

Comparative analysis of magnesium sulfate and atosiban in fetal neuroprotection during high-risk pregnancies

Lijuan Pan* and Ning Zhang

Department of Obstetrics, Affiliated Hospital of Jiangsu University, 438 Jiefang Road, Zhenjiang, Jiangsu Province, China

Abstract: Preterm births could increase the risk of neonatal conditions like cerebral palsy and neurodevelopmental delays. This trial aimed to evaluate the efficacy of magnesium sulfate and atosiban in providing neuroprotection to preterm infants. A clinical trial was conducted between 2020 and 2024, involving 102 high-risk pregnant women at multiple tertiary clinics in China. We studied the neonatal neurodevelopmental delay at 6 months and 12 months whilst also focusing on factors such as maternal side effects, gestational age, mode of delivery, and Neonatal Intensive Care Unit (NICU) admission rates. Unlike magnesium sulfate, Atosiban could reduce the fetus' breathing problems that can, in turn, lead to baby brain protection. It also has fewer maternal side effects, such as nausea and hypertension ($p = 0.03$). Magnesium sulfate had comparably higher risks of maternal and fetal complications, 49.02% and 68.63% respectively. This study's results suggest that while atosiban is not a commonly used intervention, it is a promising agent for fetal neuroprotection. It is also observed that considering maternal safety, it has fewer side effects. Future larger population studies should be carried out to corroborate the results for higher efficient and safer intervention for fetal neuroprotection

Keywords: Magnesium sulfate; atosiban; fetal neuroprotection; high-risk pregnancies

Submitted on 18-06-2024 – Revised on 07-04-2025– Accepted on 18-06-2025

INTRODUCTION

Preterm birth is a world problem, which is characterized by the birth of a baby earlier than in the normal 37 weeks (Hoffman, 2021). More than 13.4 millions or 10 per cent of all live births take place before the expected time. Regrettably, the result of these premature births also results in complications and pegs at approximately 900,000 children dying at birth and it forms one of the leading causes of children deaths below the age of five (WHO, 2023). The preterm births in China include 6.4 percent of all births, but the volume of the issue is increased due to large population of China (Liu and Wang, 2024). Preterm birth is not only associated with a severe health challenge but also generates immense social and economic burdens such as an expensive medical cost and chronic developmental problems that could extend throughout the lifespan of a child (Song *et al.*, 2022; Lakshmanan *et al.*, 2017).

Among the most significant consequences of preterm births, there is the threat of neurological disorders, such as cerebral palsy and cognitive retardation (Mornioli *et al.*, 2023). To curb it, neuroprotective interventions are created on risky pregnancies. A delay in labor is done by the use of tocolytic agents, one of such strategies. When delayed the delivery of these drugs can provide a greater chance of fetuses undergoing the development and finding remedies that enhance the development of lungs (Liu and Wang, 2024).

Another drug that is thoroughly researched is magnesium sulfate. Now, it is mainly used in the treatment of conditions such as eclampsia but later, scientists discovered that it is used in decreasing the risk of cerebral palsy among preterm newborns (Rahma *et al.*, 2024; Jafarabady *et al.*, 2024). Magnesium could protect the brain in a number of ways. It inhibits NMDA receptors thereby thwarting the tendency of calcium levels to increase at a dangerous level. In its reduced flow, magnesium can decrease glutamate, which prevents cells form injury and excitosis and also magnesium has anti-inflammatory properties that can reduce oxidizing stress and harmful cytokines (Chollat *et al.*, 2018).

Magnesium plays a crucial role in regulating vascular tone by modulating nitric oxide production, particularly when its levels are low, which can impact endothelial function. Additionally, it helps maintain calcium homeostasis and possesses anti-inflammatory properties (Chollat *et al.*, 2018). However, the administration of magnesium sulfate is not without limitations. It is associated with maternal side effects such as flushing, nausea, and, in some cases, respiratory depression (Shepherd *et al.*, 2024). These adverse effects may contribute to clinician reluctance in certain clinical scenarios, and ongoing research aims to better understand its efficacy across varying pregnancy profiles and patient populations.

Atosiban, on the other hand, is a less common and pricier option among tocolytic drugs. Unlike traditional drugs, it stops uterine contractions by blocking oxytocin, giving the baby more time to grow (Liu and Wang, 2024). It's considered safer for the lungs compared to older

*Corresponding author: e-mail: bjk1638792plj@hotmail.com

medications, but there's still a lot we do not know about how it might affect the newborn's brain as most research has focused on its role in delaying preterm labor (Al-Riyami *et al.*, 2021).

Moreover, atosiban demonstrated improved maternal tolerability as well as fewer adverse effects than other tocolytics, e.g. nifedipine or 8-mimetics (Dekker *et al.*, 2021; Liu *et al.*, 2024). In spite of the fact that the evidence, which would point to direct neuroprotective ability, remains scattered, recent studies note that longer gestation period due to the administration of atosiban could indirectly cause better neurodevelopmental outcomes in newborn babies (Chauhan *et al.*, 2023). It is with this in mind that more people are keenly interested in the comparative studies on magnesium sulfate as opposed to atosiban in assessing the aspects of fetal neuroprotection and maternal safety with regard to high risk pregnancies. Regardless of the widespread usage of magnesium sulfate, there remain numerous clinical uncertainties about its correct dose, longevity, and interaction with other therapeutic procedures (Parikh *et al.*, 2014; Chollat *et al.*, 2018).

