Ključne reči:
nova antikoagulantna terapija,
krvarenje,
starija populacija

Introduction

Direct oral anticoagulant therapy (DOACT) was introduced few years ago. One of the commonly used drugs is dabigatran whose mechanism of action is direct inhibition of thrombin. This therapy represents an alternative for antagonist of vitamin K (VKA) in prevention and treatment of thromboembolism with different etiology. The dosage of these medicaments is fixed. Their effect starts between 1 - 4 hours, they are less interactive with other medicaments than VKA and diet changing is not obligatory. During usage of these medicaments, there is no need to check INR (The International Normalized Ratio) value which is time and stress relieving for the patients to VKA, especially at elderly patients (1). This group of medicaments is becoming a gold standard in therapy of atrial fibrillation and prevention of thromboembolism (2).

Despite their advantages, the bleeding remains a significant complication. Although, a lot of studies states that frequency of bleeding while using DOACT is lower than while using VKA (3), elderly patients have numerous comorbidities which makes the risk of bleeding a significant problem. They have lower BMI, lower muscle mass, changes in glomerular filtration, different comorbidities which contribute to more frequent interactions between medicaments, and also require special dosage (4, 5).

There are just a few randomized controlled studies connected with risk of bleeding specifically in elderly population (6).

The main aim of this study is to determine whether DOAC is a better and safer choice for elderly patients with AF, in terms of bleeding complications.

Materials and Methods

Retrospective study was conducted during this research which included 60 patients older than 65 years with nonvalvular atrial fibrillation (AF), which were treated with anticoagulant therapy. A half of these patients were treated with dabigatran (examined group) and the other half was treated with warfarin (control group). Dosage of dabigatran was 2 x 110mg. None of the examinees had chronic renal failure (all patients had CrCl > 80ml/min). Patients were treated and controlled on Gerontology Department of Internal Medicine at KBC „Zvezdara“ from January 2018 until December 2019. The following parameters were followed: frequency and type of bleeding - gastrointestinal bleeding, melena, epistaxis, hematoma (as the complication of therapy), age of patients, gender, presence of cardiomyopathy, average duration of treatment, and potential thromboembolic events. None of them had previous bleeding in their anamnesis. The value of HAS - BLED score was also calculated. It is a score that indicates the risk of bleeding and the value > 3 indicates high risk. When calculating score presence of each of this parameter gives one point: hypertension, renal/hepatic insuficience, previous stroke, previous bleeding, unstable value of INR, age > 65 years, consumption of drugs and alcohol.

A statistical evaluation of obtained data was done (Hi square test) in order to find out if there were statistically significant differences and occurrence of bleeding in these two groups of patients ($p < 0.05$).

Results

Group of patients which was treated with dabigatran included 30 patients (15 woman (50%)) with the average age of 74.4 ± 5.2. Majority had been diagnosed with cardiomyopathy (70%). Average duration of usage of dabigatran was 9 months, with only two patients using therapy up to 24 months in a row.

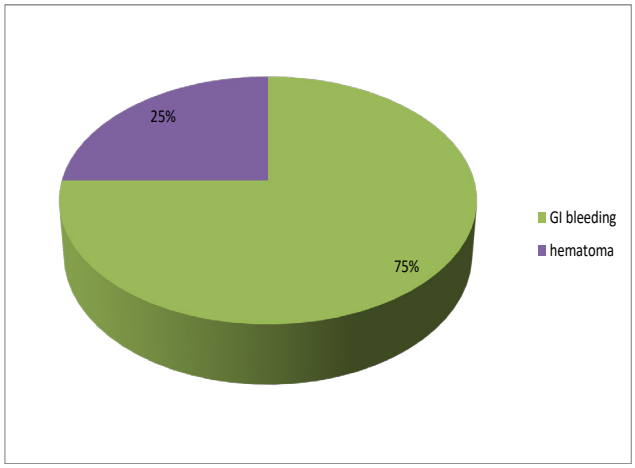

Figure 1. Types of bleeding as a complication of dabigatran (GI- gastrointestinal bleeding)

