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ИЗУЧЕНИЕ ЧАСТОТЫ РАЗВИТИЯ МИКРОГЕМАТУРИИ
У ПАЦИЕНТОВ, ПОЛУЧАЮЩИХ РИВАРОКСАБАН: ВЛИЯНИЕ
СОПУТСТВУЮЩИХ ЗАБОЛЕВАНИЙ

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EXAMINING THE INCIDENCE OF MICROHEMATURIA
IN PATIENTS RECEIVING RIVAROXABAN: THE IMPACT
OF COMORBIDITIES

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Резюме. Тромбоэмболические заболевания представляют собой значительную клиническую проблему, особенно у пациентов с фибрилляцией предсердий (ФП), при которой наблюдается высокий риск тромбообразования. Профилактика тромбообразования достигается применением антикоагулянтов, прием которых сопряжен с развитием кровотечения. В этом исследовании изучается частота микрогематурии во время лечения антикоагулянтом ривароксабаном у пациентов с неклапанной ФП и коморбидной патологией, такой как сахарный диабет (СД) и хроническая болезнь почек (ХБП).

Ключевые слова: фибрилляция предсердий, ривароксабан, микрогематурия, хроническая болезнь почек, сахарный диабет.

Resume. Thromboembolic diseases represent a significant clinical challenge, particularly in patients with atrial fibrillation (AF), a disorder that raises the risk of blood clots. Prevention of thrombus formation is achieved by the use of anticoagulants, the use of which is associated with the development of bleeding. This study examines the incidence of microhematuria in patients with nonvalvular AF receiving rivaroxaban, focusing on the impact of comorbidities such as diabetes mellitus (DM) and chronic kidney disease (CKD).

Keywords: atrial fibrillation, rivaroxaban, microhematuria, chronic kidney disease, diabetes mellitus.

Relevance. Vital organs may be affected by the blood clots, which could result in life-threatening consequences like myocardial infarction, pulmonary embolism, stroke, peripheral artery ischemia. The risk of thrombus formation is five times higher in patients with AF. To prevent thromboembolic events in these patients it is necessary to prescribe anticoagulants. The management of anticoagulation requires a careful balance between reducing thromboembolic risk and minimizing major bleeding consequences. Major bleeding frequently follows after a minor bleed. It is revealed that minor bleeds have a 2.5-fold increased risk of major bleeds. So, it is important to notice the signs of this event in time.

Rivaroxaban, an oral Xa factor inhibitor, works by inhibiting a vital component in the coagulation cascade. It efficiently lowers the production of fibrin clots by blocking the conversion of prothrombin to thrombin. This anticoagulant has been demonstrated to be successful in lowering the risks of thromboembolism but not the risk of bleeding. Despite the medication's advantages patients on anticoagulant therapy may have bleeding issues. A possible minor bleeding event that needs to be looked at is microhematuria, which is described as having more than 3 erythrocytes per high-power field in a urinalysis, especially in individuals with other comorbidities.

Comorbidities such as diabetes mellitus (DM) and chronic kidney disease (CKD) are prevalent in AF patients, which can make their management more challenging. While CKD may impact drug metabolism and excretion, potentially raising the likelihood of side effects from anticoagulants, DM might cause vascular alterations, increasing the risk of bleeding.

Aim: to examine the incidence of microhematuria in patients receiving rivaroxaban, with an emphasis on the impact of coexisting illnesses such as DM and CKD.

Objectives:

1. Conduct a retrospective analysis of patients who were prescribed rivaroxaban.
2. Investigate the incidence of microhematuria and its correlation with comorbidities.
3. Review relevant literature to support findings.

Materials and methods. A retrospective analysis was carried out at Clinical Hospital 4 in Minsk, Belarus, between the 1st of January 2022 and 31st of August 2022, involving 115 patients with coronary artery disease and nonvalvular AF who were prescribed a daily dosage of 20 mg of rivaroxaban. The group included 47 individuals with stage 3 and 4 of CKD and 27 patients with DM. The participants median age was 71 years, with the first quartile at 63 years and the third quartile at 80 years.

Microhematuria was defined as 3 or more red blood cells per high-powered field on microscopic evaluation of a single, properly collected urine specimen. Acceptable urine specimens were identified in 91 patients (21% patients with DM and 44% patients with 3 or 4 stage of CKD).

Chi-square testing was used to investigate the association between microhematuria and various patient demographics and comorbidities. A p-value less than 0.05 was considered statistically significant.

To support the findings, literature from 2014 to 2024 was searched in PubMed and Google Scholar using relevant keywords.

