ORIGINAL ARTICLE

Comparative Study between Atosiban and Salbutamol in Treatment of Preterm Labor

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ABSTRACT

Aim: To compare the efficiency of two tocolytic drugs, oxytocin antagonist (oxytocin) with those of beta-adrenergic agonist (salbutamol) in continuation of pregnancy.

Methods: A randomized clinical trial study was carried out at the Al Batool Teaching Hospital, Mosul City-Iraq, all women belonged to age group (18 to 35) years who admitted delivery room with gestational age between (24-34) weeks of pregnancy. Two hundred pregnant women with preterm labor were joined in this study during the period of (January 2009-March, 2010). The women were divided randomly into two groups,(100) women Received intravenous infusion beta-agonist drug salbutamol sulfate (ventolin obstetric injection) .The pulse rate for women and for fetal were observed. the infusion amount were controlled to avoid women heart rates to excess of 120 beat per/min. Oxytocin is administered IV in 3 successive stages : an initial bolus dose 0.9 ml intravenous infusion (6.75mg) over 1 minute with oxytocin 7.5mg/ml solution for injection ,followed by continuous high dose infusion of(300microgram/minute) of oxytocin injection with infusion rate of 24ml/hour (oxytocin e dose 18mg/hour) over 3 hours period followed by a lower dose of oxytocin (subsequent infusion100microgram/minute) with infusion rate of 8ml/hour(oxytocin e dose 6mg/hour) for up to 48 hours. Fetal pulse and uterine withdrawals just as maternal circulatory strain and heartbeat rate were surveyed like clockwork for all member patients, if maternal heartbeat rate >120 beat/minute, fetal pulse >160 beat/minute, maternal dyspnea or chest torment built up the administration ended. The 48-hour delay in delivery was the most prominent result of this study.

Results: The study finding reveals that mean age of Salbutamol and Atosiban groups is (24.22+3.54), (25.54+1.14) respectively. Gestational age for group 1 is (29.22+0.42) and for group 2(30.11+0.77). Salbutamol delayed Delivery more than 48h in (44%) of women while Atosiban delayed (26%).Salbutamol administration associated with maternal tachycardia in 44% of women, and in comparative with Atosiban, only 16 % of women record tachycardia. Neonatal respiratory distress observed in 16% in group 1 and 12% in group 2.

Conclusion: The oxytocin antagonist atosiban, with a comparable neonatal and child health profile, was found to be better tolerated by both mother and fetus than salbutamol and atosiban was as effective as salbutamol in preventing threatened preterm birth. This research assists in the clinical use of atosiban in preterm labor therapy.

Keywords: Atosiban, Salbutamol, preterm, labor

INTRODUCTION

Preterm birth remains to be a challenge for obstetricians. Nearly 1 in 8 birth is born before 37 weeks' gestational age[1]. While the reasons for preterm b are birth not surely knew, the issue of preterm birth is clear[2].. Preterm work is answerable for practically 75% of all neonatal mortality and half of the kid's neurological disorders[3,4,5]. Around the world, endurance among newborn children brought into the world very preterm contrasts by open information for obstetric and neonatal consideration, and impression of feasibility[6,7,8]. Although slight development has been made over the last 20 years in decreasing the occurrence of preterm birth, a temporary extension of pregnancy permits maternal corticosteroid administration to stimulate maturation of fetal lungs and other body part and maternal transfer before birth to a center that can offer suitable neonatal special or intensive care[9]. It is a pear-shaped muscular organ that is inverted from the female reproductive system and is located between the bladder and rectum. It works to nourish and harbor the unborn baby and the unborn baby[10]. The uterus responds to many stimuli, and subsequent differences in the level of receptor expression and joining signaling pathways within cells may be involved in regulating uterine contractions. Uterine rest during pregnancy and the improved procedures associated with spontaneous initiation of labor can be redirected through differences in the role of uterine muscle receptors[11]. During the last three decades, Tocolytics using considered the main management for the inhibition of preterm birth. Tocolytic drugs are demonstrated to expand pregnancy in women with the danger of preterm birth. The principle defense for utilization of these meds is to deferment work for in any event 48 hours for the reason to allow time for the administration impact of corticosteroids or transmission of the pregnant mother to a specific high-chance obstetrical unit[12,13]. Oxytocin (OT) is a nonapeptide integrated by the magnocellular neurons situated in the supraoptic and paraventricular cores of the nerve center and discharged to the dissemination by the back pituitary and nerve terminals accordingly to different upgrades. Oxytocin reduces energy in the uterine muscle membrane, increases the intensity and number of uterus contractions and stimulates calcium ions. Intravenous injection of 2 milliliters of oxytocin causes an effect on the viability of the uterus, and uterine contraction may not begin until several minutes after the injection stops, just as intravenous injection quickly with 500 or 1,000 milliliters of oxytocin for a woman while labor may fail to cause even one contraction.But it undoubtedly increases the sensitivity of the uterine muscle and prepares it for its rapid action from subsequent bursts of oxytocin. As for the duration of the effect, the uterus may continue to contract for an extended period of an hour or more after the discontinuation of the IV. And then it gradually decreases to wear off. Oxytocin may increase

