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ORIGINAL ARTICLE

Comparison of vaginal progesterone plus cervical cerclage versus vaginal progesterone alone in reducing preterm birth in high risk women.

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ABSTRACT… Objective: To compare the outcome of vaginal progesterone plus cervical cerclage versus vaginal progesterone alone in reducing preterm birth in high risk women. **Study Design:** Randomized Controlled Trial. **Setting:** Department of Obstetrics and Gynaecology, Bahawal Victoria Hospital, Bahawalpur. **Period:** April 2022 to October 2022. **Material & Methods:** A total of 330 high risk women aged between 18-40 with sonographically short cervix (<25 mm) were included. After randomization, in Group-A (n=165), cervical cerclage was done at 12 weeks and then 200 mg vaginal progesterone was given once daily at night till delivery while in Group-B (n=165) women, 200 mg vaginal progesterone was given once daily at night till delivery. All women were followed up till delivery and outcome (satisfactory/unsatisfactory) was noted. **Results:** In a total of 330 women, the mean age was 29.17±5.29 years while 194 (58.8%) women were aged between 18 to 30 years of age. Satisfactory outcome (no preterm birth in <37 weeks) was seen in 151 (91.5%) women in Group-A (combination of vaginal progesterone plus cervical cerclage) and 102 (61.8%) in Group-B (vaginal progesterone alone, p=0.0001. **Conclusion:** This study concluded that outcome of combination of vaginal progesterone and cervical cerclage is better as compared to progesterone alone in reducing preterm birth among high risk women.

Key words: Cervix, Cervical Cerclage, Delivery, Preterm Labour, Progesterone.

INTRODUCTION

Preterm labor (PTL) is characterized by consistent contractions of uterus that are linked with the changes in the cervix and occur prior to 37 weeks of gestational age.[1] The annual incidence of premature birth is fifteen million, and out of the three million deaths among neonates, its contribution on a yearly basis is estimated around one million.[2] Prematurity is the 2nd most common factor causing death among children aged below 5 years and is the main cause of mortality among neonates.[3]

There are several factors (current multiple gestation, smoking, previous or current PTL, and/or shortened cervix) that are more likely to cause PTL, which might not have been involved in previous premature birth.[4,5] The United States had a 9.5% occurrence rate of PTB in 2014, whereas the live birth information system (SINASC) of Brazil showed a 9.9% occurrence rate in 2012.[2] Preterm birth exists as the leading factor that independently determines the adverse infant outcome in terms as well as in survival and quality of life.[6] About one-third of preterm births occur due to preterm delivery with intact membrane and it results in a 70-80% mortality rate among neonates which are formed normally.[7,8]

Most of the efforts that have been carried out to prevent prematurity have concentrated on treating the symptoms or signs of activation of the biological pathways that lead towards parturition (i.e., increased uterine contractility, preterm cervical ripening, and/or membrane decidual activation).[4-7] Vaginal progesterone administration or cervical cerclage are the two possible interventions that might play a part in

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reducing the occurrence of PTL among women with history of preterm birth (PTB) and cervix length < 25 mm.[4] It has been recently reported that combining vaginal progesterone with pessary has produced good results in reducing the incidence of premature births in twin gestations with a cervical length less than 25mm.[8] Samie MA et al in their study found that there was a 32.0% preterm birth rate in the progesterone only group but 20.0% in the progesterone plus cervical cerclage group.[9]

On searching the literature, we have found very limited as well as no local literature in which adjunctive vaginal progesterone therapy plus cervical cerclage is evaluated in women at high risk to prevent PTB. So, we decided to conduct this study to compare the outcome of vaginal progesterone plus cervical cerclage intervention versus vaginal progesterone only in high-risk women.

MATERIAL & METHODS

This randomized controlled trial was carried out at the outpatient department of Obstetrics and Gynaecology, Bahawal Victoria Hospital, Bahawalpur, Pakistan, from April 2022 to October 2022. A sample size of 330 was calculated (165 in each group), considering the percentage of preterm delivery as 32.0% in the vaginal progesterone group and 20.0% in the progesterone plus cervical cerclage group,9 with a 5% level of significance and 80% power of the study. Simple random sampling technique was adopted.

