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ABSTRACT

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COVID-19, LIPID PROFILE DISORDERS, RENIN-ANGIOTENSIN-ALDOSTERON SYSTEM IMBALANCE: PECULIARITIES OF PATHOGENESIS AND TREATMENT (LITERATURE REVIEW)

Objective: The present study aimed to determine the peculiarities of pathogenesis and treatment of patients with lipid profile disorders, renin-angiotensin-aldosteron system imbalance and coexistent COVID-19.

Materials and methods. Articles published in 2020-2025 in the PubMed, Scopus, and Google Scholar electronic databases were analyzed.

The limitations of the review are narrative character of the work, different type and design of analyzed publications, parameters of the patients, the presence of conflicting results regarding to the effectiveness of individual therapeutic approaches.

Results and discussion. The connection between severe acute respiratory syndrome coronavirus 2 and angiotensin-converting enzyme 2 leads to the inactivation of this enzyme, increased vasoconstriction and progression of arterial hypertension.

The increased levels of serum amyloid A in patients with COVID-19 displace ApoA-I situated on high density lipoprotein, which leads to the impairment of reverse cholesterol transport, disorders of endothelium and promotion of oxidative stress.

Prescription of rosuvastatin is considered for patients with COVID-19 if it is indicated because of antiinflammotory properties, protection of endothelial cells and further reduction the risk of hospitalization and mortality. Evidence suggests that prolongation of treatment with rosuvastatin is effective for people which have received it before because of lipid profile disorders, coexistent ischemic heart disease, heart failure or increased cardiovascular risk.

The continuation of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ramipril, losartan, valsartan)

prescribed previously for treatment of arterial hypertension, heart failure, coexistent lipid profile disorders during hospitalization in patients with COVID-19 as associated with decreased mortality.

Not all clinical trials suggested the improvement of clinical outcomes and mortality rate after using statins and renin-angiotensin-aldosteron system inhibitors.

Conclusions. Management with rosuvastatin, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers prescribed previously because of arterial hypertension, lipid profile disorders, heart failure, ischemic heart disease and increased cardiovascular risk may be beneficial to continua or initiation treatment with those drugs at first in patients with COVID-19 if contraindications are absent because these changes become more severe in the case of such comorbidity for achievement the goal ranges of blood pressure and low density lipoproteins, improvement of endothelial function, reduction the progression of oxidative stress, decrease mortality and prevention of cardiovascular complications.

Keywords: dyslipidemia, COVID-19, angiotensin-converting enzyme 2, statins.

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COVID-19, ПОРУШЕННЯ ЛІПІДНОГО СПЕКТРУ, ДИСБАЛАНС РЕНІН-АНГІОТЕНЗИН-АЛЬДОСТЕРОНОВОЇ СИСТЕМИ : ОСОБЛИВОСТІ ПАТОГЕНЕЗУ ТА ЛІКУВАННЯ (ОГЛЯД ЛІТЕРАТУРИ)

Мета: Дослідження проведене з метою вивчення особливостей патогенезу та лікування пацієнтів із порушеннями ліпідного спектру, дисбалансом ренін-ангіотензин-альдостернової системи та супутньою інфекцією COVID-19.

Матеріали та методи: Проаналізовано статті, опубліковані протягом 2020-2025 рр у електронних базах даних PubMed, Scopus, and Google Scholar.

Обмеження огляду: наративний характер роботи, неоднорідність включених досліджень, відмінності у дизайні досліджень та характеристиках пацієнтів, наявність суперечливих результатів щодо ефективності окремих терапевтичних підходів.

Результати та їх обговорення. Рецептор на SARS-CoV-2 зв'язується з рецептором до ангіотензин-перетворюючого ферменту 2, інактивуючи його та призводячи до стимуляції перетворення ангіотензину I у ангіотензин II, спазму судин, підвищення артеріального тиску, що потребує його моніторингу та зниження за допомогою антигіпертензивної терапії.

