

БИОМЕДИЦИНА ВА АМАЛИЁТ ЖУРНАЛИ ЖУРНАЛ БИОМЕДИЦИНЫ И ПРАКТИКИ JOURNAL OF BIOMEDICINE AND PRACTICE

INFECTIOUS DISEASE

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REVIEW OF ARTICLES RELATED TO COVID-19 AND DIABETES MELLITUS COMORBIDITY

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ANNOTATION

This article provides summary recommendations of some manuscripts related to Covid-19 and diabetes mellitus comorbidity. Manuscripts related to this topic were searched in PubMed. The article describes the mechanisms how COVID-19 may enhance complications in individuals with diabetes mellitus and providing special considerations on anti-diabetes drugs commonly used in patients with type 2 diabetes in view of COVID-19 developed by group of researches. These recommendations can be useful for those physicians who are involved in case management of Covid-19 and diabetes mellitus.

Key words: Covid-19, diabetes mellitus, SARS CoV-2, metformin, insulin.

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COVID-19 И КОМОРБИДНОСТЬ САХАРНОГО ДИАБЕТА (ОБЗОРНАЯ СТАТЬЯ)

АННОТАЦИЯ

В этой статье представлены сводные рекомендации, собранные при анализе научных статей, касающиеся Covid-19 и сопутствующей патологии как сахарный диабет. Научные статьи, относящиеся к этой теме, были собраны на платформе PubMed. В статье описываются

механизмы, с помощью которых COVID-19 может усиливать осложнения у больных с сахарным диабетом, а также приводятся особые рекомендации по применению антидиабетических препаратов, обычно используемых у пациентов с диабетом 2 типа. Эти рекомендации могут быть полезны врачам, которые занимаются лечением Covid-19 и сахарного диабета.

Ключевые слова: Covid-19, сахарный диабет, SARS CoV-2, метформин, инсулин.

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COVID-19 ВА ҚАНДЛИ ДИАБЕТНИНГ БИРГА КЕЛИШИ

АННОТАЦИЯ

Ушбу мақолада COVID-19 ва қандли диабетнинг бирга келиши билан боғлиқ бўлган мақолалар таҳлилидан йиғилган тавсияларнинг қисқача мазмуни келтирилган. Ушбу мавзуга оид мақолалар PubMed платформасидан тўпланган. Ушбу мақолада, COVID-19, қандли диабетни бор беморларда оғир асоратларга олиб келиш механизмлари баён этилган ва қандли диабетнинг 2-тури бўлган беморларда тез-тез ишлатиладиган диабетга қарши препаратларни қўллаш бўйича аниқ тавсиялар берилган. Ушбу тавсиялар Covid-19 ва қандли диабетни даволаш билан шуғулланадиган шифорлар учун фойдали бўлиши мумкин.

Калит сўзлар: Covid-19, қандли диабет, SARS CoV-2, метформин, инсулин

Background. The outbreak of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first reported in Wuhan, China, in December 2019. On 30 January 2020, WHO Director-General Dr Tedros Adhanom Ghebreyesus declared the COVID-19 outbreak a Public Health Emergency of International Concern. The declaration is WHO's highest level of alarm – a rallying call to all countries to immediately take notice and take action.

The COVID-19 virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes. The best way to prevent and slow down transmission is to be well informed about the COVID-19 virus, the disease it causes and how it spreads. Protect yourself and others from infection by washing your hands or using an alcohol based rub frequently and not touching your face. Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. Older people, and those with underlying medical problems like diabetes mellitus (DM), cardiovascular disease, chronic respiratory disease, and cancer are more likely to develop serious illness (1).

COVID-19 and DM

Patients with DM have experienced and continue to experience significant challenges during the period of the COVID-19 pandemic. Even if they are not infected, they are at risk of dysregulated glycemic control due to the overall restrictive measures which compromise and disrupt the quality of healthcare delivery, especially to patients with chronic diseases. Moreover, restrictive measures in many countries have restricted the physical activity of city dwellers. In addition, many people with diabetes discontinued scheduled visits for diabetes control either because hospitals discontinued regular outpatient clinics or because people with diabetes, due to the fear of SARS-CoV-2 exposure in hospitals, canceled their scheduled visits. In the case of infection, patients with DM have an increased risk of developing severe and potentially fatal complications. Nevertheless, it would be inappropriate to conclude that all patients with DM have an equally increased risk for severity and mortality due to COVID-19. Certain clinical and biological characteristics determine high risk phenotypes within the DM population and such prognostic markers need to be clearly characterized

in future studies. Whether these phenotypic features include long-standing DM, advanced age, concomitant obesity and other cardiometabolic complications, profound insulin resistance or subclinical inflammation remains to be determined (2).

