NONCARDIOGENIC PULMONARY EDEMA DUE TO RITODRINE USAGE IN PRETERM LABOR

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A 34-year-old woman at 28 weeks of gestation presented at the emergency department of our hospital with shortness of breath, cough, sweating, and deterioration of consciousness, which had begun 3 days ago. The history given by her relatives revealed that she had received intravenous ritodrine (later found to be in the form of a constant infusion at 60 μg/min for 2 days) together with two doses of betamethasone (Celestone, Schering) at 12-hour intervals for accelerating fetal lung maturation in a private clinic. After this initial intervention, treatment was continued with oral tocolytic tablets (ritodrine tablets). There was nothing else notable in her medical history. Physical examination of the unconscious patient revealed a body temperature of 37.2°C, arterial blood pressure of 90/60 mmHg, pulse rate of 142/min, and respiration rate of 27/min, with hyperventilation and slight rales over bilateral lungs. She was intubated immediately. Fetal measurements were concordant with a 28-week pregnancy, and the amount of amniotic fluid was found to be normal. Ultrasonic estimation of fetal weight was 1,100 g. The hemoglobin level, hematocrit, leukocyte count and platelet counts were 12 g/dL, 37.2%, 9.100/mm^3 and 223,000/mm^3, respectively. Plasma levels of glucose, urea, creatinine and albumin were 164 mg/dL, 135 mg/dL, 3.4 mg/dL and 2.6 g/dL, respectively. Arterial blood gas analysis revealed hypoxia (PO_2, 35.5 mmHg; SaO_2, 68%) with acidosis ([HCO_3], 15 mEq/dL; pH, 7.32) and hypocapnia (PCO_2, 29.4). Chest X-ray revealed increased radiodensity in the basal lobes of the lungs, predominantly on the left side, and a diagnosis of noncardiogenic pulmonary edema due to ritodrine treatment was proposed by chest doctors. Ritodrine was stopped immediately, and supportive therapy with prophylactic antibiotics, low-dose diuretics, β-blocker agents, fluid intake restriction and mechanical ventilation was started. However, the patient died 10 hours after beginning the treatment due to cardiac arrest, and negative fetal cardiac activity was subsequently detected by ultrasound.

Many factors, such as the use of tocolytic agents, cardiac disease, fluid overload and preeclampsia, have been reported as risk factors in pregnant women for the development of pulmonary edema [1,2]. Ritodrine is the most commonly used agent among β-mimetics for tocolytic treatment [3]. The incidence of pulmonary edema arising from tocolytic treatment is about 4.4%, and it usually develops during the second day of the treatment. Infusions should be started at the lowest dose possible, as long as specific information on plasma clearance is not available. Caritis et al [4] addressed the issue of dosage and defined the pharmacokinetics of ritodrine in 13 pregnant women receiving the drug by constant intravenous infusion at 50 μg/min. In their series, two cases of acute pulmonary edema occurred 3 hours after perfusion was stopped. Pulmonary edema requiring mechanical ventilation support appears in 3–10% of cases. The mortality from pulmonary edema is 3%, and this increases if sepsis and acute respiratory distress syndrome complicate the situation [5].

Close monitoring and restriction of fluid intake can prevent the development of pulmonary edema; but if it develops, ritodrine treatment must be stopped immediately. If the patient's condition is serious, β-blockers and loop diuretics should be used to antagonize the effects of ritodrine and pulmonary edema. Controlled intravenous fluid support, maintenance of the electrolyte balance, adequate oxygenation, and support of respiration with mechanical ventilation can be used, when necessary, for the treatment of pulmonary edema [6].

In this case, there was concomitant use of steroids for lung maturation, together with ritodrine, which

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increased the suspicion of noncardiogenic pulmonary edema, as the shortness of breath, cough, sweating, and deterioration of consciousness started after the administration of steroid therapy for lung maturation. Hyperventilation with inspiratory rales and chest X-ray findings of increased pulmonary density in basal lobes supported our clinical diagnosis. In spite of aggressive treatment, the patient still died 10 hours later.

In conclusion, although preterm delivery is associated with a risk of morbidity and mortality in the newborn, the treatment of this condition also has its inherent risks, which should not be overlooked. The use of ritodrine, which has long been favored in the treatment of preterm labor, may cause potentially lethal pulmonary edema, especially with concomitant use of steroids for fetal lung maturation.

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