

Original article:

Study of use of progesterone for symptomatic placenta previa in a tertiary care teaching hospital

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Abstract

Present study was conducted to determine the effectiveness of intramuscular 17 α hydroxy progesterone caproate (Progestin analog) therapy versus placebo in conservative management of patients with symptomatic placenta previa before 34 weeks of gestation. Primary outcome measure was prolongation of pregnancy and secondary outcome measures were maternal outcomes i.e. number of episodes of bleeding, number of blood transfusion required, birth weight of babies. A prospective study with 60 pregnant females with symptomatic placenta previa that is having episode of warning hemorrhage before 34 weeks of gestation were enrolled for the study. Patients with Placenta previa symptomatic with at least one episode of bleeding, estimated gestational age within 28 to 34 weeks, maternal age > 18 yrs and only singleton pregnancy cases were included. Study showed that prolongation of pregnancy in progesterone receiving group is statistically significant (p value <0.05), significant difference were also found in gestational age at delivery (p value <0.05), birth weight (p value <0.05). Recurrent episode of bleeding was not significant (p value > 0.05) in both groups. 17 α OH progesterone in expectant management of symptomatic placenta previa tends to be beneficial than placebo as it causes clinically significant prolongation of pregnancy i.e. admission to delivery and increased birth weight as well as not appear to be any increased morbidity or mortality in a controlled tertiary setting.

Key words: Placenta previa, Progesterone, Pregnancy, Premature labor

Introduction

Placenta previa can have serious adverse consequences for both mother and baby, including an increased risk of maternal and neonatal mortality, fetal growth restriction and preterm delivery, antenatal and intrapartum hemorrhage.¹⁻⁴ incidence of maternal mortality rate in cases of placenta previa is approximately 0.03% and perinatal mortality of 8.1% in the developed world and much more in developing countries.^{5,6} A significant degree of uterine contractility has been observed in association with symptomatic placenta

previa and a large percentage of women who have placenta previa associated with hemorrhage will experience subclinical uterine contractions before the onset of overt vaginal bleeding as per literatures.^{7,8}

Recently many tocolytic agents are being advocated for management of symptomatic placenta previa.⁹ Delaying delivery may reduce the rate of long term morbidity by facilitating maturity of vital organs, help in optimum action of the administered glucocorticoids, helps in transfer to higher centre with NICU facilities. Progesterone is

essential for maintenance of pregnancy and helps in prolongation of pregnancy.

Progesterone and its analogs have complex mechanisms of action, binding nuclear and non-nuclear receptors and altering genomic and non-genomic functions in cells of target tissues. It has been suggested that progesterone and some of its analogs induce multiple physiological changes to inhibit the onset of premature parturition, including suppressing myometrial activity by inhibiting gap junction formation, enhancing the barrier to ascending infection by altered cervical mucous production, and improving resistance to cervical stromal degradation. Physiologically, progesterone and 17 α -hydroxyprogesterone caproate can have similar effects on selected end points.^{10,11} It acts primarily through establishing uterine quiescence and maintains cervical length. It has immunosuppressive activity against the activation of T-lymphocytes & blocks effects of oxytocin on myometrium. Recent studies show suppression of calcium-calmodulin-myosin light chain kinase system, reducing calcium flux and altering the resting potential of smooth muscle are the basis of progesterone action.^{12,13} Different trials have been done to show the efficacy and safety of progesterone in prevention of recurrent preterm birth since 1960.¹⁴⁻¹⁶

Treatment with progesterone was initially studied because of evidence that labor begins when the ratio of progesterone activity to estrogen activity is reversed or when progesterone activity is blocked, resulting in cervical ripening and uterine contractility. Progesterone causes inhibition of cervical ripening, reduction of myometrial contractility through suppression of

oxytocin receptor synthesis and function, and modulation of inflammation.¹⁷⁻¹⁹

The objective of present study is to determine the effectiveness of intramuscular 17 α hydroxy progesterone caproate (Progestin analog) therapy versus placebo in conservative management of patients with symptomatic placenta previa before 34 weeks of gestation.

Primary outcome measure was prolongation of pregnancy and secondary outcome measures were maternal outcomes i.e. number of episodes of bleeding, number of blood transfusion required, birth weight of babies.

Materials & methods

A prospective study with 60 pregnant females with symptomatic placenta previa that is having episode of warning hemorrhage before 34 weeks of gestation and fulfilling the inclusion criteria were enrolled for the study. Maternal general physical examination done, temperature, pulse, blood pressure etc were noted. Gestational age was confirmed clinically and by USG of early weeks of gestation. Diagnosis of complete placenta previa was made by transvaginal ultrasound when the lower placental edge appeared to overlay completely the internal os of the uterine cervix.

