ORIGINAL ARTICLE

EFFICACY OF 17-α-HYDROXY-PROGESTRONE IN PREVENTION OF PRETERM LABOUR IN HIGH RISK PREGNANT WOMEN

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Background: Preterm delivery (before 37 completed weeks of gestation) is a major determinant of infant mortality. The objective of study was to determine the efficacy of 17-alpha hydroxy-progesterone in preventing delivery before 37 weeks of gestation in high risk women. **Methods:** This study, a randomized controlled trial was conducted in Obstetrics OPD, observing all scientific and ethical protocols. The women with less than 20 weeks gestation and with a past history of preterm delivery were included. A total of 132 women fulfilled the study requirements. Two groups made were as follows: Group A (Treatment group received intramuscular 17-alpha hydroxy-progesterone) and Group B served as control (The control group revived intramuscular Neurobion). A total of 66 women were assigned to each group. The data was recorded on a specially designed proforma for statistical analysis and comparison following the standard procedure. **Results:** The criterion was strictly observed. The results showed a statistically significant (p<0.01) difference between group A as compared to group B. **Conclusion:** 17-α-Hydroxyprogesterone was found to be an effective drug in preventing delivery before 37 weeks in women at risk.

Keywords: 17-Alpha-hydroxyprogesterone; Preterm labour; High risk pregnancy

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INTRODUCTION

Preterm labour is an area of immense importance in obstetrics in terms of infant and mother mortality and morbidity.[1] It is responsible for around 80% of all infant deaths resulting from non-lethal deformities.[2] Preterm infants are at greater risk of many developmental and health problems compared to those born at term. The consequences include long-term neurological complications, intraventricular haemorrhage, acute respiratory distress, gastrointestinal necrotizing enterocolitis and immunological effects.[3] economically it puts a huge burden in pregnancy and afterwards in treatment of infant.[4]

The incidence of preterm labour is striking a high rate in developing countries including Pakistan, India and Bangladesh.[5] Because of high prevalence primary prevention is needed most of the time.[6] It is a complex cluster with unclear cause and pathology, moreover it is also a social and economic issue. Improved neonatal and antenatal management options have decreased incidence of preterm labour but possess a huge financial burden.

Multiple studies have shown increased uterine contractions in pregnant women predisposed to this condition.[7] Progesterone hormone is known to retain pregnancy and block unwanted contractions before reaching term.[8] It inhibits these unwanted contractions by working as antagonist to prostaglandin F2.[9] Studies have shown opposing action of progesterone on lipopolysaccharide induced uterine inflammation leading to preterm delivery.[10]

17-α-hydroxy- progesterone caproate is a synthetic hormone and a randomized controlled trial in America has shown its effectiveness in preventing recurrent preterm labour. Another randomized trial has shown its role in delaying pregnancy >35 weeks.[11,12] The present investigation is focusing at the use of pro-gestational agent 17-α-hydroxy-progesterone in women at high risk of spontaneous preterm birth and to improve the neonatal outcome. The results of our present study regarding the management of such women are presented in the current communication.

MATERIAL AND METHODS

This randomized control trial was conducted in Gynaecology/Obstetrics OPD and included healthy, pregnant women with singleton pregnancy at gestational age of <20 weeks having previous history of preterm birth. Selection of patients for the trial was on non-probability consecutive sampling. However, after patients were inducted in the study, they were randomly allocated to one of the two groups. A total of 66 slips each with group A, and group B written on them were put in a jar. Following the ethical norms, each time, a new patient visiting our out-patient department was asked to draw a slip from the jar. The patients with correctable causes were excluded, including patients with any history of

delivery somewhere else and women with first trimester were also excluded.

Group A was the study group and received 250 mg of intramuscular (IM) 17-α-hydroxy-progesterone caproate while the group B received Neurobion (as placebo, IM) till 37 weeks of gestation. Both the groups were followed throughout pregnancy for occurrence of preterm labour and data was collected on a specially designed proforma. The statistical analyses were conducted routinely by using SPSS-11.0.

RESULTS

A total of 132 patients attended the outpatients that fulfilled the inclusion criteria for the study. One hundred and fifty-four patients refused to be included in the study and opted for 17-α-hydroxy-progesterone Caproate. They were excluded from the study. Seven patients with incomplete records and 6 patients who were either lost to follow-up or decided to get delivered elsewhere were excluded from the study. At the end 132 patients were included in the final study.

The two groups were comparable as regards participants' age: Participants aged 31–40 years were 28.78% (n=19) in Group-A and 31.82 % (n=21) in Group-B. Similarly, participants aged >40 years constituted. 16% (n=10) in Group-A and 16.67% (n=11) in Group-B and finally X% (n=y) in group A, and Q (n=z) were aged less than 30 years. Mean and standard deviation was calculated, it was found 26.75±3.76 in Group-A and 27.99±1.43 in Group-B.