Підвищення вмісту білків сироваткового амілоїду А у пацієнтів із COVID-19 сприяє заміщенню аполіпопротеїну А-I, розташованого на поверхні холестерину ліпопротеїдів високої щільності, порушенню їх функцій, які полягають у транспортуванні холестерину з периферичних тканини до печінки, покращенні антиоксидантної активності ендотелію, що обумовлює необхідність ліпідознижуючої терапії.

Призначення розувастатину може розглядатися за наявності відповідних клінічних показань для пацієнтів із COVID-19, а

продовження його прийому показане у разі попереднього застосування з приводу верифікованих порушень ліпідного спектру крові, супутньої ішемічної хвороби серця, серцевої недостатності або підвищеного кардіоваскулярного ризику.

Пролонгація терапії інгібіторами ангіотензин-перетворюючого ферменту/блокаторами рецепторами до ангіотензину (раміприлом, лозартаном, валсартаном) показана у хворих на артеріальну гіпертензію, серцеву недостатність, дисліпідемію, госпіталізованих з приводу COVID-19.

Не всі рандомізовані контрольовані дослідження підтвердили зниження смертності або покращення клінічних наслідків на тлі терапії статинами.

Висновок. Продовження прийому розувастатину, інгібіторів ангіотензин-перетворюючого ферменту/блокаторів рецепторів до ангіотензину, призначених попередньо у зв'язку з наявністю артеріальної гіпертензії, порушень ліпідного спектру крові, серцевої недостатності, ішемічної хвороби серця та підвищеного серцево-судинного ризику або первинне їх застосування доцільне у хворих на COVID-19 за відсутності протипоказань з метою досягнення цільових рівнів артеріального тиску, покращення функціонального стану ендотелію, зниження вираженості оксидативного стресу, зменшення рівня смертності та попередження кардіоваскулярних ускладнень.

Ключові слова: дисліпідемія, COVID-19, інгібітори ангіотензин-перетворюючого ферменту, статини.

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INTRODUCTION

Today a lot of people are still infected by Coronavirus disease-19 (COVID-19) which has been appeared five years ago and provoked a lot of disorders, invalidization and dearth [1].

Dyslipidemia potentially increases mortality and severity of COVID-19. Moreover, the association was stronger in old age men with arterial hypertension (AH) [2]. A large observational study of more than 2 millions people with COVID-19 reported that dyslipidaemia was determined in three percents of patients after the first month of infection [3]. In addition, there was the association between duration of staying in hospital and appearance of lipid profile disorders [4]. Choi et al. suggested that lipid profile disorders may play a significant role in the severity of COVID-19 [5].

Jiang X. et al. have demonstrated that in the case of absence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, angiotensin-converting enzyme 2 (ACE 2) has nephroprotective action. But the age-related increase of its expression within lungs and kidneys may be relevant to the risk of COVID-19 [6]. SARS-CoV-2 uses ACE 2 as a cellular entry receptor [7].

SARS-CoV-2 causes imbalance between ACE 1 and ACE 2, renin-angiotensin-aldosteron system (RAAS) activation, which leads to COVID-19 progression, especially in patients with comorbidities, such as AH, diabetes mellitus, and cardiovascular diseases (CVD) [8].

Resultly in people with COVID-19 it is considerable to continue using drugs for inhibition of RAAS previously prescribed for management of such coexistent pathology.

Therefore, SARS-CoV-2-mediated endothelial dysfunction and impaired vascularization induced by chronic diseases increase the appearance of CVD. Pre-existing comorbidities may also be directly associated to higher rates of SARS-CoV-2 organ damage, as demonstrated in post-mortem analyses of the lungs, pharynx, kidneys, liver, and heart [9].

COVID-19 is associated with long-term cardiovascular (CV) complications, potentially driven by persistent inflammation, coagulopathy, and endothelial dysfunction [10].

