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ORIGINAL ARTICLE

Comparison of Efficacy of Oral Nifedipine Versus Vaginal Micronized Progesterone in Management of Preterm Labor

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ABSTRACT

Objective: Preterm delivery causes the deaths of approximately 1 million children annually. The World Health Organization (WHO) estimates a prevalence of 5--18% of births occur prematurely worldwide; exceptionally rare studies are published comparing nifedipine with progesterone for use in the maintenance of tocolysis. This study compares oral nifedipine to veginal micronized progesterone in preterm labor-prone women

Methods: This randomized clinical study was carried out at gynecology department from 02-march 2021 to 01-March-2022. A total of 126 women with pre-term labor ware included. In group A, women took nifedipine 20mg sublingually 3 times every 30 minutes then maintained with nifedipine SR 20mg every 12 hours until 37 weeks of gestational amenorrhea or cervical dilatation >4cm (for 48 hours). In group B, women were asked to take vaginal micronized progesterone tablets of 200mg vaginally once a day or until 37 weeks of gestation amenorrhea or cervical dilatation at >4cm (for 48 hours). We compared premature birth, mode of delivery, side effects, neonate's respiratory distress, ventilator time, ICU stay, and death rate between the groups.

Results: Patients in both groups had similar demographics in terms of age and parity of patients. Pregnancy was delayed with a mean of 19.61±6.66 days in nifedipine group, at the same time the pregnancy was delayed for 33.06±8.66 days in progesterone group (p-value < 0.001). The average birth weight was 2.99 ± 0.29 Kg in nifedipine and 3.20 ± 0.17 Kg in progesterone group (p < 0.001).

Conclusion: According to the findings of the present study, Progesterone did not affect overall mortality. Progesterone looks like a promising medicine in this aspect,

Keywords: preterm, nifedipine, progesterone, tocolysis

INTRODUCTION

Births that occur before 37 weeks of pregnancy are considered preterm labor.[1] Birth at a premature age is the single most important risk factor for infant mortality. Premature delivery causes the deaths of approximately 1 million children annually [2]. The World Health Organization (WHO) estimates a prevalence of 5-18% of births occur prematurely worldwide, which means more than 10% of newborns have this problem. Those who manage to survive often do so with permanent impairments, such as impaired vision or hearing. common reasons for premature birth are multiple pregnancies, infections, and chronic diseases including diabetes and high blood pressure. After India, China, and Nigeria, Pakistan has the fourth-highest rate of premature births at 7,48,100 per year (WHO, 2018).

If high-risk pregnant women are found and treated early, they may be able to avoid or postpone having a premature baby. There needs to be an emphasis on both delaying or preventing premature delivery and improving the health of the newborn to lessen the hazards connected with it. Treatment for acute preterm labor is often treated with pharmacological intervention, which might include the use of a wide variety of medications. Medications are essential to the improvement of human health and well-being. However, their efficient and secure use is necessary to accomplish the desired target results. Due to the mother's changing physiology and the drug's possible teratogenic effects, drug therapy is a special concern during pregnancy. tocolysis is known as the Pharmacological induction of uterine relaxation. The injection of prenatal steroids allows for fetal lung maturation after 48 hours of acute tocolysis, making it possible to further postpone the onset of preterm delivery. The goal of maintenance tocolysis is to prevent a repeat of preterm labor once it has been halted.[3]

Nifedipine, a calcium channel blocker, is a safe and effective first-line medication for acute tocolysis. Oral administration, cheap costs, and the potential to reduce newborn morbidity are all positives. [4] [5] However, results from using it for maintenance tocolysis have been mixed.[6, 7] It appears that when combined with magnesium sulfate, nifedipine's efficacy is maximized.[8] The hormone progesterone plays a crucial role in preserving uterine relaxation.[9] As a result, it is increasingly being utilized for both maintenance tocolysis, and women at risk for pre-term labor. Most countries allow tocolytic therapy for 48 hours so that corticosteroids can be given[10], although there are some exceptions. Some studies recorded better outcomes for newborns with progesterone.[11] Progesterone reduces neonatal stay in the intensive care unit.

In terms of its efficacy, Tocolytic therapy after preterm labor arrest is controversial. Exceptionally rare studies are published comparing nifedipine with progesterone for use in the maintenance of tocolysis. This study compares oral nifedipine to vaginal micronized progesterone in preterm labor-prone women.

METHODS

This randomized clinical study was carried out at department of Gynecology between 02-march 2021 to 01-March-2022. The including criteria were patients aged 18-40 years, singleton pregnancy on ultrasound. pregnancy between < 37 weeks of gestation on LMP. Definition of preterm labor, the presence of regular uterine contractions more than 4 times in 20 minutes and cervical dilatation <4cm on pelvic examination. Women with short cervical length as diagnosed by transvaginal ultrasonography scan. Patients were excluded if their medical records showed they had a history of co-morbid conditions such as hypertension, diabetes mellitus, bronchial asthma, or pre-eclampsia. Women with severe anemia (Hb <11 mg/dl), a history of placental abruption or antepartum hemorrhage, fetal distress on a cardiotocograph (CTG), or polyhydramnios (AFI >24cm or single deepest vertical pool >8cm) are excluded.

