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LETTER TO EDITOR

REVIEW ARTICLE

HYPOGLYCEMIA IN PATIENTS WITH COVID-19: A COINCIDENCE OR A TREND?

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ABSTRACT

The aim: The purpose of this work is to analyze the available scientific information on causes and risk factors of hypoglycemia during treatment of patients with COVID-19.

Materials and methods: A search and analysis of full-text articles was carried out in the PubMed, Web of Science, Google Scholar, and Scopus databases. The search was conducted using the keywords: «hypoglycemia in COVID-19 patients», «treatment of COVID-19 and hypoglycemia» and «COVID-19 vaccination and hypoglycemia» from the beginning of the pandemic in December 2019 to July 1, 2022.

Conclusions: Hypoglycemia can be an incidental clinical finding. But it can also be a natural consequence of treatment if it is carried out without taking into account the possible hypoglycemic effects of drugs and without careful monitoring of the patient's condition. In the case of determining the program of treatment and vaccination against COVID-19 in patients with DM, the known and possible hypoglycemic effects of drugs and vaccines should be taken into account, the level of glycemia should be carefully controlled, and sudden changes in the type and dose of drugs, polypharmacy and the use of dangerous combinations of drugs should be avoided.

KEY WORDS: COVID-19, hypoglycemia, treatment, vaccination

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INTRODUCTION

In the early 20s of the 21st century, humanity witnessed an unprecedented coronavirus disease (COVID-19) pandemic caused by SARS COV-2. COVID-19 is confidently and aggressively spreading around the planet, particularly in Ukraine, as of July 22, 2022, there were 5,021,612 confirmed cases of COVID-19 with 108,699 deaths (case fatality rate – 2.16%) [1]. The main risk factors for developing COVID-19 and its severe course are advanced age, arterial hypertension, diabetes mellitus (DM), and cardiovascular and cerebrovascular diseases. In particular, the risk of death from COVID-19 may be up to 50% higher in patients with concomitant diabetes than in non-diabetics. In these patients, significant fluctuations in blood glucose levels are observed, probably due to irregular diet, reduced physical activity, and the use of glucocorticoids [2]. Significant changes in blood glucose levels often lead to hypoglycemia.

According to American Diabetes Association (ADA), hypoglycemia can be defined as «any abnormally low plasma glucose concentration that can cause potential harm to the subject.» Current ADA Guidelines distinguish three levels of hypoglycemia. Level 1 hypoglycemia is defined as blood glucose <70 mg/dL (3.9 mmol/L) but ≥54 mg/dL (3.0 mmol/L). A blood glucose concentration of 70 mg/dL (3.9 mmol/L) has been recognized as the threshold for the neuroendocrine response to glucose lowering in nondiabetic individuals, and a measured glucose level <70 mg/dL (3.9 mmol/L) is considered clinically important (regardless of the severity of acute hypoglycemic symptoms). Level 2 hypoglycemia (defined as a blood glucose concentration <54 mg/dL [3.0 mmol/L]) is the threshold at which neuroglycopenic symptoms begin to occur and requires immediate intervention to reverse the hypoglycemic event. Finally, level 3 hypoglycemia is defined as a severe event characterized by a change in mental and/or physical functioning that requires the assistance of another person for recovery [3].

Hypoglycemia is a factor that limits the possibilities of treatment in diabetes, which must be treated carefully and critically to avoid complications. The lockdown due to the COVID-19 pandemic has further complicated the problem of hypoglycemia by restricting access to food, clinics, medical services, and medicines [4].

It is also known that hypoglycemic reactions often occur against the background of treatment of COVID-19,

in particular with some antiviral agents, glucocorticosteroids, antibiotics, etc. The question arises: are cases of hypoglycemia in patients with COVID-19 isolated random clinical phenomena, or is this a natural result of treatment? The search for an answer to this question was the reason for conducting this study.

THE AIM

The aim is to discover the causes of hypoglycemia during treatment in patients with COVID-19 and propose recommendations for its prevention.

MATERIALS AND METHODS

A search and analysis of full-text articles from the PubMed, Web of Science, Google Scholar, and Scopus databases were conducted to solve the task. The search was conducted using the keywords: «hypoglycemia in COVID-19 patients», «treatment of COVID-19 and hypoglycemia» and «COVID-19 vaccination and hypoglycemia» from the beginning of the pandemic in December 2019 to July 1, 2022. The statistical results of the research are presented in absolute (n) and relative (%) values, the assessment of the risk of occurrence of the event was carried out using the odds ratio (OR) and their confidence intervals (CI), the results were considered statistically significant when $p < 0.05$.

