



Use of dexamethasone, remdesivir, convalescent plasma and prone positioning in the treatment of severe COVID-19 infection in pregnancy: A case report

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ARTICLE INFO

Article history:

Received 29 October 2020

Received in revised form 16 November 2020

Accepted 18 November 2020

Available online xxxx

Keywords:

Pregnancy

COVID-19

Respiratory failure

Prone

Dexamethasone

Acute respiratory distress syndrome (ARDS)

ABSTRACT

Severe infection with COVID-19 virus in pregnancy offers unique management challenges for the obstetrician and critical care specialist. We report the case of a woman at 26 weeks of gestation with acute respiratory distress syndrome secondary to COVID-19 infection treated with dexamethasone, remdesivir, convalescent plasma and mechanical ventilation. Cesarean delivery was performed at 29 weeks due to worsening maternal status. This case offers insight into the assessment and successful use of treatment strategies, including dexamethasone, remdesivir, convalescent plasma, early prone positioning, conservative fluid management, permissive hypoxia and low tidal volume parameters with ventilator support for pregnancies affected by severe COVID-19 infection. © 2020 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

The mainstay of intensive care treatment for acute hypoxic respiratory failure due to severe COVID-19 infection is supportive with supplemental oxygen or invasive mechanical ventilation, judicious fluid management, systemic corticosteroids, and early use of vasoactive medications. Patients are monitored closely for the development of viral myocarditis, thrombotic events, and superimposed bacterial pneumonia. Several experimental drug and other therapies are currently being studied, including remdesivir, lopinavir-ritonavir, tocilizumab, azithromycin, Bacillus Calmette–Guérin vaccine and convalescent plasma [1–3].

Severe infection with COVID-19 virus in pregnancy offers unique management challenges for the obstetrician and critical care specialist. Special consideration must be undertaken regarding oxygenation and respiratory support, fluid management, use of corticosteroids and experimental therapeutics, anticoagulation, and fetal monitoring, often with limited evidence-based recommendations. This case offers insight into the assessment and use of these management strategies, most specifically the use of dexamethasone and critical care strategies with early prone positioning in those requiring ventilator support.

2. Case Presentation

A 42-year-old woman, G8P6016, presented to an outside hospital in acute hypoxic respiratory failure at 26 weeks of gestation. She had no underlying medical history. She presented with a week of increasing dyspnea and a productive cough; a PCR test for COVID-19 the day prior was positive. She was febrile with an oxygen saturation (SpO₂) of 78% on room air, and respiratory rate of 50–60. Her SpO₂ remained in the 80s by pulse oximetry despite 15 L of oxygen by non-rebreather mask and ABG showed a pH 7.42, pCO₂ 24.3, PaO₂ 46.7, HCO₃ 15.7, Base deficit –8.7 and O₂ saturation 84.3. Chest x-ray demonstrated diffuse bilateral consolidations and clinical exam revealed coarse, diminished breath sounds. She was intubated and transferred to a tertiary care center.

Upon arrival, SpO₂ remained 85% on FiO₂ of 100% and PEEP of 12 but improved to 93–95% with placement in prone position, paralysis and sedation, and adjustment of ventilator settings to 6 cc/kg with increased PEEP. A low tidal volume strategy was employed for lung protection in the setting of acute respiratory distress syndrome (ARDS) [4]. The patient remained in prone positioning for 16–18 h daily to assist with ventilation [5,6]. She received dexamethasone 20 mg IV for 5 days followed by 10 mg IV for 5 days [7,8], remdesivir 200 mg × 1 then 100 mg every 24 h for 9 days [1], and convalescent plasma [2] on HD2. She received azithromycin and ceftriaxone for empiric treatment of possible superimposed bacterial pneumonia [3]. Bilateral upper and lower

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extremity Doppler and coagulation studies were completed to assess for hypercoagulability. Therapeutic enoxaparin was initiated after identifying a basilic vein thrombosis near the upper extremity PICC site. She was eventually transitioned to a heparin infusion to allow reversal of anticoagulation in case of urgent delivery. She required an insulin infusion to maintain euglycemia through the day of delivery, suggesting both steroid-induced hyperglycemia and some degree of undiagnosed gestational diabetes. Continuous external fetal monitoring (EFM) was performed from admission to delivery. Fetal status remained reassuring throughout her hospitalization except for a period of prolonged, 8-min fetal heart rate (FHR) deceleration occurring during maternal position change from prone to supine, but recovered with standard intrauterine resuscitation measures.

On HD11, ventilator requirements gradually increased after a period of initial stabilization and SpO₂ of 95% or higher could not be maintained without risking barotrauma. After interdisciplinary discussion, this goal was adjusted to maintain SpO₂ of 90% or higher if fetal wellbeing was reassuring. This adjustment was well tolerated and allowed the pregnancy to be continued for an additional week. The evening of HD16, she was noted to have progressive hypoxia, declining lung compliance and increasing plateau pressures, requiring increasing ventilator support parameters and diuresis with furosemide to maintain SpO₂ at 90%. On HD17, Critical Care and Maternal-Fetal Medicine (MFM) discussed the therapeutic option of ECMO support in concert with cardiothoracic surgery but ultimately this was deemed to be higher risk than proceeding with cesarean delivery. Anticoagulation was held and primary cesarean delivery was performed at 29 weeks 1 day via vertical skin incision and low transverse hysterotomy. Cesarean delivery was performed in the ICU with Critical Care, MFM, Neonatology and Anesthesia teams present. A live male infant weighing 1310 g with APGAR scores of 3¹ and 6⁵ was delivered and admitted to the NICU. Arterial umbilical cord blood gases showed pH of 7.25, pCO₂ 79, pO₂ 17 and base excess 3.8. Amniotic fluid and placenta cultured negative for COVID-19. Placental pathology was only notable for few patchy areas consistent with maternal vascular malperfusion. Subsequent testing of the infant on DOL 3 and DOL 14 were negative for COVID-19.

