

COVID-19 treatment in elderly. *Short Review*

Vladislav V. Bezrukov, Liana P. Kuprash, Tetyana M. Panteleymonova, Olena V. Kuprash, Svetlana A. Gudarenko

D. F. Chebotarev Institute of Gerontology NAMS of Ukraine, Kyiv, Ukraine

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Correspondence: kuprash@geront.kiev.ua

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Abstract. Coronavirus SARS-CoV-2 disease (COVID-19) is characterized by severe and high mortality, which increases significantly with age. This poses a great threat to the elderly. The results of numerous clinical observations suggest that the interaction of drugs used in the COVID-19 treatment and concomitant pathology in elderly patients may worsen the course of the disease and lead to the development of serious complications. Therefore, a need for an individual approach to treatment. Appropriate adjustment of the doses of prescribed drugs and taking into account the interaction of drugs for the treatment of concomitant pathology will help to increase the effectiveness of COVID-19 drug therapy in the elderly.

Keywords: COVID-19; comorbid diseases; etiotropic agents; pathogenetic agents; symptomatic agents; complex therapy.

Coronavirus disease (COVID-19), an epidemic that began in late 2019 and spread rapidly in many countries, is an acute respiratory infection caused by the SARS-CoV-2 [1].

The disease is characterized by severe and high mortality, which increases significantly with age. According to the results of the study, the overall mortality in the sample of COVID-19 patients was 2.3%. Moreover, in patients under the age of 54 years, it was about 1%, at the age of 65-84 years, its value was 3-11%, and at the age of 85 years - from 10% to 27% [2].

The causative agent of COVID-19 is transmitted by airborne droplets most often. Once in the alveoli, the virus enters the cells of the body through the transmembrane exopeptidase of angiotensin-converting enzyme localized in pneumocytes [3]. There are also other ways of virus transmission into the body. SARS-CoV-2 might enter epithelial cells of the gastrointestinal tract, as well as directly into the brain.

The pathogenesis of the infection is based on a wide range of functional disorders of the immune system due to the action of the virus. It is manifested in the suppression of anti-inflammatory and activation of pro-inflammatory functions, including increased synthesis and secretion of pro-inflammatory cytokines. Cytokine release syndrome ("cytokine storm") is considered central in the pathogenesis of multiorgan inflammation in COVID-19 patients [4-5]. Proinflammatory cytokines affect coagulation processes: reduce the content of endogenous coagulants in the blood, increase thrombin formation and inhibit fibrinolysis. Therefore, the course of COVID-19 is often complicated by coagulopathy [6].

Elderly people are most vulnerable to COVID-19 (especially to its β -genotype). This is due to age-related structural and functional changes in the body. A significant role in this belongs to the expression of genes associated with aging and homeostatic imbalance. This is manifested in the suppression of anti-inflammatory and activation of pro-inflammatory mechanisms of natural immunity, as well as in the dysfunction of the homeostasis system [7].

Age-related changes in metabolic and destructive-inflammatory processes determine the severe and often fatal course of COVID-19 in the elderly.

The clinical picture of COVID-19 corresponds to respiratory infection with a variation in the severity of symptoms from a mild cold-like illness to severe viral pneumonia, which can lead to potentially fatal acute respiratory distress syndrome [8-10].

Fever (99%), dry cough (59%), fatigue (70%), anorexia (40%), dyspnea (31%), and sputum secretion (20%) are among the main clinical symptoms of COVID-19 in the general population. In addition, there may be complaints of loss of taste and smell, nasal congestion or rhinorrhea, conjunctivitis, and gastrointestinal disorders [11, 12].

In the elderly population, there are more common atypical clinical syndromes of the disease. There are delirium, risk of severe psychosis and suicidal behavior, as well as tachycardia, and low blood pressure. However, typical symptoms such as fever, cough, and shortness of breath in elderly patients may be absent [13,14]. Fever is the most common symptom of COVID-19. It is observed in more than 80% of young patients (up to 50 years) and only 20-30% of elderly patients [15].

The incidence of COVID-19 in the elderly is characterized by moderate to severe disease, as indicated by shortness of breath, shortness of breath, hemoptysis, intermittent vomiting, diarrhea, confusion, and inhibition. The condition of patients is complicated by the presence of concomitant diseases of the lungs and cardiovascular system, renal failure, diabetes, etc. [16].

In severe cases, there is often progression of lower respiratory tract disease, pneumonia, acute respiratory failure, sepsis, and septic shock [17].

Most elderly COVID-19 patients have complications from individual organs - acute respiratory syndrome (71%), acute kidney disease (20%), heart disease (33%), and liver dysfunction (15%) [18].

The incidence of COVID-19 increases with age [19].