the effectiveness of uterine muscle fibers by energy without the demise of the cellular sheathing. This observation is of great importance in determining the mechanism of the effect of oxytocin. We must not forget what was observed by confirming that oxytocin facilitates the transfer of fluid from the uterine muscle to another muscle[14,15]. Beta-adrenergic agonist drugs such as salbutamol are the commonly used tocolytic drugs[16]. It acts through c-GMP to inhibit uterine contractions by inhibiting the pass of calcium ions into the smooth muscle of the uterus and produce uterine relaxation in most instances, but the onset is variable and depends on the dosage[17].

The current study objective was to compare the efficiency of two tocolytic drugs, oxytocin antagonist (Atosiban) with those of beta-adrenergic agonists (salbutamol) in continuation of pregnancy.

METHODS

It was a randomized clinical trial study was carried out at the Al batool Teaching Hospital, Mosul City-Iraq, conducted on all women belonged to the age group (18 to 35) years who admitted the delivery room with gestational age between (24-34) weeks of pregnancy.

- Preterm labor was estimated according to the following criteria:
- Uterine contractions ≥4 30 per second during the one-hour post-admission.
- Cervical dilatation rang (Zero-3cm) for primigravida and (1 - 3 cm) for multi-gravida.
- Cervical effacement < 50 percent and the fetal heart rate is normal.

Exclusion criteria: the following criteria were used to exclude women in the present study:

- eclampsia and severe pre-eclampsia requiring delivery.
- maternal diabetes mellitus.
- gestational age less than 24 weeks or more than 34 weeks.
- premature rupture of membranes.
- abnormal fetal heart rate,
- cervical dilatation more than 3 cm.
- hypersensitivity to the active substance of the drugs used in the study.

Two hundred pregnant women with preterm labor were joined in this study during the period of (January 2009-March, 2010).

Procedure: The women were divided randomly into two groups,(100) women Received intravenous infusion beta-agonist drug salbutamol sulfate (Ventolin obstetric injection).The pulse rate for women and fetal was observed. the infusion amount was controlled to avoid women's heart rates to an excess of 120 beats per/min. The infusion rate fixed at an identical level for 1 hour and then decreased by 50% decrements at 6 hourly intervals for up to 48 hours. Second group (n=100) received oxytocin antagonist oxytocin 7.5 mg/ml concentrate for solution for infusion, each vial contain 37.5 mg oxytocin diluted in one of the following solutions: ringer's lactate solution , 0.9% sodium chloride ,5% dextrose solution. Withdrawal of "10 ml solution from a 100ml infusion bag and discarded and replaced by 10 ml oxytocin 7.5 mg/ml concentrate for solution for infusion from two 5 ml vial to obtain a concentration of 75 mg oxytocin in 100 ml".Oxytocin is administered IV in 3 successive stages: an initial bolus dose 0.9 ml intravenous infusion (6.75mg) over 1 minute with oxytocin 7.5mg/ml solution for injection,followed by continuous high dose infusion of(300microgram/minute) of oxytocin injection with an infusion rate of 24ml/hour (oxytocin e dose 18mg/hour) over 3 hours period followed by a lower dose of oxytocin (subsequent infusion100microgram/minute) with an infusion rate of 8ml/hour(oxytocin e dose 6mg/hour) for up to 48 hours. Fetal pulse and uterine withdrawals just as maternal circulatory strain and heartbeat rate were surveyed like clockwork for all member patients,if maternal heartbeat rate >120 beats/minute, fetal pulse >160 beat/minute,maternal dyspnea or chest torment built up the administration ended. The 48-hour delay in delivery was the most prominent result of this study. Pregnant women who have had contractions after 48 hours, or have reported complications of the mother or fetus, failed to continue with the pregnancy and have undergone birth. While the pregnant women who released contractions left the hospital

Statistical analysis: All data were analyzed using IBM SPSS version 23.0 (IBM, Armonk, NY, USA).

