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Original Article

Comparison of Effectiveness of Vaginal Versus Intramuscular Progesterone for the Prevention of Preterm Delivery

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ABSTRACT

Objective: To compare the effectiveness of vaginal progesterone versus intramuscular progesterone for the prevention of preterm delivery.

Study Design: Quasi-experimental study.

Place and Duration of Study: Department of Obstetrics and Gynaecology, KRL Hospital, Bahria University College of Medicine, Islamabad, from Aug 2022 to March 2023.

Methodology: A total of 170 women between 24 to 36+6 weeks of gestation with singleton pregnancy and at risk of preterm birth, with short cervical length (10th %ile for gestational age) were recruited after taking written informed consent. Patients were divided into two groups: Group A was treated with 200 mg vaginal progesterone once daily, whereas Group B received 250 mg intramuscularly each week. The intervention was maintained till completion of 34 weeks, provided the pregnancy remained ongoing. If a miscarriage or early rupture of membranes (ROM) resulted in preterm birth before 37 weeks, therapy was stopped.

Results: Median age of Group A was 27.90 (34.95 – 23.85) years and for Group B was 27.70 (34.35 – 23.75) years. In Group A, vaginal progesterone was effective in 75(88%) patients whereas in Group B, intramuscular progesterone was effective in 60 (71%) patients. Statistical analysis revealed a *p*-value of 0.0044, indicating a significant difference in effectiveness between the two treatment modalities.

Conclusion: Vaginal progesterone is more effective than intramuscular progesterone for the prevention of preterm labour.

Keywords: Intramuscular progesterone, Preterm delivery, Vaginal progesterone.

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INTRODUCTION

Birth occurring before 37 completed weeks of pregnancy, also known as premature delivery, affects between 1% and 10% of all live births across the world, being the primary contributor to illness and death among newborns and responsible for nearly 70% of neonatal deaths and 36% of infant deaths, as well as neurodevelopmental impairment in 5% of all preterm births[1]. The rates of cerebral palsy are 80 times higher in premature infants as nearly half of all preterm deliveries are preceded by early-onset labour, which is the leading cause of death and disability in children under 5 years of age[2]. The number of cases involving premature delivery is higher in India, China, Nigeria, Pakistan and the United States [2,3]. Women with limited financial resources are more likely to give birth to low-weight preterm neonates4 where impaired respiratory function, sepsis, and birth defects lead to mortality [5]. Preterm delivery frequently results from spontaneous uterine contractions with tocolytic drugs having limited effectiveness in delaying labour[6], more emphasis is now placed on preventive interventions[7]. Assessing the effectiveness of progesterone supplementation for minimizing the occurrence of spontaneous early labour and childbirth in vulnerable pregnancies is a critical research area[8] which needs to be explored as prophylaxis has limited efficacy. Even if all pregnant patients with a previous natural premature delivery are administered progesterone, it is anticipated that spontaneous preterm deliveries may decrease to only 20%, so identifying and treating patients with a shortened cervix could further lower the absolute risk by 0.02%[9]. The rationale of our study is to compare intramuscular and vaginal progesterone in our patient population, filling a crucial gap in local knowledge. Evidence based information provided to the health care professionals will result in reducing neonatal morbidity and mortality thus leading to long term health benefits to the neonates.

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METHODOLOGY

This was a quasi-experimental study conducted from 31st Aug 2022 to 2nd March 2023 in the Department of Obstetrics and Gynaecology, KRL hospital, affiliated with Bahria University College of Medicine, Islamabad. Approval was taken from Institutional Ethics Review Committee, with reference number KRL-HI-ERCiMav22/10, dated 1st May 2022. Sample size was calculated using the World Health Organization (WHO) sample size calculator, taking a 95% confidence interval and 5% margin of error where expected effectiveness of vaginal progesterone was 57% while the effectiveness in the intramuscular group was 37.80%[10]. The estimated sample size came out to be 170 participants. Patients were selected through non-probability purposive sampling and were enrolled in the study through Department of Obstetrics and Gynaecology Out-Patient Department (OPD) and Emergency at KRL Hospital, Islamabad.

Inclusion Criteria: All pregnant women within the age group 15-45 years, who had a single foetus and were at risk of premature delivery, with short length of cervix (10th percentile for gestational age) and between 24 to 34 weeks of gestation (on dating scan), were enrolled.

Exclusion Criteria: Women with twin gestation, intrauterine foetal demise, preterm prelabour rupture of membranes, chorioamnionitis, antepartum haemorrhage, anomalous ultrasound assessment or having been diagnosed with severe medical disorders like chronic liver disease, renal disease or autoimmune diseases were excluded.