A retrospective study analyzed the severity of COVID-19 in patients of different ages. In elderly patients, the severe disease was registered in 16.18%, critical - in 8.82%, and in young people, it was 5.98% and 0.77%, respectively [20].

The presence of comorbidities causes a more severe course of coronavirus disease in such patients [21].

Cardiovascular diseases (coronary heart disease, chronic heart failure, hypertension), diabetes mellitus, chronic obstructive pulmonary disease, and cancer are the most common comorbid diseases [22-24].

In a clinical study of COVID-19 elderly patients with severe disease, 86% were diagnosed with comorbidities such as chronic heart failure (43%), chronic obstructive pulmonary disease (33%), and diabetes mellitus (13%) [25].

In a multicenter clinical study in COVID-19 patients over 65 years of age, hypertension was reported in 63.1%, chronic kidney disease in 38%, and diabetes in 26.8% [26].

The presence of comorbidities significantly complicates the COVID-19 course and increases the risk of mortality [27]. The purpose of the analysis shows that the presence of hypertension in a patient increases the risk of severe disease by 2.26 times, chronic obstructive pulmonary disease – by 2.46 times, and coronary heart disease – by 3.42 times [28].

The presence of concomitant pathology, its impact on the course of COVID-19, and the interaction of drugs used in the treatment of underlying and concomitant pathology should be considered when prescribing drug therapy [16, 17].

Treatment of elderly COVID-19 patients is carried out using etiotropic, pathogenetic and symptomatic agents.

Specific etiotropic agents for the treatment of COVID-19 patients, approved by the EMA (Europe) and the FDA (USA), are not available today [18]. National protocols for the treatment of patients with this infection include drugs whose activity against SARS-CoV-2 or related coronaviruses has been established in vitro and limited clinical experience. Their effectiveness has not yet been proven in randomized multicenter clinical trials [19, 20].

Etiotropic antiviral therapy in COVID-19 patients in Ukraine is carried out by the wording of the protocol approved by the order of the Ministry of Health №852 from 10.04.2020. Remdesivir, favipiravir, hydroxychloroquine, and interferons are used to treat COVID-19 according to this protocol [29].

Prescribing antiviral therapy to elderly and senile patients slows the progression of the disease and improves the prognosis in patients of this age group [30-40].

Remdesivir reduces the replication of SARS-CoV-2 by inhibiting the action of viral RNA. This drug is active against SARS-CoV-2 and related coronaviruses in patients with severe and moderate disease reducing the duration of fever and reducing mortality. The recommended remdesivir dose for patients with severe disease is 200 mg (intravenously) on day one and 100 mg per day (intravenously) from the second day, with treatment for 5 days [41-43].

Favipiravir (a selective RNA polymerase inhibitor) increases the rate of viral clearance and has a positive effect on clinical dynamics. Normalization of COVID-19 symptoms therapy was recorded in 91.4% of patients versus 62% in the control group after treatment. The drugs are prescribed to patients with a disease of moderate severity of 1800 mg twice on the first day, then 600 mg twice a day for 10 days [17, 26, 27].

Hydroxychloroquine disrupts the binding of the SARS-CoV2 virus to the cellular adenosine-converting enzyme by raising intracellular endosomal pH, which reduces the entry of the virus into the body. Hydroxychloroquine increases the secretion of anti-inflammatory cytokines that inhibit the replication of SARS-COV2 by stopping the action of viral RNA due to its immunomodulatory properties. Clinical studies have shown that the use of hydroxychloroquine accelerates the disappearance of SARS-COV-2 RNA in nasopharyngeal smears [44].

The results of published studies indicate the effectiveness of hydroxychloroquine in low doses in patients with mild to moderate COVID-19, provided it is prescribed during the first 3-5 days of the disease. The use of hydroxychloroquine in patients with severe disease is usually ineffective, which limits its use in geriatrics [45].

Arbidol is an antiviral drug that inhibits the DNA and RNA of viruses and changes the structure of virus membranes. The efficacy of arbidol in the COVID-19 treatment has been established in retrospective cohort studies [46, 47].

Interferons are a family of cytokines with antiviral properties. α -interferon is used in the treatment of COVID-19 elderly patients in the absence of contraindications (allergies, central nervous system dysfunction, hepatic and renal failure) [48].

A multicenter prospective clinical study has shown that the combination of antiviral therapy with the inclusion of interferon A-2B reduces the duration of virus isolation and reduces the length of hospital stay [15].

Antimicrobial therapy is used in COVID-19 patients only in the presence of confirmed bacterial infection, as antibiotics do not act on the virus. Because azithromycin and doxycycline are antibiotics that inhibit interleukin synthesis, they are used in the complex COVID-19 therapy [49].

