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Pharmacotherapeutic Considerations in the Management of Hypertensive and Diabetic COVID-19 Patients

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***Abstract*—** The COVID-19 disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 has emerged as a pandemic inflicting more than 229 million people over the globe. Preexisting illnesses including diabetes, hypertension, and cardiovascular diseases are known to increase the risk of developing severe disease course and mortality. Likewise, COVID-19 potentiates the risk of acute cardiovascular events, multiorgan damages and, poor glycemic control among the patients. Special pharmacotherapeutic considerations are, therefore, essential for optimal treatment of COVID-19 patients with chronic comorbidities. In this editorial, we have summarized and interpreted the current information and guidelines about the need for pharmacotherapy adjustment in COVID-19 patients with hypertension and type II diabetes. Diabetic and hypertensive patients with mild to moderate COVID-19 disease should be encouraged to continue their usual medications with frequent monitoring. However, the choice of antidiabetic drugs needs to be reviewed in severe diseases.

Keywords: COVID-19 pandemic; Comorbidities; Diabetes, Hypertension; Pharmacotherapy; Recommendations.

1. INTRODUCTION

Coronavirus disease-19 (COVID-19) has emerged as a major cause of morbidity and mortality worldwide. Till the date of this writing, over 229 million cases of COVID-19 have been recorded. Patients with chronic illnesses including diabetes mellitus, hypertension, and cardiovascular diseases have been considered as high-risk patients for COVID-19 [1]. The high risk in these patients may manifest itself as an increased likelihood of contracting SARS-CoV-2 infection, developing severe disease, or mortality. Likewise, COVID-19 per se is associated with an increased risk of acute cardiovascular events (myocardial infarction, myocarditis, heart failure, arrhythmias, and venous thromboembolic events), renal failure, and poor glycemic control [2]. Therefore, management of chronic illnesses in COVID-19 patients should be considered a priority. As COVID-19 is likely to damage various organs and adversely affect the homeostasis of biochemical parameters, therefore, several disease-disease and disease-drug interactions are possible between COVID-19 and chronic morbidities [3]. This may require special pharmacotherapy considerations for the treatment of COVID-19 with these conditions. Here we summarize and interpret the current information and guidelines about the need for pharmacotherapy adjustment in COVID-19 patients with hypertension and type II diabetes.

Hypertension is one of the most common chronic diseases affecting over 1.4 billion of the world population [4]. Previous studies have revealed an increased risk of developing severe disease and therefore higher mortality among hypertensive COVID-19 patients [5] but there is no straight confirmation that hypertension increases the risk of new infection [6]. There is also concern about the use of renin-angiotensin system (RAS) inhibitors due to a key role of angiotensin-converting enzyme 2 receptors in the entry of the SARS-CoV-2 virus into cells. Angiotensin-converting enzymes inhibitors (ACEI) and angiotensin receptor blockers (ARBs) are the most frequently prescribed antihypertensive drugs as first-line therapy. The viral spike (S) protein uses angiotensin-converting enzyme 2 for receptor-mediated entry to the host cell, this has led to the suggestion that the use of ACEIs and ARBs may increase susceptibility to SARS-CoV-2 infection and poorer outcomes through upregulation of angiotensin-converting enzyme 2 [4].

However, current observational studies of confirmed COVID-19 patients have increased confidence that the antihypertensive drugs including ACEIs, ARBs, calcium channel blockers and thiazide diuretics are not associated with increased likelihood of either a positive coronavirus test or increased risk of severe COVID-19 illness [7-9]. As ACEIs and ARBs are considered safe, well-tolerated, and effective, and as current evidence does not support the withdrawal of ACEI and ARBs in well-controlled patients with hypertension and corona infection, therefore, major medical organizations including the American Heart Association and European Society of Cardiology have recommended the continuation of

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ACEI and ARBs in all hypertensive patients with COVID-19 [4].

Diabetes has emerged as one of the most important comorbidities affecting the prognosis of COVID-19 patients and is an independent predictor of adverse outcomes [10]. Patients with diabetes have a twofold increase in fatal outcomes than those without. Hypoglycemia and hyperglycemia are both predictors of adverse outcomes in hospitalized patients, therefore, maintaining good glycemic control is mandatory [11]. Studies have suggested adherence to ongoing therapy or intensive therapy as a wise approach for the management of diabetic patients with COVID-19. However, the choice of antidiabetic drugs needs to be reviewed in severe disease.