The research would test the hypothesis that the two conditions (magnesium sulfate and atosiban) differ regarding the protection of the fetus against brain damage, especially in high-risk pregnancies occurring at the 24-32 week of gestation. Whereas the neuroprotective effect of magnesium sulphate is generally accepted, atosiban is mostly applied as a tocolytic and has not been studied well on potential neurotoxic effect of neonatal neurodevelopment. The use of such materials as magnesium sulfate and atosiban is aimed at the direct comparison of the two with respect to the neurodevelopmental outcomes of preemies (6- and 12-months delay prevention), the maternal repercussions of their use, offers of gestation, and neonatal conditions, as the secondary research methods. This clinical trial study was conducted and compared the two drugs, not only as potential fetal neuroprotectants, but also longitudinally with quantitative neurodevelopmental outcomes in infants up to 12 months of age by using standardized developmental scales. Such a new pathway can fill in the evidence gap about the wider fetal safety profile of atosiban and provide new data on the maternal-neonatal outcomes linked to both drugs.

MATERIALS AND METHODS

Study design

This study was conducted for 4 years from 2020-2024 in multiple tertiary centres in China. Following the standard dosage guidelines, two groups of 51 individuals each were intravenously given magnesium sulfate and atosiban, respectively. The administration of these treatments was carefully monitored to ensure both their safety and effectiveness.

Study population

This trial involved 102 pregnant individuals between 24 and 32 weeks of gestation, all at high risk for preterm labor due to clinical conditions that led to early labor.

Inclusion criteria

1. Pregnant women at gestational age between 24 and 32 weeks
2. Women aged 18-45 years
3. Clinical signs of early labor, such as premature rupture of membranes (PROM) or preterm labor with uterine contractions and cervical changes
4. High-risk problems like a history of preterm deliveries, preeclampsia, gestational hypertension, diabetes, or infections
5. Consent with full knowledge

Exclusion criteria

1. Twin or triplet pregnancies
2. Pre-existing diseases like kidney or liver problems, heart issues, or poorly controlled diabetes
3. Stillbirth or congenital abnormalities
4. A history of allergic reactions to magnesium sulfate or atosiban

Outcome measures

The research's primary goal was assessing the newborns' neurodevelopmental status at 6 and 12 months. Using standardized tools like the Bayley Scales of Infant Development and the Denver Developmental Screening Test, we aimed to detect any developmental delays, motor dysfunction, or cognitive impairments.

Regarding the secondary outcomes, we examined the frequency and severity of maternal adverse effects, including hypotension, nausea, vomiting, respiratory depression, and other side effects linked to magnesium sulfate or atosiban administration. We also recorded the gestational age at delivery, along with the incidence of preterm delivery, which is defined as births occurring before 37 weeks of gestation.

Birth defects were also evaluated, focusing on diseases such as respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH), newborn infections like sepsis, necrotizing enterocolitis (NEC), and the admission rates to the Neonatal Intensive Care Unit (NICU). We also looked at any maternal complications, including preeclampsia, eclampsia and other maternal morbidities. Finally, the study documented the mode of delivery, whether vaginal or cesarean, along with any difficulties that happened during the delivery process.

Data collection

We collected data over four years, from January 2020 to December 2024. This included basic information like age, BMI, medical history, and past pregnancies, including any history of preterm births. We also recorded complications

during pregnancy, how far along participants were when they joined the study, and details about the treatments they received.

In the end, the data covered everything we were measuring, such as assessments of the babies' development at 6 and 12 months, along with information about any issues the mothers or babies experienced. The information was stored securely and handled following privacy rules and ethical guidelines in China.

Pregnancy outcomes, including fetal loss, stillbirths, and early neonatal mortality, were also recorded. Any cases of fetal demise prior to delivery or neonatal death within the first 7 days were excluded from the neurodevelopmental follow-up assessments but were documented for transparency.

STATISTICAL ANALYSIS

We summarized the demographic and baseline characteristics using averages, medians, standard deviations, and proportions. For comparing the two groups, we looked at continuous variables like neurodevelopmental scores and gestational age at delivery, using t-tests or non-parametric tests when necessary. Categorical variables, such as NICU admissions and maternal adverse effects, were studied with chi-square test.

To control for possible confounding factors like maternal age and medical history, we applied multivariate regression models. This helped us assess the independent effects of magnesium sulfate compared to atosiban on the primary and secondary outcomes. We deemed a p-value of less than 0.05 to be statistically significant. We also handled any missing data using mean imputation methods to keep our analysis strong and valid.

Ethical considerations

This study followed the guidelines set by the Declaration of Helsinki and was approved by the Affiliated Hospital of Jiangsu University ethics committees of all participating tertiary centers. (No. KY2023H0907-05) Participants were informed about the study's goals, procedures, potential risks, and benefits. Written informed consent was obtained and we kept their information anonymous and confidential throughout the research.

