

Corticosteroids in COVID-19

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Introduction

In December 2019, a novel coronavirus (severe acute respiratory syndrome coronavirus 2, or COVID-19) was identified in Wuhan, China.¹ In a few short months, COVID-19 has become an unprecedented global pandemic. While every effort is being made to flatten the curve, additional infections in pregnancy are inevitable. One of the many challenges faced by clinicians caring for critically ill pregnant women and their fetuses will be management of preterm pregnancy. More specifically, questions may arise regarding the routine administration of antenatal steroids for fetal lung maturation as the impact of corticosteroid use in COVID-19 patients is currently unclear.

Steroid use in non-pregnant COVID-19 patients

The role of corticosteroids in the treatment of severe respiratory manifestations of COVID-19, is currently unclear. While recent meta-analyses on the use of steroids in viral pneumonia (influenza, coronavirus and others)^{10,11} have suggested an association between steroid use and increased mortality, our ability to extrapolate this data is limited because included studies were not controlled trials, had significant heterogeneity, and were susceptible to confounding by indication (sicker patients more likely to be given steroids). Moreover, doses administered were typically higher and/or more prolonged than that required in one course of antenatal lung maturation (12mg of Betamethasone = 75mg of prednisone; doses typically used in adult critical care are ~50mg of prednisone for 5-10 days). Research during Middle East Respiratory Syndrome (MERS) coronavirus outbreak, found that routine treatment with corticosteroids was not beneficial and was associated with decreased viral clearance, but had no impact on 90 day mortality.¹²

In contrast, in a retrospective cohort study of 201 patients with COVID-19, almost 50% of those with ARDS (N=84) received corticosteroids, and these patients had a lower risk of mortality than those who did not receive corticosteroids (HR 0.38, 95% CI 0.20-0.72).¹³ A published (non-peer reviewed) report of 26 patients with severe COVID-19 suggested the use of methylprednisone (1-2mg/kg/day x5-7 days) was associated with decreased duration of supplemental oxygen use (8.2d vs 13.5d p<0.001) and improvement in radiographic findings.¹⁴ These findings are again limited by concerns around sample size and confounding and as such, strong conclusions cannot be drawn. This sentiment is also reflected in current guidelines where limited recommendations around the use of corticosteroids in COVID-19 patients have been made.¹⁵ A randomized control trial investigating the effectiveness of corticosteroids in COVID-19 patients is currently underway.¹⁶

What we know about the impact of antenatal corticosteroids on neonates

Antenatal corticosteroids are a cornerstone of obstetric management. Overall, administration of antenatal corticosteroids reduces the risk of respiratory distress syndrome from 18% to 12% (RR 0.66, 95% CI 0.56 to 0.77), reduces the risk of intraventricular hemorrhage from 5% to 3% (RR 0.55, 95% CI 0.40 to 0.76), and reduces the risk of perinatal death from 10% to 7% (RR 0.72, 95% CI 0.58 to 0.89).¹⁷ However, the absolute benefits of antenatal corticosteroids change as

gestational age advances and baseline risks of neonatal morbidity decrease. For example, among births <32 weeks' gestation, antenatal corticosteroids reduce the absolute risk of RDS by 20% (from 46% to 26%, RR 0.56, 95% CI 0.45, 0.71),¹⁸ while among those born between 34-36 weeks' this treatment reduces the absolute risk of severe RDS by 0.9% (from 2.3% to 1.4%, RR 0.60, 95% CI 0.33 to 0.94).¹⁹ These differences by gestational age may be helpful to keep in mind when weighing the benefits of antenatal corticosteroids against any potential or unknown maternal risks.

Summary

As our experience with this pandemic evolves, so will the evidence to support optimal care. With the evidence we have so far, a decision about the use of corticosteroids for antenatal lung maturation must be weighed between the uncertainty of effect on the mother versus the known benefit for the neonate by gestational age at birth. This assessment should, whenever possible, also take into consideration the preferences and values of the mother.

Based on the current evidence, and because definite harm to maternal health has not been demonstrated, we recommend continuing with routine administration of antenatal corticosteroids up to 34+6 weeks of gestation. If new evidence arises regarding the impact of steroids on COVID-19 patients, or in the situation of a critically unwell COVID-19 positive preterm mother, interdisciplinary collaboration and shared decision making will become even more imperative.

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