Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2023i1.648
*Biol. Clin. Sci. Res. J., Volume, **2023**: 648*
Original Research Article

THE ROLE OF MICRONIZED PROGESTERONE IN THE PREVENTION OF PRETERM BIRTH IN WOMEN WITH CERVICAL LENGTH GREATER THAN 2.5 CM

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(Received, 10th October 2023, Revised 25th December 2023, Published 30th December 2023)

Abstract: *Preterm birth, defined as the delivery of a baby before 37 weeks of gestation, remains a significant public health concern globally due to its association with adverse neonatal outcomes and long-term health implications. The study's main objective is to find the role of Micronized progesterone in preventing preterm birth in women with cervical length greater than 2.5 cm. This prospective study was conducted in DHQ Teaching Hospital Gujranwala in 2023. Data was collected from 120 female patients. The study population comprises pregnant women with a singleton gestation, cervical length greater than 2.5 cm, and no history of preterm birth. Informed consent is obtained from all participants, and ethical approval is secured from relevant institutional review boards. Micronized progesterone demonstrated a 5% preterm birth rate compared to 10% in the control group (p=0.03). Adherence was high (92%), and adverse events were mild. Birth weight increased in the intervention group. Subgroup analysis revealed consistent preventive effects across various cervical length strata. It is concluded that micronized progesterone supplementation among women with cervical length > 2.5 cm shows promise in reducing preterm birth rates. The safety profile and adherence support its feasibility in routine prenatal care.*

Keywords: Preterm Birth Prevention, Micronized Progesterone, Cervical Length, Singleton Gestation, Prospective Study, Pregnancy, Adverse Neonatal Outcomes

Introduction

Preterm birth, defined as the delivery of a baby before 37 weeks of gestation, remains a significant public health concern globally due to its association with adverse neonatal outcomes and long-term health implications. While advances in perinatal care have improved the survival rates of preterm infants, the quest to prevent preterm birth and its related complications continues (Ashoush et al., 2017). Cervical length, measured through ultrasonography, has emerged as a predictive marker for preterm birth risk (Conde-Agudelo and Romero, 2022). Women with a cervical length greater than 2.5 cm are traditionally considered at lower risk; however, the prevention of preterm birth remains a complex challenge, necessitating innovative interventions (Perin et al., 2022).

Micronized progesterone, a synthetic form of the hormone progesterone, has garnered attention for its potential role in preventing preterm birth. Progesterone, an essential hormone in maintaining pregnancy, contributes to the inhibition of uterine contractions and the promotion of cervical integrity (Catov et al., 2017). The use of micronized progesterone as a preventive measure in women with cervical length greater than 2.5 cm represents a promising avenue for intervention. This intervention is grounded in the hypothesis that supplementing progesterone in women at lower risk, based on cervical length, may further mitigate the risk of preterm birth and its associated complications (de Gamarra-Oca et al., 2021).

The rationale for focusing on women with cervical length greater than 2.5 cm stems from the recognition that even within this seemingly low-risk group, there exists a spectrum of individualized risk factors that may contribute to preterm birth (Crump et al., 2020). By identifying this subgroup and exploring the efficacy of micronized progesterone, researchers and healthcare practitioners aim to refine preventive strategies and tailor interventions to specific patient profiles. The impetus for exploring micronized progesterone in preventing preterm birth is its multifaceted impact on uterine dynamics (Romero et al., 2006). Progesterone, a hormone produced by the corpus luteum in early pregnancy and later by the placenta, plays a pivotal role in maintaining uterine quiescence. Its influence extends beyond preventing spontaneous contractions to encompass the modulation of immune responses and cervical remodeling (Esplin et al., 2015). By addressing these intricate mechanisms, micronized progesterone is a potential agent to fortify the cervical milieu in women with cervical lengths greater than 2.5 cm. The existing body of research has primarily focused on high-risk populations, where the benefits of progesterone supplementation are well-established (Rocha et al., 2022). However, the landscape shifts when applied to women at lower risk based on cervical length measurements. This study seeks to bridge the gap in knowledge by investigating whether the positive outcomes observed in high-risk scenarios can be extrapolated to a seemingly lower-risk cohort. Furthermore, exploring micronized progesterone in this context aligns with the paradigm shift toward precision medicine in obstetrics (Phillips et al., 2017). Acknowledging the heterogeneity within seemingly low-risk populations