RESULTS

Participant characteristics

A total of 102 participants were enrolled in the study, they were divided into two groups according to the intervention methods: 51 women were assigned to take magnesium sulfate, while the other 51 women were assigned to the atosiban group as shown in fig. 1. They delivered at ≤ 32 weeks of gestation in tertiary centres in China. At the onset of the trial, the demographic and clinical characteristics of

the two groups were found to be similar, which ensures comparability and strengthens the validity of the findings (table 1). Of the 102 enrolled pregnancies, all resulted in live births. There were no reported fetal losses or stillbirths during the study period. However, two neonates (one in each group) died within the first 48 hours due to extreme prematurity and severe respiratory failure. These cases were excluded from the neurodevelopmental outcome analysis at 6 and 12 months but were included in the NICU and neonatal complication statistics.

Both groups had similar average gestational ages at enrollment, recorded at 28.3 weeks with a standard deviation of 2.1 weeks. This further maintains the comparability of the groups at the start of the trial. Coming to obstetric history, neither group showed any significant differences. Approximately 40% of women in each group had a history of preterm birth, emphasizing a common risk factor for both treatments. Additionally, 25% of participants in both groups were found to have multiple gestations, and 20% had experienced preeclampsia or other hypertensive conditions during pregnancy.

Regarding maternal health, hypertension was present in 15% of women in both groups, while gestational diabetes affected around 10% of participants in each group. These characteristics support that both groups were similar in terms of risk factors related to preterm birth and maternal health. Ultimately, these comparable features provide a solid foundation for the analysis of both treatments in the study.

Primary outcome: Neurodevelopmental delay at 6 and 12 months

The study's primary goal was to observe how the neurodevelopment of newborns progresses at 6 and 12 months, using standardized tools like the Bayley Scales of Infant Development (BSID) and the Denver Developmental Screening Test (table 2).

When we followed up at 12 months, the trends remained consistent as seen in fig. 2. In the magnesium sulfate group, 20 neonates (39.2%) still had developmental delays, particularly in their motor skills and cognitive abilities. Meanwhile, in the atosiban group, only 10 neonates (19.6%) had ongoing delays at this stage, with this result also being statistically significant ($p = 0.03$). These findings support that atosiban treatment is beneficial for long-term neurodevelopment compared to magnesium sulfate.

Secondary outcomes

The study's secondary outcomes consisted of maternal adverse effects (hypertension and nausea/vomiting), gestational age at delivery, NICU admission rate, neonatal complications, mode of delivery, and maternal complications (table 3).

Maternal adverse effects

In the magnesium sulfate group, 11 out of 51 women (21.6%) experienced hypotension during treatment, which required management through intravenous fluids or temporary discontinuation of the medication. Additionally, 14 women (27.4%) reported nausea or vomiting as a side effect, with some requiring antiemetic treatment. Notably, one participant experienced respiratory depression, which necessitated temporary respiratory support.

In contrast, the atosiban group reported significantly fewer maternal adverse effects. Only 4 out of 51 women (7.8%) experienced hypotension, which is a notably lower rate compared to the magnesium sulfate group ($p = 0.02$). Furthermore, 6 women (11.8%) reported nausea or vomiting, also lower than the magnesium sulfate group ($p = 0.03$), and no cases of respiratory depression were reported in the atosiban group. These percentages indicate that atosiban is associated with fewer maternal adverse effects, suggesting it may be a safer option for maternal health (fig. 3).

NICU admission rates and neonatal complications

When examining NICU admission rates, the magnesium sulfate group had 39 neonates (76.5%) admitted for preterm complications such as respiratory distress, feeding difficulties, and infections. Conversely, only 28 neonates (54.9%) in the atosiban group required NICU admission ($p = 0.02$), indicating fewer complications necessitating intensive care.

Regarding neonatal complications (fig. 3), the magnesium sulfate group reported 15 neonates (29.4%) developing respiratory distress syndrome (RDS), 5 (9.8%) with intraventricular hemorrhage (IVH), and 3 (5.9%) with necrotizing enterocolitis (NEC). In comparison, the atosiban group had 10 neonates (19.6%) with RDS, 2 (3.9%) with IVH, and 1 (2%) with NEC. These numbers demonstrate a statistically significant reduction in neonatal complications such as RDS, IVH, and NEC in the atosiban group, underscoring the advantages of atosiban in mitigating the severity of neonatal issues.

Maternal complications

The incidence of maternal complications also differed between these two groups. In the magnesium sulfate group, 10 women (19.6%) developed complications such as preeclampsia, eclampsia, or uterine rupture. Conversely, only 5 women (9.8%) in the atosiban group experienced similar complications, which represents a statistically significant reduction compared to the magnesium sulfate group ($p = 0.04$) (fig. 3).

Gestational age at delivery

The average gestational age at delivery in the magnesium sulfate group was 34.2 ± 2.4 weeks, with a median gestational age of 34 weeks; notably, 40% of women delivered before 34 weeks. In comparison, the atosiban

group had an average gestational age at delivery of 35.5 ± 2.1 weeks, with a median of 35 weeks ($p = 0.01$). Only 25% of women in the atosiban group delivered before 34 weeks. These results imply that atosiban may effectively delay preterm delivery, providing more time for fetal development.

Mode of delivery

The mode of delivery in the magnesium sulfate group as seen in fig. 4 showed that 30 women (58.8%) underwent cesarean deliveries, while 21 women (41.2%) had vaginal deliveries. This high rate of cesarean sections reflects the obstetric complications and the necessity for emergency deliveries. In contrast, the atosiban group experienced a higher proportion of vaginal deliveries, with 40 women (78.4%) delivering vaginally and 11 women (21.6%) having cesarean deliveries ($p = 0.04$).