Inclusion criteria were females of 18-40 years of age, at high risk, having a singleton pregnancy of gestational age ≤20 weeks (assessed on last menstrual period) and a sonographic transvaginal scan (TVS) showing short cervix (<25 mm) at 12 weeks. Exclusion criteria were antepartum hemorrhage (assessed on history and clinical examination), pregnancy-induced hypertension or gestational diabetes mellitus, antiphospholipid syndrome, and / or congenital fetal malformations. Any of the couples with chromosomal abnormalities were also excluded. All women with a previous history of PTB were considered to be at high risk. Birth before 37 complete weeks of gestation was labeled as PTB. Informed and written consent were obtained. Approval from the "Institutional Ethical Committee" was also taken (letter number:2141).

At the time of enrollment, socio-demographic and clinical characteristics were documented. All study patients with PTL were provided mixed slips (half of the slips contained the letter 'A' and the remaining half contained the letter 'B'). Groups were allocated according to the pick of their slips. In Group-A, cervical cerclage was done at 12 weeks, and then 200 mg vaginal progesterone was given once daily at night till delivery, while in Group-B patients, 200 mg vaginal progesterone was given once daily at night till delivery. Researchers followed both groups by themselves until delivery and recorded the outcome as satisfactory or unsatisfactory. If there was no PTB, the outcome was taken as satisfactory or otherwise (unsatisfactory). All data was noted a customized proforma.

Statistical analysis was done using "Statistical Package for Social Sciences (SPSS)", version 26.0. Quantitative variables like age, gestational age, parity, and cervical length were represented as mean and standard deviation (SD). Qualitative variables such as place of living and outcome were described by frequency and percentages. Chi-square test was used to compare the outcome between both groups. Stratification was done for age, gestational age, parity, cervical length and place of living (rural/urban). Post-stratification chi-square was applied taking $p<0.05$ as significant.

RESULTS

In this study, the mean age was 29.17±5.29 years. There were 194 (58.8%) women aged between 18 to 30 years. The mean gestational age was 14.11±2.43 weeks while 245 (74.2%) women were between 13 to 20 weeks of gestation. The mean parity was 2.4 ±0.78. The mean cervical length was 16.25±3.92 cm. Comparison of baseline charactersitics of women in both study groups is shown in Table-I.

Table-II shown comparison of outcome (no

preterm birth in <37 weeks) and it was seen that in 151 (91.5%) women in Group-A (combination of vaginal progesterone plus cervical cerclage) and 102 (61.8%) in Group-B (vaginal progesterone alone), p=0.0001 (Table-II).

Stratification of outcome between two groups with respect to baseline characteristics is shown in Table-III.

Characteristics		Total (n=330)	Group-A (n=165)	Group-B (n=165)	P-Value
Age (years)	18-30	194(58.7%)	94(56.9%)	100(60.6%)	0.502
	31-40	136(41.3%)	71(43.1%)	65(39.4%)	
Gestational age (weeks)	≤12 weeks	85(25.7%)	44(26.6%)	41(24.8%)	0.706
	13-20 weeks	245(74.3%)	121(73.4%)	124(75.2%)	
Parity	0-2	163(49.3%)	85(51.5%)	78(47.2%)	0.441
	>2	167(50.7%)	80(48.5%)	87(58.8%)	
Cervical length (cm)	≤12 cm	48(14.5%)	25(15.1%)	23(13.9%)	0.755
	13-24 cm	282(85.5%)	140(84.9%)	142(86.1%)	
Place of living	Rural	117(35.4%)	61(36.9%)	56(33.9%)	0.565
	Urban	213(64.6%)	104(63.1%)	109(66.1%)	

Table-I. Comparison of baseline characteristics of women in both study groups
Group-A: Combination of vaginal progesterone plus cervical cerclage; Group-B Vaginal progesterone alone.

Outcomes	Group-A (n=165)	Group-B (n=165)	P-Value
Satisfactory	151(91.5%)	102(61.8%)	0.0001
Unsatisfactory	14(8.5%)	63(38.2%)	

Table-II. Comparison of outcome both groups (N=330)
Group-A: Combination of vaginal progesterone plus cervical cerclage; Group-B Vaginal progesterone alone

