Intrapartum Atosiban Treatment During Tachysystole and Non-reassuring Fetal Monitoring: A Retrospective Cohort Study

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ABSTRACT **Background:** Uterine tachysystole during labor can lead to a decrease in fetal oxygen saturation and intracerebral oxygen saturation. Acute tocolysis using atosiban can inhibit uterine smooth muscle activity, potentially improving fetal status and facilitating vaginal delivery or allowing time to prepare for operative delivery.

Objectives: To compare maternal and neonatal outcomes in cesarean and vaginal deliveries following atosiban administration during fetal prolonged deceleration and tachysystole at gestational age 37 0/7 to 43 0/7 weeks.

Methods: We conducted a single-center, descriptive retrospective cohort study at a large tertiary referral center.

Results: Of the 275 patients treated with atosiban, 186 (68%) delivered vaginally (either spontaneous delivery or instrumental delivery) and 89 (32%) underwent a cesarean delivery. In a univariate analysis, cesarean delivery was associated with higher body mass index (27.9 ± 4.3 vs. 30.2 ± 4.8, P = 0.003). Second stage atosiban administration was associated with vaginal delivery (89.3% vs. 10.7%, P = 0.01). Cesarean delivery was associated with lower Apgar at 1 and 5 minutes and a higher rate of neonatal intensive care unit admissions. The incidence of PPH among women treated with atosiban in our study (2.3–4.3%) was higher than the incidence reported in the literature (1–3%)

Conclusions: Atosiban may be an effective acute intervention for non-reassuring fetal heart rate during tachysystole, increasing the rate of vaginal delivery and potentially reducing the need for cesarean delivery. However, the potential risk of postpartum hemorrhage should be taken into consideration.

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KEY WORDS: atosiban, cesarean delivery, non-reassuring fetal heart rate, tachysystole

Uterine contractions compress the maternal spiral arteries and increase the intra-placental pressure, profoundly reducing the placental blood flow when that pressure exceeds the pressure of maternal perfusion to the placenta [1]. It has been reported that a contraction of 30 mmHg or more can diminish or even interrupt the maternal blood flow to the placenta and can potentially reduce the fetal oxygenation status [1,2]. Normal labor with sufficient physiological relaxation time allows the oxygenation level of an uncompromised baby to be restored between contractions. The compensatory feto-placental mechanism may no longer be effective in the presence of uterine tachysystole. Uterine tachysystole is usually associated with strong contractions of 80 mmHg or more [3] and significantly shortened relaxation time. Strong contractions contribute to further compression of maternal spiral arteries, while a shortened relaxation time presumably does not allow the blood supply to the placenta to return to baseline levels before the next contraction [4]. Uterine tachysystole was found to be associated with a progressive decrease of fetal oxygen saturation [5] and with a fall in fetal intracerebral oxygen saturation [4]. Acute tocolysis is an intervention that inhibits uterine smooth muscle activity [6] and has been used based on the assumption that such relaxation improves placental perfusion and may enhance fetal oxygenation [5]. The intervention is employed to either improve fetal status and facilitate vaginal delivery or as an interim method to improve fetal status while preparations for operative delivery are made [5,7]. Atosiban is a tocolytic drug. Its mechanism of action is by inhibition of oxytocin. We studied the effects of intrapartum atosiban administration during tachysystole and non-reassuring fetal heart rate on maternal and neonatal outcomes.

PATIENTS AND METHODS

We conducted a single-center, descriptive retrospective cohort study at a large tertiary referral center. Data were collected from January 2010 to August 2020. The study was approved by the research ethics board (RMB-0086-20). Eligibility criteria for inclusion were intrapartum atosiban treatment during fetal prolonged deceleration, tachysystole, and gestational age between $37^{0/7}$ and $43^{0/7}$ weeks. The data were retrieved from the combined maternal and fetal medical records and included antenatal, intra-

partum, and postpartum characteristics. The primary objective of this study was to compare maternal and neonatal outcomes in cesarean compared to the outcomes in vaginal delivery following atosiban administration. Maternal outcome data included demographic data, medical data, and maternal outcomes. Estimated blood loss of > 500 ml during a vaginal delivery and more than 1000 ml during a cesarean delivery were used to define postpartum hemorrhage. Neonatal outcomes included Apgar scores at 1 and 5 minutes, umbilical artery cord pH, and admission to the neonatal intensive care unit (NICU).

STATISTICAL ANALYSIS

Descriptive statistics were reported as mean ± standard deviation for continuous variables and as numbers (percentages) for categorical variables. Univariate analyses were performed using chi-square test or Mann–Whitney test to compare the groups on cesarean and vaginal deliveries. The threshold of statistical significance was $P < 0.05$. Statistical analysis was performed by IBM Statistical Package for the Social Sciences statistics software, version 25 (SPSS, IBM Corp, Armonk, NY, USA).

RESULTS

Overall, 275 patients were treated with atosiban. Of those, 186 (68%) were delivered vaginally (either spontaneous delivery or instrumental delivery), and 89 (32%) underwent a cesarean delivery. Eighty-seven gravidas (31.6%) underwent induction of labor, and 16 and 7 had gestational diabetes mellitus and pre-eclampsia, respectively [Table 1].

In a univariate analysis, cesarean delivery was associated with higher body mass index (27.9 ± 4.3 vs. 30.2 ± 4.8, $P = 0.003$), whereas second stage administration was associated with vaginal delivery (89.3% vs. 10.7%, $P = 0.01$). Cesarean delivery was associated with lower Apgar at 1 and 5 minutes and a higher rate of NICU admissions. Fetal weight was similar in both groups. The maternal age, gestational age, median dilation at drug administration, time therapy, gestational diabetes mellitus, pre-eclampsia, meconium, and postpartum hemorrhage (PPH) rates were similar in both groups [Table 2].

