

## Effect of Tractocile (Atosiban) Therapy in Prevention of Preterm Labor in Singleton and Multiple Pregnancies

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### Abstract

**Objectives:** This research aims at studying Atosiban efficacy in terms of prolongation of pregnancy in the cohort of multiple and singleton pregnancy respectively.

**Methodology:** A retrospective observational study of 84 pregnant women with a diagnosis of threatened preterm labor, who received Atosiban as a tocolytic in the period 1st January 2015 till 31st December 2015 and their follow up till the timing of their delivery. Data were collected retrospectively using hospital online recording system [Cerner; version 12.4.0 (441592)-2016 Citrix Systems, Inc]. The inclusion criteria included pregnant women aged between 18 years and 35 years old in whom gestational age ranged between 24 weeks and 33 weeks and 6 days. The data were kept anonymously in an Excel sheet [(Microsoft Office -2016 (16.0.6769.2017)]. Analysis was carried out using Wizard Pro (version 1.9.26). A P-value less than 0.05 was considered statistically significant.

**Results:** Total of 84 cases were studied. 19% were multiple pregnancy cases versus 81 singletons. Mean Maternal age ( $27,4 \pm 4,77$  years). Maternal age didn't defer between both groups [p value 0.64]. Gestational age at diagnosis of preterm labour was ( $30,7 \pm 2,6$  weeks). Majority of multiple gestations came with PL < 32 weeks (p value 0.04).

The mean cervical dilatation at diagnosis was  $1.9 \pm 0.3$  cm. There was no significant defence between both groups taking the mean cervical dilation [p = 0.61]. There was no significant defence for the duration of Atosiban [p = 0.4]. The two groups did not significantly defer for The mean Atosiban Stopping-Delivery interval [p = 0.48]. Mean gestational age at delivery was 32.6 weeks (SD 2) and 34.2 weeks (SD 0.9) for Multiple and singleton respectively [P = 0,054] with no significant defence.

**Conclusion:** Our study didn't find any significant difference of the effect of Tractocile (Atosiban) on the singleton or multiple gestations on the means of prolongations of pregnancy and the gestational age at delivery.

**Keywords:** Tractocile; Atosiban; Preterm Labor

### Introduction

Preterm birth is defined as delivery at less than 37 weeks gestation and is the leading cause of perinatal morbidity and mortality [1]. More than 1 in 10 of the world's babies born in 2010 were born prematurely, making an estimated 15 million preterm births (defined as before 37 completed weeks of gestation), of which more than 1 million died as a result of their prematurity [2]. Prematurity is now the second-leading cause of death in children under 5 years and the single most important cause of death in the critical first month of life [3]; thus, research studies have been focused on identifying the best method to prevent preterm birth. Atosiban, an oxytocin receptor blocker which has been used in our institute, in cases of suspected preterm labor for thirteen years.

### Objectives of the Study

This research aims at studying Atosiban efficacy in terms of prolongation of pregnancy for singleton and multiple respectively and find out if significant deference between both groups in term of prolongation of pregnancy, gestational age at delivery and the preterm labour variables.

### Methodology

We undertook a retrospective observational study of 84 pregnant women admitted to the hospital with a diagnosis of threatened pre-term labor, and who received Atosiban as a tocolytic for prevention of preterm delivery (suppression of uterine contractions) in the period 1<sup>st</sup> January 2015 till 31<sup>st</sup> December 2015 and their follow up till the timing of their delivery, data were collected retrospectively using an online data collecting system through hospital online recording system [Cerner; version 12.4.0 (441592)-2016 Citrix Systems, Inc]. The inclusion criteria included pregnant women aged between 18 years and 35 years old in whom gestational age ranged between 24 weeks and 33 weeks and 6 days. Patient was excluded for the study if any she has any of the following:

1. Reproductive age group less than 18 years old or more than 35 years old
2. Gestational age less than 24 weeks or 34 weeks and more
3. Cervical dilatation 5 cm or more on admission
4. Cervical dilatation 4 cm and effacement 100% on admission
5. Severe vaginal bleeding
6. Signs of fetal distress
7. Signs of intrauterine infection
8. Fetuses with suspected chromosomal abnormalities or anomalies incompatible with life.