With approval from the institute ethics committee and research department, 126 women undergoing preterm labor who fulfilled inclusion criteria were enrolled in the Department of Obstetrics and Gynecology (indoor ward setting) of the hospital. The husband of the patient gave his consent after being informed of the study's confidentiality and the lack of risk to his wife.

Patients' baseline characteristics were recorded, including their age, gestational age, parity, smoking status, and body mass index. In this study, Patients were given progesterone or nifedipine at random. based on the instructions printed on an opaque envelope and opened upon the patient's arrival (lottery method).

A total of 63 individuals were assigned to the oral nifedipine group (Group A) and another identical number (63 patients) were

assigned to the vaginal progesterone group (Group B). In group A, women took nifedipine 20mg sublingually 3 times every 30 minutes then maintained with nifedipine SR 20mg every 12 hours until 37 weeks of gestational amenorrhea or till cervical dilatation >4cm (for 48 hours). In group B, women were asked to take vaginal micronized progesterone tablets of 200mg vaginally once a day until 37 weeks of gestational amenorrhea or till cervical dilatation >4cm (for 48 hours).

The data were analyzed through a statistical tool for analysis (IBM-SPSS v22). Quantitative variables such as age, gestational age, parity, BP, hemoglobin, prolongation of pregnancy, and body mass index were provided as means ± SD. Qualitative variables were analyzed using frequency and percentage calculations; these included a mother's history of premature birth, mode of delivery, side effects, neonate's respiratory distress, ventilator time, ICU stay and death rate. A Chi-square test was performed to assess the effectiveness of the two different groups, and a result of < 0.05 was considered statistically significant.

RESULTS

Patients in both groups had similar demographics in terms of age and parity of patients, statistically insignificant. When comparing the two groups, neither had a significant advantage in terms of weight, body mass index, or hemoglobin (p = 0.632, 0.280, and 0.313, respectively). There was a statistically insignificant difference in the number of previous preterm births across the groups (p = 0.089). Women in Group A had a mean gestational age of 34.38 ± 2.34 weeks when they were admitted with preterm labor, while those in Group B had a mean gestational age of 35.77 ± 0.97 weeks, there was a significant difference between the groups in the average gestational age of the patients admitted for labor (p-value 0.001). Cervical dilation over 4 centimeters occurred in 77% of patients in group A and 65% of patients in the group = 0.115). The average cervical length is measured by ultrasonography. In group A, the pulse rate mean was 75.10 ± 3.64 beats per minute (bpm), the mean blood pressure (MBP) of 87.76 ± 4.90 mmHg, and in group B, the pulse rate was 75.27 ± 3.84 bpm, and MBP of 90.57± 4.18. there was a statistically significant between the two groups (p < 0.001). Prolongation of pregnancy has been delayed with a mean of 19.61±6.66 days in group A, at the same time the prolongation of pregnancy was 33.06±8.66 days in group B, and there was a statistically significant prolongation of pregnancy between the two groups. a p-value < 0.001.

Table 1: Preterm labor patients' demographic data.

Demographic data	Nifedipine (Group A) (N=63)	Progesterone (Group B) (N= 63)	p-value
Patient age (years) mean ± SD	29.62 ± 3.14	28.75±3.06	0.117
Weight (Kg) mean ± SD	56.26 ± 6.19	55.74 ± 5.92	0.632
BMI (Kg/m^2) mean ± SD	24.98 ± 4.89	25.90 ± 4.60	0.280
Parity mean ± SD	1.94 ± 1.44	1.87 ± 1.37	0.753
Pulse rate (bpm) mean ± SD	75.10 ± 3.64	75.27 ± 3.84	0.001
Blood pressure (mmHg) mean ± SD	87.76 ± 4.90	90.57± 4.18	0.001
Hemoglobin(g%) mean ± SD	13.51± 1.06	13.71± 1.19	0.313
Gestational age at delivery (weeks) mean ± SD	34.38±2.34	35.77±0.97	0.001
Prolongation of pregnancy (days) mean ± SD	19.61±6.66	33.06±8.66	0.001
History of preterm n (%)	10 (15.87%)	4(06.34%)	0.089
Side effects n (%)	16(25.39%)	7(11.11%)	0.038
Mode of delivery			
Vaginal delivery n (%)	14 (22.22%)	22(34.9%)	0.115
Cesarian section n (%)	49(77.77%)	41(65.07%)	