The understanding the peculiarities of SARS-CoV-2 action on lipid profile and RAAS is reasonable for

further treatment of such patients especially with comorbidities.

MATERIALS AND METHODS. The authors have analysed 46 articles written in 2020-2025 in PubMed, Scopus, and Google Scholar. In general we have found 95 publications. There are comprehensive reviews; meta-analyses; RCTs; prospective cohort studies; case-control studies; multicenter, prospective studies; international, open science, cohort analysis; prospective, parallel group, randomised, controlled, open-label trial among them.

Data were retrieved using predefined keywords “dyslipidemia”, “COVID-19”, “angiotensin-converting enzyme 2”, “statins”, “lipid profile disorders”, “renin-angiotensin-aldosteron system”, “angiotensin-converting enzyme inhibitors”, “angiotensin receptor blockers”.

The inclusion criteria are COVID-19, arterial hypertension, hypercholesterolemia, dyslipidaemia, stroke in anamnesis, chronic kidney disease, coronary artery disease, type 2 diabetes mellitus.

The exclusion criteria are cancer, organ transplantation, acute kidney injury, and other infection diseases in the period of exacerbations.

THE LIMITATION OF THE REVIEW are narrative character of the work, different type and design of analyzed publications, parameters of the patients, the presence of conflicting results regarding to the effectiveness of individual therapeutic approaches.

RESULTS AND DISCUSSION

Relationship between ACE 2 and COVID-19

The inflammatory response in moderate and severe COVID-19 has been variously described as a pro-inflammatory cytokine storm [11]. There are the elevation of interleukin (IL)-6, IL-8 and IL-1β, D-dimer, IL-37 [12, 13, 14], activation of coagulation pathways and extracellular trap formation [11].

A lot of people with lipid profile disorders have confirmed AH. RAAS inhibitors in combination with calcium channel blockers CCBs or diuretics are the first-line therapy for treatment of AH [15].

We try to analyze relathionship between the RAAS and COVID-19 for better understanding the advantages and disadvantages of using ACE inhibitors and ARB for reduction of BP and systemic inflammation in people with such comorbidity.

SARS-CoV-2 enters into host cells after binding with ACE 2 receptor [16], and both SARS-CoV-2 and ACE 2 are assimilated by endocytosis. The surface of the last one is downregulated, resulting in Ang II accumulation [17] and overactivation of RAAS [18].

In physiological conditions, the ACE metabolizes angiotensin I (Ang I) to angiotensin II (Ang II). The last one increases vasoconstriction, inflammation, fibrosis, lung damage and edema. ACE 2 inactivates Ang I and protect vessels from the actions of this enzyme. SARS-CoV-2 reduses the expression of ACE2, which leads to overactivation of lung damage and edema [18], conversion of Ang I in Ang II, which lead to vasoconstriction.

The ACE 2 receptors are particularly overexpressed on intestinal epithelial cells of the gut, endothelial and smooth cells of blood vessels, heart (adipocytes, fibroblasts, myocytes, coronary arteries), lung (macrophages, bronchial and tracheal epithelial cells, type 2 pneumocytes), brain, testis, and tubular epithelial cells in kidneys [19].

ACE2 is a transmembrane protein which involved in counterbalancing the function of ACE [20]. There are two parts of it. They are the N-terminal extracellular protease ectodomain and a short cytoplasmic C-terminus. Protease enzymatic activity is situated in the ectodomain called protease domain, containing the carboxypeptidase catalytic site. The receptor binding site for SARS-CoV-2 is more toward the N-Terminus, involving the N-terminal helix [21;22].

A coronavirus has spike proteins, commonly called S-protein, distributed on its lipid layer. It has two functional units called S1 and S2. While S1 contains the receptor-binding domain (RBD) for binding to ACE 2 [23]. Connection between spike protein RBD and ACE 2 brings the virion into proximity with the host cell surface membrane. It induces conformational changes in this domain that initiate the process of membrane fusion [21;24]. Spike protein facilitates entry into the cell with subsequent damage by alveolar macrophages [25].