DISCUSSION

In this study, we looked at how magnesium sulfate and atosiban help when it comes to protecting fetal brains in high-risk pregnancies, especially in terms of how the babies develop after birth. The results show that atosiban might be a better choice overall. It appeared to outperform magnesium sulfate in several key areas, including fetal neurodevelopment, maternal safety, timing of delivery, and the overall reduction in neonatal health complications.

One of the significant findings in this study was how much better babies did at 6 and 12 months when their mothers were treated with atosiban instead of magnesium sulfate. Fewer babies in the atosiban group showed developmental delays, based on tests like the Bayley Scales and the Denver Developmental Screening Test. At 6 months, only 17.6% of babies in the atosiban group had delays, compared to 31.4% in the magnesium sulfate group. By 12 months, the difference was even clearer – just 19.6% in the atosiban group had delays, while 39.2% of the magnesium sulfate babies did. This difference is pretty significant ($p = 0.03$), which suggests atosiban might be doing a better job protecting babies' brains overall.

As we know, magnesium sulfate helps by blocking calcium from getting into cells, which helps protect the brain from overstimulation (Chollat *et al.*, 2018). It's effective, but it can also cause problems for the mother, like low blood pressure and breathing issues, which in turn would affect the baby (Shepherd *et al.*, 2024). This stays consistent with what other studies have found, like the one by Nijman *et al.*, 2018, showing atosiban could be good for protecting fetal brains. Even though magnesium sulfate is still the standard treatment for preterm labor, atosiban seems to be a solid alternative for both the mother and baby. It could definitely be worth considering in high-risk pregnancies.

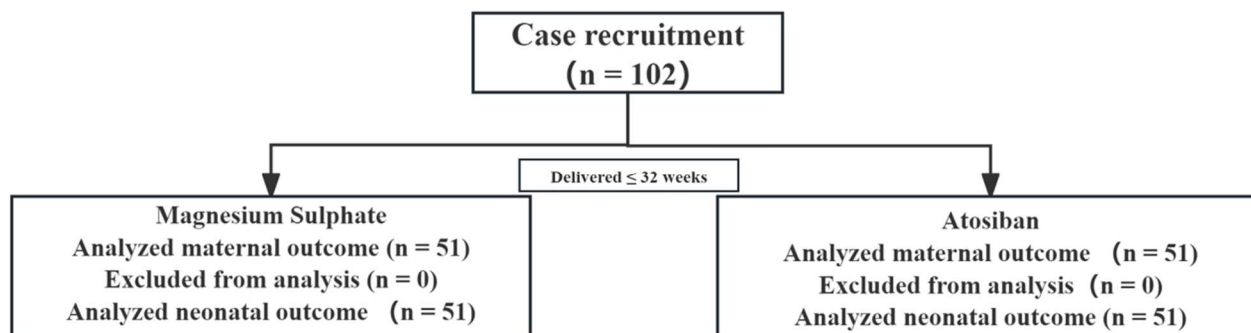


Fig. 1: Flowchart showing participants included in the trial

Table 1: Demographic Characteristics of Participants

Characteristic	Magnesium Sulfate (n = 51)	Atosiban (n = 51)	Total (n = 102)
Age (mean \pm SD)	30.5 \pm 4.1 years	30.3 \pm 3.9 years	30.4 \pm 4.0 years
Gestational Age at Enrollment (mean \pm SD)	28.3 \pm 2.1 weeks	28.3 \pm 2.1 weeks	28.3 \pm 2.1 weeks
Obstetric History			
History of Preterm Birth (%)	40% (n = 20)	40% (n = 20)	40% (n = 40)
Multiple Gestations (%)	25% (n = 13)	25% (n = 13)	25% (n = 26)
History of Preeclampsia or Hypertensive Disorders (%)	20% (n = 10)	20% (n = 10)	20% (n = 20)
Maternal Health Conditions			
Hypertension (%)	15% (n = 8)	15% (n = 8)	15% (n = 16)
Gestational Diabetes (%)	10% (n = 5)	10% (n = 5)	10% (n = 10)

In terms of age distribution, the average age of participants in the magnesium sulfate group was 30.5 years, with a standard deviation of 4.1 years. Conversely, the atosiban group had an average age of 30.3 years, with a standard deviation of 3.9 years. This indicates that the participants in both groups were of comparable age, contributing to the overall balance of the study.

