Inhaled Corticosteroids in early COVID-19 – a tale of many facets

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To the Editor,

Following our early report in Allergy [1], there was several studies published in the same direction showing the benefit of continuation of inhaled steroids in COVID-19. Inhaled budesonide represents a standard of care for patients with asthma, allergic rhinitis and chronic rhinosinusitis [1-3]. It is recommended that in COVID-19, patients with chronic inflammatory airway diseases should continue guideline-based pharmacological

treatment including ICS and/or biological therapies [1, 2]. New data indicate that patients with various asthma endotypes may show a different risk profile for SARS-CoV-2 infection and a different course of COVID-19. Patients suffering from allergic asthma (type 2 inflammation) seem to have a lower risk of developing COVID-19 than patients with non-type 2 asthma [4].

Ramakrishnan et al. performed an open-label, parallel-group, randomized controlled trial to compare standard of care with the additive use of inhaled budesonide [5]. The authors claim that this is an easily accessible and effective intervention in early COVID-19. Their data also suggest a potential benefit in the prevention of long COVID-19.

However, these statements may not be sufficiently proven. This was an open study, in which patients and staff were aware of the therapy used.*Placebo* effects, for example for inhalant asthma drugs, can be observed in 21 to 46% of cases, especially for subjective outcomes [6]. Effects assessed during this study, including the primary endpoint (COVID-19-related urgent care visit, including emergency department visits or hospitalization), may all be influenced by the subjective perception of the patients and their treating physicians. Secondary endpoints, including objective measures like blood oxygen saturation and SARS-CoV-2 load, were not different between the groups. The study population was small, including 146 participants of which 73 were randomized to usual care and 73 to the budesonide group. A cautious interpretation of these data is warranted, since an updated interim analysis from a larger phase-III study, including 2,617 people with risk factors for adverse outcomes with COVID-19, did not show such favorable results [7]. Inhaled budesonide reduced the time to self-reported recovery by a median of 3 days. However, it did not meet the primary outcome parameter (COVID-19 hospitalizations/deaths) even though these rates were lower in the budesonide versus the usual care group (59/692 (8.5%) and 100/968 (10.3%) respectively) [7].

Ramakrishnan et al. hypothesized that an early administration of inhaled budesonide is beneficial at the early stage of COVID-19. Importantly, this would suggest a low-cost and safe therapy. However, based on the evidence from this and other studies, more research is still necessary to support this recommendation.

Literatur

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