Furthermore, we suggest that SARS-CoV-2 infection considered as a dual phase phenomenon. Therefore, in the first phase, expression a higher number of ACE 2 receptors stimulate the viral penetration. In the second phase of infection, ACE 2 receptors may be protective of SARS-CoV-2 mediated acute lung injury [18].

ACE 2 targeted strategy could be employed as a potential therapeutic intervention for the treatment of COVID-19 disease [19;26;27].

In conclusion, SARS-CoV-2 connects with ACE 2 and inactivate it which leads to the conversation of Ang I to Ang II and increased constriction of vessels. The action of ACE is also the stimulation of this conversation. Based on this finding it is reasonable to continua prescription of ACE inhibitors in patients with COVID-19 for reduction vasoconstriction and prevent cardiovascular complications in future.

Lipoprotein changes in COVID-19

The level of high density lipoprotein-cholesterol (HDL-C) is low in COVID-19 patients with dyslipidemia [28; 29] and independently associated with

severity and mortality [30]. These particles have the greatest affinity for binding and neutralization of pathogen-associated lipids (eg, lipopolysaccharide, lipoteichoic acid) that mediate the excessive immune activation [25;31].

HDL also induces the production of cyclooxygenase-2, which is responsible for secretion of anti-inflammatory prostaglandins [32].

It has been suggested that overactivation of immune system due to SARS-CoV-2 infection causes a surge of proinflammatory factors, referred to as "cytokine storm," resulting in host organ damage, such as increased endothelial and epithelial permeability of the lungs, impaired gas exchange and severe respiratory failure with a high mortality rate [25;33;34].

The inflammation due to cytokine storm, immune response and vascular dysfunction are the main factors of long COVID. The key links between SARS-CoV-2, obesity, dyslipidemia are determined on Figure 1 [35].

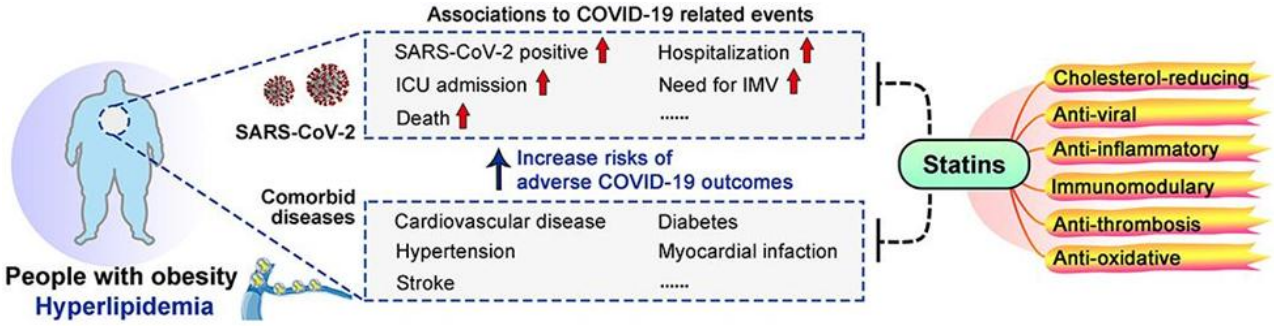

Figure 1. Key links between COVID-19, obesity and dyslipidemia (Source: https://doi.org/10.3389/fnut.2022.927092)

Paraoxonase 1 (PON1) is an enzyme with protective role against poisoning by organophosphate metabolites. It is used as a biomarker of diseases resulted by oxidative stress, inflammation and liver disorders [36]. This enzyme is synthesized primarily in the liver and appears mainly in serum, where is associated to HDL. Impaired PON 1 function on HDL, and excessive inflammatory response leads to further lipid oxidation [37]. Excessive production of oxidative HDL stimulates the lipoprotein transport alteration and impairment of the reverse cholesterol transport (RCT) pathway [38].