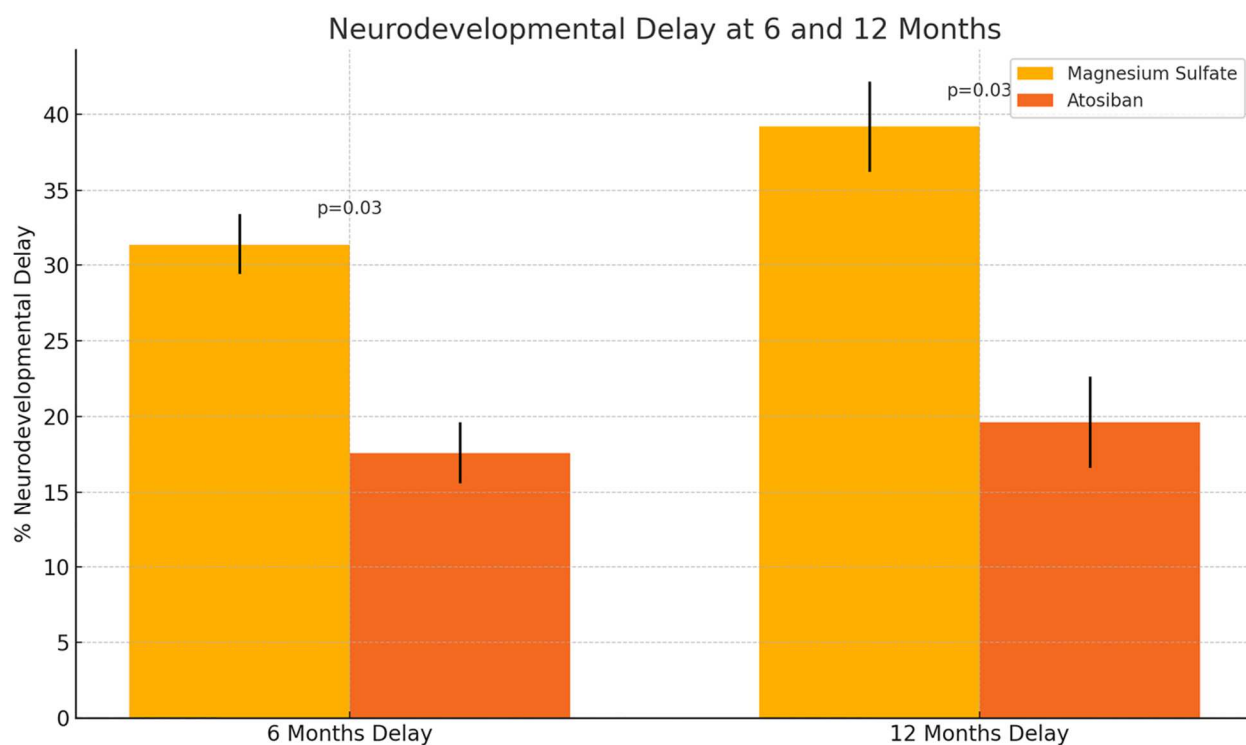


Fig. 2: Graphical representation of the neonatal neurodevelopmental delay at 6 months and 12 months.

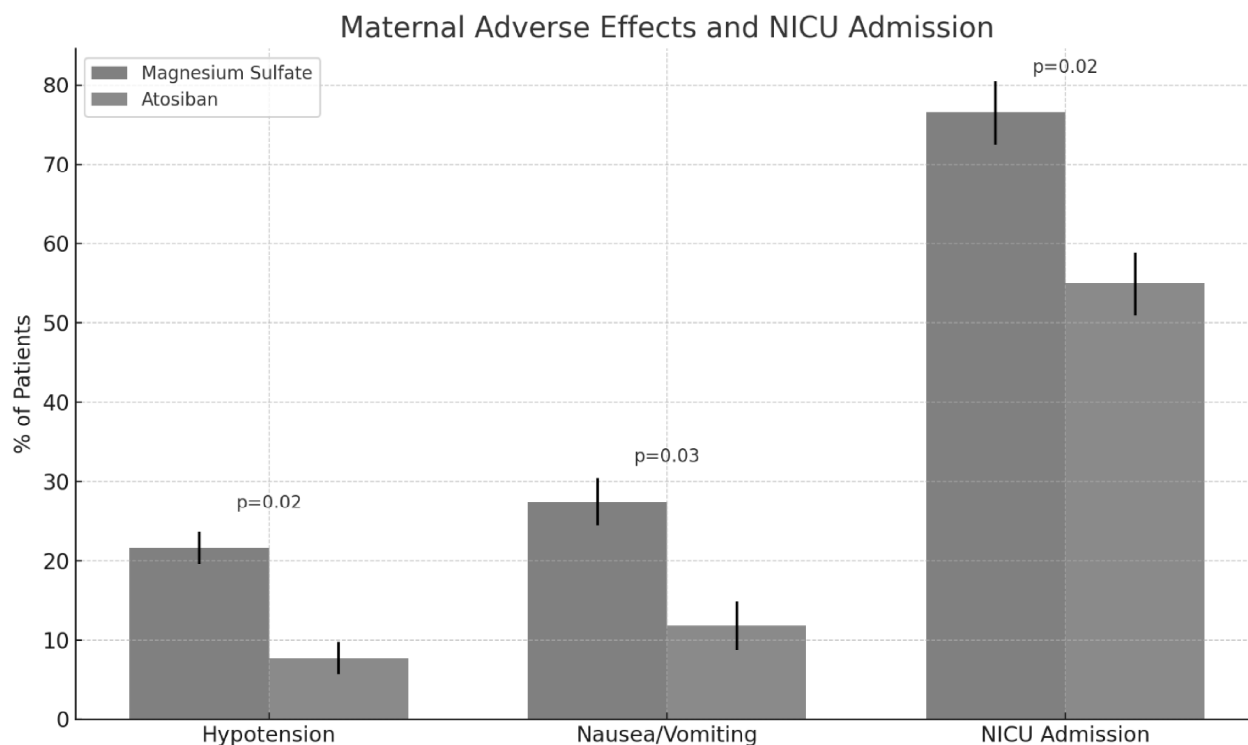
Table 2: Primary Outcome of the Study

Outcome	Magnesium Sulfate (n = 51)	Atosiban (n = 51)	p-value
Neonatal Neurodevelopmental Delay (at 6 months)	31.4% (n = 16)	17.6% (n = 9)	0.03
Neonatal Neurodevelopmental Delay (at 12 months)	39.2% (n = 20)	19.6% (n = 10)	0.03