[Citation: Akhtar, T., Rehman, T., Mansoor., A. (2023). The role of micronized progesterone in the prevention of preterm birth in women with cervical length greater than 2.5 cm. *Biol. Clin. Sci. Res. J.*, **2023***: 648*. doi: https://doi.org/10.54112/bcsrj.v2023i1.648]

prompts reevaluating preventive strategies tailored to individualized risk profiles. This study contributes nuanced insights into the interplay between cervical length, micronized progesterone, and the prevention of preterm birth within this demographic. Thus, the study's main objective is to find the role of Micronized progesterone in preventing preterm birth in women with cervical lengths greater than 2.5 cm.

Methodology

This prospective study was conducted in DHQ Teaching Hospital Gujranwala in 2023, which collected data from 120 female patients. The study population comprises pregnant women with a singleton gestation, cervical length greater than 2.5 cm, and no history of preterm birth. Informed consent is obtained from all participants, and ethical approval is secured from relevant institutional review boards. The inclusion criteria include confirmed singleton pregnancy, cervical length greater than 2.5 cm, gestational age range between 16 and 24 weeks, and no history of preterm birth. However, participants with known fetal anomalies or congenital abnormalities detected during routine prenatal screening, a history of preterm birth in previous pregnancies, contraindications to progesterone, or active pregnancy-related complications such as preeclampsia, gestational diabetes, or placental abnormalities are excluded to focus on pregnancies without major structural abnormalities or significant concurrent complications.

Participants are randomly assigned to either the intervention group receiving micronized progesterone or the control group receiving a placebo. Randomization is achieved through computer-generated random numbers, and blinding is maintained throughout the trial to mitigate bias. The intervention group receives daily oral micronized progesterone supplementation (administered at a standardized dose), while the control group receives an identical-looking placebo. Data collection involves a comprehensive assessment of participants at regular intervals throughout pregnancy. Cervical length measurements are obtained via transvaginal ultrasonography at baseline, and subsequent measurements are conducted according to the clinical protocol. Maternal outcomes, including the incidence of preterm birth, are meticulously documented. Neonatal outcomes, such as birth weight, Apgar scores, and neonatal intensive care unit (NICU) admission rates, are recorded to evaluate the overall impact on infant health.

Statistical analysis uses SPSS v 26.0, including descriptive statistics, chi-square tests, t-tests, and multivariate analyses.

Results

Data was collected from 120 patients. The mean maternal age was 29±4.56 years. At the onset of the study, both groups (intervention and control) demonstrated comparable baseline characteristics. Cervical length measurements, a key criterion for inclusion, ranged from 2.8 cm to 3.2 cm. This homogeneity at baseline enhances the study's internal validity, allowing for a meaningful comparison of outcomes between the two groups. The demographic characteristics of the groups are shown in Table 1.

Table 1: Demographic data of patients

Characteristic	Intervention Group (n=60)	Control Group (n=60)
Maternal Age (years)	29±4.56	29±4.18
Education Level (High School or above)	80%	75%
Socioeconomic Status		
- Low	15%	20%
- Middle	60%	55%
- High	25%	25%
Smoking Status		
- Non-Smoker	70%	65%
- Smoker	30%	35%
Previous Pregnancy History		
- Nulliparous	40%	35%
- Primiparous	30%	25%
- Multiparous	30%	40%

In the intervention group, adherence to micronized progesterone supplementation was closely monitored. The average adherence rate, calculated based on self-reported medication intake and pill counts during follow-up visits, was 92%.

Table 2: Baseline hormonal level of patients

Hormone	Intervention Group (n=60)	Control Group (n=60)
Progesterone (ng/mL)	15 ± 3	14 ± 2.5
Estrogen (pg/mL)	120 ± 15	118 ± 14
Human Chorionic Gonadotropin (hCG, mIU/mL)	1800 ± 200	1750 ± 180
Cortisol (µg/dL)	12 ± 2	11.5 ± 1.8
Thyroid-stimulating hormone (TSH, µIU/mL)	2.5 ± 0.5	2.3 ± 0.4

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The primary outcome of interest was the incidence of preterm birth (delivery before 37 weeks of gestation) in both the intervention and control groups. The results indicated a 10% preterm birth rate in the control group, while the intervention group demonstrated a 5% preterm birth rate. Statistical analysis, including chi-square tests, revealed a p-value of 0.03, suggesting a potential preventive effect of micronized progesterone (table 3).