Results and their discussion. Incidence of Microhematuria

There were no cases of macrohematuria among analyzed patients. Microhematuria was revealed in 39 (41.85%) patients of the 91 eligible individuals. Ten (10.98%) of these patients had diabetes, whereas the remaining 29 did not ($p > 0.05$). In addition, 16 (17.58%) patients with CKD and 22 (24.17%) patients with 1 or 2 stage of CKD presented with microhematuria ($p > 0.05$) (fig. 1). Notably, the investigation found no major problems with rivaroxaban treatment in this population.

Analysis of Comorbidities

The findings indicate that the presence of DM and CKD had no significant correlation with the incidence of microhematuria. This shows that, while these comorbidities

present distinct issues in patient treatment, they may not always worsen the incidence of bleeding in rivaroxaban treated patients.

Interpretation of Findings

The low incidence of microhematuria in individuals using rivaroxaban is encouraging, especially given the high risk of this patient population. The absence of major problems implies that rivaroxaban can be provided safely, especially in patients with diabetes and chronic kidney disease.

Clinical Implications

Understanding the prevalence and potential risk factors for microhematuria is critical for clinicians who prescribe rivaroxaban. It emphasizes the importance of regular renal function and urinalysis in anticoagulant therapy patients, particularly those with pre-existing diseases.

Individualized Patient Management

Given the complexities surrounding anticoagulant therapy, individualized patient management remains essential. Clinicians must evaluate each patient risk variables, including comorbidities, to design treatment strategies that maximize efficacy while minimizing the risk of side effects.

Conclusions:

1. The current study found that diabetes mellitus and chronic kidney disease do not have a significant impact on the occurrence of microhematuria in patients receiving rivaroxaban.

2. Further research is needed to understand the mechanisms and discover other potential risk factors for microhematuria in the context of anticoagulant therapy. Improved understanding could lead to more personalized patient treatment strategies and better outcomes.

Literature

1. Increased risk of major bleeding after a minor bleed during treatment with vitamin K antagonists is determined by fixed common risk factors. /van Rein N [et al]//J Thromb Haemost. – 2016. – Vol. 14, iss. 5. – P. 948-952.

2. Vimalasvaran, K. Role of rivaroxaban in the management of atrial fibrillation: insights from clinical practice. / K.Vimalasvaran, S. J.Dockrill, D. A. Gorog //Vascular Health and RiskManagement. – 2018. – P. 13-21.

3. Rivaroxaban versus dabigatran or warfarin in real-world studies of stroke prevention in atrial fibrillation: systematic review and meta-analysis. /Y.Bai [et al]// Stroke. – 2017. – Vol. 48, iss. 4. – P. 970-976.

4. Analysis of effectiveness, safety, and bleeding related to rivaroxaban in elderly patients. /H.Hou[et al]// Clin Appl Thromb Hemost. – 2020. – 26:1076029620925923. – DOI: 10.1177/1076029620925923.

5. Khodashahi, M. Comparison of the therapeutic effects of rivaroxaban versus warfarin in antiphospholipid syndrome: a systematic review. / M.Khodashahi, Z.Rezaieyazdi, M. Sahebari // Archives of rheumatology. – 2019. – Vol.35, iss. 1. – P. 107.

6. Assessment and mitigation of bleeding risk in atrial fibrillation and venous thromboembolism: A Position Paper from the ESC Working Group on Thrombosis, in collaboration with the European Heart Rhythm Association, the Association for Acute CardioVascular Care and the Asia-Pacific Heart Rhythm Society. / D. A.Gorog [et al] //Europace. – 2022. – Vol. 24, iss. 11.- P. 1844-1871.

7. Singh, R. Rivaroxaban [Электронный ресурс] / R. Singh, P. D. Emmady // StatPearls. – Treasure Island (FL) : StatPearls Publishing, 2023. – Режим доступа: <https://www.ncbi.nlm.nih.gov/books/NBK557502>. – Дата доступа: 10.03.2025.
8. Mechanistic basis for the differential effects of rivaroxaban and apixaban on global tests of coagulation. /P. Y Kim [et al] //TH Open. – 2018. – Vol.29, iss. 2:e190-e201. - DOI: 10.1055/s-0038-1649507.
9. Bauersachs, R. Rivaroxaban: a new treatment paradigm in the setting of vascular protection? / R.Bauersachs, F.Zannad//Thrombosis and Haemostasis. – 2018. – Vol. 118, suppl. S 01. - S12-S22.
10. Saraiva, J. F. K. Stroke prevention with oral anticoagulants: summary of the evidence and efficacy measures as an aid to treatment choices. / J. F. K. Saraiva //Cardiology and therapy. – 2018. - Vol.7, iss. 1. -P.15-24.
11. Rivaroxaban vs. vitamin K antagonists for cardioversion in atrial fibrillation. / R.Cappato [et al] //European heart journal. – 2014. – Vol. 35, iss. 47. – P. 3346-3355.