At the 6-month mark, we noticed some interesting differences between the two treatment groups. Of the 51 neonates who received magnesium sulfate, 16 of them (or 31.4%) showed signs of neurodevelopmental delays. These delays included issues with motor skills, speech, and some mild cognitive challenges. On the other hand, the atosiban group, which also had 51 neonates, performed better overall-only 9 of them (17.6%) experienced similar delays, and the difference was statistically significant ($p = 0.03$). This indicates that atosiban might lead to better neurodevelopmental outcomes.

Table 3: Secondary Outcome of the Study

Outcome	Magnesium Sulfate (n = 51)	Atosiban (n = 51)	p-value
Maternal Adverse Effects			
Hypotension	21.6% (n = 11)	7.8% (n = 4)	0.02
Nausea/Vomiting	27.4% (n = 14)	11.8% (n = 6)	0.03
Gestational Age at Delivery	34.2 \pm 2.4 weeks	35.5 \pm 2.1 weeks	0.02
NICU Admission Rate	76.5% (n = 39)	54.9% (n = 28)	0.02
Neonatal Complications			
Respiratory Distress Syndrome (RDS)	35.3% (n = 18)	15.7% (n = 8)	0.04
Intraventricular Hemorrhage (IVH)	25.5% (n = 13)	9.8% (n = 5)	0.02
Necrotizing Enterocolitis (NEC)	7.8% (n = 4)	3.9% (n = 2)	0.35
Mode of Delivery			
Vaginal Delivery	41.2% (n = 21)	78.4% (n = 40)	0.01
Cesarean Section	58.8% (n = 30)	21.6% (n = 11)	0.01
Maternal Complications			
Preeclampsia	Preeclampsia	Preeclampsia	Preeclampsia

**Fig. 3:** Graphical representation of secondary outcomes of the study showing atosiban as more favorable in terms of maternal side effects, NICU admission rates, maternal and neonatal complications.

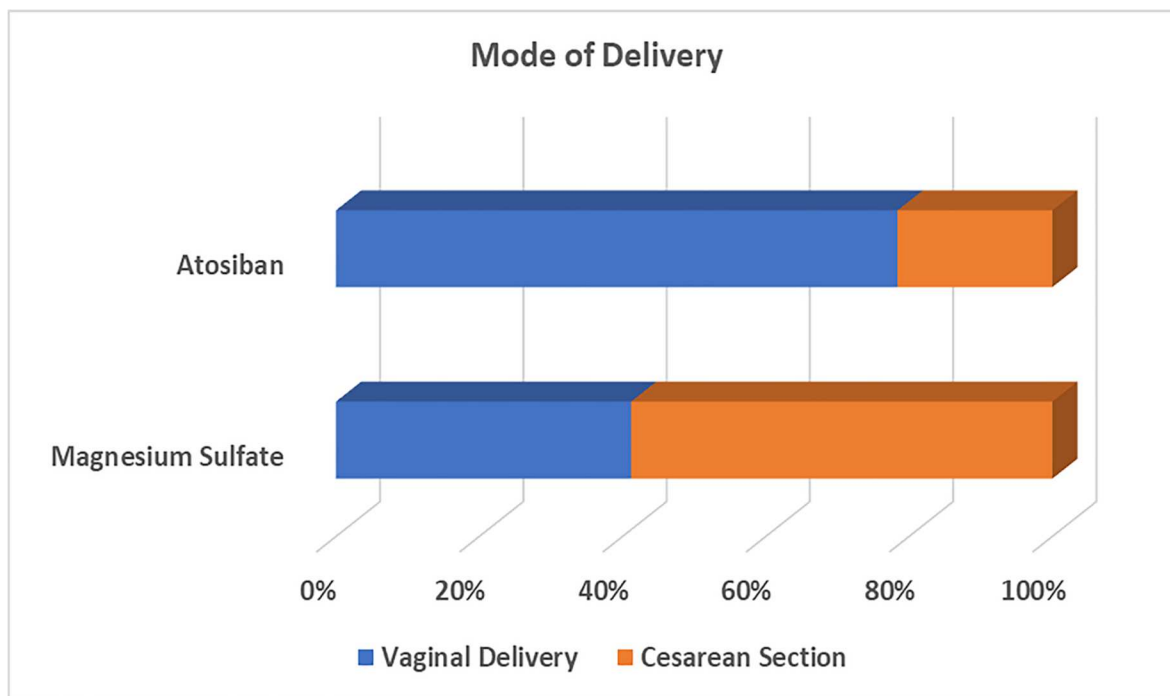


Fig. 4: Graphical representation of mode of delivery showing atosiban leading to more normal deliveries as compared to magnesium sulfate.

