PROPHYLACTIC USE OF 17OH PROGESTERONE FOR PREVENTION OF PRETERM LABOUR IS EFFECTIVE

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ABSTRACT

Objective: To show efficacy of 17OH progesterone in prevention of preterm labor in comparison with frequent monitoring.

Study Design: Randomized clinical trial.

Place and Duration of Study: Department of Obstetrics and Gynecology, Combined Military Hospital Attock, from May 2011 to Dec 2011.

Methodology: Total 100 patients of high risk preterm delivery were selected from outpatient department. Patients were divided into two groups, fifty patients in group A, who were managed by frequent monitoring only and no treatment used for them. Fifty patients in group B, were given injection Proluton depot prophylactically (17OH progesterone) on weekly basis from 16 weeks of pregnancy till 37 weeks. Women included in study were educated about signs and symptoms of preterm labor, and about the importance of early diagnosis and treatment. The women were followed according to their group assignments until either preterm delivery or 37 weeks.

Results: Out of 50 patients, 41 (82%) deliveries in group A were between 32 -36 weeks of pregnancy, there was no delivery at or >37 weeks as compared to group B, in which 14 (28%) deliveries were beyond 37 weeks of gestation. Only 4 (8%) patients in group B, were delivered before 31 weeks of pregnancy as compared to group A in which this number was 9 (18%) (*p*-value <0.001).

Regarding neonatal outcomes, respiratory distress syndrome was seen in 30 (60%) babies in group A and in 18 (36%) babies in group B (*p*-value 0.016). Neonatal death (NND) occurred in 5 (10%) newborns in group A and only 2 (4.0%) in group B. However this difference in NND was not statistically significant (*p*-value 0.24). APGAR score was poor in 14 (28%) babies in group-B as compared to group A, in which poor APGAR score was seen in 30 (60%) babies (*p*-value <0.001).

Conclusion: Prophylactic use of 17OH progesterone in prevention of preterm labor is effective. It improves neonatal outcome and reduces the incidence of preterm deliveries.

Keywords: 17OH Progesterone, Preterm labor, Neonatal death.

INTRODUCTION

Term is defined as period from 37 to 41 completed weeks of gestation[1]. Delivery before 37 weeks is preterm[2] with incidence of 5.5%[2]. Preterm delivery is divided into three groups on basis of gestational age.

- Mild preterm (32-36) weeks
- Moderate preterm (28-31) weeks
- Extremely preterm (24 to 27) weeks[2]

Preterm labor is defined as regular, effective uterine contractions with cervical dilatation and decent of presenting part before 37 weeks of gestation[3]. Threatened preterm labor is defined as effective uterine contraction without cervical dilatation[4]. It has two subclinical types iatrogenic and spontaneous[5].

Patients going into spontaneous labor are 50%, out of which 30% are with premature rupture of membranes (PPROM), however iatrogenic preterm deliveries due to fetomaternal indication are 20%[3]. Preterm delivery itself is associated with increased risk of operative delivery, intra-uterine infections, financial and psychological stress for parents[5]. Fetal implications include prematurity, infections, metabolic disorders,

hypoglycemia, hypocal-cemia[5]. Low I/Q, poor progress in school, neurological impairment, and respiratory distress syndrome (RDS)[5]. 70% of neonatal mortality[3]. intrauterine growth retardation (IUGR), necrotizing enterocolitis, septicemia, and intracranial hemorrhage[3].

Before 32 weeks, prematurity and related mortality and morbidity is approximately 75% and 50% respectiely[6,3]. The frequency of RDS decreases with increase in gestation. Term infants are rarely affected by RDS. Incidence of RDS in preterm is 50%[6], it is 87% with weight of 500 gm (fetus) and 27% with gestational weight of 1500 gm (fetus)[7,8]. Common causes of preterm labor are vaginal and urinary tract infection, cervical incompetence, recurrent bleeding episodes, uterine anomaly, and progesterone deficiency, low socioeconomic status[8]. Previous preterm delivery, a significant risk factor increasing incidence by 15% after 1, 30% after 2, and 45% after 3 preterm deliveries[9].