After taking written informed consent, all women were subjected to detailed history and clinical examination. Baseline investigations were done, including blood count, urinalysis, and obstetric ultrasound to confirm gestational age and fetal viability. Two groups were formed by assigning patients randomly through the lottery method to either Group A, which received a daily dose of 200 mg vaginal progesterone pessary or Group B, which received intramuscular progesterone injections of 250 mg weekly. In both groups, therapy was maintained up to the completion of 37 weeks of pregnancy and follow-up was done at routine antenatal visit while compliance to the prescribed treatment was monitored through self-reporting and pill/vial counts during subsequent visits. Additionally, telephone calls were utilized to ensure continued participation and minimize losses. All demographic data, such as, age, education level, employment status, family type and area of residence was recorded in a data collection tool. Data was analyzed by using Statistical Package for Social Sciences (SPSS) version 22.00. Normality of data was checked by Shapiro-Wilk test which showed that age was non-normally distributed represented by using median and interquartile range (IQR). Qualitative data was represented by using percentage and frequency while chi-square test was applied for qualitative variables where *p*-value of ≤ 0.05 was considered as statistically significant.

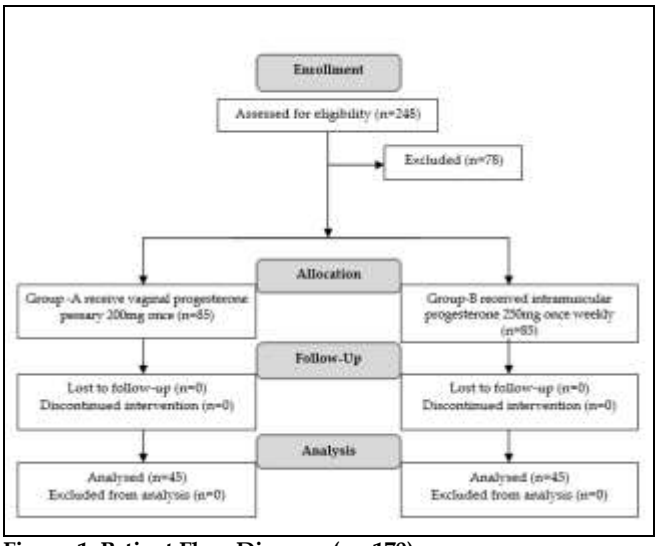

Figure-1: Patient Flow Diagram (n= 170)

RESULTS

A total of 170 participants were included in the study. Median age of Group A was 27.90 (34.95 – 23.85) years and Group B was 27.70 (34.35 – 23.75) years. Most respondents were in the 25–29 years age group 62(36.50%), while least represented age category was under 20 years 5(2.90%). Most patients reported having primary to matric education 55(32.40%), while the smallest proportion had no formal education 18(10.60%). Most participants were unemployed 118(69.40%), and majority belonged to joint families 95(55.90%). In terms of residence, urban participants constituted 105(61.80%), whereas some 65(38.2%) resided in rural areas. Demographic characteristics of study participants shown in Table-I.

Age-related data was compared between both groups, where it was found that in Group A, a total of 53 patients (62.0%) belonged to the 15–30 years age group and 32(38%) patients were in age bracket 31-45 years while in Group B, 54(64%) participants were

aged between 15 - 30 years, while 31(36%) belonged to the 31 - 45 years age bracket. Gravidity patterns were examined between the two groups, revealing that in Group A, 54(64%) participants belonged to primigravida category, while 31(36%) fell under multigravida in contrast to Group B where 55(65%) patients were classified as primigravida, while 30(35%) were multigravida, as shown in Table II.

Table-I: Demographic Characteristics of Study Participants (n = 170)

Variable		n (%)
Age (years)	20–24	28(16.50%)
	Under 20	5(2.90%)
	25–29	62(36.50%)
	30–34	45(26.50%)
	35 and above	30(17.60%)
Education Level	No formal education	18(10.60%)
	Primary to Matric	55(32.40%)
	Intermediate	49(28.80%)
	Bachelor's and above	48(28.20%)
Employment Status	Employed	52(30.60%)
	Unemployed	118(69.40%)
Family Type	Nuclear	75(44.10%)
	Joint	95(55.90%)
Area of Residence	Urban	105(61.80%)

Table-II: Distribution of Effectiveness Across Groups Compared to Demographic Variables (n=170)