Maternal safety is the biggest factor when it comes to treatments during pregnancy, especially in high-risk cases. We noticed that atosiban caused fewer issues to the mothers as compared to magnesium sulfate in this study. The magnesium sulfate group had more cases of low blood pressure (21.6%) and nausea/vomiting (27.4%) than the atosiban group, where those numbers were much lower - 7.8% and 11.8%, respectively. Magnesium sulfate also led to a case of respiratory depression, which needed temporary breathing support, but nothing like that happened in the atosiban group.

While magnesium sulfate does help protect the baby's brain, it also causes side effects for mothers, like low blood pressure, breathing issues, and higher magnesium levels. These side effects can lead to more treatments and possibly longer hospital stays for the patient. Atosiban, however, was much easier on them, with fewer to no side effects, making it a safer option for handling preterm labor, especially for women who are already at high risk for issues with magnesium sulfate.

In fact, atosiban managed to delay delivery by about 1.3 weeks, which makes a difference. This extra time can help lower the chances of problems like breathing issues or brain bleeds. What's interesting is that this result lines up with a study by Younger *et al.*, 2017, which also found that atosiban can delay delivery without putting either the mother or baby at risk.

When we looked at NICU admission rates, we found that only 54.9% of newborns from the atosiban group were sent to the NICU, compared to about 76.5% from the magnesium sulfate group ($p = 0.02$). Additionally, the newborns in the magnesium sulfate group faced more challenges, such as trouble breathing, brain bleeding, and gut problems.

This aligns with previous studies indicating that atosiban reduces the risk of serious complications like respiratory distress and hemorrhage (Yu *et al.*, 2020). Such complications can lead to long-term health problems for the fetus, including developmental delays or lung diseases. By reducing the likelihood of these issues, atosiban seems to offer the fetus a better chance for a healthy future. It's interesting that the delivery method differed between the two groups. Most women in the atosiban group (78.4%) had normal deliveries compared to those in the magnesium sulfate group (41.2%). This likely ties back to how atosiban works by stopping uterine contractions (Liu and Wang, 2024). By reducing contractions, atosiban can make delivery less urgent, giving more chances for a vaginal birth. On the other hand, cesarean sections were more common in the magnesium sulfate group, probably because of complications from preterm labor.

Normal deliveries are considered to be healthier for the mother as c-section has higher risks, like infection, bleeding, and longer recovery time. With atosiban, the rate for c-section was way lower making the mothers recover faster and shortening their hospital stay.

Strengths

The randomized controlled trial design is a key strength of this study, minimizing selection bias and ensuring robust comparisons between the two intervention groups. Additionally, the inclusion of standardized neurodevelopmental assessments at 6 and 12 months provides reliable and clinically relevant measures of fetal neuroprotection. The multi-center approach enhances the generalizability of the results, as it accounts for differences in patient demographics and clinical practices.

Limitations

Despite its strengths, the study is not without limitations. The study size of 102 participants, while sufficient to detect significant differences, limits the power to explore subgroup analyses or detect smaller effect sizes. Future studies with larger cohorts could provide more definitive insights into the comparative effectiveness of these interventions.

Another limitation is the reliance on maternal self-reporting and clinical documentation for some secondary outcomes, such as adverse effects. While efforts were made to standardize data collection, the potential for reporting bias cannot be entirely ruled out. Additionally, the study's outcomes may not fully apply to populations outside the gestational age range of 24 to 32 weeks or those with unique comorbidities or demographic characteristics. Lastly, while the study focused on the effects of magnesium sulfate and atosiban on neuroprotection, other treatments (like corticosteroids or other tocolytics) might have affected the results. Future research should try to take in account these factors to get a clearer picture of the drugs' effects.

Clinical implications

This study gives us some really interesting insights that could change the way we treat preterm labor. Atosiban seems to work as well as magnesium sulfate for protecting babies, but with fewer side effects for the mothers, and it might even help delay delivery longer. This makes it a great option for people who have trouble with magnesium sulfate or in cases where managing side effects is tricky. What's even better is that atosiban seems gentler on the mothers, which could make it a better choice for high-risk pregnancies that need to be managed over a long period of time or with repeated treatments. But, like with anything, it's important to weigh the pros and cons, especially since atosiban's main purpose is to stop labor, not necessarily to protect the baby.

CONCLUSION

In conclusion, this multi-center clinical trial demonstrates that atosiban may serve as a viable and potentially superior alternative to magnesium sulfate in the management of high-risk preterm labor when considering both fetal neuroprotection and maternal safety. The study found that

infants exposed to atosiban showed a lower incidence of neurodevelopmental delays at both 6 and 12 months of age compared to those treated with magnesium sulfate. This suggests that atosiban's ability to delay preterm birth and provide a more stable intrauterine environment may indirectly contribute to better neurological outcomes.

Additionally, atosiban was associated with significantly fewer maternal side effects, including lower rates of hypotension and nausea, as well as lower NICU admission rates and fewer neonatal complications, such as respiratory distress syndrome and intraventricular hemorrhage. It also resulted in a higher proportion of vaginal deliveries and extended gestational duration, which are favorable for both maternal and neonatal outcomes. These findings provide important insights for clinicians managing high-risk pregnancies and underscore the importance of individualized, evidence-based therapeutic decisions. However, larger-scale randomized trials and long-term neurodevelopmental follow-up beyond 12 months are warranted to validate these results and further define the role of atosiban in fetal neuroprotection.

