

# A Rare Side Effect of Ritodrine Hydrochloride in the Treatment of Preterm Labor: A Case Report

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A patient at the 29<sup>th</sup> week of gestation was hospitalized because of preterm labor and treated with intravenous ritodrine hydrochloride. After greater than 2 weeks of therapy erythematous maculopapular pruritic lesions appeared initially on the forearms and later extended to extremities and the rest of the body. Cutaneous side effects have been described rarely in the literature. We encountered a case of erythema multiforme in the treatment of preterm labor with ritodrine hydrochloride.

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Preterm labor is traditionally defined as contractions that result in cervical change at less than 37 weeks of gestation. An alternative definition is six to eight contractions per hour even in the absence of cervical change. The incidence of preterm labor has remained at 9-11% of all live births despite the use of tocolytic agents. In addition, preterm birth is the cause of at least about 75% of neonatal deaths that are not attributable to congenital malformations.<sup>1</sup> Ritodrine hydrochloride is used frequently and widely for the treatment of preterm contractions since the Food and Drug Administration approval in 1980.<sup>2</sup>

Common side effects of ritodrine hydrochloride include palpitations, tremor, tachycardia, nausea and flushing. These side effects are relatively frequent but occur only in 3-10% of patients a change of therapy.<sup>3,4</sup> More serious side effects include hyperglycemia, hypopotassemia, hypotension, pulmonary edema, cardiac insufficiency including cardiac arrhythmias, myocardial ischemia.

Though rare, they may cause fatal outcomes.<sup>3-6</sup> Cutaneous side effects have been described rarely in the literature. We encountered a case of erythema multiforme in the treatment of preterm labor with ritodrine hydrochloride. To our knowledge erythema multiforme has been reported in only three cases after prolonged  $\beta_2$ -sympathomimetic tocolysis with ritodrine hydrochloride.<sup>5,6</sup>

## Case Report

A 33-year-old woman, gravida 1, para 0, at the 21<sup>th</sup> week of gestation with mild contractions, without any significant medical history or any history of allergic reaction presented.

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She was placed on bed rest and started on a regime of oral ritodrine hydrochloride 10 mg every two hours. She had stayed on this regime for six weeks when she again noted mild contractions. At this point she was admitted to our hospital with preterm labor. At that time she had a ultrasonography consistent with her dates, a cervical examination showing minimal bleeding, no dilatation or effacement. The cardiocography revealed contractions every five to six minutes.

She was set on ritodrine hydrochloride 50 mg/min i.v. as an initial dosage, and was gradually increased to 200 mg/min to suppress the contractions. Meanwhile, for fetal lung maturation, she received betamethasone acetate 12 mg intramuscular. At the 29<sup>th</sup> week of gestation (8 weeks after admission) erythematous maculopapular pruritic lesions appeared initially on the forearms and later extended to extremities and the rest of the body (Figure 1, 2). There was no lesions on her mucosal membranes.



Figure 1. Erythematous maculopapular pruritic lesions on the body

Laboratory work-up was completely normal (hemoglobin, hematocrit, trombocyte count, electrolyte levels, liver function tests and clotting tests). CMV, EBV, rubella and coxsackie infections were ruled out. After consultation by dermatology she was started on cetirizine p.o 10 mg once a day and carbamide cream (10%) externally. This medication did not stop pruritus and lesions did not regress after two

days of treatment. She was started on betamethasone acetate 3 mg intramuscularly. Although pruritus decreased, maculopapular lesions persisted. Finally we stopped ritodrine hydrochloride and she was set on a regime of oral nifedipin 20 mg every six hours and 20 mg nitroglycerin once a day. Two hours after ritodrine hydrochloride has been stopped, pruritus and maculopapular lesions regressed and finally disappeared within a week. She gave birth at 34 weeks of gestation to a healthy 2100 gr female infant by cesarean section because of an placenta previa marginalis.



Figure 2. Erythematous maculopapular pruritic lesions on the forearms

## Discussion

The adrenergic receptors are located on the outer surface of the smooth muscle cell membrane, where specific agonists can couple with them. Two classes of b-adrenergic receptors: b1-receptors, dominant in the heart and intestines; and b2-receptors, dominant in the myometrium, blood vessels, and bronchioles are known. Ritodrine hydrochloride is a b2-sympathomimetic agent that significantly inhibits uterine contractions and is frequently used as a tocolytic agent for treatment of preterm labor. The use of ritodrine, as well

Our patient was seen with erythema multiforme that was persistent throughout a prolonged ritodrine hydrochloride therapy (8 weeks). Maculopapular lesions resembling erythema multiforme were seen after treatment with ritodrine hydrochloride. Maculopapular lesions have been reported in only three other cases after treatment with ritodrine hydrochloride.<sup>5,6</sup> Other cutaneous complications has been rarely related to ritodrine hydrochloride. In one patient acute cutaneous vasculitis was seen after treatment with ritodrine therapy. In another patient a mild skin rash was described. The ritodrine hydrochloride was stopped, the patient delivered at the same day (32<sup>th</sup> week of gestation) and rash disappeared gradually within two days without any treatment. In none of the cases the authors could describe the reason for this allergic reactions.<sup>4-6</sup>

The clinician should always consider unusual side effects like maculopapular cutaneous lesions in the treatment of preterm labor with ritodrine hydrochloride. Our aim was to show that patients with preterm labor need to be carefully monitored when treated with ritodrine hydrochloride.

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