AGE		Effectiveness	Group A (n=85)	Group B (n=85)	*p*-value
15-30 years		Effective	47(89.00%)	39(72.00%)	0.0321
		Not effective	6(11.00%)	15(28.00%)	
31-45 years		Effective	28(88.00%)	21(68.00%)	0.0593
		Not effective	4(12.00%)	10(32.00%)	
Primigravida		Effective	48(89.00%)	39(71.00%)	0.0193
		Not effective	6(11.00%)	16(29.00%)	
Multigravida		Effective	27(87.00%)	21(70.00%)	0.1030
		Not effective	4(13.00%)	9(30.00%)	
Period of Gestation	24-30 weeks	Effective	51(88.00%)	39(70.00%)	0.0166
		Not effective	7(12.00%)	17(30.00%)	
	31-34 weeks	Effective	24(89.00%)	21(72.00%)	0.1209
		Not effective	3(11.00%)	8(28.00%)	

When comparing effectiveness of therapy, in Group A, vaginal progesterone proved beneficial in 75(88%) participants and did not demonstrate efficacy in 10(12%) participants while in Group B, intramuscular progesterone showed effectiveness in in 60(71%) participants and did not yield favorable results in 25(29%) participants. Statistical analysis revealed a *p*-value of 0.0044, confirming a significant variation in effectiveness between the two treatment modalities as shared in Table-III.

Table-III: Comparison of Effectiveness Between Vaginal and Intramuscular Progesterone(n=170)

Effectiveness	Group A n=85	Group B n=85	*p*-value
Effective	75(88.00%)	60(71.00%)	0.004
Not effective	10(12.00%)	25(29.00%)	

DISCUSSION

Preterm birth complicates 9 to 12 % of births worldwide and is the foremost cause of health complications and death in newborns leading 11. The greater efficacy of vaginal progesterone in preventing preterm birth may be attributed to its direct action on the cervix and uterus, facilitating better absorption and a localized effect, in contrast, intramuscular progesterone, despite its systemic circulation, may have variability in absorption and metabolism. As one of the main contributors to early labour and low birth weight, the occurrence of spontaneous preterm labour leads to perinatal mortality and morbidity[12,13]. Given the limited success of tocolytic therapy in delaying delivery among patients with spontaneous preterm labour, recent focus has shifted toward preventive measures[14,15]. Our findings are consistent with those of another researcher, where 40% of women getting intramuscular progesterone required NICU admission versus only 11.40% in the vaginal group[16]. Similarly, another study on patients with cervical shortening to 25 mm or less, who were treated with received 400 mg progesterone via vaginal route at night, had lower preterm labour rates (48% vs. 80%) and less neonatal deaths (2% vs. 16%) than the untreated group, further supporting the use of vaginal progesterone for patients at risk of preterm delivery [17]. A quantitative review of randomized intervention studies appraising outcomes of progesterone therapy via vaginal route in pregnancies with single babies and reduced cervical length18 demonstrated a noteworthy decrease in preterm birth <34 weeks, with a relative risk (RR) of 0.65 (95% CI: 0.51–0.83), as vaginal progesterone decreased neonatal problems such as respiratory distress syndrome (RR 0.47) and NICU admissions (RR 0.68). These findings support the effectiveness of vaginal progesterone, aligning closely with our study results. Additionally, patients between 24–30 weeks of gestation demonstrated a notable difference in effectiveness (*p*=0.0166), reinforcing the potential benefit of early intervention with vaginal progesterone. While this variation was not statistically meaningful in multigravida women and in those with

a pregnancy duration ranging from 31–37 weeks, a higher success rate was still observed with vaginal progesterone. The inclusive subgroup analysis not only reinforces the evidence base for preferring vaginal progesterone but also highpoints potential clinical variables that may affect treatment response.

LIMITATIONS OF STUDY

This study has several limitations that should be considered when interpreting its findings. First, the quasi-experimental design, introduces the risk of selection bias and limits the strength of causal inference compared to a true randomized controlled trial. Second, the single-centre setting at restricts the generalizability of the findings to broader or more diverse obstetric populations. Third, the relatively short study duration may have constrained the sample size and limited the ability to capture a more representative spectrum of patients at risk of preterm birth. Finally, the study did not account for potential confounding variables such as parity, prior preterm birth history, cervical cerclage, or coexisting obstetric complications, any of which may have independently influenced the outcome. Future randomized controlled trials with larger, multicentre cohorts and more rigorous outcome monitoring are needed to confirm these findings.

CONCLUSION

Vaginal route of progesterone administration was more beneficial for preterm birth prevention in women with a known history of premature delivery than intramuscular route.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

KF & SQ: Data acquisition, data analysis, critical review, approval of the final version to be published.

NA & AB: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

BR & NJ: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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