Out of participants in group A, majority, 65.15%, (n=43) reached 37 weeks of gestation, another 28.79% (n=9) delivered before reaching 37 weeks, and only 6.06% (n=4) delivered beyond 37 weeks of gestation. In Group B, the majority, 59.09% (n=39) delivered before 37 weeks, 37.88% (n=25) delivered at 37 weeks and 3.03% (n=2) delivered beyond the 37th week of gestation.

When compared, from amongst the group A, 28.79 %(n=19) had preterm labour while in Group-B 59.09% (n=39) had preterm labour. (p<0.01).

Table-1: Age distribution of the subjects (n=132)

	Group-A (n=66)		Group-B (n=66)	
Age in years	No. of cases	Percentage	No. of cases	Percentage
20–30	37	56.06	34	51.51
31–40	19	28.78	21	31.82
>40	10	15.16	11	16.67
Mean and S.D.	26.75±3.76		27.99±1.43	
Total	66	100	66	100

Regarding mean age, the two-tailed p-value equals 0.6287. By conventional criteria, this difference is considered to be not statistically significant. (Chi-square test).

Table-2: Gestational age of the subjects at the time of delivery

Gestational Age (in weeks)	Group-A (n=66)		Group-B (n=66)	
	No. of cases	Percentage	No. of cases	Percentage
<37	19	28.79	39	59.09
37	43	65.15	25	37.88
>37	04	6.06	02	3.03
Mean and S.D.	36.35±1.36		34.51±3.33	
Total	66	100	66	100

Regarding Mean Gestational Age, The two-tailed p-value equals 0.0600. By conventional criteria, this difference is considered to be not quite statistically significant.

Table-3: Occurrence of preterm labour

Pre-term labour	Group-A (n=66)		Group-B (n=66)	
	No. of cases	Percentage	No. of cases	Percentage
Yes	19	28.79	39	59.09
No	47	71.21	27	40.91
Total	66	100	66	100

The chi-square statistic is 12.302. The p-value is .000452. This result is significant at p<0.05

DISCUSSION

Preterm delivery is the major cause of infant mortality and morbidity in developing and developed countries and is a cause of increased neonatal mortality.[13] In a developed country like USA the incidence has increased in last two decades from nine percent to twelve percent.[14] Many trials conducted worldwide have evaluated the effectiveness of different strategies varying from reduced activity to use of pharmacological agents like tocolytics, antibiotics but no single effective and reproducible method of preventing preterm delivery has been devised.[15]

Our findings are in full agreement with the use of 17-alpha-hydroxy-progesterone which was

found to be effective in protecting the preterm birth. Our observations are also contradictory with the reports indicating no effect of such a treatment on lowering the preterm delivery.[16,17] In addition, our findings were not in agreement with the earlier work where various progesterone derivatives could not express effectiveness in reducing risk of preterm delivery.[18] As per the design of our present study women who were at high risk for preterm delivery were given 17-alpha-hydroxy-progesterone on a weekly basis, beginning at 16–20 weeks of gestation and continued to delivery or 36 weeks of gestation. There was a significant reduction in the rate of preterm delivery before 37 weeks, 35 weeks, and 32 weeks of gestation. As a consequence, in the treatment group reduced rates of prematurity were found among the infants born.

The role of progesterone on uterus is dual it decreases contractile action of oestrogen on uterus and increase synthetic function in myometrial cells to retain nutrients for growing foetus.[19] It prolongs the pregnancy near 37 weeks and by hormonal assay noted as progesterone withdrawal leading to uterine contractions.[20]

A recent randomized controlled trial undertaken by a maternal foetal medicine unit network shows that 17 alpha hydroxy progesterone caproate has the capability to decrease preterm birth in high risk women. Progesterone was also administered in second trimester and revealed a significant reduction in preterm birth rate. American College of Obstetrics and Gynaecology has also advocated use of 17 alpha hydroxy progesterone for patients with previous preterm birth; recommendation based on several trials.[21] This study demonstrates that treatment with 17 Alpha hydroxy progesterone on a weekly basis till delivery or 36 weeks of gestation, reduces the risk of preterm labour in high risk group.

Another study concluded that women taking 17 alpha-hydroxyprogesterone caproate and women in the control group showed 39.2% versus 60.8% respectively reduction in preterm birth. These results are also in agreement with the current study.[22]

CONCLUSION

In light of the results of above mentioned studies and current study, the hypothesis of this study, i.e., "17 Alpha Hydroxyprogesterone is effective in preventing delivery at less than 37 weeks in women at risk for preterm birth" is found to be justified. However, the limitation of the study is that we did not compare any side effects of the drugs, but no complaint regarding adverse effect/complications due to drug was found. Further studies may be carried out in future to evaluate the adverse effects/complications and efficacy of 17 Alpha Hydroxyprogesterone so that it can be used in routine in clinical practice with more confidence.

Declaration: The authors' do not bear any conflict of interest.

