МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
БУКОВИНСЬКИЙ ДЕРЖАВНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ
ДЕПАРТАМЕНТ ОХОРОНИ ЗДОРОВ'Я ЧЕРНІВЕЦЬКОЇ ОБЛАСНОЇ ДЕРЖАВНОЇ АДМІНІСТРАЦІЇ
ГРОМАДСЬКА ОРГАНІЗАЦІЯ «АСОЦІАЦІЯ ТЕРАПЕВТІВ БУКОВИНИ»

Науково-практична конференція з міжнародною участю

«АКТУАЛЬНІ ПРОБЛЕМИ КОМОРБІДНОСТІ У КЛІНІЦІ ВНУТРІШНЬОЇ МЕДИЦИНИ»

ТЕЗИ ДОПОВІДЕЙ

присвячена 100-річчю від Дня народження
професора Самсон Олени Іларіонівни

м. Чернівці
15-16 квітня 2021 року

УДК: 616.1/.4-008.9-07-08(063)
ББК: 54.15я434
М54

Актуальні проблеми коморбідності в клінці внутрішньої медицини: Матеріали науково-практичної конференції з міжнародною участю (Чернівці, 15-16 квітня 2021 р.) – Чернівці: Медуніверситет, 2021. – 168 с.

У збірнику представлені матеріали тез науково-практичної конференції з міжнароднлю участю «Актуальні проблеми коморбідності в клінці внутрішньої медицини» (Чернівці, 15-16 квітня 2021 р.) із стилістикою та орфографією у авторській редакції. Публікації присвячені актуальним проблемам гастроентерології, кардіології, нефрології, пульмонології, ревматології. Наукова та загальна редакція – професор, д.мед.н. О.І.Федів

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Буковинський державний
медичний університет, 2021

УДК 616.12-008.46-036.1:[612.018:616.15]:615.363:615.22

MODERN POSSIBILITIES TARGETING THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM BLOCKADE IN PATIENTS WITH CHRONIC HEART FAILURE: FOCUS ON VALSARTAN

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Background. The prevalence of chronic heart failure (CHF) has reached a pandemic level, and its further growth is projected. Commonly, the patients with heart failure have a significant level of co-morbidities, and comorbidity index increases with age. In such patients, it is important to avoid polypharmacy to maintain a satisfactory adherence to the recommended treatment. Therefore, it is better to choose drugs that act simultaneously on the common links in the pathogenesis of CHF and other cardiovascular pathology. Use of sartans, which affect the main pathogenetic links of both CHF and comorbid conditions, is justified in terms of reducing the total number of drugs taken by the patient, which, consequently, decreases the economic burden on the patient and improves adherence to treatment. The latter, in turn, will help improve the quality of life, reduce the number of hospitalizations and make the prognosis better.

The aim. To analyze the literature regarding valsartan to reveal its benefits compared to other drugs affecting the renin-angiotensin-aldosterone system activity in the treatment of the patients with CHF.

Materials and methods. A search and analysis of available literature sources for the last 30 years in the PubMed database using a combination of keywords "chronic heart failure", "valsartan", "sartan" was conducted. According to the search results, 123 articles were selected for detailed analysis.

Results. Activation of the renin-angiotensin-aldosterone system (RAAS) is one of the key common links in the pathogenesis of CHF and the diseases that led to its occurrence (hypertension (AH), coronary artery disease (CAD), or complicated its course (chronic kidney disease (CKD), arrhythmias). Therefore, it is reasonable to prescribe drugs inhibiting this activation, which has been shown to reduce the frequency of hospitalizations and improve survival in

patients with CHF. It is known that ACE inhibitors do not completely block the production of angiotensin II (ATII), because its synthesis can occur through alternative enzymatic pathways (chymases and other proteases). And this alternative production increases in case of prolonged use of ACE inhibitors. In contrast to ACE inhibitors, ATII receptor blockers (ARBs) achieve the desired effect by blocking type 1 receptors to ATII, neutralizing the effects of the latter, regardless of how it was synthesized. In addition, ARBs do not have the kinin-dependent side effects (dry cough and angioedema) may occur with ACE inhibitors and cause a decrease in the treatment adherence. Essential thing to remember is that there are several types of ATII receptors. Cardiovascular effects of ATII are realized through receptors of 1 and 2 types, and their stimulation leads to opposite manifestations. Therefore, not only the ability to block ATII receptors matters, but also the selectivity of it. In valsartan, this selectivity is the most pronounced of all ARBs: its affinity for type 1 receptors is 20,000 times greater than for type 2 ones, which means it securely blocks the negative effects of ATII mediated by type 1 receptors, having almost no influence on the effects mediated by type 2 receptors. However, ARBs differ not only in the selectivity of the receptors block, but also in the strength of this block. Unlike most of the ARBs, valsartan causes non-competitive antagonism, which is better, because in this case the receptor remains inactive even when the blood concentration of ATII rises. Another major aspect of the ARBs action, which distinguishes them one from another, is the effect on the synthesis of aldosterone, increased blood concentration of which is one of the key links in the pathogenesis of CHF. This effect is mediated via ATII receptors in two independent ways: through the G protein and β-arrestin-dependent pathway. Only a complete block of both pathways will inhibit aldosterone synthesis, but not all ARBs equally affect the β-arrestin pathway. Valsartan is one of the most potent sartans in blocking the synthesis of aldosterone, also due to inhibition of the β-arrestin pathway.

Conclusion. Blockade of RAAS with ARBs, on the one hand, affects the common link in the pathogenesis of CHF, AH, CAD, CKD, reducing the number of drugs has to be taken by patient, and, on the other hand, does not cause the "ACE escape" and side effects inherent in ACE inhibitors. However, not all sartans are the same in clinical and pharmacological effects. Valsartan`s ability

to irreversibly bind ATII type 1 receptors makes its effects more stable even at the high blood concentrations of ATII. Given the complex hormonal interaction underlying the pathogenesis of CHF, in which ATII and aldosterone play central roles, it is reasonable to prescribe a drug that would affect both participants in this process simultaneously. The potential of valsartan to block the alternative (β- arrestin) pathway of aldosterone synthesis in the adrenal glands distinguishes it from other ARBs in the treatment of CHF.