

Multiple drugs

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Lack of efficacy, off-label use and exposure during pregnancy: 3 case reports

In a case series, 3 women aged 27–43 years, were described, who exhibited lack of efficacy during treatment with paracetamol, and off-label treatment with ceftriaxone, dexamethasone or tocilizumab for COVID-19 infection. Two of these three women exhibited lack of efficacy during pregnancy.

Case 1: The 27-year-old woman (gravida 2 para 1) had a history of urinary tract infections and a previous caesarean section. She was admitted at 18 weeks and 6 days of gestation due to cough, fever and dyspnoea. Before admission, she was found positive for COVID-19 infection. At admission, her chest X-ray revealed patchy infiltrates indicative of pneumonia. She was started on off-label ceftriaxone and paracetamol along with unspecified low molecular weight heparins as prophylaxis and oxygen. On hospital day 2, her general condition worsened (lack of efficacy). She was then referred to the COVID-center. At that time, suspicion of bacterial superinfection was made, and she was placed on high-flow nasal cannula (HFNC) along with pantoprazole, dexamethasone, azithromycin and piperacillin/tazobactam treatment. Despite the HFNC, her RR was 45–50 breaths/minute and oxygen saturation (SaO₂) was 76–78%. Subsequently, due to the severe acute respiratory distress syndrome (ARDS), she was transferred to the ICU. She was intubated and prone. At 19 weeks and 6 days of gestation, she was placed on veno-venous extracorporeal membrane oxygenation. Methicillin-resistant *Staphylococcus aureus* was isolated, and she was treated with vancomycin. During the following weeks, recovery in her respiratory function was noted. Further, she received olanzapine due to the episodes of psychomotor agitation. Subsequently, she was admitted again to our obstetric ward at 37 weeks and 1 day of gestation and underwent a caesarean section. She delivered a healthy male neonate with a birth weight of 2670g and Apgar score of 9 at 1 and 5 mins.

Case 2: The 38-year-old woman (gravida 2 para 1) presented at 28 weeks and 4 days of gestation due to fever and myalgia since 6 days. She was admitted because of dyspnoea and positive SARS-CoV-2 test. Prior to COVID-19, her pregnancy was complicated by gestational diabetes (GDM). She started receiving treatment with paracetamol and IV off-label dexamethasone 8mg daily along with unspecified low molecular weight heparins as prophylaxis due to severe COVID-19 infection. However, her respiratory condition worsened with the onset of tachypnoea and increase of inflammation indices (lack of efficacy). Due to worsening hypoxia maximum ventilation support was needed. She was placed on veno-venous extracorporeal membrane oxygenation at 30 weeks and 1 day of gestation. Methicillin-resistant *Staphylococcus aureus* was isolated, and she was treated with oxacillin. At 31 weeks and 6 days of gestation, she underwent precipitous premature vaginal delivery. She delivered a male neonate with a birth weight 1880g and Apgar score of 1 and 7 at 1 and 5 mins, respectively.

Case 3: The 43-year-old woman (gravida 2 para 1) was admitted to the obstetric ward at 38 weeks and 2 days of gestation due to cough for 1 week. She was found positive for COVID-19 infection. Subsequently, she underwent a caesarean section, and delivered a neonate with COVID-19 infection, weighing 3080g with Apgar score of 9 and 10 at 1 and 5 mins respectively. Subsequently, her condition deteriorated. Further, she was referred to the COVID-19 center due to the respiratory failure associated with respiratory alkalosis. At that time, she was started on off-label IV dexamethasone 8 mg/day. Despite this ongoing therapy, progressive worsening of respiratory exchanges was noted (lack of efficacy). At that time, she required non-invasive ventilation. Further, she received off-label tocilizumab. However, worsening of respiratory exchanges and worsening of parenchymal thickening was noted. Therefore, she was referred to the ICU. Subsequently, she was placed on veno-venous extracorporeal membrane oxygenation. However, 143 days after the caesarean section, she died due to sepsis and multiple organ failure.