Atosiban was given as a single loading intravenous dose, 6.75 mg in 0.9% sodium chloride solution, followed by an intravenous infusion of 300 micrograms/min in 0.9% sodium chloride solution for the first 3 hours and then 100 micrograms/min for another 45 hours. The choice of the dose regimen for Atosiban was consistent with the recommendations of the product labeling.

Assigned treatment was planned for up to 48 hours. Maintenance therapy after the first 48 hours was not provided. In addition, tocolytic drugs were discontinued when progression to a cervical dilatation of 5 cm or more.

Prophylactic antibiotics for group B streptococcus and corticosteroids were administered according to standard clinical indications. Uterine contractions were monitored continuously by an external tocodynamometer for 2 - 4 hours after initiation of the study drug followed by two to three times a day for 30 - 60 minutes if contractions are subsiding.

The data were kept anonymously in an Excel sheet [(Microsoft Office -2016 (16.0.6769.2017)]. Descriptive and inferential statistics were employed as adequate using Wizard Pro (version 1.9.26). The statically differences were calculated using the t-test for the means and the Mann-Whitney test for the medians. A P-value of less than 0.05 was considered statistically significant.

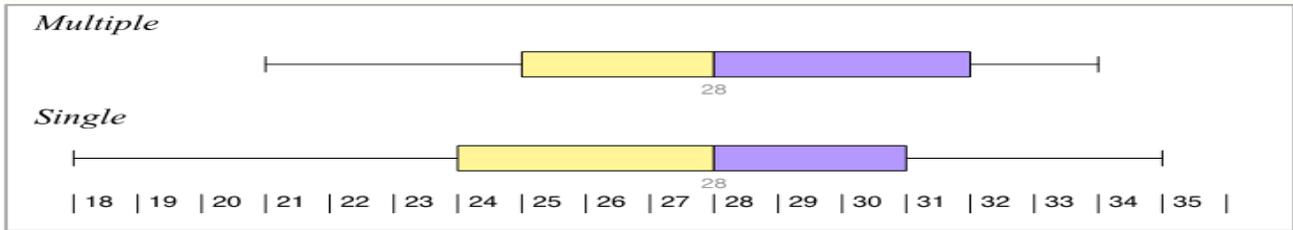
Ethical approval was not required as this was an audit as a quality assurance project and all data were unidentifiable.

### Results

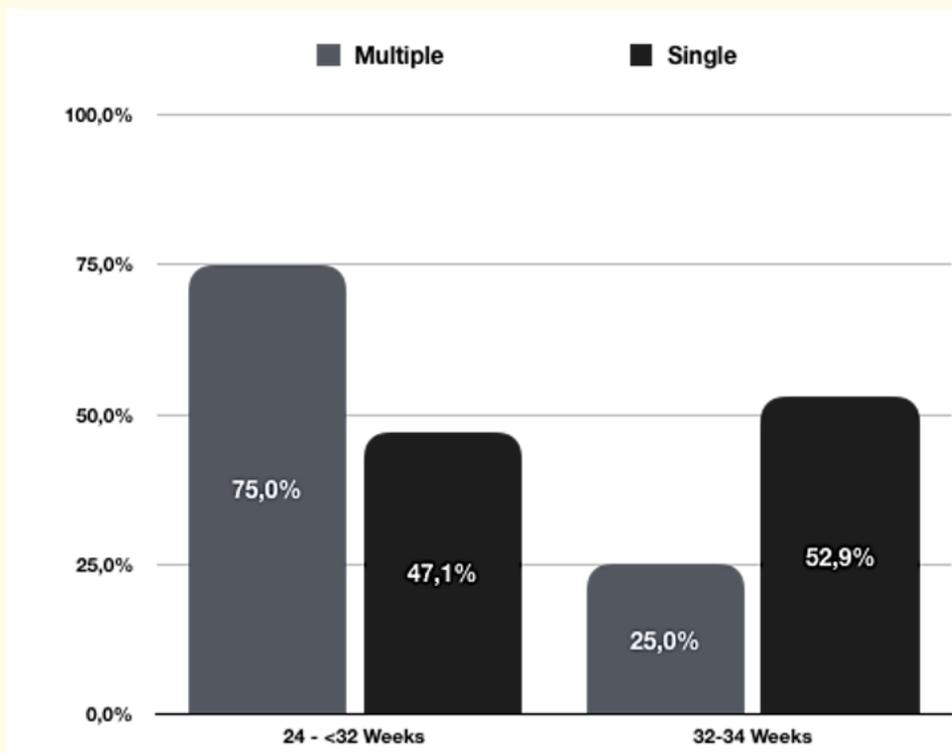
Total of 84 cases were studied. Singletons were 81% and multiple gestation 19%.

