Evolving evidence for immunosuppressants in COVID-19

Aust Prescr 2021;44:7
https://doi.org/10.18773/austprescr.2020.086

I read with great interest the informative article on the role of immunosuppression in the treatment of COVID-19.[1] While appreciating their efforts, I wish to make a few observations.

In the section where the authors have stated the role of systemic corticosteroids, there are two more findings that are worth mentioning. First, a study found that SARS patients treated with high-dose pulse therapy of methylprednisolone had systemic damage along with metabolic alterations at 12-years follow-up.[2] Second, in the RECOVERY trial, treatment with a daily dose of dexamethasone for up to 10 days was associated with reduced 28-day mortality in COVID-19 patients with respiratory support.[3]

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The authors of the article comment:

Evidence in COVID-19 continues to evolve at a rapid pace. While the promise of certain therapeutic options has not materialised, other medicines have emerged from clinical trials with proven clinical efficacy.

While early observational data were promising, tocilizumab failed to improve clinical status and reduce mortality in the COVACTA trial[1] or prevent intubation in the BACC Bay trial.[2] Dexamethasone, in contrast, has demonstrated some clinical and mortality benefit in advanced disease in the RECOVERY trial.[3] As Ajay Shukla points out, the adverse effects of corticosteroids are broad and potentially long-term and should be closely monitored.[4,5] Despite dexamethasone, mortality rates remain high. Successful strategies potentially hinge on strategic selection of the mode and timing of immunomodulation in appropriate clinical settings. Refining this treatment paradigm may only be achieved through rigorous clinical trial evaluation.

Trials evaluating the efficacy and safety of multiple immunosuppressive therapies, including tumour necrosis factor inhibitors[6] and tyrosine kinase inhibitors,[7] continue as we still grapple with this evolving global health crisis. Resources such as the Australian National COVID-19 Clinical Evidence Taskforce's Living Guidelines[8] provide a useful reference point, with important clinical information and summation of emerging evidence for healthcare workers.

While evidence evolves, therapies will either be discounted as unsafe or ineffective or be validated and approved as standard of care. As therapeutic validation occurs, it is important to remember that prescribing outside of clinical trials remains off label and should be conducted in an ethical and considered manner.[9]

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