Future directions

While these results are promising, we definitely need more research to dig deeper. Bigger studies with more participants would help confirm if atosiban really works as well as magnesium sulfate, and it would also be useful to follow babies past the first year to see how they develop long term. It'd also be helpful to understand exactly how atosiban works. Does it mainly improve blood flow to the placenta, or is there something else going on? Figuring this out could lead to even more targeted and effective treatments.

Finally, we should think about comparing the costs of both treatments, especially in areas where resources are limited, and preterm birth brings a heavy financial burden.

Consent to participate

Written informed consent was obtained and we kept their information anonymous and confidential throughout the research.

Data availability statement

The data that support the findings of this study are available from the corresponding author, upon request.

Conflicts of interest

The authors declare that they have no financial conflicts of interest.

REFERENCES

- Al-Riyami N, Al-Badri H, Jaju S and Pillai S (2021). Short-term outcomes of atosiban in the treatment of preterm labour at the Sultan Qaboos University Hospital, Muscat, Oman. *Sultan Qaboos Univ. Med. J.*, **21**(2): e260-265.

- Arrowsmith S, Neilson J and Wray S (2016). The combination tocolytic effect of magnesium sulfate and an oxytocin receptor antagonist in myometrium from singleton and twin pregnancies. *Am. J. Obstet. Gynecol.*, **215**(6): 789.e1-789.e9.
- Chollat C, Sentilhes L and Marret S (2018). Fetal neuroprotection by magnesium sulfate: From translational research to clinical application. *Front Neurol.*, **9**: 247.
- Hoffman MK (2021). Prediction and prevention of spontaneous preterm birth: ACOG practice bulletin, number 234. *Obstet. Gynecol.*, **138**(6): 945-946.
- Jafarabady K, Shafiee A, Eshraghi N, Salehi SA, Mohammadi I, Rajai S, Zarcian Z, Movahed F and Bakhtiyari M (2024). Magnesium sulfate for fetal neuroprotection in preterm pregnancy: a meta-analysis of randomized controlled trials. *BMC Pregnancy Childbirth*, **24**(1): 519.
- Lakshmanan A, Agni M, Lieu T, Fleegler E, Kipke M, Friedlich PS, McCormick MC and Belfort MB (2017). The impact of preterm birth <37 weeks on parents and families: a cross-sectional study in the 2 years after discharge from the neonatal intensive care unit. *Health Qual. Life Outcomes*, **15**(1): 38.
- Liu H and Wang X (2024). Use of tocolytic agents in preterm labor: A cross-sectional analysis from a chinese real-world study from 2016 to 2021. *J. Clin. Pharm. Ther.*, **2024**(1): 1-11.
- Mornioli D, Tiraferri V, Maiocco G, De Rose DU, Cresi F, Coscia A, Mosca F and Gianni ML (2023). Beyond survival: The lasting effects of premature birth. *Front Pediatr*, **11**: 1213243.
- Nijman TAJ, Goedhart MM, Naaktgeboren CN, de Haan TR, Vijlbrief DC, Mol BW, Benders MJN, Franx A and Oudijk MA (2018). Effect of nifedipine and atosiban on perinatal brain injury: Secondary analysis of the APOSTEL-III trial. *Ultrasound Obstet. Gynecol.*, **51**(6): 806-812.
- Parikh LI, Reddy UM, Männistö T, Mendola P, Sjaarda L, Hinkle S, Chen Z, Lu Z, Laughon Shaheen RS, Ismail RA, Salama EY, Korini SM and Elsaedy AS (2024). Efficacy and safety of 12-hour versus 24-hour magnesium sulfate in management of patients with pre-eclampsia and eclampsia: A systematic review and meta-analysis. *BMC Womens Health*, **24**(1): 421.
- Shepherd ES, Goldsmith S, Doyle LW, Middleton P, Marret S, Rouse DJ, Pryde P, Wolf HT and Crowther CA (2024). Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. *Cochrane Database Syst. Rev.*, **5**(5): CD004661.
- Song Q, Chen J, Zhou Y, Li Z, Li H and Liu J (2022). Preterm delivery rate in China: A systematic review and meta-analysis. *BMC Pregnancy Childbirth*, **22**(1): 383.
- Tsao PC. (2023). Pathogenesis and prevention of intraventricular hemorrhage in preterm infants. *J. Korean Neurosurg. Soc.*, **66**(3): 228-238.
- Wadhwa PD, Entringer S, Buss C and Lu MC (2011). The contribution of maternal stress to preterm birth: issues and considerations. *Clin. Perinatol.*, **38**(3): 351-384.
- World Health Organization (WHO). (2023). Preterm birth. Preterm Birth; World Health Organization: WHO.
- Younger JD, Reitman E and Gallos G (2017). Tocolysis: Present and future treatment options. *Semin Perinatol*, **41**(8): 493-504.
- Yu Y, Yang Z, Wu L, Zhu Y and Guo F (2020). Effectiveness and safety of atosiban versus conventional treatment in the management of preterm labor. *Taiwan J. Obstet. Gynecol.*, **59**(5): 682-685.