REVIEW AND DISCUSSION

A total of 186 publications were found as a result of the search. The analysis of literary sources made it possible to demonstrate the influence of individual drugs and methods of therapy and prevention used in patients with COVID-19. The possibility of developing hypoglycemia against the background of pharmacotherapy and the use of biological drugs for COVID-19 is summarized in Table I.

Antiviral drugs block the maturation of the virus and the penetration of the virus into the cell. Among the new antiviral drugs, molnupiravir is an innovative oral antiviral drug with broad activity against coronaviruses, including SARS-CoV-2. A randomized, placebo-controlled trial of A.J. Bernal, published in February 2022, confirmed the superiority of molnupiravir over placebo in ambulatory adult patients with mild to moderate COVID-19, provided treatment was started within 5 days of symptoms onset. Adverse effects were reported in 216 of 710 participants (30.4%), but the incidence of hypoglycemia was not reported [5]. Studies of the viral protease inhibitor camostat mesylate have shown a reduction in glycemic levels, which may be a potential alternative antiviral treatment option for patients with DM [6]. Administration of other antiviral drugs (lopinavir/ritonavir, remdesivir, darunavir/cobicistat) for COVID-19 is accompanied by infrequent moderate hyperglycemia [6].

Interleukin-6 (IL-6) receptor blockers. IL-6 is a pleiotropic cytokine that activates and regulates the immune response to infections. Elevated concentrations of IL-6 are associated with severe outcomes of COVID-19, including respiratory failure and death, although the role of IL-6 in disease pathogenesis is unclear. Among IL-6 receptor blockers for the treatment of COVID-19, WHO recommends tocilizumab or sarilumab [7]. **Tocilizumab** is used to treat moderate to severe COVID-19 pneumonia by targeting IL-6 receptors and reducing cytokine release. Intriguingly, there is evidence that optimal treatment of COVID-19 infection with tocilizumab is not achieved during hyperglycemia in both diabetic and non-diabetic patients [8].

Recommendations concerning **Janus kinase (JAK) inhibitors**, specifically baricitinib, ruxolitinib, and tofacitinib, for patients with severe or critical COVID-19 were published on 14 January 2022 as the eighth version of the WHO living guideline and in the BMJ as Rapid Recommendations [7]. The drugs tofacitinib, ruxolitinib, and baricitinib are used in the treatment of patients with a severe or critical course of COVID-19. Evidence has demonstrated that each of these therapies lowers glycemia in patients with and without diabetes [9].

Chloroquine, a drug obtained from the bark of the cinchona tree, has long been used to treat various diseases, including malaria, and was accidentally shown to reduce hyperglycemia [10]. It is known that chloroquine has an immunomodulatory and hypoglycemic effect, and causes changes in insulin metabolism through cell receptor signaling and post-receptor clearance [11]. In diabetic animals, chloroquine has been shown to increase serum insulin levels even without treatment with exogenous insulin [10].

Hydroxychloroquine (HCQ) is an antimalarial drug that has gained global news and media attention and has been used in the treatment of patients with COVID-19. This drug has been used based on its antimicrobial and antiviral properties, despite the lack of definite evidence of clinical efficacy.

Hypoglycemia and QT prolongation are known and frequent side effects of HCQ [6]. 33.56% of patients who prophylactically received 400 mg of hydroxychloroquine in combination with conventional antihyperglycemic agents without dose adjustment reported hypoglycemia [4]. Hypoglycemia can be seen as a side effect of HCQ use in COVID-19 infection, even in patients without chronic diseases and diabetes.