	Singletons	Multiple Gestation	P value
Maternal Age (Years) - [Mean ± SD]	28,1 ± 2,3	27,3 ± 1,2	0,5
Preterm labour gestation -[Mean ± SD]			
24 - < 32 Weeks gestation	47,1%	25%	0,04
32 - 34 Weeks	52,9%	75%	0,04
Cervical Dilatation at Presentation (cm) - [Mean ± SD]	1,9 ± 0.3	2,1 ± 0,6	0.61
Atosiban Duration (Hours) - [Mean ± SD]	35.9 ± 3.7	30,7 ± 1	0,4
Atosiban Cessation-Delivery interval (Days) - [Mean ± SD]	22.9 ± 5.8	18.3 ± 11.9	0,48
Gestational Age at Delivery (Weeks) - [Mean ± SD]	34.2 ± 0.9	32.6 ± 2	0,054

**Table 1:** Patients variables as well as Atosiban Effect among the two groups.



Graph 1: Median Maternal age for both groups [p = 0,64].

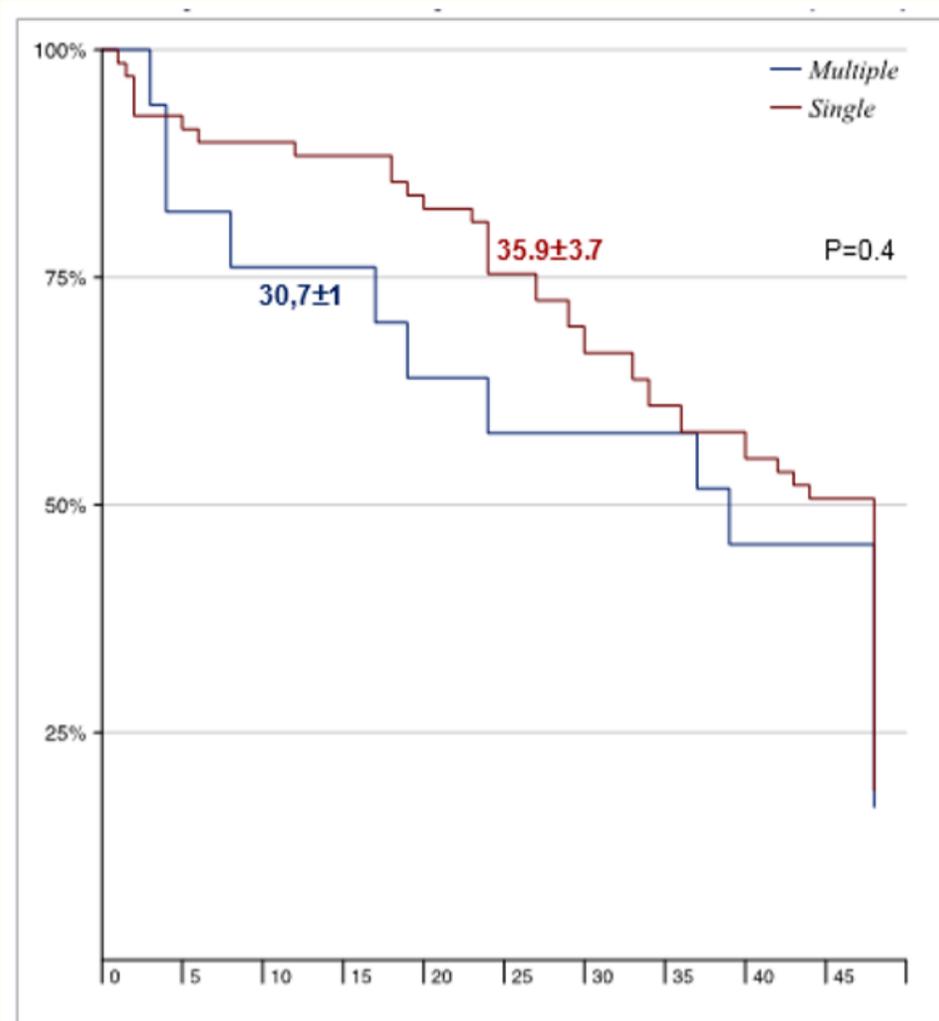


Graph 2: Gestational age at the diagnosis of preterm labour [p = 0.04].

