Navigating Through the COVID-19 Pandemic: New Lessons on Diabetes and the Cardiovascular System

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MULTIDISCIPLINARY care is the future of medicine, as it becomes increasingly apparent that a single patient treated by a single doctor is an old-fashioned and restrictive approach. This year's European Association for the Study of Diabetes (EASD) Virtual Meeting showcased the importance of such cross-disciplinary care by timetabling multiple cross-curricular sessions, including 'Navigating Through the COVID-19 Pandemic and New Lessons from Cardiovascular Outcome Trials', which served to update clinicians across the endocrinology and cardiology therapeutic areas on coronavirus disease (COVID-19) patient management.

CARDIOVASCULAR RISK MANAGEMENT IN PATIENTS WITH DIABETES AND COVID-19

"There is no doubt that diabetes is one of the most important contributors to the worst prognosis in COVID-19," began Prof Antonio Ceriello, Head of the Diabetes Department, IRCCS MultiMedica, Milan, Italy. However, he was quick to interject that we have already learnt many valuable lessons about patient care in diabetes and COVID-19 since the start of the pandemic, including the control of hyperglycaemia, and the prescribing of antidiabetic drugs, angiotensin-converting enzyme inhibitors (ACEi) and angiotensin II receptor blockers (ARB), corticosteroids, and hydroxychloroquine.

Hyperglycaemia

A recent study has analysed the mortality rate among 7,300 patients with COVID-19 and Type 2 diabetes mellitus; those with well-controlled blood glucose (upper limit: $\leqslant 10$ mM), as opposed to those with poorly-controlled blood glucose (upper limit: >10 mM), showed a strong association to a lower death rate. Looking further into this relationship, Prof Ceriello reported on another study's findings: "What appeared to be most important was the level of the hyperglycaemia at admission, more than previous glycaemic control." There are several other

studies that have since confirmed this evidence, suggesting that the level of HbA1c before admission to hospital does not have a negative effect on the prognosis of these patients with COVID-19 and diabetes.

The link between hyperglycaemia at hospital admission and severity of COVID-19 has also been observed in other studies, though Prof Ceriello noted: "Hyperglycaemia worsened the prognosis, but this was particularly in people without previous history of diabetes." Hyperglycaemia therefore appears to be a very good predictor of the prognosis, but it does appear to be more dangerous in people without diabetes. Other study findings discussed by Prof Ceriello included the recent observations that admission hyperglycaemia is an independent risk factor for poorer outcomes in people with lung disease, sepsis, and in those who experience a cardiac event.

"The control of hyperglycaemia should be considered a key action for the management of this disease," concluded Prof Ceriello.
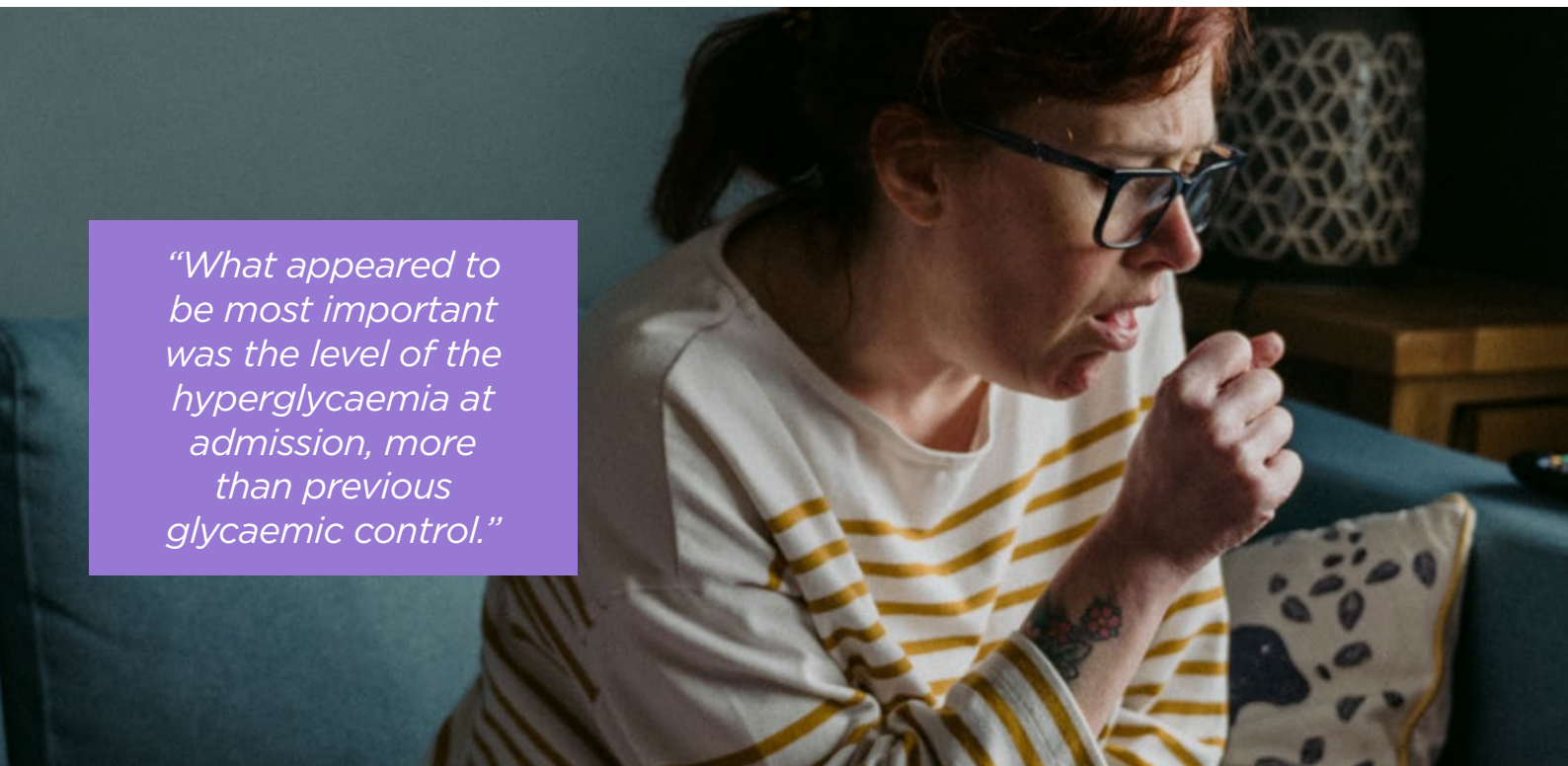
Antidiabetic Drugs