Table 1. Maternal and neonatal baseline characteristics

Characteristic	Value
Maternal characteristics	
Age at delivery, mean ± SD	29.9 ± 5.3
BMI, mean ± SD	28.7 ± 4.6
Gestational age at birth, mean ± SD	39.8 ± 1.1
Induction of labor, n (%)	87 (31.6%)
Gestational diabetes mellitus, n (%)	16 (5.8%)
Pre-eclampsia, n (%)	7 (2.5%)
Meconium, n (%)	50 (18.2%)
Cesarean delivery, n (%)	89 (32.4%)
Post-partum hemorrhage, n (%)	10 (3.6%)
Dilation, median	5
Neonatal characteristics	
Weight (grams), mean ± SD	3271 ± 411
Apgar at 1 minute, mode	9
Apgar at 5 minutes, mode	10
Admission to NICU, n (%)	16 (5.8%)

NICU = neonatal intensive care unit, SD = standard deviation

DISCUSSION

Atosiban is an oxytocin antagonist. It is a synthetic analogue that has the nonapeptide structure of oxytocin, thus competing with oxytocin for its receptors in the myometrium [8]. This property of atosiban was found to inhibit uterine contractions and delay preterm delivery [9].

In this study, we used the oxytocin antagonist property of atosiban as an intrapartum intervention for prolonged fetal heart rate deceleration in the second stage of labor to decrease the rate and the strength of uterine contractions during tachysystole and to avoid the need of emergency instrumental or cesarean section in the indication of non-reassuring fetal heart rate.

In our study, atosiban administration during labor was associated with 68% vaginal or instrumental delivery and only 32% cesarean delivery. The low rate of cesarean delivery during non-reassuring fetal heart rate as a result of tachysystole can be explained by atosiban induced myometrial relaxation that restores the oxygenation level of the fetus.

Furthermore, endogenous and exogenous oxytocin has uterotonic function during the third stage of labor. Thus, prophylactic oxytocin used after birth can reduce blood loss and decrease the rate of postpartum hemorrhage [10,11]. The incidence of PPH among women treated with atosiban in our study (2.3–4.3%) was higher than the incidence reported in the literature (1–3%) [12,13]. This finding may be a result of the oxytocin receptor antagonist mechanism of the atosiban, which diminishes the physiologic uterine contraction after the delivery and as a result causes higher blood loss.

We found only one randomized trial in the literature that compares atosiban vs. hexoprenaline treatment for uterine tachysystole or suspected fetal distress [14]. The study presented similar effects for stopping uterine contractions. Atosiban had significantly fewer adverse events compared to hexoprenaline, and uterine contractions resumed more promptly in the atosiban group. However, the incidence of cesarean delivery and epidural use was significantly lower compared to the literature and the findings in our study, which makes the study difficult to extrapolate for the general population.

Table 2. Comparison of risk factors associated with cesarean delivery

Variable	Vaginal and instrumental delivery (N=186)	Cesarean delivery (N=89)	*P*-value
Maternal characteristics			
Age in years at delivery, mean ± SD	29.5 ± 5.2	30.6 ± 5.5	0.12
BMI, mean ± SD	27.9 ± 4.3	30.2 ± 4.8	**0.003**
Gestational age in years, mean ± SD	39.8 ± 1.2	39.8 ± 1.0	0.88
GDM, n (%)	8 (4.3%)	8 (9.1%)	0.11
Pre-eclampsia, n (%)	3 (1.6%)	4 (4.5%)	0.15
Meconium, n (%)	29 (15.6%)	21 (23.9%)	0.10
Time from atosiban to delivery (hour)	6.6 ± 7.2	7.0 ± 7.4	0.92
Second stage administration	25 (89.3%)	3 (10.7%)	**0.01**
Dilation at administration; median	5	4.5	0.12
PPH, n (%)	8 (4.3%)	2 (2.3%)	0.4
Neonatal characteristics			
Weight (grams), mean ± SD	3264 ± 404	3287 ± 431	0.62
Apgar at 1 minute < 8	17 (9.1%)	31 (41.4%)	**< 0.001**
Apgar at 5 minutes < 9	6 (3.2%)	16 (18.6%)	**< 0.001**
Admission to NICU, n (%)	4 (2.2%)	12 (13.6%)	**< 0.001**

BMI = body mass index, GDM = gestational diabetes mellitus, NICU = neonatal intensive care unit, PPH = postpartum hemorrhage, SD = standard deviation
Bold indicates $P < 0.05$

Our results encourage the use of atosiban in the second stage of labor as an acute intervention for non-reassuring fetal heart rate during tachysystole to increase vaginal delivery rate and to avoid cesarean delivery. However, atosiban may be associated with higher incidence of PPH. The active third stage of delivery should be considered after administration of atosiban.

The study limitations include its descriptive retrospective nature and the fact that we did not have a control group without atosiban treatment. Additional randomized prospective studies are needed to confirm our results.

CONCLUSIONS

Atosiban in the second stage of labor may be an acute intervention for non-reassuring fetal heart rate during tachysystole to increase vaginal delivery rate and avoid cesarean delivery. Atosiban may be associated with higher incidence of postpartum hemorrhage and the active third stage of delivery should be considered after administration of atosiban.

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Little strokes, fell great oaks.

Benjamin Franklin (1705–1790), one of the Founding Fathers of the United States. A polymath and leading author, politician, scientist, inventor, civic activist, statesman, and diplomat, Franklin is known for his discoveries and theories regarding electricity, as well as lightning rod, bifocals, and the Franklin stove, among other inventions