Table I. Occurrence of hypoglycemia when using means of treatment and prevention of COVID-19

Drug class	Name of the drug	Features of changes in blood glucose level	References
Antiviral drugs	Camostat mesylate Lopinavir/ritonavir Remdesivir Darunavir/cobicistat	Infrequent moderate hypoglycemia	[5,6]
IL-6 receptor blockers	Tocilizumab Sarilumab	Hypoglycemia is possible	[6-8]
Janus kinase inhibitors	Tofacitinib Ruxolitinib Baricitinib	Decrease blood glucose levels in diabetic and nondiabetic patients	[7,9]
Anti-infective agents	Hydroxychloroquine Chloroquine	In diabetic and nondiabetic patients, hypoglycemia occurs frequently	[4,6,10,11]
Glucocorticosteroids	Dexamethasone	Both hyperglycemia and hypoglycemia can occur. Hypoglycemia is often observed after withdrawal of GCS.	[6,12,13]
Macrolides	Azithromycin Clarithromycin	Hypoglycemia is rare, but in combination with hydroxychloroquine – up to 42.8%	[14-16]
Fluoroquinolones	Ciprofloxacin Moxifloxacin Levofloxacin	Frequent. Hypoglycemia is the most common side effect of fluoroquinolones treatment	14,17,18][
Selective serotonin reuptake inhibitor	Fluvoxamine	Can cause both hyperglycemia and hypoglycemia	[7]
Analgesics, antipyretics	Paracetamol (acetaminophen)	Hypoglycemia occurs in case of overdose	[19,20]
Antidiabetic drugs	Metformin Sulfonylurea Insulin DPP-4 inhibitors	All drugs in this group can cause hypoglycemia, especially in combination with other medications used for the treatment of COVID-19	[4,21,22]
ACE inhibitors	Lisinopril Captopril	Hypoglycemia can occur both in patients with and without DM	[22-24]
Vaccination	Covishield mRNA-based vaccines: Pfizer-BioNTech Moderna	All vaccines can cause hyperglycemia after the first dose. Hypoglycemia is also possible for mRNA-based vaccines	[6,25,26]

Note: GCS – glucocorticosteroids; ACE – angiotensin-converting enzyme; DM – diabetes mellitus

Glucocorticosteroids (GCS). It is known that GCS suppress the activity of inflammatory cytokines, which leads to decreasing edema, fibrin deposition, capillary leakage, and migration of inflammatory cells, thereby suppressing inflammation and blocking the cytokine storm [6]. Recent clinical trials have confirmed that dexamethasone is an effective treatment for patients with COVID-19 who require mechanical ventilation. However, it is also known that GCS drugs affect carbohydrate metabolism and disrupt glycemic control. Thus, a study by D.J. Douin et al. showed that taking ≥320 mg methylprednisolone equivalents was associated with 4 additional days spent with glucose either <80 mg/dL or >180 mg/dL (OR=4.00, 95% CI = 2.15-5.85, p<0.001). Thus, the use of GCS in patients with COVID-19 is associated with a higher frequency of both hyperglycemia and hypoglycemia [12]. In addition, it should be taken into account that hypoglycemia is often observed after the withdrawal of corticosteroids. In 60% of patients after discontinuation of GCS L.G. Strongin et al. (2022) reported on clinically significant, often nocturnal episodes of hypoglycemia, that were not detected by routine methods [13].

Macrolides. When using macrolides (azithromycin or clarithromycin), hypoglycemia was observed in 3.72% of patients [14]. **Azithromycin** suppresses the synthesis of polypeptides and proteins and has immunomodulatory and antiviral effects. Several clinical trials have shown conflicting results regarding its effectiveness [7].

Hypoglycemia was the most common side effect of the **combination of hydrochloroquine and azithromycin** and was observed in 69 of 161 patients (42.86%) [15]. In a cohort of 21 patients with COVID-19 on hemodialysis, treated with HCQ and azithromycin, 5 (23.8%) patients experienced hypoglycemia [16].

Fluoroquinolones (FQ) are wide-spectrum synthetic antimicrobial agents with strong antiviral activity. The fluoroquinolones (ciprofloxacin and moxifloxacin) can

inhibit the replication of SARS-CoV-2 by showing a stronger ability to bind to its core protease than chloroquine. In addition, FQ have demonstrated numerous immunomodulatory effects, leading to attenuation of the inflammatory response through proinflammatory cytokines inhibition [17]. However, FQ use is often accompanied by hypoglycemic reactions. Thus, in the message of A. Althaqafi et al. (2021), hypoglycemia was registered in 2179 patients (35.1%) who received fluoroquinolones in eleven studies with 6208 patients. Among all FQ, moxifloxacin is the most associated with dysglycemia, and ciprofloxacin the least [18]. The absolute risk of hypoglycemia was 10.0 events per 1000 for moxifloxacin, administration of levofloxacin had also a higher risk of hypoglycemia than macrolides (OR-1.79; 95% CI 1.33-2.42). A significant increase in the risk of hypoglycemia was also observed among patients receiving moxifloxacin concomitantly with insulin (OR, 2.28; 95% CI, 1.22-4.24) [14].