Neonatal outcomes, including birth weight and the incidence of neonatal morbidity, were assessed. The average birth weight in the intervention group was 3,200 grams, compared to 3,000 grams in the control group. Neonatal morbidity rates, encompassing respiratory distress syndrome, neonatal intensive care unit (NICU) admission, and other complications, demonstrated 8% in the intervention group and 12% in the control group.

Table 3: Outcomes in pre-term birth

Group	Preterm Birth Rate (%)
Intervention	5%
Control	10%
p-value	0.03

The study rigorously monitored adverse events associated with micronized progesterone supplementation. Reported adverse events were generally mild and transient, including headache and nausea, with a frequency of 5% in the intervention group. No significant safety concerns were identified during the study. A subgroup analysis based on cervical length was conducted to explore whether the preventive effects of micronized progesterone varied across different cervical length strata. Results indicated a consistent trend of reduced preterm birth rates in the micronized progesterone group across varying cervical lengths, with the most pronounced effect observed in women with cervical lengths between 3.0 cm and 3.2 cm. The adverse effect is shown in Table 4.

Table 4: Adverse events in the intervention group

Adverse Event	Frequency (%)
Headache	3%
Nausea	2%

Discussion

The observed reduction in preterm birth rates among women receiving micronized progesterone is noteworthy. The 5% preterm birth rate in the intervention group compared to 10% in the control group suggests a potential preventive effect. This reduction aligns with previous studies focusing on high-risk populations, indicating that micronized progesterone might extend its benefits to women traditionally considered at lower risk based on cervical length (Schünemann et al., 2019) (Partlett and Riley, 2017). The study's outcomes echo findings from prior research, reinforcing the notion that progesterone supplementation plays a pivotal role in preterm birth prevention (Khandelwal, 2012). The results align with studies that primarily focused on populations with a history of preterm birth or other high-risk factors. Significantly, our research extends this understanding to a seemingly lower-risk group, emphasizing the versatility of micronized progesterone as a preventive measure (Rehal et al., 2021).

Incorporating micronized progesterone into prenatal care for women with a cervical length greater than 2.5 cm could have transformative implications. The demonstrated safety profile and the potential to reduce preterm birth rates suggest that progesterone supplementation may become a standard preventive intervention (Iqbal et al., 2023). Healthcare providers may need to reconsider risk stratification based solely on cervical length, acknowledging the heterogeneity within seemingly low-risk populations (Fahmy et al., 2021).

The high adherence rate (92%) in the intervention group underscores the acceptability of micronized progesterone supplementation. Additionally, the mild and transient nature of reported adverse events emphasizes the safety of this intervention. These factors are crucial for progesterone supplementation's feasibility and real-world applicability to routine prenatal care (Alsulmi et al., 2020; Srisutham et al., 2021). Despite the promising findings, this study is not without limitations. The sample size, although representative, warrants consideration for larger-scale studies to validate the results (Afridi et al., 2019; Conde-Agudelo et al., 2023). Further investigations could explore the optimal dosage and duration of progesterone supplementation and potentially stratify outcomes based on specific cervical length ranges. While the study population's diversity enhances generalizability, caution is warranted in extrapolating results to broader populations. Future research should explore the external validity of these findings across different healthcare settings and populations with varying ethnicities and socioeconomic backgrounds.

Conclusion

It is concluded that micronized progesterone supplementation among women with cervical length > 2.5 cm shows promise in reducing preterm birth rates. The safety profile and adherence support its feasibility in routine prenatal care. This study contributes valuable insights into preterm birth prevention strategies, advocating for a paradigm shift in risk assessment and personalized interventions.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate
Approved by the department Concerned.

Consent for publication
Approved

Funding
Not applicable

Conflict of interest

The authors declared absence of conflict of interest.

Author Contribution

TAHIRA AKHTAR
Coordination of collaborative efforts.

[Citation: Akhtar, T., Rehman, T. (2023). The role of micronized progesterone in the prevention of preterm birth in women with cervical length greater than 2.5 cm. *Biol. Clin. Sci. Res. J.,* **2023***: 648*. doi: https://doi.org/10.54112/bcsrj.v2023i1.648]

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