Oxidized LDL is also a powerful stimulator that can activate endothelial cells and monocytes and increase the expression of inflammatory proteins and receptors [28;39]. These lipoproteins can also induce endothelial cell apoptosis through LDL receptor-1-mediated nuclear factor-κB signal, caspase 3 and 9 which leads to elevation of monocyte levels, platelet activation, and vascular smooth muscle cell migration induced by collagen exposure [28;40;41]. This culminates in decreased return of cholesteryl esters to the liver either directly after interaction with hepatic scavenger receptor B1 or indirectly after transfer to LDL by cholesteryl ester transfer protein. The results of studies showed that the lung injury of COVID-19 patients was caused by endothelial cell pyroptosis and apoptosis [28].

Moreover, the "cytokine storm" underlying COVID-19 produces immune-mediated inflammatory dyslipoproteinemia, leading to low HDL-C and increased LDL-cholesterol (LDL-C) levels, elevated triglycerides, increased lipoprotein oxidation, low apolipoprotein E (ApoE) levels, and impaired inflammation resolution [25].

Resultly there is the increase of proinflammatory cytokines and chemokines promoting attraction of macrophages, neutrophils, and T-cells. This leads to uncontrolled inflammation and immune dysregulation, which culminates in the modulation of HDL [25]. This leads to the structural changes of HDL granules and accumulation of serum amyloid A (SAA), which increased dynamically to the severity of COVID-19 disease [42].

The results of meta-analysis defined same results. SAA concentrations were significantly higher in patients with severe COVID-19 and non-survivors (SMD = 1.20, 95% confidence interval 0.91–1.49, $P < 0.001$) [43].

It can elevate to 1000-fold within the first 24–48 h of an acute phase response [43]. The production of SAA is increased in the liver as a result of elevated tumor necrosis factor (TNF), IL-1β, IL-6, and interferon gamma (IFN-γ) [43;44].

Moissl-Blanke AP et al in comprehensive review summarizes that lipophilic SAA proteins interact with specific receptors and have been implicated in tissue remodeling through metalloproteinase, local tissue

changes in atherosclerosis [45]. SAA proteins displaced apolipoprotein A-I (ApoA-I) situated on HDL which leads to the impairment of HDL's atheroprotective functions such as improving of endothelium function, RCT and antioxidative activity [46]. RCT defined as a migration of cholesterol from the periphery to the liver [25;47]. SAA prevents the ability of HDL to protect low-density lipoprotein (LDL) from pro-atherogenic modifications such as oxidation and glycation [48].

It is possible that severe COVID-19 may contribute to lipoprotein X (LpX) accumulation independently of liver function [49]. This abnormal lipoprotein predominantly composed of phospholipids, free cholesterol and albumin [50]. Sometimes it can be a cause of hyperlipidemia [51].

Resultly, the increased levels of SAA proteins in patients with COVID-19 displace ApoA-I situated on HDL which leads to the impairment of HDL's functions such as migration of cholesterol from the periphery to the liver, improving of endothelium qualities, and antioxidative activity.

Atherosclerotic cardiovascular disease incidence is increased during acute COVID-19 infection. It has been recommended to use lipid-lowering medication in the period of active infection [53].

TREATMENT OF COVID-19.

Peculiarities of statins prescription in COVID-19.

Statins are well-known medications with a huge number of pleiotropic effects [30]. These drugs are used for treatment of COVID-19 and can reduce pro-inflammatory cytokines such as IL and TNF [53].