Insulin administration alongside continuous glucose monitoring to avoid insulin-induced hypoglycemia is considered as the treatment of choice in COVID-19 critical patients with diabetes. Certain beneficial effects have been ascribed for insulin when used for the management of diabetes in COVID-19 patients. Insulin reportedly reduced markers of inflammations in hospitalized patients with a critical illness [12]. Intravenous insulin treatment had strong beneficial effects on inflammation and coagulation in hospitalized type 2 diabetic patients with COVID-19 over a period of 2 weeks [13]. As with other severe infections, diabetic ketoacidosis (DKA) has been reported in DM patients with COVID-19. Available evidence highlighted that subcutaneous insulin therapy was a useful strategy for uncomplicated DKA during the pandemic [14]. Experimental studies have shown that insulin downregulates ACE2 receptors, which reduce the risk of viral infection.

Emerging evidence found that treatment with Metformin in DM patients with coronavirus infection is not harmful and could possibly be beneficial [15], however, the recent guidelines for the management of diabetes during the COVID-19 pandemic have recommended stopping metformin in those with fever and acute illness (body temperature >38.5 °C, GFR <30 ml/min/1.73m2) [16]. Pioglitazone has been recommended to discontinue in critically ill patients due to its adverse effect of fluid retention and the suggested upregulation of ACE2 receptors, however, it has been found beneficial in patients with mild to moderate disease. Similarly, DPP4 inhibitors may also be continued in mild to moderate COVID-19. Similarly, the other oral hypoglycemic agents are recommended to be used in mild to moderate disease but discontinue in critically ill patients of COVID-19. The beneficial and adverse effects of various antidiabetic drugs as reported in the literature previously and the recommendations of their use in COVID-19 patients are given in **Table 1** [10,17].

Pharmacotherapy of COVID-19 in diabetic patients also requires careful considerations. RECOVERY study on corticosteroid treatment has shown that dexamethasone decreases mortality in patients suffering from the severe forms of COVID-19 disease. However, previous studies seem to show a worse prognosis in COVID-19 patients with corticosteroids therapy. As hyperglycemia has been shown to have deleterious effects on the outcome of disease, therefore, advantages of using corticosteroids in COVID-19 patients with diabetes are lost possibly due to damage caused by hyperglycemia [11]. This emphasizes the need for frequent monitoring and glycemic control in diabetic COVID-19 patients.

Remdesivir is the only FDA-approved drug for the treatment of the severe forms of COVID-19. Although studies on Remdesivir treatment impact on diabetic patients are lacking, its potential to promote liver and kidney damage warrants an evaluation of diabetic patients for the presence of prior liver and kidney diseases as well as frequent monitoring of liver and kidney functions after the onset of therapy [11].

Table 1. Potential risks and benefits of antidiabetic agents in relation to SARS-CoV-infection [10,17]

Antidiabetic agent	Beneficial effect	Disadvantages	Recommendation
Insulin	ACE 2 downregulation and reduced inflammatory markers	Require frequent monitoring for hypoglycemia	Drug of choice for severely ill patients
Metformin	Reduced risk of uncomplicated diabetes ketoacidosis, lowered death and, Interleukin-6 levels	Risk of lactic acidosis, increased risk of poor prognosis	Stop treatment in those with fever, hypoxia, and acute illness
Pioglitazone	Lowered mortality among hospitalized patients, inhibited viral replication Decreased pro-inflammatory cytokines	Up-regulated ACE2 Risk of fluid retention and edema	Stop if severely ill with hemodynamic instability, or hepatic or cardiac dysfunction
DPP4 inhibitors	Inhibits SARS-CoV-2 replication, reduces levels of pro-inflammatory cytokines Preserve endothelial functions Low risk of hypoglycemia and possible to use for a wide range of renal functions		Continue in mild to moderate COVID-19
SGLT2 inhibitors	Anti-inflammatory action, reduced cardiovascular and renal complications, reduced mortality and improved clinical outcome	Increased risk of dehydration and euglycemic ketoacidosis	Continue in mild to moderate COVID-19 and stop if oral intake is not tolerated and in severely ill patients.
GLP-1RAs	Exerts anti-inflammatory effects and reduced inflammatory cytokines Reduced hypoglycemia and glucose variability	Gastrointestinal side effects and risk of aspiration	Stop in severely ill patients

