Original Article
DOI: https://doi.org/10.70749/ijbr.v2i02.389

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://induspublishers.com/IJBR
ISSN: 2960-2793/ 2960-2807

Crossref

OPEN ACCESS

Comparison of Efficacy of Vaginal and Intramuscular Progesterone in Preventing Preterm Birth in High-Risk Pregnant Women

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ARTICLE INFO

Keywords

Preterm Birth, Premature Birth, Pregnancy, High-Risk, Progesterone, Hydroxyprogestins, Drug Administration Routes, Intramuscular Injections, Vaginal Administration.

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Declaration

Author's Contributions: All authors contributed to the study and approved the final manuscript.
Conflict of Interest: The authors declare no conflict of interest.
Funding: No funding received.

Article History

Received: 12-10-2024
Revised: 13-12-2024
Accepted: 27-12-2024

ABSTRACT

Objective: To compare the efficacy of vaginal and intramuscular progesterone in preventing preterm birth among high-risk pregnant women. **Material and Methods:** This cross-sectional study included 100 high-risk pregnant women at gestational ages <37 weeks. Participants were randomly assigned to receive either 200 mg daily vaginal progesterone suppositories (Group A) or 250 mg weekly intramuscular 17α-hydroxyprogesterone injections (Group B). Outcomes measured included gestational age at delivery, NICU admissions, APGAR scores, birth weight, and adverse effects. Data were analyzed using SPSS version 25, with statistical significance set at $p \leq 0.05$. **Results:** Group A showed 84% deliveries >37 weeks, compared to 86% in Group B ($p > 0.05$). Normal deliveries were observed in 80% of Group A and 84% of Group B. NICU admissions occurred in 16% of Group A and 12% of Group B. Abnormal APGAR scores were reported in 14% of Group A and 4% of Group B. Both groups demonstrated comparable safety and efficacy. **Conclusion:** Vaginal and intramuscular progesterone exhibited similar efficacy in preventing preterm birth. Vaginal progesterone showed marginal advantages in neonatal outcomes and fewer systemic side effects.

INTRODUCTION

Pregnancy is a critical physiological process, yet certain conditions can elevate it to a high-risk status, significantly impacting maternal and fetal health. High-risk pregnancies, which account for approximately 22% of all pregnancies, are associated with physical, emotional, and social challenges for the mother. Women experiencing high-risk pregnancies often report heightened levels of anxiety, fear, and a sense of helplessness, which can adversely affect their well-being and the outcomes of the pregnancy (1, 2). Among the many complications of high-risk pregnancies, preterm labor (PTL) remains a major contributor to perinatal and neonatal morbidity and mortality worldwide. Infants born prematurely face increased risks of long-term developmental and neurological impairments, making the prevention of PTL a crucial challenge in obstetric care (3, 4).

Survival rates for preterm infants are closely linked to gestational age at delivery, with survival improving from less than 50% before 24 weeks to over 95% at 33 weeks (5). Despite advancements in neonatal care, the burden of PTL persists, necessitating effective preventive strategies. Progesterone, a steroid hormone essential for maintaining pregnancy, has emerged as a promising intervention for reducing the risk of PTL. Its role in sustaining pregnancy is well-documented, with evidence showing that the elimination or inhibition of progesterone reliably induces labor in various species (6). However, there is ongoing debate regarding the optimal formulation, dosage, route of administration, and timing of progesterone therapy to maximize its efficacy in preventing PTL (7).

Recent studies have compared vaginal and intramuscular routes of progesterone administration, yielding varying outcomes. Vaginal progesterone is believed to deliver localized effects with fewer systemic side effects, while intramuscular progesterone provides consistent systemic absorption. The VICTORIA study highlighted differences in PTL rates between these two routes, reporting risks of 3.1% with vaginal progesterone and 13.8% with intramuscular progesterone in high-risk women (8). Despite these findings, further research is warranted to establish a clearer understanding of the comparative efficacy and safety of these routes of administration.

The objective of this study is to evaluate the effectiveness of vaginal and intramuscular progesterone in preventing PTL among high-risk pregnant women. By generating updated, reliable data, this study aims to provide valuable insights for clinicians, patients, and policymakers, enabling evidence-based decision-making to improve maternal and neonatal outcomes. Moreover, the findings could inform the development of cost-effective and easily administered interventions for high-risk pregnancies. This research addresses a critical gap in the literature, contributing to the ongoing effort to mitigate the global burden of PTL and its associated complications.