It is obvious the majority of our cohort has singletons, on the other hand majority of multiple gestations came with PL < 32 weeks (p value 0.04).

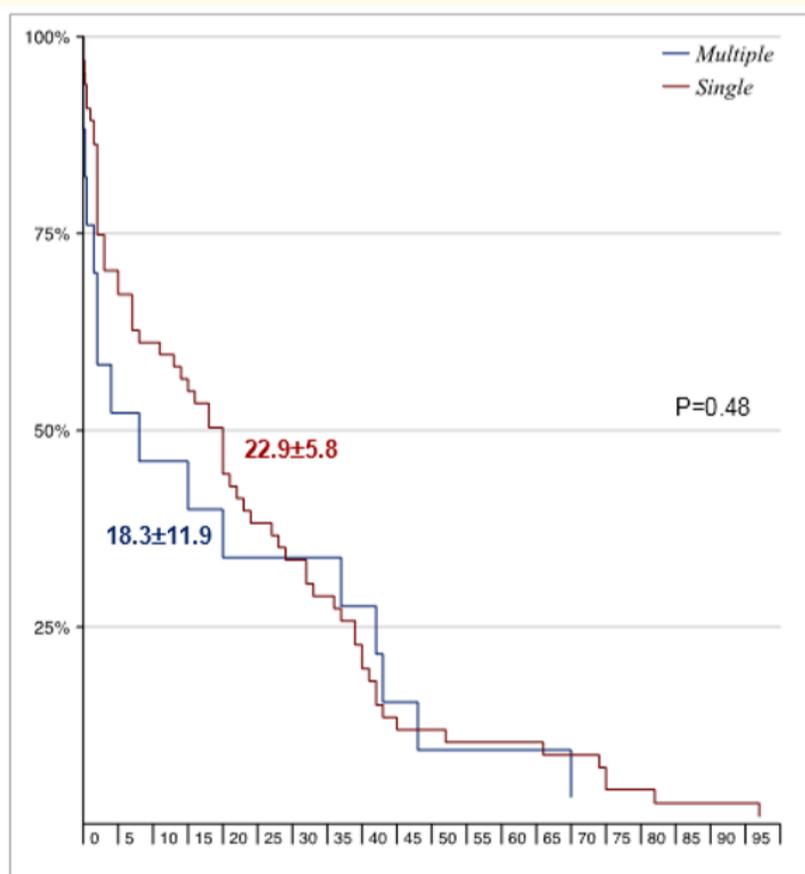
The mean cervical dilatation at diagnosis was  $1,9 \pm 0,3$  cm for singleton and  $2,1 \pm 0,6$  cm for Multiple gestation. There was no significant difference between both groups taking the mean cervical dilation [p value 0.61].

Atosiban was used in a mean duration of  $35,9 \pm 3,7$  hours for singleton and  $30,7 \pm 1$  hour for multiple pregnancies with no significant difference between both groups for the duration of Atosiban [p value 0.4]