Characteristics		Groups	Outcome		P-Value
			Satisfactory	Unsatisfactory	
Age (years)	18-30	Group-A	85 (90.4%)	9 (9.6%)	0.0001
		Group-B	51 (51.0%)	49 (49.0%)	
	31-40	Group-A	66 (92.9%)	5 (7.1%)	0.015
		Group-B	51 (78.4%)	14 (21.6%)	
Gestational age (weeks)	≤12 weeks	Group-A	44(100%)	0(0%)	0.0001
		Group-B	28(68.2%)	13(31.8%)	
	13-20 weeks	Group-A	107(88.4%)	14(11.6%)	0.0001
		Group-B	74(59.6%)	50(40.4%)	
Parity	0-2	Group-A	76(89.4%)	9(10.6%)	0.0001
		Group-B	22(28.2%)	56(71.8%)	
	>2	Group-A	75(93.7%)	5(6.3%)	0.654
		Group-B	80(91.9%)	7(8.1%)	
Cervical length (cm)	≤12 cm	Group-A	25(100%)	0(0%)	0.006
		Group-B	17(73.9%)	6(26.1%)	
	13-24 cm	Group-A	126(90%)	14(10%)	0.0001
		Group-B	85(59.8%)	5740.2%)	
Place of living	Rural	Group-A	52(85.2%)	9(14.8%)	0.003
		Group-B	34(60.7%)	22(39.3%)	
	Urban	Group-A	99(95.1%)	5(4.9%)	0.0001
		Group-B	68(63.5%)	41(36.5%)	

Table-III Stratification of Baseline Characteristics of Women with respect to Outcomes in Both Study Groups (N=330)
Group-A: Combination of vaginal progesterone plus cervical cerclage; Group-B Vaginal progesterone alone

DISCUSSION

Although, for years, clinicians and reproductive biologists have focused on detecting increased uterine contractility and the evidence that has emerged on the basis of clinical and laboratory findings suggests that for the identification and prevention of premature births among patients at risk, multiple techniques might be developed by focusing on the uterine cervix.[10,11] Data for 2 meta-analysis revealed that the effectiveness of progesterone, cervical cerclage, and cervical pessary is comparable to placebo or standard care in reducing PTB for those women who are at risk.[12,13]

According to our study, satisfactory outcome (no preterm birth in <37 weeks) was seen in 91.5% of patients in combination of vaginal progesterone plus cervical cerclage group versus 61.8% with vaginal progesterone alone (p=0.0001). Data from different randomized clinical trials[14,15] and from another study revealed that among those women who had a sonographically short cervix, the rate of premature birth and neonatal morbidity or mortality decreased using vaginal progesterone.[16] Usually, the use of cervical cerclage is opted for those women who have acute cervical insufficiency[17,18], and probably in a few patients who have a previous history of premature birth and a sonographically short cervix of <25mm.[19,20] Hence, vaginal progesterone administration and a cervical cerclage are seemingly the two interventions that reduce the incidence of premature birth in those patients who have a previous history of preterm delivery and a cervix of <25mm. Global bodies have endorsed that among cases of singleton pregnancy with history of spontaneous premature birth and cervical length below 25 mm prior to 24th weeks might be managed through cervical cerclage.[21,22]

Some researcher have suggested that the risk of premature delivery at and perinatal morbidity and mortality were significantly reduced among women who had cervical cerclage.[23] On the other hand, another meta-analysis manifested a major decrease in PTB risk and composite neonatal morbidity and mortality with vaginal progesterone among high risk women.[16]

The women having a history of pregnancy losses in mid-trimester due to cervical insufficiency, are more likely to be treated with cervical cerclage while replacing cervical cerclage with progesterone is not advocated as having additional advantages for women.[25] A randomized trial was carried out for a secondary analysis to evaluate cerclage and showed that a similar incidence of birth prior to 35th week of gestation was noted between women having a previous history of spontaneous premature delivery, a short cervix (≤ 25 mm), and a cerclage and the women who were not served with progesterone supplementation.[24] Berghella et al also described in their meta-analysis that cerclage was advantageous for those women who had a singleton pregnancy, a short cervix, and a previous history of preterm delivery.[25]

CONCLUSION

This study concluded that outcome of combination of vaginal progesterone and cervical cerclage is better as compared to progesterone alone in reducing preterm birth among high risk women.

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2	Rukhsana Aziz	Data collection, Drafting.	
3	Tahira Nazir	Data Collection, Assembly of data.	
4	Khadija Sundas	Data collection, Data analysis.	
5	Ayesha Amin	Literature review, Discussion.	
6	Abdul Ahad	Literature review, References.