The mechanisms of antihyperglycaemic drugs must be considered in the management of COVID-19 and diabetes, stressed Prof Ceriello. For example, the effect of lowering inflammatory stress and peripheral insulin resistance by reducing the infiltrate with macrophages, via glucagon-like peptide 1 (GLP-1)-dependant signalling by regulating M1/M2 macrophage polarisation, have been described with dipeptidyl peptidase (DPP4) inhibition and GLP-1 receptor activation. Given the significance of preserving the cardiovascular system and kidney function in this pandemic, alongside the known benefits of drugs such as GLP-1 receptor agonists and SGLT-2 and DPP4 inhibitors in achieving this, Prof Ceriello resolved that: "These drugs have a very strong anti-inflammatory activity which can probably help patients with COVID-19."

Angiotensin-Converting-Enzyme Inhibitors and Angiotensin II Receptor Blockers

Given the ACE2 receptor is the entry point for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) into cells, it was hypothesised that patients with cardiac diseases, hypertension, or diabetes who were treated with ACE2-increasing drugs, were at higher risk of severe COVID-19 infection. However, Prof Ceriello then presented the findings of several further studies which found no such link between ACEi or ARB with in-hospital death. Prof Ceriello believes this first report of ACEi and severe COVID-19 could have been very damaging: "Nobody knows how many people stopped using ACEi and ARB, or how many cardiovascular deaths or vascular deaths there were because people stopped use of these drugs."

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Corticosteroids

"At the beginning, the guidelines were suggesting that corticosteroids must be avoided for the treatment of COVID-19," began Prof Ceriello. Now, we have evidence that, in patients hospitalised with COVID-19, dexamethasone can be life-saving; one study concluded that the drug resulted in lower 28-day mortality among those who were receiving either invasive mechanical ventilation or oxygen alone, but not among those receiving no respiratory support. However, corticosteroids are known to increase glycaemia; "When they are used in diabetes, we must pay attention to the balance between the benefits of use and the damage caused by high glucose," emphasised Prof Ceriello.

Hydroxychloroquine

At the beginning of the pandemic, hydroxychloroquine was suggested to be very beneficial for the treatment of COVID-19; however, the articles which advocated its use were subsequently retracted on the grounds of serious methodological issues. "It is well known that this compound can cause some heart damage, as well as increasing the risk of hyperglycaemia in diabetes," warned Prof Ceriello. Unfortunately, the benefits of this treatment are still unclear and under research.

LESSONS LEARNT

There has been much controversy amongst study authors so far in this pandemic, which has led to consequences such as hyperglycaemia (in diabetes and nondiabetes) not being identified as an issue in COVID-19 treatment earlier; "The communications between different specialists has failed," said Prof Ceriello. Purely scientific hypotheses have been considered as true evidence without significant proof, and preliminary therapeutic data were not interpreted with enough caution. However, he did provide some possible solutions to these global challenges: he suggested collaboration between healthcare professionals, patients, professional bodies and organisations, government decision makers, and the mass media, in order to share both best and worst practices.

Prof Ceriello then ended the session with the words: "Effective communication, collaboration, and trust, leading to evidence-based science and decisions, are essential between all 'players' involved in the pandemic of COVID-19."