People with diabetes do not exhibit increased susceptibility to SARS-CoV-2 infection. However, COVID-19 infection results in increased rates of hospitalization and greater severity of illness in people with type 1 diabetes, type 2 diabetes, or obesity. A few illustrative reports highlight the extent of these findings, with relative proportions often differing across centers. On November 20, 2020, the International Severe Acute Respiratory and Emerging Infection Consortium (<https://isaric.tghn.org/>), representing dozens of countries and multiple continents, reported 95,966 clinical COVID-19 cases (93.4% with laboratory-confirmed SARS-CoV-2 infection) wherein prevalence of diabetes was 17.4% (3). Yongli Yan et al reported that of 193 patients with severe covid-19, 48 (24.9%) had diabetes. Compared with patients with severe covid-19 without diabetes, patients with diabetes were older, susceptible to receiving mechanical ventilation and admission to ICU, and had higher mortality. In addition, patients with severe covid-19 with diabetes had higher levels of leukocyte count, neutrophil count, high-sensitivity C reaction protein, procalcitonin, ferritin, interleukin (IL) 2 receptor, IL-6, IL-8, tumor necrosis factor α , D-dimer, fibrinogen, lactic dehydrogenase and N-terminal pro-brain natriuretic peptide. Among patients with severe covid-19 with diabetes, more non-survivors were men (30 (76.9%) vs 9 (23.1%)). The authors concluded that the mortality rate in patients with severe covid-19 with diabetes is considerable. Diabetes may lead to an increase in the risk of death (4).

COVID-19 may enhance complications in individuals with DM through an imbalance in angiotension-converting enzyme 2 (ACE2) activation pathways leading to an inflammatory response. ACE2 imbalance in the pancreas causes acute β -cell dysfunction and a resultant hyperglycemic state. These individuals may be prone to worsened COVID-19 complications including vasculopathy, coagulopathy as well as psychological stress. It can also be associated with a higher basal level of pro-inflammatory cytokines present in patients with diabetes, which enables a hyperinflammatory “cytokine storm” in response to the virus. Apart from general preventive measures, remaining hydrated, monitoring blood glucose regularly and monitoring ketone bodies in urine if on insulin is essential. All this while concurrently maintaining physical activity and a healthy diet (5).

Research works in many countries demonstrates that DM in patients with COVID-19 is associated with a two-fold increase in mortality as well as severity of COVID-19, as compared to non-diabetics (6). Further studies on the pathogenic mechanisms and therapeutic implications need to be done. Multiple datasets from China, Italy and the USA have consistently reported that the clinical course of COVID-19 is more severe in patients with advanced age (>70 years old) and pre-existing comorbidities, predominantly DM, hypertension and cardiovascular disease (7).

Recommendations for health care managers and clinicians to mitigate severe complications for COVID and DM comorbidities.

The group of researches leading by Prof. Stefan R Bornstein reviewed guidelines for the management of COVID-19 published by WHO, American Diabetes Association, and the US Centers for Disease Control and Prevention. They also reviewed relevant references cited in retrieved articles. Articles published in English, Italian, and Chinese were included. The final reference list was generated on the basis of relevance to the topics, with the aim of emphasizing the multiple challenges the health-care professionals from practitioners to intensive care staff might face in the management of patients with diabetes and at risk of or with COVID-19. Based on analysis of those resources they provided the following special considerations on anti-diabetes drugs commonly used in patients with type 2 diabetes in view of COVID-19 (8).

Consideration of potential metabolically interfering effects of drugs in suspected or COVID-19 positive patients with type 2 diabetes

Metformin

- Dehydration and lactic acidosis will probably occur if patients are dehydrated, so patients should stop taking the drug and follow sick day rules

- During illness, renal function should be carefully monitored because of the high risk of chronic kidney disease or acute kidney injury

Sodium-glucose-co-transporter 2 inhibitors

- These include canagliflozin, dapagliflozin, and empagliflozin
- Risk of dehydration and diabetic ketoacidosis during illness, so patients should stop taking the drugs and follow sick day rules
- Patients should avoid initiating therapy during respiratory illness
- Renal function should be carefully monitored for acute kidney injury

Glucagon-like peptide-1 receptor agonists

- These include albiglutide, dulaglutide, exenatide-extended release, liraglutide, lixisenatide, and semaglutide
- Dehydration is likely to lead to a serious illness so patients should be closely monitored
- Adequate fluid intake and regular meals should be encouraged

Dipeptidyl peptidase-4 inhibitors

- These include alogliptin, linagliptin, saxagliptin, and sitagliptin
- These drugs are generally well tolerated and can be continued

Insulin

- Insulin therapy should not be stopped
- Regular self-monitoring of blood-glucose every 2–4 hours should be encouraged, or continuous glucose monitoring
- Carefully adjust regular therapy if appropriate to reach therapeutic goals according to diabetes type, comorbidities, and health status

Connected Health models and Telemedicine should be used to continue regular reviews and self-management education programmes virtually and ensure patients are adherent to therapy.

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