Statins in high dose is prescribed for LDL-lowering to achieve the goal ranges respectively to the levels of CVD risk according to SCORE-system (IA). For people with low risk LDL should be less than 3,0 mmol/l (IIb-A), moderate – 2.6 mmol/l (IIa-A), high – 1.8 mmol/l (IA), very high – 1.4 mmol/l (IA). For patients with high or very high risk the reduction of LDL more than 50% from baseline is recommended too (IA). Furthermore, this drugs is the first step of treatment of hypertriglyceridemia with more than 2.3 mmol/l levels of TG (IB) [54].

Liu C et al. determined that statins inhibit viral life cycle, reduce inflammation and modulate immune response to COVID-19 [35]. The mechanisms are defined on Figure 2.

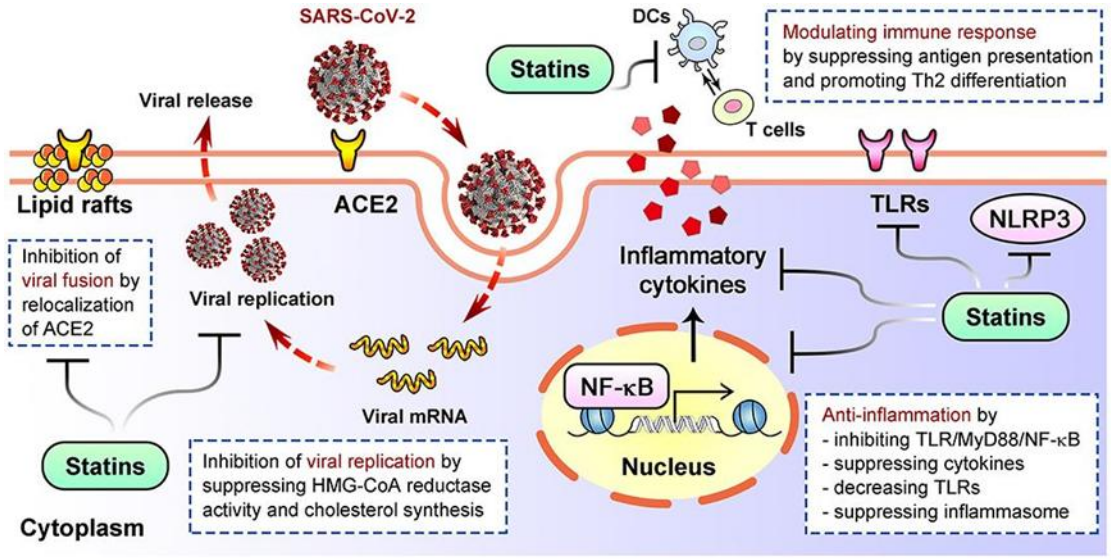

Figure 2. The relationship between statins and COVID-19 (Source: https://doi.org/10.3389/fnut.2022.927092)

Iqbal Z et al, suggested that statin therapy prescribed for dyslipidaemia, hyperlipidaemia, atherosclerotic heart disease should be continued in patients with confirmed diagnosis of COVID-19. It should be stopped if creatine kinase rises 10-fold to levels above 2000 IU/L in asymptomatic patients or at a lower level of 5-fold upper limit of normal in symptomatic patients (I, B-R), or dose reduced if ALT or AST is greater than 3 times the upper limit of normal (I, B-R) [53].

Iqbal Z et al, summarized the data about interactions between statins and other antiviral medications [53]. Atorvastatin, simvastatin, and lovastatin should be avoided in patients treated with remdesivir that is connected with Cytochrome P450 pathway of metabolism [53].

Low-doses of rosuvastatin and atorvastatin was recommended in patients with COVID-19 treated with lopinavir/ritonavir [53]. Lovastatin and simvastatin are

contraindicated in such patients because of the increased risk of rhabdomyolysis [55].

