

## CASE REPORT

# Nifedipine induced pulmonary edema

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## ABSTRACT

Tocolytics (also called anticontraction or labor suppressants) are the medications used to suppress premature labor. The tocolytic therapy gives time for the administration of steroid (a glucocorticoid drug) which greatly accelerates fetal lung maturity. There is no ideal tocolytic agent in use; various types of agents used for tocolysis include beta-2 adrenergic agonists, calcium channel blockers, oxytocin antagonists, magnesium sulphate and NSAIDs, with varying success rates and side effects. We are reporting a case of pulmonary edema following tocolysis with nifedipine, a calcium channel blocker.

**Key words:** Tocolysis; Nifedipine; Pulmonary edema

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## INTRODUCTION

Tocolytics are also called anticontraction or labor repressant drugs. These are usually used to suppress premature labor. The therapy gives time for betamethasone to accelerate fetal lung maturity. There are a variety of drugs used for tocolysis.<sup>1-3</sup> These include beta-2 adrenergic agonists e.g. terbutaline, ritodrine, salbutamol etc., calcium channel blockers e.g. nifedipine and nicaldipine, oxytocin antagonists (atosiban), NSAIDs (indomethacine) and magnesium sulphate, with varying success rates and side effects. Calcium channel blockers and oxytocin antagonists can delay delivery by 2-7 days.<sup>4</sup> Otherwise tocolysis is rarely successful beyond 24-48 hrs. However, gaining 48 hrs may be sufficient to allow the pregnant women to reach specialized centers for management of preterm labor and receive steroids to accelerate fetal organ maturity.<sup>5,6</sup>

Nifedipine is used by many obstetricians as a preferred tocolytic drug in the prevention of premature labor. Its tocolytic effect is equivalent to  $\beta_2$ -adrenergic receptors, but with a better safety profile. When nifedipine is administered as a tocolytic, it binds inside myometrial L-type voltage dependent calcium channels, making them to remain closed and hence inhibiting contractility. However, these L-type channels are also present in other types of smooth muscle cells such as vascular smooth muscles.<sup>7,8</sup>

Pulmonary edema during tocolysis with  $\beta_2$ -adrenergic receptors has been described, but with nifedipine

which is a calcium channel blocker, it is not so common. Here we report a case of pulmonary edema induced by nifedipine used for tocolytic therapy.

## CASE REPORT

A 38 years old lady with 27 wks twin pregnancy was admitted in obstetric ward with a complaint of pain abdomen. For tocolysis she received tab. nifedipine 20 mg stat and 6 hourly afterwards, and betamethasone 12 mg/day IV to improve fetal organ maturity. She was infused one liter of dextrose-normal saline solution as maintenance fluid. Before the use of nifedipine her blood pressure was 110/70 mmHg, PR 90/min and there was mild anemia (Hb= 9 gm/dl). There was no history suggestive of any heart disease, diabetes, preeclampsia or any infection.

On the second day, she developed tachycardia (HR 130/min) and hypotension (90/50 mmHg) for which she received 500 ml of normal saline. Soon after, she complained of breathlessness. On chest auscultation there were bilateral coarse crepitations. With oxygen supplementation (4 lit/min with ventimask) her SpO<sub>2</sub> remained at 90%, so for further management she was shifted to intensive care unit.

At the time of ICU admission she had severe breathlessness and dry cough. She had a pulse rate 140/min regular and BP 130/84 mmHg. She was pale, normal heart sounds and bilateral coarse crepts. Bilateral perihilar haziness was

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seen in chest x-ray suggestive of pulmonary edema. ECG was normal except sinus tachycardia. ABG's depicted mild hypoxia (PaO<sub>2</sub> 40 mmHg, PaCO<sub>2</sub> 30 mmHg and pH 7.45). Echocardiography was normal. All blood investigations including hemogram, complete cell count, random blood sugar, kidney function tests, liver function tests, thyroid function tests and cardiac enzymes were within normal limits. Patient was managed with diuretics, a prop-up position and CPAP (continuous positive airway pressure) ventilation with a tight fitting mask. With above treatment pulmonary edema resolved within a few hours. After 48 hrs she was shifted to the ward. After one week the patient went into labor. In view of prematurity of the babies and being a precious pregnancy, she was rushed for an emergency cesarean section. Cesarean section was carried out under spinal anesthesia with 2 ml of bupivacaine and 25 µg fentanyl. The whole of the course remained uneventful, twin babies were delivered and shifted to NICU for further management.

## DISCUSSION

Pulmonary edema during tocolytic therapy with calcium channel blocker (nifedipine) and steroids is a rare incidence. The rapid clinical improvement and a negative echocardiography report eliminate the possibility of peripartum cardiomyopathy. Patient's course of events suggests that nifedipine may be responsible for progressive tachycardia. Moreover, at 27 weeks gestational age the stroke volume was near maximal which could have been

further increased with steroid therapy because of water and sodium retention. Therefore this patient might have developed an acute diastolic dysfunction as a result of both tachycardia and volume overloading. By blocking the calcium channels nifedipine might increase the vascular permeability and as a result increase the alveolocapillary membrane permeability also, thus playing a role in this patient's clinical course.<sup>7</sup> Calcium channel blockers are widely accepted in the treatment of premature labor.<sup>7-9</sup> The mechanism of action in tocolysis involves the blockade of L-type Ca<sup>++</sup> channels.<sup>6</sup> In clinical practice efficacy of nifedipine is superior or comparable to those of beta agonists and oxytocin antagonists.<sup>10-12</sup> Additionally it has favorable safety profile as compared with the majority of other tocolytics. The most frequent and well tolerated side effects of calcium channel blockers are tachycardia, headache and hypotension.<sup>13</sup>

In tocolytic therapy, currently a combination of tocolytic agents is being used, that yields a better therapeutic result.<sup>6</sup> The calcium channel blockers are likely to remain one of the important groups of drugs for rapid inhibition of premature uterine contractions. This significance may be magnified in due course of time by further clinical studies as their combined use with other drugs.

In conclusion, the use of nifedipine as a tocolytic drug is increasing due to its safety index, but clinicians must keep in mind the rare risk of pulmonary edema, especially if it is co-administered with steroids.

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