The side effects of headache and hypotension were observed in 16 (25.39%) women of group A, and 7 (11.11%) women of group B, statistically significant (p= 0.038). there were 14 (22.22%) vaginal delivery and 49(77.77%) caesarian section delivery in Group A, and in group B the mode of delivery was 22(34.9%) vaginal, 41(65.07%) caesarian section. (p= 0.115). (Table 1)

The neonates were born into the two groups, as shown by the demographic data (Table 2) collected during the first month of life. The average birth weight was 2.99 ± 0.29 Kg in group A and 3.20 ± 0.17 Kg in group B. Statistically, the difference between the two groups was significant (p < 0.001). Both groups contained infants who required admission to an intensive care unit (ICU) and ventilator assistance. the numbers were 17 (26.98%) and 12 (19.04%) in group A, and 7 (11.11%) and 3 (04.76%) in group B (p-value of 0.02 and 0.013, respectively). Among the 8 infant deaths, 6 occurred in Group A and 2 occurred in Group B.

Table 2: Neonatal demographic data

Neonatal data	(Group A) (N=63)	(Group B) (N= 63)	p-value
Birth weight (Kg) mean ± SD	2.99 ± 0.29	3.20 ± 0.17	0.001
Respiratory distress n (%)	15 (23.80%)	6 (09.52%)	0.31
ICU admission n (%)	17 (26.98%)	7 (11.11%)	0.023
Ventilator support n (%)	12 (19.04%)	3 (04.76%)	0.013
Death n (%)	6 (09.52%)	2 (03.17%)	0.14

DISCUSSION

Preterm birth problems are the main cause of death among children younger than 5 years old. Three-quarters of these deaths might be averted using existing, cost-efficient therapies. Based on gestational age, there are subcategories of preterm birth: extremely preterm (< 28 weeks) mild to late preterm (28 to 32 weeks), and very preterm (32 to 37 weeks). A healthy pregnancy is the first step in preventing deaths and consequences from preterm birth. Preterm birth avoided counseling on healthy food and optimal nutrition, and fetal measures, including the use of ultrasound to assess gestational age and optimal fetal development.[12]

Although the Cochrane review (2003) concluded that ca^{+2} channel blockers are better than other assessed tocolytic drugs, particularly beta-mimetics, Some additional research has cast doubt on the effectiveness of nifedipine as a maintenance tocolytic[7].

The present study mimicked Kamat et al.[13] and We looked at how well nifedipine and progesterone worked and how well they were tolerated to prolong tocolysis following halted preterm labor and the researchers discovered no significant difference in gestation. We detected insignificant parity between the nifedipine and progesterone groups, which contradicts the conclusions of Rabei et al.[14] and Chawanpaiboon et al.[15].

It was reported by Eldesouky et al.[16] that the gestational age was between 25 to 40 weeks, with a mean of 36.10 ± 3.27 weeks, and that The progesterone group had considerably higher gestational ages at delivery than the placebo group. (37.16 ± 1.81 vs. 35.04 ± 4.03 weeks, respectively). According to Rabei et al [14]., there was insignificant GA among the groups. our study results agree with Eldesouky et al results with gestational age 34.38 ± 2.34 in nifedipine and 35.77±0.97 in progesterone.

As of our present study results, Prolongation of pregnancy has been delayed with a mean of 19.61±6.66 days in the nifedipine group, at the same time the prolongation of pregnancy was 33.06±8.66 days in the progesterone group. Ding et al.[17] found that in maintenance tocolysis therapy following halted preterm birth, progesterone was substantially more efficacious than nifedipine. However, these findings run counter to those of another research. It was reported by O'Brien et al.[18] that there was an insignificant rate of preterm delivery at less than or equal to 32 ± 0 weeks of gestation. Women in the nifedipine group had significantly more preterm births than women in the progesterone group, and this gap could not be explained by any other factor[13]. There was significantly less birth weight in neonates born in the nifedipine versus progesterone group.

Newborns exposed to either nifedipine or progesterone did not show statistically significant differences in respiratory distress. According to the results of AM. Abdelgaied et al.[19], newborn Respiratory distress were much lower when vaginal progesterone therapy was used instead of nifedipine. Our results same as mentioned above. In our statistical analysis, there were more nifedipine group neonates admitted to ICU and ventilated compared to the progesterone group. The death rate was negligible in groups A and B.

Limitation of the study: Present study was conducted in a less population, it is advised to do multicenter research with a larger study population to improve the outcome.

CONCLUSION

In conclusion, progesterone is superior to nifedipine for maintaining tocolysis. Prolonged pregnancy has also reduced newborn morbidity and ICU stays. Progesterone did not affect overall mortality. Our less sample size prevents us from recommending veginal micronized progesterone for tocolysis maintenance. Progesterone looks like a promising medicine in this aspect, but further research is needed.

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