Should dexamethasone be used for COVID-19?

This clinical evidence summary outlines existing evidence on the use of dexamethasone as a potential treatment for patients with COVID-19. The information may be revised as new evidence emerges. The summary is not exhaustive of the subject matter and does not replace clinical judgement. The responsibility for making decisions appropriate to the circumstances of the individual patient remains at all times with the healthcare professional.

Background

Dexamethasone is a corticosteroid that has been used since the 1960s to reduce inflammation. It is included in the World Health Organization (WHO) Essential Medicines List[1] and is approved by regulatory agencies (including US FDA, EMA and HSA) for a range of conditions, including adrenocortical insufficiency, inflammatory disorders, cancer and shock.

The full spectrum of COVID-19 infection ranges from asymptomatic disease to mild respiratory tract illness to severe pneumonia, acute respiratory distress syndrome (ARDS), multiorgan failure, and death. Clinical presentation of some critically ill patients with COVID-19 suggest a "Cytokine Storm Syndrome" or hyperinflammatory state in which the immunosuppressive effects of corticosteroids may be beneficial.[2]

Corticosteroids were widely used during outbreaks of severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), however, their efficacy has been controversial and largely based on observational studies with conflicting results.[3, 4]

Clinical evidence

Preliminary findings from the RECOVERY trial published in the New England Journal of Medicine suggest that dexamethasone reduces mortality in patients with severe disease[5].

RECOVERY is a large, multicentre, open-label, randomised controlled trial (RCT) conducted in the United Kingdom to assess a range of treatments for patients hospitalised with COVID-19. Over 11,500 patients were enrolled in the trial, of which 2104 patients were randomised to receive dexamethasone 6 mg orally or intravenously for 10 days and 4321 patients were randomised to receive usual care. The primary outcome was 28-day all-cause mortality. Preliminary findings demonstrated that dexamethasone reduced the absolute risk of 28-day mortality by 2.8% compared with usual care (22.9% versus 25.7%; age-adjusted rate ratio, RR 0.83; 95% CI, 0.75 to 0.93). Prespecified subgroup analyses showed that patients receiving mechanical ventilation achieved the greatest benefit (29.3% versus 41.4%; RR 0.64; 95% CI, 0.51 to 0.81) followed by patients receiving oxygen without mechanical ventilation (23.3% versus 26.2%; RR, 0.82; 95% CI, 0.72 to 0.94). Of note, no benefit was seen in patients not requiring respiratory support (17.8% versus 14.0%; RR, 1.19; 95% CI, 0.91 to 1.55).[5]

Several other international trials of dexamethasone for treating COVID-19 have been registered and are in planning or active recruitment stages with data anticipated to mature in the near future (Table 1).

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Table 1: Studies registered internationally for dexamethasone in patients with COVID-19

Study identifier	Study Design	Intervention	Comparator(s)	Date of primary completion
NCT04381936[6] EudraCT 2020-001113-21[7] (RECOVERY)	MC*, OL, phII/III, randomised, factorial assignment	6 intervention groups: • Dexamethasone (low dose) • Lopinavir-ritonavir • Azithromycin • Convalescent plasma • Tocilizumab • Hydroxychloroquine	Standard of care	December 2020
NCT04325061[8] EudraCT 2020-001278-31[9] (DEXA-COVID19)	MC^, OL, phIV, randomised, parallel assignment	Dexamethasone	Standard of care	October 2020
NCT04347980[10] EudraCT 2020-001333-13[11] (DHYSCO)	MC‡, SB, phIII, randomised, parallel assignment	Dexamethasone plus hydroxychloroquine	Hydroxychloroquine	June 2020
NCT04395105[12]	MC†, OL, phIII, randomised, parallel assignment	Dexamethasone	Standard of care	December 2020
NCT04344730[13] EudraCT 2020-001457-43[14] (COVIDICUS)	MC‡, QB, randomised, factorial assignment	Dexamethasone	Placebo	December 2020
NCT04360876[15]	SC#, DB, phIIa, randomised, parallel assignment	Dexamethasone	Placebo	September 2020
NCT04327401[16] (CoDEX)	MCα, OL, phIII, randomised, parallel assignment	Dexamethasone	Standard of care	August 2020
IRCT20151227025726N17[17]**	SC, OL, phII/III, randomised, parallel assignment	Dexamethasone plus standard of careΔ	Standard of careΔ	NA
IRCT20120215009014N354[18]	SC, QB, phII, randomised, parallel assignment	3 intervention groups: • Dexamethasone • Methylprednisolone • Hydrocortisone	Standard of care	NA

Abbreviations: DB, double blind; MC, multicenter; NA, not available; OL, open label, phII, phase II; phIII, phase III; phIV: phase IV; QB, quadruple blind; SB, single blind; SC, single center.
*UK; ^Spain; ‡France; †Argentina; #USA; αBrazil; ** Iran; Δ includes lopinavir/ritonavir

Recommendations from professional bodies

Guidelines issued by the National Institutes of Health (NIH, USA), were recently updated recommending dexamethasone 6 mg for up to 10 days for treating COVID-19 in patients on mechanical ventilation and in patients who require supplemental oxygen. Recommendation against using dexamethasone in patients not requiring supplemental oxygen remained unchanged.[19]

Interim guidelines issued by the National Centre for Infectious Disease (NCID, Singapore) do not recommend the routine use of corticosteroids for COVID-19 unless indicated (e.g. refractory shock, documented hypocortisolism), however, they state that dexamethasone 6 mg for 10 days or its equivalent may be considered in patients with severe COVID-19 (i.e. those requiring oxygen or mechanical ventilation) who have had symptoms for more than 7 days.[20]

The WHO and European Society of Intensive Care Medicine/Society of Critical Care Medicine (ESICM/SCCM) guidelines have yet to be updated and currently do not recommend the routine use of systemic corticosteroids for COVID-19 unless indicated.[21, 22]

Conclusion

Preliminary results from the RECOVERY trial showed that dexamethasone is effective in severely ill patients with COVID-19. Several ongoing studies are likely to report results in the months ahead, and their findings will determine whether dexamethasone should be used more widely in this setting.

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