Atorvastatin is metabolized by $CYP_{34}A$ and rosuvastatin by CYP_2C_9 [56]. Atorvastatin prescribed previously for treatment of dyslipidaemia and coexistent ischemic heart disease, heart failure showed a statistically significant reduction in the risk of hospitalization (aOR = 0.83; 95% CI: 0.74–0.92, p < 0.001) and mortality (aOR = 0.70; 95% CI: 0.53-0.93, p = 0.014) in patients with COVID-19 in population-based case-control study based on 2821 cases and 52 318 controls [57].

However the results of other RCT showed that in COVID-19 patients, atorvastatin (20 mg/day) was not associated with a significant reduction of thrombosis and all-cause mortality. On the other hand, such treatment was safe [58].

According to the results of COLSTAT trial prescription of rosuvastatin (40 mg/day) with colchicine for the treatment of hospitalized COVID-19 patients was safe and recommended. The authors suggested that rosuvastatin has direct antiviral properties by binding and inhibiting the active site of the main protease enzyme of SARS-CoV-2. Patients treated by statins previously received rosuvastatin 40 mg as other participants of RCT [59].

Other RCT showed the effectiveness of emtricitabine, tenofovir, disoproxil, colchicine and rosuvastatin (40 mg/day) during 14 days for reduction of 28-day all-cause mortality by 22%. Rosuvastatin was prescribed as a protector of endothelial cells. The patients treated by statins previously were excluded from this RCT [60].

Furthermore, respectively to the results of prospective cohort study rosuvastatin increase 25-OH vitamin D levels in blood. It could be mediated by Niemann-Pick C1 like 1 membrane transporter which stimulates the intestinal absorption of vitamin D. Low levels of this vitamin are associated with higher risk of cardiovascular morbidity and mortality [61].

Resultly, rosuvastatin has additional pleotropic effect connected with the elevation of vitamin D levels.

Combination with ezetimibe is recommended if the goal of LDL is not achieved by the maximum dose of statin (IB). If such two drugs are not effective in patients with high CVD risk the adding of PCSK9 inhibitor is recommended (IA) [54].

Not all clinical trials suggested the improvement of clinical outcomes and mortality rate after using statins and renin-angiotensin-aldosteron system inhibitors.

Peculiarities of ezetimibe and PCSK9 inhibitor in patients with COVID-19

Israel A et al. in case-control study suggested that ezetimibe, decreased the risk of hospitalization (OR=0.488, 95% CI [0.377 to 0.622], p < 0.001) in COVID-19 patients. Same effect was confirmed for rosuvastatin (OR=0.673, 95% CI [0.596 to 0.758], p < 0.001), which was prescribed because of comorbidity such as ischemic heart disease (IHD) and heart failure (HF) in about a quarter of hospitalized and non-hospitalized people with COVID-19 [62].

On the opinion of Vuorio A et al, the combination of statins and a PCSK9 inhibitor for patients with hypercholesterolaemia can improve the prognosis of COVID-19 via the efficient lowering of the LDL cholesterol level and via preventing the reduction in the expression of antiviral genes, notably those of the type I interferons [63].

Resultly, prescription of rosuvastatin is recommended for all patients with COVID-19 because of antiinflammotory properties and protection of endothelial cells for reduction the mortality and risk of hospitalization. It is recommended to continua treatment with rosuvastatin for people which have received it before because of lipid profile disorders, coexistent IHD, HF or increased cardiovascular risk.

It has been shown that blockade of RAAS exerts potent anti-atherosclerotic effects, not only through the anti-hypertensive pathway, but also through anti-inflammatory, anti-proliferative and antioxidant properties [64]. That is why it is considerable to prescribe inhibitors of this system in patients with dyslipidemia and COVID-19.

Effects of RAAS in COVID-19

People with elevated blood pressure (BP) and a SCORE2 or SCORE2-OP CVD risk of ≥ 10% have the increased risk for CVD for the purposes of risk-based management of their elevated BP (IB) [15].

Resultly, reduction of BP with antihypertensive drugs is important.