AUTHORS' CONTRIBUTION

WS: Study conception and design, acquisition of data, analysis and interpretation of data, WS, SR: drafting of manuscript. WS, SR &FA: Critical revision.

REFERENCES

1. Butler AS, Behrman RE, editors. Preterm birth: causes, consequences, and prevention. Washington (DC): National Academies Press; 2007.
2. Rush RW, Davey DA, Segall ML. The effect of preterm delivery on perinatal mortality. Br J Obstet Gynaecol 1978;85(11):806–11.
3. Nelson DB, McIntire DD, McDonald J, Gard J, Turrichi P, Leveno KJ. 17-alpha Hydroxyprogesterone caproate did not reduce the rate of recurrent preterm birth in a prospective cohort study. Am J Obstet Gynecol 2017;216(6):e600–1.
4. O'Brien JM, Adair CD, Lewis DF, Hall DR, Defranco EA, Fusey S, *et al*. Progesterone vaginal gel for the reduction of recurrent preterm birth: primary results from a randomized, double-blind, placebo-controlled trial. Ultrasound Obstet Gynecol 2007;30(5):687–96.
5. Bittar ER, Yamasaki AA, Sasaki S, Zugaib M. Cervical fetal fibronectina in patients at increased risk for preterm delivery. Am J Obstet Gynecol 1996;175(1):178–81.
6. Cunningham FG, Gant NF, Leveno KJ, Gilstrap III LC, Hauth JC, Wenstrom KD. Preterm and postterm pregnancy and fetal growth retardation. In: Williams' obstetrics. 20th ed. New Jersey: Prentice-Hall International, 1997; p.797–826.
7. Erny R, Pigne A, Prouvost C, Gamerre M, Malet C, Serment H, *et al*. The effects of oral administration of progesterone for premature labor. Am J Obstet Gynecol 1986;154(3):525–9.
8. Check JH, Lee G, Epstein R, Vetter B. Increased rate of preterm deliveries in untreated women with luteal phase deficiencies. Gynecol Obstet Invest 1992;33(3):183–4.
9. Lockwood CJ, Senyei AE, Dischie MR, Casal D, Shah KD, Thug SN, *et al*. Fetal fibronectina in cervical and vaginal secretions as a predictor of preterm delivery. N Engl J Med 1991;325(10):669–74.
10. Michal A, Elovitz, MD, Conjecvarm M. The use of progestational agents for preterm birth: lessons from a mouse model. Am J Obstet Gynecol 2006;195(4):1004–10.
11. Society for Maternal-Fetal Medicine (SMFM) Publications Committee. The choice of progestogen for the prevention of preterm birth in women with singleton pregnancy and prior preterm birth. Am J Obstet Gynecol 2017;216(3):B11–3.
12. Romero R, Yeo L, Miranda J, Hassan SS, Conde-Agudelo A, Chaiworapongsa T. A blueprint for the prevention of preterm birth: vaginal progesterone in women with a short cervix. J Perinat Med 2013;41(1):27–44.
13. Paneth NS. The problem of low birth weight. Future Child 1995;5(1):19–34.
14. Mattison DR, Damus K, Fiore E, Petrini J, Alter C. Preterm delivery: a public health perspective. Paediatr Perinat Epidemiol 2001;15(2):7–16.
15. Creasy RK. Preterm birth prevention: where are we? Am J Obstet Gynecol 1993;168(4):1223–30.
16. Johnson JW, Austin KL, Jones GS, Davis GH, King TM. Efficacy of 17alpha-hydroxyprogesterone caproate in the prevention of premature labor. N Engl J Med 1975;293(14):675–80.

17. Hauth JC, Gilstrap LC 3rd, Brekken AL, Hauth JM. The effect of 17 alpha-hydroxyprogesterone caproate on pregnancy outcome in an active-duty military population. Am J Obstet Gynecol 1983;146(2):187–90.
18. Hobel CJ, Ross MG, Bemis RL, Bragonier JR, Nessim S, Sandhu M, *et al*. The West Los Angeles Preterm Birth Prevention Project. I. Program impact on high-risk women. Am J Obstet Gynecol 1994;170(1 Pt 1):54–62.
19. Fuchs F, Stakemann G. Treatment of threatened premature labor with large doses of progesterone. Am J Obstet Gynecol 1960;79:172–6.
20. Fuchs AR, Fuchs F. Endocrinology of human parturition: a review. Br J Obstet Gynaecol 1984;91(10):948–67.
21. American college of obstetricians and gynaecologists. ACOG committee opinion: use of progesterone to reduce preterm birth. Obstet Gynecol 2003;102(5 Pt 1):1115–6.
22. Rittenberg C, Newman RB, Istwan NB, Rhea DJ, Stanziano GJ. Preterm birth prevention by 17 alpha-hydroxyprogesteronecaproate vs. Daily Nursing Surveillance. J Reprod Med 2009;54(2):47–52.

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