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REFERENCES

1. de Almeida-Pititto B, Dualib PM, Zajdenverg L, Dantas JR, de Souza FD, Rodacki M, Bertoluci MC. . Severity and mortality of COVID 19 in patients with diabetes, hypertension and cardiovascular disease: a meta-analysis. Diabetology & Metabolic Syndrome. 2020;12:75. doi: https://doi.org/10.1186/s13098-020-00586-4.
2. Longo M, Caruso P, Maiorino MI, Bellastella G, Giugliano D, Esposoito K. Treating type 2 diabetes in COVID-19 patients: the potential benefits of injective therapies. Cardiovascular Diabetology. 2020;19:115. doi: https://doi.org/10.1186/s12933-020-01090-9.
3. Kumar D, Trivedi N. Disease-drug and drug-drug interaction in COVID-19: Risk and assessment. Biomedicine & Pharmacotherapy. 2021;139:111642. doi: https://doi.org/10.1016/j.biopha.2021.111642.
4. Antwi-Amoabeng D, Beutler BD, Moody AE, Kanji Z, Gullapalli N, Rowan CJ. Management of hypertension in COVID-19. World Journal of Cardiology. 2020;12(5):228-230. doi:10.4330/wjc.v12.i5.228
5. Clark, C.E., McDonagh, S.T.J., McManus, R.J. Martin U. COVID-19 and hypertension: risks and management. A scientific statement on behalf of the British and Irish Hypertension Society. Journal of Human Hypertension 2021;35,304–307. https://doi.org/10.1038/s41371-020-00451-x.
6. Kario K, Morisawa Y, Sukonthasarn A, Turana Y, Chia YC, Park S, Wang TD, Chen CH, Tay JC, Li Y, Wang JG. Hypertension Cardiovascular Outcome Prevention, Evidence in Asia (HOPE Asia) Network. COVID-19 and hypertension-evidence and practical management: Guidance from the HOPE Asia Network. The Journal of Clinical Hypertension (Greenwich). 2020;22(7):1109-1119. doi: 10.1111/jch.13917.
7. Mancia G, Rea F, Ludergnani M, Apolone G, Corrao G. Renin–angiotensin–aldosterone system blockers and the risk ofcovid-19. New England Journal of Medicine. 2020;382:2431–40. doi: 10.1056/NEJMoa2006923.
8. Reynolds HR, Adhikari S, Pulgarin C, Troxel AB, Iturrate E,Johnson SB, et al. Renin–angiotensin–aldosterone system inhibitorsand risk of covid-19. New England Journal of Medicine. 2020;382:2441–2448. doi: 10.1056/NEJMoa2008975.
9. Mehta N, Kalra A, Nowacki AS, Anjewierden S, Han Z, Bhat P.Association of use of angiotensin-converting enzyme inhibitors andangiotensin II receptor blockers with testing positive for coronavirusdisease 2019 (COVID-19). JAMA Cardiology. 2020;5:1020–1026. doi: 10.1001/jamacardio.2020.1855.
10. Sun B, Huang S, Zhou J. Perspectives of Antidiabetic Drugs in Diabetes With Coronavirus Infections. Frontiers in Pharmacology. 2021;11:592439. doi:10.3389/fphar.2020.592439
11. Ceriello A, Prattichizzo F. Pharmacological management of COVID-19 in type 2 diabetes. Journal of Diabetes and Its Complications. 2021;35(7):107927. doi: 10.1016/j.jdiacomp.2021.107927.
12. Hansen TK, Thiel S, Wouters PJ, Christiansen JS, Van den Berghe G. Intensive insulin therapy exerts antiinflammatory effects in critically ill patients and counteracts the adverse effect of low mannose-binding lectin levels. Journal of Clinical Endocrinology and Metabolism 2003;88(3):1082–1088. doi: 10.1210/jc.2002-021478.
13. Sardu C, D'Onofrio N, Balestrieri ML, et al. Outcomes in patients with hyperglycemia affected by COVID-19: can we do more on glycemic control? Diabetes Care 2020;43:1408-15. doi: https://doi.org/10.2337/dc20-0723.
14. Palermo NE, Sadhu AR, McDonnell ME. Diabetic ketoacidosis in COVID-19: unique concerns and considerations. Journal of Clinical Endocrinology and Metabolism. 2020;105(8):dgaa360. doi: 10.1210/clinem/dgaa360.
15. Kumar Singh A, Singh R. Is Metformin ahead in the race as a repurposed host-directed therapy for patients with diabetes and COVID-19? Diabetes Research and. Clinical Practice. 2020;165:108268. Doi: 10.1016/j.diabres.2020.108268.
16. Sinclair A, Dhatariya K, Burr O, Nagi D, Higgins K, Hopkins D, Patel M, Kar P, Gooday C, Howarth D, Abdelhafiz A, Newland-Jones P, O'Neill S. Guidelines for the management of diabetes in care homes during the Covid-19 pandemic. Diabetic Medicine. 2020;37(7):1090-1093. doi: 10.1111/dme.14317.
17. Corrao S, Pinelli K, Vacca M, Raspanti M, Argano C. Type 2 Diabetes Mellitus and COVID-19: A Narrative Review. Frontiers in Endocrinology. 2021;12:609470. doi:10.3389/fendo.2021.609470