



Article Appraisal

Article: Dexamethasone in Hospitalized Patients With Covid-19- Preliminary Report.

Date of Journal Club: 15/9/20

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Background and Study Objective(s):

Glucocorticoids may modulate inflammation-mediated lung injury and thereby reduce progression to respiratory failure and death. The objective of this study was to investigate whether 6mg of dexamethasone reduced 28 day mortality compared to standard care in patients with confirmed or suspected COVID-19. Secondary outcomes included time to discharge, and need for new mechanical ventilation in patients (including ECMO). Other clinical outcomes included cause-specific mortality, receipt of renal hemodialysis or hemofiltration, major cardiac arrhythmia, and duration of ventilation.

Study Design:

This was a non-blinded, randomized control trial involving 6425 hospitalized patients across 176 sites in the UK who were diagnosed with or suspected of having Covid-19. Patients were excluded if they, in the opinion of the treating physician, had clear indications or contraindications for steroids. Initially patients were only enrolled if >18 years of age but during the course of the trial this age limit was lifted. Pregnant and breastfeeding women were also included in the trial. Eligible and consenting patients were assigned in a 2:1 ratio to receive either standard of care alone or 6mg PO/IV dexamethasone once daily in addition to standard care for up to 10 days, or until hospital discharge. This study was part of a larger trial evaluating other interventions for Covid-19 (e.g. azithromycin, antivirals).

Results:

89% of patients had PCR confirmed Covid-19. In the dexamethasone group, 95% of patients received at least one dose of dexamethasone; median duration of treatment was 7 days. All cause mortality was 22.9% in the patients receiving 6mg dexamethasone daily compared to 25.7% in the control group (RR 0.83, 95% CI 0.75 to 0.93 P<0.001). In pre-specified analyses, patients receiving mechanical ventilation at the time of randomization showed the greatest reduction in all cause mortality (29.3% vs. 41.4%, RR 0.64, 95% CI 0.51 to 0.81). A lesser benefit was observed in patients receiving oxygen (23.3% vs 26.2%, RR 0.82, 95% 0.72-0.94), and there was no benefit patients not requiring any respiratory support at randomization (17.8% vs 14%, RR 1.19, 95% CI 0.91-1.55).

Validity of Results:

Quality assessment using V 2.0 of the Cochrane Risk of Bias tool demonstrates that results are valid and at low risk of bias given the study's randomization structure, concealment of allocation, completeness of follow-up, pre-specification of analysis, limited cross-over between treatment arms, and similar baseline characteristics between the patient populations in each treatment arm. While the study was not blinded, this is unlikely to introduce bias to the primary outcome (all cause mortality).

Generalizability of Results:

Trial centers are similar to Canadian hospitals and it would be safe to assume that similar results would be observed here in patients presenting with confirmed or suspected Covid-19 and requiring respiratory support. The September 2020 meta-analysis in JAMA by the REACT working group on steroids (including predominantly dexamethasone and hydrocortisone, as well as methylprednisone) in Covid-19 for critically ill patients confirmed a reduction in mortality with steroid use, and as such the WHO now recommends corticosteroids as standard of care for critically ill Covid-19 patients.

The Bottom Line:

6mg dexamethasone PO/IV reduces all cause 28d mortality in patients admitted to hospital with confirmed or suspected Covid-19, with greater effects seen in patients receiving respiratory support. Steroids are now considered standard of care for critically ill Covid-19 patients.