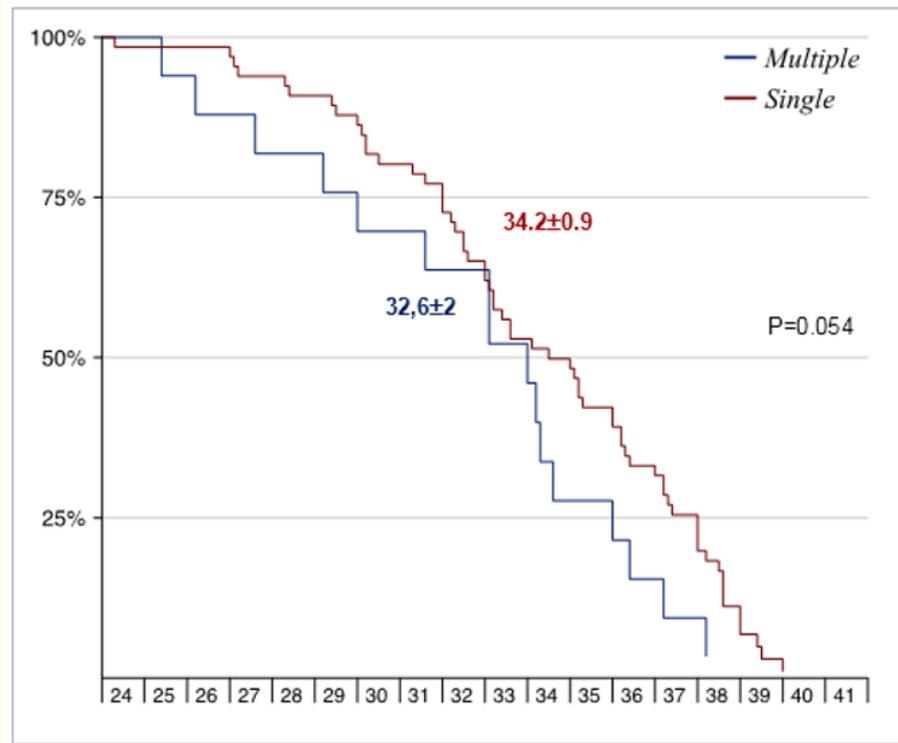
**Graph 3:** Kaplan-Meier estimator for the duration of Atosiban administration (Hours) among the two cohorts.

The mean Atosiban Cessation-Delivery interval was 22.9 ± 5.8 days for Singleton and 18.3 ± 11.9 days for multiple pregnancies respectively and was not significantly defer for the mean [p value 0.48].



**Graph 4:** Kaplan-Meier estimator for the Atosiban cessation-Delivery interval (days) among the two cohorts.

Mean gestational age at delivery was 34.2 weeks (SD 0.9) 32.6 weeks (SD 2) for singleton and Multiple respectively [P value 0,054] with no significant defence.



Graph 5: Kaplan-Meier estimator for the Gestational age at delivery (Weeks).

**Discussion**

Multiple pregnancies e.g. twins, are especially confounded by higher rates of preterm birth with 50 - 60% of twins reported to deliver preterm compared to 11% of singletons, suggesting there is a twin-specific risk to preterm delivery [4,5].

The preterm birth prevention strategies applied to singleton pregnancies have not been found to be effective in twin pregnancies 12 and the evidence for the use of tocolysis in twins is limited [6,7].

Arrowsmith S., *et al.* suggest that on spontaneous contractions, indomethacin and progesterone are as potent in suppressing myometrial contractions in twin and singleton pregnancies; similarly, for Atosiban, it is as potent in suppressing oxytocin-induced contractions in twins as it is in singletons [8].

Arrowsmith S., *et al.* other work was very comprehensive but specific toward the relaxant effect of Magnesium Sulfate (MgSO<sub>4</sub>) on spontaneous and oxytocin-augmented contractions of human myometrium from singleton and twin pregnancies and wither that effect can be augment with Atosiban; it was not meant to specifically address the effect of Atosiban [7].

Our study demonstrates that clinical Response to Atosiban did not significantly defer between singleton and multiple gestations, however, the clinical significance cannot be overlooked. Singleton pregnancies showed apparent longer Atosiban Cessation-Delivery interval and almost two weeks longer on the gestational age at delivery. These findings are of crucial importance during counselling and managing these groups. The statistical insignificance, however, will encourage further studies with a larger number.

The limitation of this research is the retrospective nature with its limitations and the small number, especially for multiple pregnancy arm.

### Conclusion

Our study didn't find any significant difference of the effect of Tractocile (Atosiban) on the singleton or multiple gestations on the means of prolongations of pregnancy and the gestational age at delivery. This Study should encourage more prospective research with a more significant number of patients in order to find conclusive evidence regarding the use of Tractocile in multiple gestations.

### Disclosure

There is no financial interest associated with the study.

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