Pathogenetic therapy of coronavirus infection includes anti-inflammatory and antithrombotic agents.

Based on the activation of the virus by the immune system and the significant increase in pro-inflammatory cytokines released due to this, COVID-19 patients have been prescribed corticosteroids (low doses of dexamethasone or hydrocortisone). Systemic corticosteroid therapy improves the clinical course of the disease and reduces mortality in COVID-19 patients. The use of corticosteroids reduced mortality in patients with critical (38%) and severe (17%) diseases. According to WHO guidelines, corticosteroids are the drugs of choice for critically ill patients. Corticosteroids are not recommended for use in mild patients. And corticosteroids are used in the early stages of the disease, in low doses and with prolonged administration in patients with acute distress syndrome [50-53].

Due to the significant release of cytokines in COVID-19 patients may develop increased blood clotting - hypercoagulation. Age-related changes in the homeostasis system and increased risk of thrombotic complications in elderly COVID-19 patients justify the need for antithrombotic therapy. Its effectiveness has been established in several clinical studies. The treatment regimen of such patients should include drugs of low molecular weight heparin (heparin, fraxiparin), vitamin K inhibitors (warfarin), and inhibitors of platelet aggregation (clopidogrel, dipyridamole). Cumulative changes in the general analysis of blood (thrombocytopenia) and coagulogram (increase in prothrombin time) are the criteria for prescribing drugs [54-56].

Elderly patients with severe COVID-19 need oxygen support. Oxygen therapy in COVID-19 patients should be performed when hemoglobin is saturated with oxygen in the elderly (60-75 years) in the range of 91-93%, senile age (over 75 years) - 88-91%. High-speed oxygen therapy and non-invasive positive pressure ventilation are used for this purpose [57].

Symptomatic treatment of COVID-19 patients includes antipyretics, nasal decongestants, mucolytics, bronchodilators, and other drugs (vitamins, metabolic drugs) [58].

Treatment of comorbid diseases is very important in the comprehensive treatment of elderly COVID-19 patients. The use of certain groups of drugs along with antiviral therapy is appropriate for patients of this age group. Antiviral drugs (remdezivir, favipiravir) are inhibitors or activators of certain cytochromes and proteins (drug transporters), and they may alter plasma concentrations and efficacy of drugs metabolized by these cytochromes or transported by proteins. Therefore, it requires appropriate adjustment of doses of drugs intended for the treatment of concomitant pathology in elderly COVID-19 patients [59].

Beta-blockers, ACE inhibitors, calcium channel blockers, and statins are included in the complex therapy of patients with concomitant cardiovascular pathology (coronary heart disease, chronic heart failure, hypertension). RAAS blocker therapy is prescribed to patients with concomitant cardiovascular disease, given the established role of angiotensin-converting enzyme-2 receptors in the mechanism of COVID-19 virus penetration into cells and the lack of experimental or clinical data on adverse effects on such patients [60, 61].

Corticosteroids are effectively used in the treatment of viral infection as immunosuppressants in patients with concomitant diabetes. But they cause hyperglycemia due to insulin resistance and pancreatic β -cell dysfunction. Optimal glycemic control is necessary in such cases. Insulin is considered the choice of antidiabetic drugs for severe COVID-19 patients, and metformin or sulfonylureas in mild COVID-19 patients [62-64].

Corticosteroids (prednisolone) are prescribed to COVID-19 patients with concomitant chronic obstructive pulmonary disease. Antibiotics (azithromycin, ceftriaxone) are prescribed to such patients to suppress the accompanying microflora [65].

Cancer patients belong to the risk group of severe coronavirus infection due to suppressed immunity in the background of antitumor treatment. A significantly higher rate of COVID-19 severe complications was found among patients receiving anticancer therapy. According to the recommendations of the American Society of Clinical Oncology, with a positive laboratory COVID-19 test in cancer patients, all specific anticancer treatments, including chemotherapy, should be stopped and resumed only after receiving a negative COVID-19 test [66, 67].

The results of numerous clinical observations suggest that the interaction of drugs used in the treatment of elderly COVID-19 patients with concomitant pathology may worsen the course of the disease and lead to the development of serious complications. This must be taken into account in the treatment of such patients [68-70].

Conclusions:

Coronavirus disease infection caused by the SARS-COV-2 virus (COVID-19) poses a major threat to the elderly due to severe disease, high morbidity, and mortality. In the treatment of this category, patients use the same drugs recommended for COVID-19 treatment in the general population. But the atypical course of the disease characteristic of these patients, and the high level of comorbidity necessitate an individual approach to treatment. Appropriate adjustment of the doses of prescribed drugs, taking into account the interaction of drugs for the treatment of comorbidities will help increase the effectiveness of drug therapy in elderly COVID-19 patients.

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