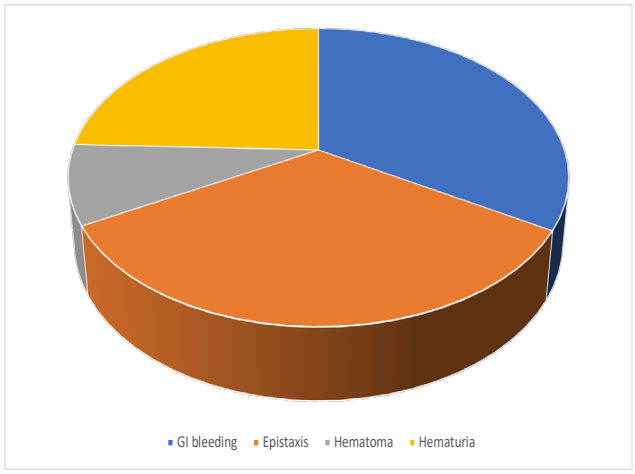

Figure 2. Types of bleeding as a complication of treatment with vitamin K antagonist

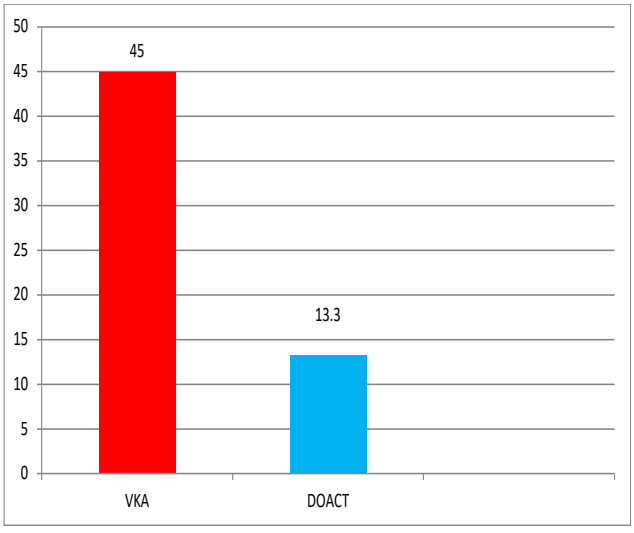

Figure 3. Rate of bleeding in patients treated with different anticoagulant therapy

In DOACT group, in 13% of patients, bleeding was verified as the consequence of treatment. Bleeding manifestations were gastrointestinal (75%) and hematoma on the skin (25%), so the treatment was discontinued (**figure 1**). The value of INR stayed stabile at 95% of patients. The aPTT was increased at 45% of patients. The mean value of HAS - BLED in this group is 3.9.

Group of patients which was treated with warfarin included also 30 patients with equal percentage of both genders, with the average age of 81.3 ± 3.8 years. Presence of the cardiomyopathy was verified at 66.7% of patients. Bleeding was verified as the complication at 45% of patients. Bleeding manifestation were gastrointestinal (33.5%), epistaxis (33.5%), hematoma on the skin (8.6%) and hematuria (24.4%) (**figure 2**). The mean value of HAS - BLED score in this group is 3.4.

During statistical analysis it was determined that there is no statistically relevant difference between the group of patients treated with dabigatran and group of patients treated with warfarin in terms of age ($p = 0.702$).

Also, there is no statistically relevant difference in value of HAS - BLED score between these groups.

Patients treated with dabigatran had significantly fewer bleeding events than patients treated with warfarin (Hi-square = 4.286; $p = 0.038$) (**figure 3**).

Discussion

Analyzing the literature, different results may be found. Some studies have shown that in patients aged ≥65 years with atrial fibrillation, treated with dabigatran, there was less hospitalization occurrence than in patients treated with VKA (7). Additional studies show higher risk of bleeding in elderly while using DOACT, but lower rate of mortality (8). Others claim that morbidity rate is lower and risk of cerebrovascular hemorrhage is lower with the usage of the DOACT (9).

Similar studies show lower risk of bleeding in patients with atrial fibrillation who were treated with dabigatran, in comparison with patients treated with rivaroxaban, but without significant difference in occurrence of cerebrovascular insult (10). One Japanese study shows lower risk of occurrence of bleeding in patients treated with DOACT, in comparison with patients treated with VKA, but there was the same mortality rate and the same occurrence of cerebrovascular insult (11). Also, there is a study that does not show any statistically relevant difference in occurrence of bleeding between two groups (12).

Administrating anticoagulant therapy in elderly poses a risk itself due to fear of bleeding. That is the reason why numerous physicians do not prescribe DOACT to elderly patients. It is important to emphasize that elderly patients are at greater risk of occurrence of thromboembolism, so the therapy is in this case needed (13).

Results acquired during this study are encouraging. Lower risk of bleeding and more comfortable usage potentially brings better prevention of thromboembolism at elderly patients following lower risk of fatal outcome.

Conclusion

In the examined group of patients older than 65 years, there was a significantly lower percent of verified bleeding as the complication of the usage of DOACT (dabigatran), in comparison with the group of patients using warfarin.

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