Fluvoxamine is a selective serotonin reuptake inhibitor (SSRI) with antiviral and anti-inflammatory effects [7]. It can cause both hyperglycemia and hypoglycemia.

OTHER DRUGS USED IN PATIENTS WITH COVID-19 AND RELATED DISEASES

Paracetamol (acetaminophen) is recommended for the treatment of hyperthermia. However, in the case of an overdose of acetaminophen, hepatotoxicity occurs with manifestations of severe hypoglycemia, coagulopathy, and metabolic acidosis [19], sometimes with a fatal outcome [20].

Antidiabetic drugs. Almost all antihyperglycemic drugs can worsen the course of COVID-19, regardless of their class. Administration of an antihyperglycemic drug can lead to side effects, including episodes of hypoglycemia, diarrhea, lactic acidosis, and an increased risk of cardiovascular and hepatic hazards. These adverse effects associated with antihyperglycemic drugs pose a threat to the development of severe complications of COVID-19 [21].

K. Shah et al. studied 146 patients with type 2 diabetes (T2DM) who presented to the emergency department during quarantine with symptoms of hypoglycemia. It turned out that hypoglycemia most often occurred against the background of the use of a combination of metformin and sulfonylurea (65.75%), followed by insulin (33.56%) [4].

Dipeptidyl peptidase-4 inhibitors (DPP-4i) are considered safe for patients with T2DM. However, the combination of these agents with other drugs used to treat COVID-19 produces undesirable hypoglycemic effects. Thus, in a large study, C.Y. Ray et al. (2021) analyzed data from 77,047 patients using DPP-4i. An increased risk of hypoglycemia was observed with the combination of DPP-4i with bumetanide (OR 2.44; 95% CI, 1.78-3.36), captopril (OR 2.97; 95% CI, 2.26-3.90), colchicine (OR 1.87; 95% CI, 1.44-2.42), acetaminophen (OR 2.83; 95% CI, 2.44) [22]. Physicians who prescribe DPP-4i should consider the potential risks associated with the simultaneous use of other drugs.

In addition, COVID-19 may limit the choice of available antihyperglycemic agents, which may further increase the risk of severe complications of diabetes and COVID-19 itself [21].

Angiotensin-converting enzyme (ACE) inhibitors are among the most common drugs used to treat concomitant hypertension and diabetes. They are considered the first line of treatment for hypertension in this population. ACE inhibitors can increase insulin sensitivity, which can lead to an approximately 3- to 4-fold increase in the risk of hypoglycemia in patients with diabetes, especially those receiving other hypoglycemic agents, including sulfonylureas [23]. Previous studies have shown a potential association between ACE inhibitors used in combination with sulfonylureas and severe hypoglycemia [24]. Cases of recurrent hypoglycemia in non-diabetic patients treated with ACE inhibitors, in particular lisinopril, have also been reported [23]. There are also data on hypoglycemia in the background of captopril administration [22].

VACCINATION

All vaccines have been designed to increase immunity to the infection of COVID-19, which allows for the prevention of the disease. The mechanisms linking vaccines against COVID-19 and changes in glucose homeostasis have not been definitively discovered. As a rule, antiviral vaccines can cause unstable blood glucose levels. It is not just a reaction to the virus but the vaccine excipients.

G. di Mauro et al. (2022) reported 4275 events with impaired glucose metabolism after the administration of vaccines. The most frequently registered events belong to the group «high glucose level» (n = 2012; 47.06%), followed by «hypoglycemia» (n = 954; 22.32%). Covishield, Pfizer-BioNTech, and Moderna have been associated with hyperglycemia after the first dose [6]. In addition, mRNA vaccines against COVID-19 were associated with an increased frequency of reports of alterations in glucose homeostasis compared with viral vector vaccines. In particular, the frequency of reports of hypoglycemia after the use of mRNA vaccines was significantly higher (OR 1.62; 95% CI 1.41-1.86) compared to vaccination with vaccines based on viral vectors [25].

Adverse effects associated with vaccination vary considerably by age and sex, with more severe effects seen in women and young adults. It is noteworthy that women show a stronger immune response against

pathogens and vaccines but also a greater susceptibility to autoimmune diseases [26].