Mortality with prematurity is 90% at 23 weeks and 2% at 34 week, and also high even in those babies who survive[10,11].

Preterm labor is prevented by 60% by treating asymptomatic bacteuria and bacterial vaginosis[12]. Cervical cerclage another way to avoid preterm labor is applied after 14 weeks of pregnancy and removed after 37 weeks[13]. It has role in prevention of preterm labor but with low predictive value[13,6].

Use of progesterone in form of injections, tablets, and suppostries is common practice to prevent preterm labor. Routes are oral, vaginal, rectal and injectables. Substances in common use are injection proluton, cyclogest pessary, and tablet Duphaston[14]. Progesterone can prevent preterm labor in 60% patients[14]. Tocolysis is only indicated for inutero transfer of baby and to gain time for dexamethasone. 17OH Progesterone is available with composition of 250 mg hydroxy progesterone caproate in oily solution (1ml)[15] and stored below 30 C and protected from light. Common indication for use are habitual miscarriage. Contra indication are past history of anaphylactoid reaction, cardiac, pulmonary and liver disease and caution use in diabetics. It is administered in gluteal region. Side effects are pain at site of injection and allergic reaction[15].

Frequent monitoring means frequent antenatal visit to assess fetal and maternal well being. Avoidance of smoking, complete bed rest, home monitoring of uterine activity, social and psychological support, sexual abstinence are part of frequent monitoring[16].

The study was done to throw light on the importance of 17OH Progesterone in prevention of preterm labor and its role in improvement of neonatal and maternal outcome.

METHODOLOGY

This interventional study was conducted from May 2011 to Dec 2011, in department of obstetrics and gynecology, Combined Military Hospital Attock.

One hundred patients high risk for preterm labor, were selected from outpatient department by non-probability consecutive sampling technique and divided into two groups, 50 patients in group A and 50 patients in group B. Written informed consent was taken from all patients prior to inclusion in study.

Patients with age >18 years, booked or unbooked accurately dated singleton pregnancy with cephalic presentation in preterm labor were included in study. Patients with previous preterm delivery, were considered at high risk of preterm labor. Patients who need hospital stay for administration of antenatal steroid for fetal well-being were included in this study.

Patients with age <18 years, with PROM, cervical cerclage, cervical dilatation >4cm, chorioamnionitis, poly-hydramnios, multi-parity, and twin pregnancy, were excluded from study. Cases with multiple fetal and uterine abnormality, intrauterine death, placenta previa were ruled out from study.

Preterm labor was diagnosed by palpable effective contraction and vaginal examination, which was repeated after 4 hours to find any

change in bishop score. Patients in group A high risk for preterm delivery on basis of history and examination, were called frequently at twice weekly interval just for fetomaternal monitoring and no treatment was given. Feto-maternal well-being was assessed by their symptoms, ultra-sound for fetal well being and measurement of cervical length by transvaginal sonography (TVS) on weekly basis. Women were educated about signs and symptoms of preterm labor, like changes in vaginal discharge, cramping, and backache and also told about the importance of early diagnosis of preterm labor and treatment. They were also educated about the way to palpate themselves for uterine contractions. Regular uterine contractions were defined for the women as four or more contractions per hour. They were advised to avoid exertion and to report earlier if develop any of above symptoms.

Group B was administered injection Proluton depot on weekly basis from 16 weeks of gestation. They were assessed for fetomaternal well-being twice a month. They were advised to report earlier if develops uterine contraction or PROM or vaginal bleeding. Abdomen was palpated for palpable contractions, fundal height, fatel heart rate (FHR), lie and presentation of fetus. Patients were advised to lie in left lateral position and to maintain fetal kick count chart. The women were followed according to their group assignments until either preterm delivery or 37 weeks' gestation.

Neonatal outcome was assessed on basis of their APGAR score.

APGAR score was defined as general appearance of baby at 1 and 5 minute of birth assessed by respiration, heart, body color, tone and activity.

APGAR score >3 at 1 minute and 5 min. was taken as poor and more than` 7 at 1 min and 10 at 5 minute, was considered as good APGAR score.