Ethical considerations: The study was approved by the Ethical Committee of Nineveh Health directorate. All women completed and signed the" informed consent form.

RESULT

The study finding reveals that the mean age of Salbutamol and Atosiban groups is(24.22+3.54),(25.54=1.14) respectively. Gestational age for group 1 is (29.22+0.42) and for group 2 (30.11+0.77). Salbutamol delayed Delivery more than 48h in (44%) of women while Atosiban delayed (26%).Salbutamol administration associated with maternal tachycardia in 44 % of women, and in comparison, with Atosiban, only 16 % of women record tachycardia. Neonatal respiratory distress observed in 16 % in group 1 and 12 % in group 2.

Table 1: Characteristics of the two study groups comparing the patient's age (years),parity, gestational age(weeks), cervical dilatation(cm), number of uterine contractions and intensity of contraction(seconds).

Characteristic	Group 1 (Salbutamol) N = 100	Group 2 (Atosiban) N = 100	P-value
Age (years)	24.22+3.54	25.54+1.14	0.379
Gestational age	29.22+0.42	30.11+0.77	0.638
Parity	1 (0-3)	1(0-4)	0.624
Number of uterine	2.44+1.61	2.94+0.62	0.14
Intensity of uterine contraction(seconds)	28.13+1.13	29.16+2.23	0.649
Cervical dilatation (cm)	3.11+1.31	2.11+0.51	0.379

Table 2: Outcome of pregnancy in the two study groups comparing the time of delivery.

Delivery time	Group 1 (Salbutamol)		Group 2 (Atosiban)		P-value
	No.	%	No.	%	
Delivery within 48 hours	36	36	22	22	0.123
Delivery after 48 hours	44	44	26	46	0.841
Delivery after 7 days	20	20	32	32	0.171
Total	100	100	100	100	

Table 3: Maternal and fetal complications in the two study groups.

Maternal and fetal complications	Group 1 (Salbutamol)		Group 2 (Atosiban)		P-value
	No.	%	No.	%	
Maternal tachycardia	44	22	16	16	0.05

Fetal tachycardia	16	8	8	8	0.867
Maternal chest pain	24	12	8	8	0.112
Maternal dyspnea	12	6	4	4	0.617

Table 4: Neonatal complications in women with preterm labor in the two study groups.

Neonatal **complications**	**Group 1 (Salbutamol)**		**Group 2 (Atosiban)**		**P-value**
	No.	**%**	**No.**	**%**	
Respiratory distress	18	18	16	16	0.79
Intra cranial hemorrhage	12	12	10	10	0.749
Sepsis	12	12	6	6	0.487
Total	42	42	32	32	0.3

DISCUSSION

Fetal heartbeat and uterine withdrawals similarly as maternal circulatory strain and heartbeat rate were reviewed as expected for all part patients,if maternal heartbeat rate >120 beats/minute, fetal heartbeat >160 beats/minute,maternal dyspnea or chest torment developed the organization finished[18].

In the present study, the clinical efficacy and side effects of atosiban (oxytocin antagonist drug) were compared with those of salbutamol (a beta-agonist drug) in inhibition of preterm labor and keeping expansion of pregnancy for few days, and Which will positively reflect on the life of the fetus by completing a corticosteroid or not having to transfer it to neonatal intensive care.

Previous studies displayed that the use of Atosiban in preterm birth management found that the suppression of the contraction of the uterus via IV injection was associated with prolonging in labor like other tocolytic agents[19,20,21,22]. Four diverse dosing schedules of Atosiban compared with the regular dosage of salbutamol revealed that no significant difference in delivery within 48 hours or the requirement for alternative tocolysis between the ideal dosing schedule for oxytocin and salbutamol, although rarer side effects were related with Atosiban[23,24,25].

New as of late examination detailed that fetal and maternal unfavorable occasions were comparable post organization of oxytocin or fake treatment, aside from subcutaneous infusion site responses which happened all the more now and again in upkeep treatment with oxytocin. This preliminary demonstrated no distinction in the postponement of conveyance among oxytocin and fake treatment[26].

CONCLUSION&RECOMMENDATION

The oxytocin antagonist atosiban, with a comparable neonatal and child health profile, was found to be better tolerated by both mother and fetus than salbutamol and atosiban was as effective as salbutamol in preventing threatened preterm birth. This research assists in the clinical use of atosiban in preterm labor therapy.

Ethical consideration: Before data collection, an official permission was obtained from the Ministry of Education/ Nineveh Directorate , and Written approval of participants was obtained prior to the start of data collection.

Conflicts of interest: Nil

Source funding: Self

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