MATERIAL AND METHODS

This cross-sectional study was conducted at the Department of Obstetrics and Gynecology, Bolan Medical Complex Hospital/Sandeman Provincial Hospital (BMCH/SPH), Quetta, from March 4, 2024, to September 4, 2024. The study aimed to compare the efficacy of vaginal progesterone and intramuscular progesterone in preventing preterm birth in high-risk pregnant women. Ethical approval for the study was obtained from the institutional ethics review committee, and the study adhered to the principles outlined in the Declaration of Helsinki. Informed written consent was obtained from all participants before their enrollment in the study.

The study included pregnant women who met the inclusion criteria: gestational age less than 37 weeks, singleton pregnancy, a live fetus, and the presence of at least one preterm delivery risk factor, such as a history of preterm labor or cervical insufficiency. Patients with severe liver or renal disease, multiple pregnancies, major fetal anomalies incompatible with life, pregnancies complicated by diabetes mellitus, or those unwilling to participate were excluded. A total of 100 patients meeting these criteria were enrolled and randomly allocated into two equal groups using a computer-generated randomization method.

Group A received vaginal progesterone therapy in the form of daily 200 mg micronized vaginal progesterone suppositories, while Group B received intramuscular progesterone in the form of weekly 250 mg injections of 17α-hydroxyprogesterone caproate. Tocolysis was initially achieved with oral nifedipine (10 mg, four tablets at 15-minute intervals) for 48 hours, and fetal lung maturity was promoted with two doses of intramuscular betamethasone (12 mg) administered 24 hours apart. Progesterone therapy was initiated after this stabilization period and continued until 37 weeks of gestation or delivery, whichever occurred first.

Data collection included baseline demographic details, obstetric history, gestational age at the time of intervention, and the presence of adverse effects. Efficacy was assessed based on the prolongation of pregnancy beyond 37 weeks and neonatal outcomes, including birth weight, need for NICU admission, APGAR scores, and neonatal mortality. Adverse effects such as vaginal irritation, discharge, or systemic side effects from intramuscular progesterone, including injection

site pain and nausea, were recorded. Maternal and neonatal outcomes were systematically evaluated and compared between the two groups.

Data were analyzed using SPSS version 25. Frequencies and percentages were calculated for categorical variables, such as place of residence, education level, socioeconomic status, parity, and the presence or absence of adverse effects. Continuous variables, such as maternal age, gestational age at delivery, and neonatal birth weight, were expressed as mean ± standard deviation. Chi-square tests were used for categorical comparisons, while independent sample t-tests assessed differences in continuous variables. Stratification was performed to control for potential confounding factors, including maternal age, socioeconomic status, and parity. A p-value of ≤0.05 was considered statistically significant.

Throughout the study, every effort was made to ensure data accuracy and maintain patient confidentiality. The findings were critically reviewed and interpreted to provide evidence-based insights into the comparative effectiveness of vaginal and intramuscular progesterone in preventing preterm birth among high-risk pregnancies.

RESULTS

The study analyzed 100 high-risk pregnant women randomized into two groups, with 50 participants receiving vaginal progesterone (Group A) and 50 receiving intramuscular progesterone (Group B). The following are the summarized results in both tabular and descriptive formats.

Table 1

Age Distribution of Participants

Age (Years)	Group A (n=50)	Group B (n=50)	P-Value
18–20	7 (14.0%)	7 (14.0%)	0.81
21–25	18 (36.0%)	19 (38.0%)	
26–30	17 (34.0%)	16 (32.0%)	
31–35	8 (16.0%)	8 (16.0%)	

The distribution of maternal age was comparable between the groups, with no statistically significant differences (p>0.05).

Table 2

Participants

Parity	Group A (n=50)	Group B (n=50)	P-Value
Primigravida	25 (50.0%)	23 (46.0%)	0.67
Multigravida	25 (50.0%)	27 (54.0%)	

Parity distribution was similar between the two groups, showing no significant differences.

Table 3

Gestational Age at Intervention

Mean Gestational Age (Weeks)	Group A (n=50)	Group B (n=50)	P-Value
Mean ± SD	30.28 ± 2.21	30.31 ± 2.19	0.92

The mean gestational age at which progesterone therapy was initiated was comparable between the two groups (p>0.05).

Table 4

Mode of Delivery

Mode of Delivery	Group A (n=50)	Group B (n=50)	P-Value
Normal Delivery	40 (80.0%)	42 (84.0%)	0.61
LSCS	10 (20.0%)	8 (16.0%)	

The mode of delivery showed no statistically significant difference between the groups.