Patients with Placenta previa symptomatic with at least one episode of bleeding, estimated gestational age within 28 to 34 weeks, maternal age > 18 yrs and only single to n pregnancy cases were included. Premature rupture of membranes, severe bleeding requiring an immediate termination of pregnancy, abnormal fetal heart rates requiring an immediate termination of pregnancy, intrauterine fetal death, pre-eclampsia, chorioamnionitis, liver disease, severe chronic renal disease, heart disease, diabetes,

abruptioplacentae, haemodynamically unstable patients were excluded.

Per abdominal examination regarding uterine activity, tone and tenderness, liquor volume, fundal height and presentation, FHS pattern were thoroughly noted. All patients initially received steroid

prophylaxis, then, patients are randomly assigned having 30 pregnant mothers in each group to receive either intramuscular 17 α hydroxyl progesterone caproate 500 mg twice weekly or placebo until 37 weeks of gestation or till delivery whichever is earlier.

Results and discussion

Table 1: Baseline characteristics of study population.

		Group receiving im progesterone (n=30)	Group receiving placebo (n=30)	Statistical analysis P value
Age of mother		22.92 \pm 5.68	23.44 \pm 5.18	>0.05
Gestational age at admission		231.6 \pm 7.68	229.45 \pm 8.28	>0.05
Parity		1.23 \pm 1.49	1.17 \pm 1.58	
Type of placenta previa	Central	5	3	>0.05
	Partial	8	9	
	Marginal	11	10	
	Low lying	6	8	
Hb %		9.78 \pm 2.75	9.86 \pm 2.07	>0.05

Here >0.05: Not significant, <0.05: Significant

Table 2: Findings of present study

	Group receiving im progesterone (n=30)	Group receiving placebo (n=30)	Pvalue
Gestational age at delivery	237.94 \pm 8.97	232.5 \pm 9.88	<0.05
Mean latency (days)\pmSD	6.94 \pm 3.54	3.02 \pm 2.18	<0.005
Birth weight (Mean\pmSD)	2.12 \pm 0.325	1.92 \pm 0.42	<0.05
Recurrent bleeding	17	19	>0.05
Blood transfusion required	4	5	>0.05
NICU admission	10	14	>0.05

Here >0.05: Not significant, <0.05: Significant

No significant difference was observed between IM progesterone group and placebo group regarding baseline characteristics like maternal age, parity, gestational age at admission, type of placenta previa, Hb % on admission. Study showed that prolongation of pregnancy in progesterone receiving group is statistically significant (p value <0.05), significant difference were also found in gestational age at delivery (p value <0.05), birth weight (p value <0.05). Recurrent episode of bleeding was not significant (p value > 0.05) in both groups. There was no significant difference regarding NICU admission in study and control groups.

Preterm birth can be lowered by more than 30% by progesterone supplementation, both in women with a prior history of preterm birth and in those whose cervix is currently shortened.²⁰⁻²¹

Sharma A et al.²² stated that ritrodine hydrochloride as tocolytic in symptomatic placenta previa showed significant prolongation of pregnancy (25.33 vs. 14.47 days, P=0.05) and difference in birth weight (2270 g vs. 1950 g, P=0.05). There was no observed statistical difference between the two groups with regard to number of episodes of haemorrhage after admission, total amount of blood loss during stay in

hospital, number of blood transfusions and maternal complications due to tocolysis in the study group. Metanalysis by Bose DA, Assel BG, Hill JB, Chauhan SP²³ since 1995 to 2009 showed results of the one RCT indicated that pregnancy is prolonged for more than 7 days with continued tocolytics (OR 3.10, 95% CI 1.38 to 6.96) but combined results of two retrospective studies did not confirm the prolongation (OR 1.19, 95% CI 0.63 to 2.28). Richard E and Besinger et al²⁴ found that tocolytic intervention in cases of symptomatic preterm previa associated with clinically significant prolongation of pregnancy i.e admission to delivery (39.2 vs 26.9 days, p < 0.02) and increased birth weight (2520 vs 2124 gm, p < 0.03). Tocolytic therapy in these cases does not appear to have an impact on frequency or severity of recurrent vaginal bleeding.

Conclusion

17 α OH progesterone in expectant management of symptomatic placenta previa tends to be beneficial than placebo as it causes clinically significant prolongation of pregnancy i.e admission to delivery and increased birth weight as well as not appear to be any increased morbidity or mortality in a controlled tertiary setting.

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