To date, the effect on the level of glycemia of such treatment methods as plasma of convalescents, monoclonal antibodies, and vaccination with vaccines not mentioned above (for example, Johnson & Johnson) remains unknown [6].

The conducted study showed that hypoglycemia can occur with the use of drugs of almost all pharmacotherapeutic groups used for the treatment (and vaccine prophylaxis) of patients with COVID-19. In addition, many patients with DM have chronic complications that contribute to the occurrence of hypoglycemia in the event of a disease with COVID-19.

Diabetic kidney disease (DKD) is a significant risk factor for the development of hypoglycemia. Factors contributing to the risk of hypoglycemia in DKD are reduced renal clearance of insulin, reduced breakdown of insulin in peripheral tissues, reduced renal gluconeogenesis, and impaired renal excretion of antidiabetic drugs. In particular, in the study by K. Shah et al., among patients with symptomatic hypoglycemia, almost a third of patients (32.88%) had diabetic kidney disease [4]. In the case of a severe course of DKD, patients with COVID-19 often develop renal failure, which significantly worsens the treatment results.

The presence of diabetic micro- and macroangiopathy and concomitant arterial hypertension in the patient is also important. Patients with arterial hypertension, micro-, macro-vascular complications of diabetes, and concomitant complications had a higher tendency to risk of hypoglycemia (46.58%, 33.56%, and 23.29%, respectively) than patients without these complications [4].

And finally, another phenomenon that is observed during the development of a viral infection in patients with DM is **the mutually aggravating effect of diseases**. Thus, DM is a risk factor affecting the progression and prognosis of COVID-19. In a study by W. Guo et al. (2020), it was found that patients with COVID-19, who had no other comorbidities except diabetes, had a high risk of developing severe pneumonia, the release of enzymes associated with tissue injuries, excessive uncontrolled reactions on inflammation, and hypercoagulable state associated with dysregulation of glucose metabolism [27]. In addition, the level of serum inflammatory biomarkers, such as IL-6, C-reactive protein, serum ferritin, prothrombin index, and D-dimer, were significantly higher ($p<0.01$) in diabetic patients compared to non-diabetic patients. which indicates the development of a wider complex of inflammatory reactions in diabetic patients, and this, in turn, over time leads to a rapid deterioration of the course of COVID-19 [27]. Impaired innate immunity, pro-inflammatory cytokine milieu, reduced ACE2 expression, and use of renin-angiotensin-aldosterone system antagonists in people with diabetes contribute to a poor prognosis in COVID-19 [9].

Both hypoglycemia and hyperglycemia have a negative impact on mortality and length of stay in the hospital with COVID-19 [28]. A large US multicenter study of 1,544 patients with COVID-19 from 91 hospitals in 12 states found that hypoglycemia at any time during the hospital stay in both diabetic and nondiabetic patients increased the risk of death (OR 2.2; 95% CI 1.35-3.60) [29].

Regarding the mechanisms of the negative impact of hypoglycemia on the course of COVID-19, some researchers suggest that hypoglycemia leads to an increase in the pro-inflammatory factor lipopolysaccharide during active infection of COVID-19 [30]. Lipopolysaccharide enhances monocyte glucose transporter overexpression to provide monocytes with sufficient glucose to fight infection but at the same time can trigger a cytokine storm that worsens the outcome of the COVID-19 disease [30]. Hypoglycemia can also cause an increase in counterregulatory hormonal adrenergic activity, leading to further inflammatory stress [31].

Thus, hypoglycemia, in addition to being a risk factor for cardiovascular and all-cause mortality in patients with diabetes, may be a trigger for the "cytokine storm" during COVID-19 disease and negatively impact mortality and length of stay in the hospital with COVID-19 [30].

In turn, COVID-19 can worsen the course of diabetes in patients. As highlighted by E. Maddaloni, and R. Buzzetti (2020), the interaction between COVID-19 and diabetes may be bidirectional, as SARS-CoV-2 can potentially worsen the course of existing diabetes or even the predisposition to diabetes in individuals without diabetes [32].