Among all medications ACE inhibitors, angiotensin receptor blockers (ARBs), dihydropyridine calcium channel blockers (CCBs), and diuretics (thiazides and thiazide-like drugs such as chlorthalidone and indapamide) have demonstrated the most effective reduction of BP and CVD events, and are therefore recommended as first-line treatments to lower BP (IA) [15].

Yehualashet AS et al, in review suggested that the inhibitors of RAAS can restore the balance between ACE1 and ACE2 in patients with COVID-19 [65]. Several studies have also confirmed the protective effects of ARBs during COVID-19 by increasing ACE2 levels [66].

Respectively to the results of multicenter, prospective study the continuing of ACE inhibitors / ARB during hospitalization was associated with decreased mortality (OR 0.22, 95% CI 0.073-0.67; P =

0.008). AH was confirmed in 94 %, IHD in 17,6 %, dyslipidaemia in 33,5 %, heart failure in 16,3 %, obesity in 40 %, smoking in 20 %, chronic kidney disease (CKD) in 15 % of patients treated by RAAS blockers before COVID-19. Lisinopril and losartan were the most frequently used ACE-I (46 of 90) and ARB (71 of 155), respectively [67;68].

RAAS blockers can decrease mortality of COVID-19 by 35 % [69]. These drugs reduce inflammation [70], the risk of severity in 29 % and mortality in 43 % in hypertensive patients [71]. However, some investigators did not suggest the significant association between ACE inhibitors, ARBs and plasma ACE2 consentration [72].

Morales D et al, in international, open science, cohort analysis has been found that ACE inhibitors, ARBs and its combination with hydrochlorothiazide and amlodipine (cilazapril, ramipril/hydrochlorothiazide, losartan/hydrochlorothiazide, valsartan/amlodipine) decrease hospitalization in patients with COVID-19 with previously diagnosed AH [72]. Metabolic disorders occurring with nephropathy are associated with the production of free radicals resulting in structural-functional disturbances of the cellular membranes of different organs and systems [73]. RAAS inhibitors protect kidney from damage [15].

Furthermore, losartan has the additional effect connected with significantly reduction of uric acid levels [74], which is important for prevention of CV complications [75].

On the other hand, the results of prospective, parallel group, randomised, controlled, open-label trial showed that discontinuation of RAAS inhibitors in COVID-19 had no significant effect on the maximum severity of COVID-19 but may lead to a faster and better recovery [76].

The continuing of ACE inhibitors/ARB (ramipril, losartan, valsartan) prescribed previously for treatment of AH with HF, coexistent lipid profile disorders during hospitalization in patients with COVID-19 was associated with decreased mortality.

CONCLUSIONS

The connection between SARS-CoV-2 and ACE 2 leads to the inactivation of this enzyme, further conversation of Ang I to Ang II, increased constriction of vessels and progression of AH.

The increased levels of SAA in patients with COVID-19 displace ApoA-I situated on HDL, which leads to the impairment of HDL's functions such as reverse cholesterol transport, improvement of endothelium qualities, and antioxidative activity.

Management with rosuvastatin, ACE inhibitors/ARB prescribed previously because of AH, lipid profile disorders, HF, IHD and increased cardiovascular risk may be beneficial to continua or prescribed at first in the absence of contrindications in patients with COVID-19.

It is considerable not only for achievement the goal ranges of BP and LDL, but for improvement endothelial function, reduction the progression of oxidative stress, decrease mortality and prevention of cardiovascular complications.

PROSPECTS FOR FUTURE RESEARCH

Prospect for future research is the assessment of markers of COVID-19 and lipid profile in patients with this coexistent pathology after prescription of statins, RAAS inhibitors and carnitine.

ETHICAL CONSIDERATIONS

The study was conducted without involving human subjects.

AUTHOR CONTRIBUTIONS

All authors substantively contributed to the drafting of the initial and revised versions of this paper. They take full responsibility for the integrity of all aspects of the work.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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