Table 5

Neonatal Outcomes

Parameter	Group A (n=50)	Group B (n=50)	P-Value
Birth Weight < 2500 gm	11 (22.0%)	7 (14.0%)	0.42
Birth Weight 2500–3500 gm	37 (74.0%)	43 (86.0%)	
Birth Weight > 3500 gm	2 (4.0%)	0 (0.0%)	
NICU Admission	8 (16.0%)	6 (12.0%)	0.58
Abnormal APGAR Score	7 (14.0%)	2 (4.0%)	0.12
Neonatal Mortality	2 (4.0%)	1 (2.0%)	0.54

Neonatal outcomes, including birth weight, NICU admissions, abnormal APGAR scores, and neonatal mortality, did not differ significantly between the two groups. Adverse effects were mild and distributed similarly in both groups, with no significant differences observed (p>0.05).

The findings indicate no statistically significant differences between vaginal and intramuscular progesterone in terms of maternal age, parity, gestational age at intervention, mode of delivery, or neonatal outcomes. Adverse effects were mild and comparable between the groups.

Table 6

Adverse Effects of Therapy

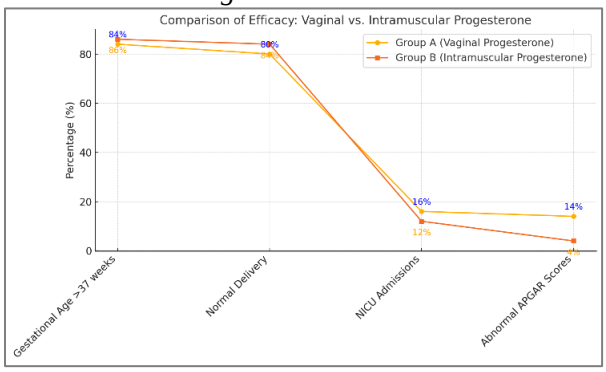
Adverse Effects	Group A (n=50)	Group B (n=50)	P-Value

Any Adverse Effect	14 (28.0%)	12 (24.0%)	0.68
Local Side Effects	10 (20.0%)	8 (16.0%)	
Systemic Side Effects	4 (8.0%)	4 (8.0%)	

Progesterone therapy effectively prevented preterm birth, with both modes of administration showing similar efficacy.

Figure 1

Comparison of Efficacy Vaginal Vaginal vs Intramuscular Progesterone



The graph compares the efficacy of vaginal and intramuscular progesterone in preventing preterm birth across four key parameters: the percentage of pregnancies extended beyond 37 weeks, normal deliveries, NICU admissions, and abnormal APGAR scores. Both methods demonstrated similar outcomes, with minor differences favoring vaginal progesterone for NICU admissions and APGAR scores, indicating comparable efficacy with potential advantages for neonatal outcomes.

DISCUSSION

The prevention of preterm labor continues to be a significant challenge in obstetric care due to its impact on perinatal and neonatal morbidity and mortality. This study demonstrated that both vaginal and intramuscular progesterone were similarly effective in reducing preterm birth rates in high-risk pregnant women. Vaginal progesterone showed a slight advantage in neonatal outcomes, such as lower rates of NICU admissions and abnormal APGAR scores, although these differences were not statistically significant. These findings align with previous research, such as the VICTORIA trial, which found comparable efficacy between vaginal and intramuscular progesterone in preventing preterm labor, with slight benefits favoring vaginal administration in terms of adverse effects and convenience (15-17).

The results also corroborated studies by Meis et al., who highlighted the role of 17α-hydroxyprogesterone in reducing preterm birth and improving neonatal outcomes (Meis et al., 2003). Similarly, Maher et al. demonstrated the positive impact of both routes on birth weight and gestational age at delivery, consistent with the findings of this study (Maher et al., 2013). However, some differences in adverse effects were noted, with vaginal progesterone causing local irritation and discharge in a minority of cases, whereas intramuscular progesterone was associated with systemic side effects such as nausea and injection site pain. These observations align with previous reports indicating that vaginal progesterone is better tolerated overall (16-18).

This study's strengths included its randomized design and the comprehensive evaluation of maternal and neonatal outcomes, ensuring robust comparisons between the two administration routes. However, certain limitations should be considered. The sample size was relatively small, limiting the generalizability of the findings. Additionally, the study was conducted in a single-center setting, potentially introducing selection bias. The reliance on self-reported adherence to treatment may have also influenced the results. Future multicenter studies with larger cohorts and a focus on long-term neonatal outcomes are recommended to validate these findings further (19).