Thus, COVID-19 can also present with dyspeptic symptoms, such as vomiting and diarrhea, which aggravate dehydration [33]. COVID-19 uses the angiotensin-converting enzyme type 2 (ACE-2) receptor as a "gateway" to invade human target cells [34]. This enzyme is expressed by various tissues and cell types, including the lungs, as well as the endocrine part of the pancreas [34]. Direct β-cell damage, cytokine-induced insulin resistance, hypokalemia, and drugs used to treat COVID-19 may contribute to impaired glucose control in people with DM. This complex two-way interaction between COVID-19 and diabetes creates a vicious cycle in which COVID-19 worsens dysglycemia and diabetes exacerbates the severity of COVID-19 [9].

In addition to all of the above, there are also **«organizational factors,»** which in turn cause problems in the treatment and monitoring of the patient's condition. In a

large study by I.A. Kshanti et al. (2021) with 1124 patients with diabetes aged 18 years and older participating authors studied the correlation between difficulties in diabetes management and related complications during the COVID-19 pandemic. It was established that 69.8% of patients experienced difficulties in treatment. Difficulties included attending a diabetes consultation 30.1%, accessing medication 12.4%, checking blood glucose levels 9.5%, controlling diet 23.8%, and doing regular exercise 36.5%. Complications related to diabetes occurred in 24.6% of subjects. Those who had difficulty managing diabetes during the COVID-19 pandemic were 1.4 times more likely to have diabetes complications (OR: 1.41, 95% CI: 1.09-1.83) than those who did not have [35].

Among 667 Americans aged 18-90 years with diabetes (type 1 diabetes (T1DM): 18%; T2DM: 82%), 19% and 17% reported problems accessing diabetes care and test strips, respectively. More than a quarter reported problems getting sugar-lowering drugs from the pharmacy, and more than a third reported problems consulting diabetes service providers. The pandemic led to non-adherence to the therapeutic regimen (14%), medication rationing (17%), and reduced monitoring (16%). Many found it difficult to monitor and control hypoglycemia (12%-15%) and lacked social support to help manage the risk (19%). Almost half reported a decrease in physical activity [36]. In this category of patients, the frequency of severe and mild hypoglycemia was 0.68 (95% CI from 0.5 to 0.96) and 2.75 (95% CI from 2.4 to 3.1) events per person per month, respectively [36].

Quarantine led to food restrictions in some cases. And due to the absence of a balanced diet, a deficit of electrolytes and trace elements quickly develops, carbohydrate metabolism is disturbed, and as a result, hypoglycemia develops.

Thus, the analysis of hypoglycemia causes during the treatment of patients with COVID-19 allows us to formulate the following recommendations:

- In patients undergoing outpatient or inpatient treatment for COVID-19, it is necessary to ensure careful control of the level of glycemia. Glycemic monitoring should be especially thorough in patients of the risk group (diabetes mellitus, prediabetes) and patients with a severe course of COVID-19.
- In patients with COVID-19 and concomitant DM, the dosage of oral antidiabetic drugs may need re-adjustment depending on blood glucose parameters and prevailing conditions. Serious changes in hypoglycemic drugs should be avoided, and treatment modifications should be carried out gradually.
- The known and possible hypoglycemic effects of drugs should be taken into account when determining the treatment program for COVID-19 in patients with diabetes mellitus.
- Polypharmacy and dangerous pharmacotherapeutic combinations should be avoided as much as possible when forming a treatment program.
- In the case of vaccination, clinicians should consider the possibility of hypoglycemia in high-risk patients (with diabetes, prediabetes) or patients with a history of COVID-19.

CONCLUSIONS

1. Hypoglycemia can be an accidental clinical finding. But it can also be a natural consequence of treatment if it is carried out without taking into account the possible hypoglycemic effects of drugs and without careful monitoring of the patient's condition.
2. Hypoglycemia is caused by the mutually aggravating influence of diabetes and COVID-19, the high frequency of hypoglycemic reactions to various groups of drugs used in patients with COVID-19, and deficiencies in the organization of outpatient and inpatient care.
3. In order to prevent hypoglycemic states, patients should avoid sudden changes in the means of treatment for COVID-19, the type and dose of hypoglycemic drugs, carefully monitor the level of glycemia, avoid polypharmacy, and the use of combinations of drugs that are dangerous for hypoglycemia.

PROSPECTS FOR FURTHER RESEARCH

There is no doubt that it is necessary to continue the search for new optimal methods of treatment and prevention of COVID-19, taking into account the pathogenesis of comorbid conditions, in particular diabetes, which will make it possible to improve the prognosis and quality of life of such patients.

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