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Original article:

Role of micronized progesterone in women with arrested Preterm labor

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ABSTRACT:-

Objective: To evaluate the efficacy of vaginal micronized progesterone in arrested preterm labor.

Methods: It was a prospective randomized controlled study conducted in the department of Obstetrics and Gynecology,Rohilkhand Medical College and Hospital, Bareilly, U.P. from June 2017 to December 2017. A total 80 patients with preterm symptomatic singleton pregnancy between 24 to 34 weeks were included in the study. Patients were divided into two groups, Study group and control group and each group had 40 patients. Study group was given 200mg micronized progesterone pervaginum (after having taken informed consent) and the Control group was given placebo. The treatment was continued till 34 weeks of gestation or till PROM delivery, which ever was earlier.

Results: There was prolongation of gestational age more than 34 weeks in 20 (50%) of the patients in progesterone group compared to placebo group of 10 patients (25%) and neonatal death was noted less in progesterone group 2 (5%) compared to placebo group 6 (15%) but it is not statistically significant.

Conclusion: Maintenance tocolytics with vaginal micronized progesterone significantly prolonged pregnancy and decreased the number of preterm births. The present study supports the use of micronized progesterone as a maintenance tocolytic for prolongation of pregnancy in cases of preterm labor.

Keywords: Progesterone, Preterm Labor, PROM, Tocolytics, Neonatal death.

INTRODUCTION:-

Preterm labor and delivery are major determinants of neonatal morbidity and mortality. Prematurity is strongly associated with long-term developmental disabilities, accounting for 1 in 5 children with mental retardation, 1 in 3 children with vision impairment, and almost half of children with cerebral palsy. Importantly, low-birth weight infants who are spared significant neonatal morbidity are at higher risk for cardiovascular disease (myocardial infarction, stroke, and hypertension) and diabetes as adults.[1] Patients with arrested preterm labor are at increased risk of recurrence, but to this point, continued tocolytic treatment with any agent after arrest of acute preterm labor is of questionable value in extending gestation or improving outcome.[2,3] Spontaneous preterm birth, that is preterm birth after labor or rupture of the membranes, represents approximately 75% of all preterm births.[4,5] Progesterone has been shown to prevent the formation of gap junctions, to have an inhibitory effect on myometrial contractions, and to prevent spontaneous abortion in women in early pregnancy after excision of the corpus luteum.[6] Progesterone is useful in allowing pregnancy to reach its physiologic term because at sufficient levels in the myometrium, it

blocks the oxytocin effect of prostaglandin F2α and α-adrenergic stimulation and therefore, increases the α-adrenergic tocolytic response.[7] Natural progesterone is free of any disturbing teratogenic, metabolic, or hemodynamic effects. This is not true for certain artificial progestagens and mimetics.[8] Many diagnostic and prophylactic measures have been investigated including tocolytic therapy, routine culture and antibiotic treatment of subclinical vaginosis. Till now, none of these have made a significant demonstrableimpact in the incidence of preterm delivery. Natural progesterone is completely innocuous. The only side effect is somnolence. There is no fetal toxicity where as beta mimetics have cardiovascular side effects.

In a study published in 2007, vaginal progesterone treatment reduced the rate of preterm birth among women who were at high risk for preterm birth because of a short cervix .[10] Progesterone has long been considered important agent in the maintenance of uterine quiescence and has been used extensively in primary and secondary prevention of preterm labor. [9,11]

OBJECTIVE:

To evaluate the efficacy of vaginal micronized progesterone in arrested preterm labor.

METHOD:

It was a prospective randomized controlled study conducted in the department of Obstetrics and Gynecology, Rohilkhand Medical College and Hospital, Bareilly, U.P. from June 2017 to December 2017. A total 80 patients with preterm symptomatic singleton pregnancy between 24 to 34 weeks were included in the study. Patients were divided into two groups, Study group and control group and each group had 40 patients. Study group was given 200mg micronized progesterone per vaginum (after having taken informed consent) and the Control group was given placebo. The treatment was continued till 34 weeks of gestation or till PROM delivery, which ever was earlier.

INCLUSION CRITERIA:

Singletonpregnancy with gestation age < 34 weeks of gestation with threatened preterm labor.

EXCLUSION CRITERIA:

Multiple pregnancies

Fetal malformations

Documented evidence of uterine malformation

Prophylactic cerclage operation

Evidence of chorioamniotis

PROM

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RESULTS :-

All the parameters were statically analyzed by mean +/- S.D., properties, frequency, chi-square test. Percentage reduction in the quantitative variables was calculated using the formula of (n-1)/n X 100.

Table 1- Demographic distribution :

	Study Group (n=40)	Control Group (n=40)	P value
Age	25.6+/-2.5	24.8 +/- 2.8	0.1816 #
Weight (kg)	60+/- 4.5	58.6 +/-6.6	0.1822 #
Height (cm)	162.2+/-2.4	161.4+/-2.8	0.1740 #

Table 2-Comparison of pregnancy outcome:

	Progesterone + Isosuxpurine	Isosuxprine + Placebo	P value
Maternal			
Delivery before < 34 weeks	20	30	0.0209*
After >34 week	20	10	0.0209*
Perinatal			
Fetal Death	2	2	0.6080#
Neonatal Death	2	6	0.2636#

Table 3-Comparison of stay of newborn babies in the NICU

	Study group		Control group		P value
	No.	%	No.	%	
<24 hours	4	10%	8	20%	0.3476#
24 hours-1 week	4	10%	10	25%	0.1412#
>1 week	1	2.5%	2	5%	1.000#

not significant * significant

DISCUSSION:-

In the present study there was a prolongation of gestational age more than 34 weeks in 20 (50%) of the patients in progesterone group compared to placebo group of 10 patients (25%) and neonatal death was noted less in progesterone group 2 (5%) compared to placebo group 6 (15%) but it is not statistically significant.

In 2005, Roberta Mackenzie et al.[12] conducted a meta-analysis evaluating the use of progesterone for women with high risk of preterm birth. Three trials were eligible for inclusion. There was a significant reduction in risk of

delivery at less than 37 weeks with progestational agents. There was no significant effect on perinatal mortality or serious neonatal morbidity. The finding was similar to our study. In 2006, a meta-analysis by AravinthanCoomarasamyet al.[13] evaluated the use of progesterone in prevention of preterm delivery in high risk patients. A total of nine randomized control trials were evaluated comprising of about 500 patients. Meta-analyses showed reductions in delivery rates before 37 weeks as well as in respiratory distress syndrome with progestational agents. A similar study was carried out by Sedigheh BORNA and Noshin SAHABI [14] in Tehran in 2004, where progesterone was given to women after threatened preterm labor in one arm where as another arm of patients received no treatment. There was significant increase in mean latency until delivery, decrease in respiratory distress syndrome, and decrease in low birth weight in progesterone arm group.

The limitation of our study was small sample size.

CONCLUSION:-

Maintenance tocolytics with vaginal micronized progesterone significantly prolonged pregnancy and decreased the number of preterm births. The present study supports the use of micronized progesterone as a maintenance tocolytic for prolongation of pregnancy in cases of preterm labor.

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