



COMPARISON OF MATERNAL ARTERIAL BLOOD GAS DIFFERENCES BETWEEN OXYTOCIN ANTAGONIST ATOSIBAN AND BETAAGONIST TERBUTALINE IN FETAL SURGERIES FOR CORRECTION OF MYELOMENINGOCELE - PROSPECTIVE COHORT STUDY



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Introduction

- Myelomeningocele (MMC) is a malformation that affects approximately 3.4 pregnancies per 10,000 in USA.
- Intrauterine surgical repair reduces the exposure of fetal neural tissues to the environment inside the uterus and potentially can decrease the incidence and intensity of neurological deficits.
- In 2011, the MOMS trial (Management of Myelomeningocele Study) showed a better neurological prognosis for children undergoing a prenatal repair compared with postnatal treatment.
- One of the most important perioperative goals in intrauterine MMC repair is the avoidance of uterine contractions and placental abruption, with the use of tocolytic agents. Many agents can be used and they can be associated with maternal or fetal effects.
- Terbutaline is a beta-adrenergic agonist widely used as a tocolytic drug for preterm labour. It is associated with tachycardia and arrhythmias, hyperglycemia, hypokalemia, hyperlactatemia and hypocalcemia.
- Atosiban is an oxytocin and vasopressin receptor antagonist as effective as the beta-adrenergic agonists with a higher uterine specificity and less systemic side effects.
- There are no studies comparing those two tocolytic agents for in utero MMC repair.

Primary objective: compare the maternal arterial blood gas analysis repercussions resulting from terbutaline or atosiban use as tocolytic agent during intrauterine MMC repair.

Methods

- Research Ethics board approval, patient's written informed consent and Clinical Trials registration

Inclusion criteria: > 18 years, single pregnancy, fetuses with normal karyotype and GA 19 - 26 weeks with a diagnosed MMC by ultrasound

Exclusion criteria: fetus with malformations unrelated to MMC, ASA $\geq$ 3)

Groups:

- 1- Terbutaline: 2.5 mg in 500 mL of saline started during anesthetic induction, at an IV infusion rate of 150 mcg/h for 24 hours
- 2- Atosiban: IV loading dose 6.75 mg started during anesthetic induction and IV maintenance of 300 mcg/min for the first 3 hours, followed by an IV infusion of 100 mcg/min for 21 hours

Perioperative protocol:

- Aspiration prophylaxis: metoclopramide 10 mg and ranitidine 50 mg
- Monitorization: ECG, pulse oximetry, invasive blood pressure, BIS, neuromuscular monitor, esophageal temperature.
- Anesthetic technique: general + epidural
- Epidural catheter insertion: T11-T12, T12-L1 or L1-L2 level
- Induction of general anesthesia (rapid sequence intubation): fentanyl 4-6 mcg/kg, lidocaine 1.5 mg/kg, propofol 1-2 mg/kg and rocuronium 1.2mg/kg
- Maintenance: sevoflurane 2-3 MAC
- Additional tocolysis: bolus of IV nitroglycerine (100 mcg)
- Maternal systolic blood pressure: maintained at the patient's baseline levels, avoiding decreases of more than 10% of the baseline, for systolic blood pressure. Metaraminol was used as vasopressor 2.5-10 mg/h or intermittent bolus (200 mcg)
- Restrictive fluid management strategy to avoid postoperative pulmonary edema (total perioperative fluid intake of 500-2000 mL)
- During uterus was closure: loading dose of IV magnesium sulfate (5 g in 20 minutes) and maintenance infusion of 1 g/h for 5 hours
- Post-anesthesia care unit (PACU): oral nifedipine (80 mg daily) and vaginal progesterone (400 mg daily)

Blood gas samples:

- 1- After induction and intubation (baseline)
- 2- At the end of surgical procedure (before extubation)
- 3- At PACU discharge, 2 hours after surgery was finished

Variables:

- 1- Demographic characteristics
- 2- Arterial blood gases
- 3- Total fluid intake
- 4- Estimated blood loss
- 5- Vasopressors consumption
- 6- Fetal outcomes



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Results

Data collection: October 2015 to December 2019

Sample size: 25 (16 in the Atosiban group and 9 in the Terbutaline group)

Table 1 - Maternal baseline demographic data			
Variables	Groups		P
	Atosiban (n=16)	Terbutaline (n=9)	
Maternal age (years)	29.06 ± 6.83	27.11 ± 5.58	0.473
Weight (kg)	69.31 ± 12.89	76.11 ± 10.79	0.194
Height (cm)	158.81 ± 6.59	163.89 ± 5.44	0.062
Gestational age (weeks)	24.37 ± 1.08	24.44 ± 1.67	0.9

Student`s t test. Data is shown as Mean ± SD.

Variables	Table 2 – Maternal arterial blood gas analysis		P
	Atosiban (n=16)	Terbutaline (n=9)	
pH			
Baseline	7.395 ± 0.03	7.371 ± 0.04	0.124
Before extubation	7.396 ± 0.02	7.347 ± 0.05	0.006
PACU	7.382 ± 0.03	7.352 ± 0.04	0.058
pCO2 (mmHg)			
Baseline	33.66 ± 1.87	35.73 ± 2.77	0.053
Before extubation	32.68 ± 2.17	35.33 ± 5.70	0.253
PACU	34.18 ± 3.02	29.20 ± 4.99	0.010
Bicarbonate (mEq/L)			
Baseline	20.30 ± 0.93	20.22 ± 1.12	0.899
Before extubation	19.74 ± 1.22	18.84 ± 2.32	0.196
PACU	19.72 ± 1.12	15.87 ± 3.03	0.001
Base excess			
Baseline	-3.40 ± 1.15	-3.87 ± 1.76	0.480*
Before extubation	-3.73 ± 1.28	-5.66 ± 2.40	0.014*
PACU	-4.14 ± 1.04	-8.12 ± 3.37	0.020*
Lactate (mg/dL)			
Baseline	12.66 ± 3.57	17.55 ± 9.72	0.146
Before extubation	13.06 ± 6.35	28.33 ± 12.76	0.001
PACU	13.73 ± 4.96	44.66 ± 18.9	0.001

*Student T test.

Bonferroni correction for the others. Data is shown as Mean ± SD.



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Table 3 – Fluid and hemodynamic management			
	Groups		P
	Atosiban (n=16)	Terbutaline (n=9)	
Crystalloids (mL)	1321.87 ± 536	1655.55 ± 655	0.095
Estimated blood loss (mL)	987.5 ± 471.2	755.4 ± 462.8	0.246*
Metaraminol consumption (mg)	21.58 ± 6.26	19.17 ± 9.12	0.487

*Student`s t test.
Mann-Whitney test for the others. Data is shown as Mean ± SD.

Table 4 – Delivery and newborn data			
	Groups		P
	Atosiban (n=16)	Terbutaline (n=8)	
Newborn weight (g)	2318.5 ± 813	2275.66 ± 648	0.664
Newborn umbilical artery pH	7.222 ± 0.03	7.244 ± 0.07	0.491
Gestational age (weeks)	33.9 ± 4.3	33.2 ± 2.63	0.557

Mann-Whitney. Data is shown as Mean ± SD.

Conclusion

- Patients who received terbutaline had higher maternal acidosis and higher levels of arterial lactate, compared to those who received atosiban as a tocolytic in fetal surgery for myelomeningocele repair.

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