Following delivery, the patient quickly tolerated increasing durations of supine positioning, improved lung compliance, reduction in plateau pressures, and ability to wean FiO₂ and PEEP settings. Due to continued fevers, she underwent bronchoscopy on HD18 and two sputum cultures showed growth of *Enterobacter cloacae*, which was treated with cefepime. On HD30, she underwent tracheostomy. She was weaned from the ventilator and transferred to intermediate care on HD40. The tracheostomy was decannulated on HD50 and she was discharged to home on HD52 requiring home oxygen at night and continued nursing care. The infant experienced adrenal insufficiency, likely due to maternal dexamethasone treatment; however, overall, the infant had an uncomplicated NICU course and was discharged home on DOL 57, a postmenstrual age of 37 weeks, in good condition.

3. Discussion

This case of severe COVID-19 infection in pregnancy required prone positioning, mechanical ventilation and the use of experimental treatment therapies. Our experience is unique given the rapidly changing course of recommended treatment for individuals with COVID-19. At the time of clinical decision making, no obstetric guidelines were available supporting the use of dexamethasone in pregnancy. With extensive discussion, we elected to administer this for the benefit of decreased morbidity among those receiving invasive respiratory treatment in COVID-19 infection, supported by both RECOVERY trial data [9] and data on use of dexamethasone in ARDS [7,8], as this outweighed the risk for fetal harm with prolonged corticosteroid exposure beyond the typical 4 doses of dexamethasone 6 mg used for fetal lung maturity [10,11]. One notable potential outcome for providers when considering use of dexamethasone is adrenal insufficiency in the neonate. The neonate was initially treated with

hydrocortisone from DOL 1 to DOL 5 due to in utero prolonged exposure to dexamethasone; however, cortisol levels remained low at both DOL 18 (63.48 nmol/L) and DOL 56 (33.40 nmol/L), diagnosing adrenal insufficiency. This infant will require stress-dosing of steroids with any future surgery or signs of clinical illness.

Beyond low tidal volume strategies for lung protection in ARDS, a conservative fluid management approach has been demonstrated to improve lung function and shorten mechanical ventilation without an increase in non-pulmonary organ failure [15] and this was safely used in the pregnant state. Furosemide was used for fluid management and can be used in pregnancy for diuresis as needed [16]. Another point of discussion is the goal for maintenance of O₂ saturations. In pregnancy, it is recommended to maintain SpO₂ of 95% or greater [12,13] and 92% or greater in non-pregnant patients, particularly with COVID-19 [14]. In this case, permissive hypoxia to SpO₂ of 90% or greater was utilized for maternal lung protection given reassuring fetal status by EFM and allowed this pre-term pregnancy to continue an additional week for fetal benefit.

The question of vertical transmission of COVID-19 in pregnancy is still under investigation. COVID-19 cultures were collected from the amniotic fluid and placenta at delivery and returned negative; however, it is worth noting that due to novel testing and laboratory processing procedures, these specimen sources have not yet been validated at our institution. Subsequent negative neonatal testing in this case does, however, strengthen their reliability.

4. Conclusion

Dexamethasone may provide significant maternal benefit and decrease mortality in pregnant women with severe COVID-19 infection requiring mechanical ventilation and at the same time promote fetal lung maturity. Neonatal concerns regarding its use in pregnancy include hyperglycemia with resulting neonatal hypoglycemia as well as the potential for the development of adrenal insufficiency. Generally, maternal benefit of this protocol outweighs risks of neonatal harm in the critically ill patient. None of the experimental clinical therapeutics are considered contraindicated and compassionate use of these therapeutics should be considered in pregnant women with severe illness due to COVID-19.

Lung protective ventilator strategies for COVID-related ARDS are well tolerated in the pregnant patient. Use of prone positioning in the pregnant patient was achieved safely, with oxygenation benefit and no prolonged distress to the fetus noted over routine 16 to 18 h of prone positioning. When supine, a left lateral tilt was employed to avoid compression of the inferior vena cava and aorta by the gravid uterus. A conservative fluid management approach with ARDS as well as diuresis can safely be used in pregnancy. Fetal heart rate tracing can offer an additional clinical indicator of maternal oxygenation status and should be employed in the critically ill pregnant patient. Permissive hypoxia may be considered to advance fetal maturity and minimize barotrauma, but this approach should be undertaken with caution and only with continuous EFM to ensure fetal tolerance.

Contributors

Jennifer Jacobson drafted the paper and is the lead author.
Kathleen Antony contributed to critical revision of the paper.
Michael Beninati contributed to critical revision of the paper.
William Alward contributed to critical revision of the paper.
Kara K. Hoppe contributed to critical revision of the paper.

Conflict of Interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

Funding

No funding from an external source supported the publication of this case report.

Patient Consent

Obtained.

Provenance and Peer Review

This case report was peer reviewed.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.crwh.2020.e00273>.

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