All findings were documented on patient's performas. Results were analyzed by SPSS-11 and interperated in terms of percentages and frequency. Mean ± SD was calculated for qualitative value. Chi Square test was applied and *p*-value in both groups regarding gestation at delivery and neonatal outcome, was found out.

RESULTS

Total 100 women fulfilling the criteria included in this study, were more than 18 years of age. It was observed that patient in group B were taken closer to 37 weeks.

41 (82%) deliveries in group A were between 32 -36 weeks of pregnancy, there was no delivery at or >37 weeks as compared to group B, in which 14 (28%) deliveries were beyond 37 weeks of gestation and only 32 (64%) deliveries were between 32 to 36 weeks of gestation. Only 4 (8%) patients in group B, were delivered before 31

Table-I: Comparison of gestational age at the time of delivery in group A and group B.

Gestational Age	Group A	Group B	*p*-value
37 Weeks	-	14 (28%)	<0.001
32-36 Weeks	41 (82%)	32 (64%)	
28-31 Weeks	9 (18%)	4 (8%)	

Table-II: Comparison of neonatal outcomes between group A and group B.

Outcome		Group A	Group B	*p*-value
Respiratory Distress Syndrome (RDS)		30 (60%)	18 (36%)	0.016
Neonatal death (NND)		5 (10%)	2 (4%)	0.24
APGAR Score	Good	20 (40%)	36 (72%)	0.001
	Poor	30 (40%)	14 (28%)	

weeks of pregnancy as compared to group A in which this number was 9 (18%) (*p*-value<0.001) (table-I).

Neonatal outcome were poor in group A as compared to group B. RDS seen in 30 (60%) babies in group A and in 18 (36%) babies in group B (*p*-value 0.016). Neonatal death (NND) occurred in 5 (10%) newborns in group A and only 2 (4.0%) in group B. However this difference in NND was not statistically significant (*p*-value 0.24).

APGAR score was poor in 14 (28%) babies in group B as compared to group A, in which poor APGAR score was seen in 30 (60%) babies and

this difference was statistically significant (*p*-value 0.001). On the whole, 72% babies were discharged with mother.

No maternal morbidity or mortality was observed. None of patients developed any side effect from injection. Injections were easily available.

DISCUSSION

Our study clearly emphasizes the importance of progesterone supplementation in prevention of preterm labor. Patients in group B delivered at 37 weeks of gestation were 14 (28%) when compared with group A with frequent monitoring in which no patient was delivered at or >37 weeks. Neonatal outcome was also good in 72% of cases in group B. Patient's compliance with injection was satisfactory and no reaction, abcess or pain at site of injection was noted in group B.

In our study, between 28-31 weeks, 9 patients were delivered in group A and 4 in group B. Double blind placebo based study was done with objective to evaluate the effects of prophylactic vaginal progesterone in decreasing preterm birth rate in high risk women. Placebo or 100 mg progesterone was given in form of vaginal suppositories on daily basis to 142 women. Patients were monitored for uterine contractions between 24 to 34 weeks. Results showed 18.5% PPROM birth in placebo group than in progesterone group 2.7%[17].

Prematurity is associated with multiple complications with mental and physical disability. No such morbid outcome was seen in our study[18].

Our study showed 82% patients delivered from 32-36 weeks in group A monitored frequently. It was compared with another study, including 2422 pregnant women with risk factors for preterm labor. They were monitored with frequent antenatal visit and to have one of the following: weekly contact with a nurse, and home monitoring of uterine activity. Women were educated for their symptoms and signs of preterm labor. Objective was to find the incidence of birth at or <35 weeks' gestation[16] and concluded that women who have daily contact with a nurse, with home monitoring of uterine activity, have no better pregnancy outcomes than women who have weekly contact with a nurse[16,6].

Counseling regarding reduction of preterm labor should be individualized in each pregnant women. Women with symptoms of preterm labor should observe activities which aggrevates symptoms and should bring behavioural changes accordingly.

CONCLUSION

Prophylactic use of 17 OH Progesterone in prevention of preterm labor is standard and safe care. It improves neonatal outcome and reduces possibility of preterm deliveries.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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