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EDITORIAL

Diabetes mellitus and SARS-CoV-2 infection[☆]

Diabetes mellitus e infección por SARS-CoV-2

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In the present article, Marcos M. Lima-Martínez et al. conduct an in-depth review of the numerous pathophysiological mechanisms reported in the literature involved in the higher morbi-mortality of individuals with diabetes mellitus (DM) and SARS-CoV-2 infection in comparison with those who do not have DM. The work also analyses the effect of glycaemic control on parameters related with the course of the infection and examines recommendations as regards glycaemia-lowering, blood pressure, and anti-coagulant treatments in subjects with DM and COVID-19 (coronavirus infection).

Type 2 DM (DM2) is the second most common comorbidity in patients hospitalised for COVID-19, after high blood pressure.¹ Similarly, obesity, highly prevalent in individuals with DM2 and considered another pandemic of the XXI century, has also been associated with a worse evolution in obese patients with SARS-CoV-2 infection, both in patients who have DM, as well as in those who do not.^{2,3}

In the review, the authors emphasize the two-way relationship that exists between DM and COVID-19. Recently diagnosed DM is a relatively commonplace phenomenon. Close to 14% of the patients hospitalised due to COVID-19 suffer from DM.⁴ It has been suggested that hyperglycaemia,

both *de novo* as well as that present in subjects already diagnosed with DM, could be secondary to the decreased pancreatic secretion of insulin due to the fact that the ACE2 (SARS-CoV-2 virus receptor) is present in pancreatic beta cells. Another possible cause of hyperglycaemia, in these patients, would be the development of insulin resistance secondary to the degree of inflammation associated with the cytokine storm and that, in turn, would also affect pancreatic beta cell functioning.⁵ In this regard, it must be pointed out that suggestion has been made that the virus might be the cause of some cases in which DM appears for the first time in the form of diabetic ketoacidosis and the absence of any pancreatic reserve of insulin with negative autoimmunity.⁶ It is worth highlighting that individuals with recently diagnosed DM display a higher risk for hospitalisation in Intensive Care Units (ICU) and for mortality than those patients with DM that was already known prior to hospitalisation.⁷

In a recent meta-analysis, subjects with known DM and with SARS-CoV-2 infection were shown to exhibit a twofold risk of hospitalisation in an ICU and close to a threefold risk of in-hospital mortality.⁸ The increase in mortality has been reported in subjects with DM2, as well as in those with DM1.^{9–11} The factors that have been correlated with said increment in morbimortality in subjects with DM include those having to do with metabolic control in DM, in addition to the high prevalence of other comorbidities in these patients.¹²

The data published to date have stressed the importance of glycaemic control during hospitalisation as a factor associated with the prognosis of patients with DM hospitalised for COVID-19. It is worthwhile to note that, at

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present, in-hospital hyperglycaemia in individuals with or without a previous diagnosis of diabetes is widely accepted to be associated with a higher risk of complications and mortality.¹³ The glycaemic control targets in subjects who are hospitalised on a conventional [medical] ward (non-critical condition) set by the American Association of Clinical Endocrinology and the American Diabetes Association are preprandial glycemia of <140 mg/dl and random glycemia of <180 mg/dl.¹⁴ More recently, the American Diabetes Association recommends a target glycemia for hospitalised patients in non-critical condition of between 140 and 180 mg/dl.¹⁵

In subjects hospitalised for COVID-19, it has been reported that hyperglycaemia (glycemia >180 mg/dl), particularly when it is present in the first few days of hospitalisation is associated with a worse prognosis in subjects with DM.^{16,17} On the other hand, hypoglycaemia (glycemia <70 mg/dl), a common side effect in people treated with insulin, has also been reported to be correlated with greater mortality in subjects with DM who are infected with SARS-CoV2.¹⁶ With respect to the relationship with glycaemic control prior to admission, several retrospective studies have reported that hospitalisation relates to both the risk of contracting SARS-CoV-2 infection as well as their prognosis (need for hospitalisation, mortality).^{18–20}

The second aspect that the COVID-19 pandemic has illustrated is the importance of telemedicine and telemonitoring as valuable tools to optimize glycaemic control in people with DM. Telemedicine makes it possible to decrease the number of in-person appointments and is highly beneficial to monitor those patients who are unable to travel, as in the situation of home confinement due to COVID-19. In this regard, the use of continuous glucose monitoring (CGM) devices, in individuals with DM1 who are confined to their home, during the pandemic, improves glycaemic without increasing the risk of hypoglycaemia.^{21–23} The improvement was more evident in who did not commute to their workplace and could, at least in part, be due to the possibility of following regular schedules, the decreased work-related stress, as well as more time to dedicate to the self-care DM calls for.²⁴ The result obtained with these CGM devices is impacted in large part, by the patient's degree of motivation to enhance their glycaemic control. It has therefore been suggested that these outcomes are not applicable to individuals with DM1 who are less motivated to control or to those who do not use CGM systems, and/or whose social and labour situation compete for the time dedicated to diabetes management.²⁵ In subjects with DM2 who have not used CGM systems, the results with respect to glycaemic control during confinement are disparate. Thus, some studies have reported higher HbA1c values,²⁶ whereas, others have found HbA1c to improve.²⁷ In patients with DM2, medical care during the COVID-19 pandemic by means of teleconsultation (via telephone or telematic visits) has exponentially surpassed in-person appointments.²⁸

The use of CGM devices might be a good option to optimize glycaemic control in subjects with DM who are in the hospital. CGM lowers the risk of infection for nursing staff, inasmuch as it substantially lowers the number of finger sticks needed. Furthermore, their use in hospitalised DM patients has been associated with having their glycaemia in range for longer.^{29,30}

In short, there are two actions aimed at glycaemic control that appear to be most suitable to improve prognosis in people with DM and COVID-19, according to the data in the literature to date: avoiding hyperglycaemia (>180 mg/dL) and hypoglycaemia (<70 mg/dL) in hospitalised patients right from the time of admission, and optimising glycaemic control in individuals following an outpatient regime by means of telemedicine with telemonitoring. In this type of DM1 patient, the use of these tools, especially CGM devices, has proven to be useful to enhance metabolic control. In addition, it lowers the number of in-person appointments. These appointments should be reserved for those individuals who cannot avail themselves of telemedicine. One vitally important element to the successful consolidation of teleconsultations in the post-COVID era, is that they be good quality, both in terms of the connection, as well as their content. For this to happen, technological resources must be improved, as well as the training of healthcare professionals and patients. However, we must not lose sight of the fact that the limitations of teleconsultations must co-exist with in-person appointments.³¹

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