Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Tackling the pillars of ageing to fight COVID-19

Patients with type 2 diabetes show an increased rate of mortality in relation to COVID-19 when compared with individuals without type 2 diabetes. A chronic status of low-grade inflammation (ie, inflamm-ageing) and an accelerated ageing of the immune system have been proposed among the potential mechanisms explaining the higher susceptibility to worst outcomes of patients with type 2 diabetes and other age-related diseases.[1] In their article, Bramante and colleagues report the results of an elegant retrospective cohort study showing that the use of home metformin in female patients affected by obesity or type 2 diabetes was associated with statistically significantly reduced in-hospital mortality for COVID-19.[2]

From a gerontological perspective, the results from the study by Bramante and colleagues are not surprising. Epidemiological data have suggested that metformin might foster health span and lifespan when compared with both type 2 diabetes patients on other therapies and age-matched patients without diabetes, protecting against a large range of age-related endpoints, including all-cause mortality.[3] In spite of their observational nature, the solidity of the results has finally prompted the design of the Targeting Aging with Metformin trial, specifically aimed at testing whether metformin can reduce the rate of ageing by measuring a number of surrogate endpoints in a large cohort of heterogenous subjects.[4]

Mechanistically, years of research have indicated that metformin might interfere with most hallmarks of ageing, such as genomic instability, epigenetic alterations, nutrient-sensing pathways, mitochondrial dysfunction, cellular senescence, stem cell dysfunction, loss of proteostasis, microbiota shifts, and development of inflamm-ageing, although, which (if any) of the proposed effects might represent the key putative anti-ageing mechanism of metformin remains unknown.[5] However, the drug favourable effects also on mortality rates in patients with sepsis[6] might support a metformin immune-modulating action that could restrain inflamm-ageing. Consistently, metformin users show lower levels of circulating cytokines, including IL-6, a prototypical marker of inflamm-ageing, and a predictor of poor prognosis in patients with COVID-19.[1,5]

Broadly, given the key role of age and age-related diseases in determining COVID-19 outcomes,[1] it is conceivable that a candidate ageing-modifying drug with interlaced reverberations on the function of the immune system, such as metformin, might favourably affect COVID-19-related mortality.

Overall, additional studies are needed to substantiate the metformin protective role against COVID-19 and explore the potential underpinnings. The assessment of a range of inflammatory mediators in large cohorts of patients treated with metformin before and during SARS-CoV-2 infection might help understand whether and how this drug affects the complex interplay among ageing, inflamm-ageing, and COVID-19. More importantly, Bramante and colleagues' data should boost a research effort in studying the pillars of ageing and identifying the interventions able to promote healthy longevity. This approach might not only prevent or delay common age-related diseases, but also limit the deleterious consequences of communicable infectious diseases, such as the ongoing pandemic.

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