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Use of Steroids in COVID-19 Patients: What is known?

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ABSTRACT

COVID-19 pandemic has exaggerated the role of steroids in the standard of care despite minimum direct evidence of their efficacy in COVID-19 patients and their well-known adverse effects. The literature abounds on the side effects of steroids affecting different organ systems of the body. COVID-19 patients, who are on long-term steroids, are more susceptible to their adverse effects. We, herein, briefly review the potential uses and the adverse effects of steroids on different organ systems of the body.

Key Words: Steroids, COVID-19, Adverse effects.

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The anti-inflammatory properties of corticosteroids are well known. They modify lymphocyte/eosinophil functions and minimise hypersensitivity reactions, mainly mediated *via* gene transcription repression.¹ During recent years, glucocorticoids are becoming the standard of care in reducing inflammation and regulation of immune responses, especially during the pandemic of COVID-19 era. However, the incoherent use of steroids in COVID-19 patients makes them more susceptible to their adverse effects. Steroid use may have some benefits as well as several adverse effects, but front-line physicians often recommend short-term glucocorticoid therapy with low to medium doses with some beneficial effects among COVID-19 patients with severe clinical conditions. The synthetic forms of corticosteroids have been documented with various side effects and toxicity depending on dosage, duration, and route of administration.

The purpose of this study was to review the beneficial or delirious effects of steroids in patients with COVID-19 infection.

During the present pandemic, there was initially a dilemma of drug choice and reliable treatment options as no vaccine or definitive treatment was available; hence, the steroids were used as anti-inflammatory and immune modulators, especially in the lung-related manifestations, despite the paucity of evidence.² The use of steroids in adult respiratory distress syndrome (ARDS), with or without COVID-19, has been evaluated with conflicting results on safety and mortality.³

The uncertainty persists on the effectiveness of glucocorticoids use in patients with COVID-19. Many guidelines for the treatment of such patients have stated that glucocorticoids are either not recommended or contraindicated. Although in China, glucocorticoids were used in severe cases. However, practice varied widely across the world.⁴

The recent WHO guidelines for COVID-19 did not recommend the use of steroids as routine therapy unless there is a clear indication for its usage because of possible deleterious effects and increased mortality rate, which has been identified from studies with other coronavirus infections and influenza.⁵ Few small scale studies identified increased mortality with severe COVID-19 infection.² However, data also suggest the promising effects of steroid therapy in patients with COVID-19 patients, who are on mechanical ventilation, though doubt still persists in diabetic elderly patients.⁶ The UK Recovery trial⁴ and others have used an individualised approach with different steroid dosages, depending upon the host response.⁷ The recovery trial showed benefit to patients in whom steroids (dexamethasone, 6 mg once daily for 10 days) were used with reduced 28-day mortality (29.3% vs. 41.4%; rate ratio, 0.64; 95% CI, 0.51 to 0.81) as compared to usual care group. However, there was no evidence of benefit of steroid use in patients who were not receiving respiratory support.⁴ Berton *et al.* identified reduced mortality if steroids were used early (within the first 14 days) in the presence of severe respiratory failure despite standard therapy.⁸ Some guidelines advocate for short course and dosage of steroids in patients admitted in critical care. On the contrary, other clinicians do not support steroid use because of its hazardous side effects.⁹ Similar meta-analysis identified neither a benefit on length of hospital stay, nor the mortality was reduced in less sicker or critically ill patients.¹⁰ Even the dose did not have any beneficial effect on patient outcomes, and the analysts identified heterogeneity of data; hence, results were not

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conclusive.¹⁰

The WHO recommends the use of steroids in COVID-19 patients, who are under clinical trial.⁵ European Union (EU) regulatory body also approves its use in critically ill COVID-19 patients. Steroid treatment has shown promising results when used as life-saving therapy among COVID-19 patients.⁹ A recently published multicentre study from Spain on tocilizumab treatment alone, demonstrated a reduction in mortality by 14.7%, (RRR 46.7%), and in combination with steroids demonstrated a reduced mortality by 29.1% (RRR 72.8%).⁹ Lu *et al.* in a meta-analysis on safety and efficacy of steroids in COVID-19 cases gathered information from a vast number of studies; and concluded that steroid use in COVID-19 patients did not reduce the risk of death among sick cases, though the duration and intensity of fever were reduced. However, the length of hospital stay was not reduced.¹⁰

There have been increasing reports from across the world on COVID-19-related multisystem inflammatory conditions (MIS-C), whose symptoms match with other inflammatory syndromes like Kawasaki disease (KD) or toxic shock syndrome. There are no widely accepted guidelines, but several organisations, like CDC and RCPCH, published their own guidelines with a multidisciplinary team approach, and most cases need supportive care and may need treatment with standard protocol for Kawasaki disease, like intravenous immunoglobulin with or without aspirin. Inotropics or steroids have also been used, as in recovery trial.^{2,4}

There are ample data on steroids crossing placenta with the adverse effects on fetus in utero, with some evidence showing high possibility of mental and behavioural disorders in children, who were exposed to steroids during their antenatal period. Though data is not sufficient, however, the use of steroids for severe COVID-19 pregnant women should be limited to those cases where these are potentially needed and beneficial.

The COVID-19 treatment guidelines panel recommends the use of dexamethasone in mechanically ventilated COVID-19 patients and those who are on supplemental oxygen. It should be cautiously administered with close monitoring to observe the adverse effects. The conflicting role of corticosteroid therapy in COVID-19 demands extensive study and clinical trials to reach a definitive conclusion; and the clinicians must consider individual potential risks and benefits of corticosteroids in patients with COVID-19. The specific mechanisms by which steroids act on sustained lung inflammation, the definition of the best drug to use, and the appropriate treatment duration, are still objectives of ongoing clinical trials.

CONFLICT OF INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

All authors were actively involved in writing of this paper, starting from topic selection to writing this paper.

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