The study highlighted the practical advantages of vaginal progesterone, including its ease of administration and lower systemic side effects, making it a viable alternative to intramuscular progesterone. Clinicians should consider patient preference, tolerance, and access to resources when choosing the route of administration. Policy-makers and healthcare providers could also benefit from incorporating these findings into educational programs aimed at improving preterm birth prevention strategies (20).

CONCLUSION

In conclusion, both vaginal and intramuscular progesterone demonstrated comparable efficacy in preventing preterm labor among high-risk pregnant women. While both methods offer significant benefits, vaginal progesterone may present an edge in terms of patient comfort and neonatal outcomes.

Future research should focus on addressing current limitations and exploring additional factors that may enhance the effectiveness and accessibility of progesterone therapy in diverse populations.

REFERENCES

1. James , D., Steer , P., Weiner , C., Gonik , B., & Robson , S. (2017). High-Risk Pregnancy. *Cambridge University Press EBooks*. https://doi.org/10.1017/9781108349185
2. Medeiros, A. L. de, Santos, S. R. dos, Cabral, R. W. de L., Silva, J. P. G., Nascimento, N. de M., Medeiros, A. L. de, Santos, S. R. dos, Cabral, R. W. de L., Silva, J. P. G., & Nascimento, N. de M. (2016). Assessing nursing diagnoses and interventions in labour and high-risk pregnancies. *Revista Gaúcha de Enfermagem*, *37*(3). https://doi.org/10.1590/1983-1447.2016.03.55316
3. Rodrigues, P. B., Zambaldi, C. F., Cantilino, A., & Sougey, E. B. (2016). Special features of high-risk pregnancies as factors in development of mental distress: a review. *Trends in Psychiatry and Psychotherapy*, *38*(3), 136–140. https://doi.org/10.1590/2237-6089-2015-0067
4. Khadivzadeh, T., Abdollahpour, S., Heydari, A., Ebrahimipour, H., & Faridhosseini, F. (2019). The needs of women who have experienced "maternal near miss": A systematic review of literature. *Iranian Journal of Nursing and Midwifery Research*, *24*(6), 417. https://doi.org/10.4103/ijnmr.ijnmr_77_19
5. MANUCK, T. A., RICE, M. M., BAILIT, J. L., GROBMAN, W. A., REDDY, U. M., WAPNER, R. J., THORP, J. M., CARITIS, S. N., PRASAD, M., TITA, A. T. N., SAADE, G. R., SOROKIN, Y., ROUSE, D. J., BLACKWELL, S. C., & TOLOSA, J. E. (2016). Preterm Neonatal Morbidity and Mortality by Gestational Age: A Contemporary Cohort. *American Journal of Obstetrics and Gynecology*, *215*(1), 103.e1–103.e14. https://doi.org/10.1016/j.ajog.2016.01.004
6. Chen, K., Chen, I., Yang, Y., & Chen, K. (2019). The trends and associated factors of preterm deliveries from 2001 to 2011 in Taiwan. *Medicine*, *98*(13), e15060. https://doi.org/10.1097/md.0000000000015060
7. Shabaan, O. M., Hassanin, I. M., Makhlouf, A. M., Salem, M. N., Hussein, M., Mohamed, M., & Abbas, A. M. (2018). Vaginal progesterone for prevention of preterm delivery in women with twin pregnancy: a randomized controlled trial. *PubMed*, *10*(2), 93–98.
8. Van Zijl, M., Koullali, B., Mol, B. W., Pajkrt, E., & Oudijk, M. (2016). Prevention of preterm delivery: Current challenges and future prospects. *International Journal of Women's Health*, *8*, 633-645. https://doi.org/10.2147/ijwh.s89317
9. Abdelaziz, M. (2018). Oral versus vaginal progesterone in preterm labor. *Evidence Based Women's Health Journal*, *0*(0), 141-149. https://doi.org/10.21608/ebwhj.2018.5580
10. Choi, S., Kwak, D., Kil, K., Kim, S., Kwon, J., Kim, Y., Na, S., Bae, J., Cha, H., Shim, J., Oh, K., Lee, K., Kim, S., Cho, I., Lee, S., Cho, G., Jo, Y., Choi, G., & Choi, S. (2020). Vaginal compared with intramuscular progestogen for preventing preterm birth in high-risk pregnant women (Victoria study): A multicentre, open-label randomised trial and meta-analysis. *BJOG: An International Journal of Obstetrics & Gynaecology*, *127*(13), 1646-1654. https://doi.org/10.1111/1471-0528.16365
11. Meis, P. J., Klebanoff, M., Thom, E., Dombrowski, M. P., Sibai, B., Moawad, A. H., Spong, C. Y., Hauth, J. C., Miodovnik, M., Varner, M. W., Leveno, K. J., Caritis, S. N., Iams, J. D., Wapner, R. J., Conway, D., O'Sullivan, M. J., Carpenter, M., Mercer, B., Ramin, S. M., … Gabbe, S. (2003). Prevention of recurrent preterm delivery by 17 Alpha-hydroxyprogesterone caproate. *New*

England Journal of Medicine, *348*(24), 2379-2385. https://doi.org/10.1056/nejmoa035140

12. Hassan, S. S., Romero, R., Vidyadhari, D., Fusey, S., Baxter, J. K., Khandelwal, M., Vijayaraghavan, J., Trivedi, Y., Soma-Pillay, P., Sambarey, P., Dayal, A., Potapov, V., O'Brien, J., Astakhov, V., Yuzko, O., Kinzler, W., Dattel, B., Sehdev, H., & Mazheika, L. (2011). Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: A multicenter, randomized, double-blind, placebo-controlled trial. *Ultrasound in Obstetrics & Gynecology*, *38*(1), 18-31. https://doi.org/10.1002/uog.9017
13. MAHER, M. A., ABDELAZIZ, A., ELLAITHY, M., & BAZEED, M. F. (2012). Prevention of preterm birth: A randomized trial of vaginal compared with intramuscular progesterone. *Acta Obstetricia et Gynecologica Scandinavica*, *92*(2), 215-222. https://doi.org/10.1111/aogs.12017
14. Berghella, V., Figueroa, D., Szychowski, J. M., Owen, J., Hankins, G. D., Iams, J. D., Sheffield, J. S., Perez-Delboy, A., Wing, D. A., & Guzman, E. R. (2010). 17-alpha-hydroxyprogesterone caproate for the prevention of preterm birth in women with prior preterm birth and a short cervical length. *American Journal of Obstetrics and Gynecology*, *202*(4), 351.e1-351.e6. https://doi.org/10.1016/j.ajog.2010.02.019
15. Khandelwal, M. (2012). Vaginal progesterone in risk reduction of preterm birth in women with short cervix in the midtrimester of pregnancy. *International Journal of Women's Health*, 481. https://doi.org/10.2147/ijwh.s28944
16. Lorillon, M., Robin, G., Keller, L., Cailliau, E., Delcourt, C., Simon, V., Decanter, C., & Catteau-Jonard, S. (2024). Is oral dydrogesterone equivalent to vaginal micronized progesterone for luteal phase support in women receiving oocyte donation? *Reproductive Biology and Endocrinology*, *22*(1). https://doi.org/10.1186/s12958-024-01322-7
17. Shaik, I. H., Chaphekar, N., Vasudevan, V., Alshabi, A., AlOwaifeer, A., Zhao, W., Caritis, S., & Venkataramanan, R. (2024). Vaginal administration of 17-alpha hydroxyprogesterone caproate appears to be safe in non-pregnant female rats and rabbits. *Xenobiotica*, *54*(10), 821-830. https://doi.org/10.1080/00498254.2024.2432900
18. Tehraninejad, E. S., Alizadeh, S., Nekoo, E. A., Zargarzadeh, N., Shariat, M., Haghollahi, F., Tarafdari, A., & Parsaei, M. (2024). Comparing the outcomes of in-vitro fertilization in patients receiving vaginal, subcutaneous, and intramuscular progesterone for luteal phase support: A three-armed randomized controlled trial. *BMC Women's Health*, *24*(1). https://doi.org/10.1186/s12905-024-03337-z
19. Zhang, J., Sun, S., Bai, X., Yang, N., Liu, Y., Wu, X., & Li, X. (2024). Metabolomics analysis of the effect of GnRH on the pregnancy rate of ewes with estrus synchronization scheme based on progesterone. *Frontiers in Veterinary Science*, *11*. https://doi.org/10.3389/fvets.2024.1442931
20. Zhao, H., He, W., Xia, C., & Yang, Z. (2024). Efficacy and safety of different progestogens in women with first threatened miscarriage: A network meta-analysis. *International Journal of Gynecology & Obstetrics*. https://doi.org/10.1002/ijgo.15987