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The Effects of Vaginal Probiotic Administration on Perinatal Outcomes in Patients with Premature Preterm Rupture of Membrane

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Abstract

Background: Preterm premature rupture of membrane (PPROM) is the rupture of fetal membrane before 37 weeks of gestation.

Objectives: The aim of the current study was to assess the effects of vaginal probiotic administration on perinatal outcomes in patients with PPROM.

Methods: Sixty pregnant women with PPROM were randomly divided into two groups (n=30). In the first group, in the first 48 hours of hospitalization, 2 gr of intravenous ampicillin and 500-mg amoxicillin capsules were administered for five days. In the second group, the patients received one vaginal probiotic supplement for ten days in addition to receiving an antibiotic treatment similar to the first group. Finally, the perinatal outcomes were examined.

Results: NICU hospitalization was significantly lower in the second group than in the first group (P<0.05). The Apgar scores 1 and 5 minutes after birth and the newborns' weight at birth were higher in the second group than in the first group (P<0.05). Pregnancy duration was longer in the second group than in the first group (P<0.05).

Conclusion: The results of this study showed that the administration of vaginal probiotics in PPROM patients may be effective in delaying childbirth and reducing neonatal complications.

Keywords: Probiotic, Vaginal, Preterm premature rupture of membrane

Abbreviations: PPROM: Preterm Premature Rupture of Membrane; TNF-α: Tumor Necrosis Factor Alpha; IL -6: Interleukin 6

Introduction

Preterm premature rupture of membrane is the rupture of the chorionic-amniotic membrane and leakage of amniotic fluid before the onset of labor pains and prior to the 37th week of pregnancy. Preterm premature rupture of membrane (PPROM) occurs in 3% of pregnancies and is the cause of about 25 to 30% of all preterm births [1]. PPROM is an important contributor to perinatal morbidity [2]. One of the reasons for the importance of PPROM is its association with the short interval between the rupture of the membranes and delivery. This issue is very important due to the birth of premature infants in patients

with PPROM [3]. During the interval between the rupture of the amniotic sac and delivery, the probability of pathogenic microorganisms ascending from the vagina to the amniotic cavity increases and is thought to play a role in increasing intrauterine infection [4-6].

Probiotics are non-pathogenic living microorganisms that have beneficial effects on human health. It has been previously shown that probiotics can play a protective role against genital infections and regulate the microbial flora of the vagina [7,8]. Researchers have turned their attention to a better understanding of the effects of probiotics on the immune system [9]. Probiotics are used to treat diseases principally due to their role in immune system modulation and their anti-inflammatory effects. Probiotics reduce the expression of pro-inflammatory cytokines such as tumor necrosis factor alpha (TNF-α) and interleukin 6 (IL-6) [10]. The goal of the current study was to investigate the effects of vaginal probiotic administration on perinatal outcomes in women with PPROM.

Materials and Methods

This study was performed from September 2020 to September 2021 on 60 pregnant women with PPROM who had a gestational age of 28-34 weeks and attended the perinatal care clinic of Besat Hospital, Sanandaj, Iran. The study protocol was approved by the Ethics Committee of Kurdistan University of Medical Sciences.

A total of sixty pregnant women with PPROM were randomly divided into two groups. In the first group (n=30) (administration of antibiotics), in the first 48 hours of hospitalization, 2 gm of intravenous ampicillin (Farabi Pharmaceutical Company, Tehran, Iran) was administered every 6 hours. Then, 500 mg amoxicillin capsules (Farabi Pharmaceutical Company, Tehran, Iran) were administered every 8 hours for five days. In addition to receiving an antibiotic treatment similar to the first group, the patients in the second group (n=30) received one vaginal probiotic supplement (Zist Takhmir Pharmaceutical Company, Tehran, Iran) for ten days. In both groups, two doses of betamethasone (Farabi Pharmaceutical Company, Tehran, Iran) 12 mg were injected intramuscularly with an interval of 24 hours. Careful monitoring of maternal vital signs and fetal health assessment were performed with sonography (twice a week) and cell blood count (daily).

Also pre-pregnancy body mass index (BMI) [kg/m^2, median (range)], Age (year), Apgar score: 1 minute, Apgar score: 5 minutes, Weight of the newborn (gr), Hospitalization in NICU (day), Respiratory distress syndrome, weight of the newborn infants, and Newborn sepsis patients in different study were recorded.

Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) statistical software (version: 22). The quantitative variables were presented as the mean ± standard deviation. The two groups were compared using the chi-square test for the categorical data and the Student's t-test for the continuous parameters.

Results

Sixty patients with PPROM were included. The mean and standard deviation of the body mass index (BMI) in the first group were 25.02 and 2.13, respectively, whereas, in the second group, they were 27.24 and 1.45, respectively. No significant difference was observed between the two groups (P=0.93). The mean and standard deviation of age in the first group were 28.70 and 5.39, respectively, whereas, in the second group, they were 29.33 and 4.53, respectively. No significant difference was observed between the two groups (P=0.62) (**Table 1**).

The mean and standard deviation of the Apgar score (1 minute) in the first group were 7.96 and 0.99, respectively. They were significantly different from those of the second group (mean=8.23, SD=0.93) (P=0.02). The mean and standard deviation of the Apgar score (5 minutes) in the first group were 9.46 and 0.93, respectively. They were significantly different from those of the second group (mean=9.73, SD=0.78) (P=0.01) (**Table 1**). The mean and standard deviation of the weight of the newborn infants in the first group were 2170.33 gm and 380.74, respectively. They were not significantly different from those of the second group (mean=2368.33, SD=396.11) (P=0.02) (**Table 1**). The mean and standard deviation of NICU hospitalization in the first group were 10.73 and 4.79, respectively. They were significantly different from those of the second group (mean=7.96, SD=1.91) (P=0.02) (**Table 1**). The mean and standard deviation of hospitalization duration after intervention in the first group were 1.18 and 2.04, respectively. They were significantly different from those of the second group (mean=2.85, SD=1.22) (P=0.001). The mean and standard deviation of gestational age in the first group were 30.53 and 2.16, respectively. They were not significantly different from those of the second group (mean=29.88, SD=1.87) (P=0.21) (**Table 1**). The mean and standard deviation of the age of delivery in the first group were 31.71 and 2.80, respectively. They were not significantly different from those of the second group (mean=32.73, SD=1.76) (P=0.09) (**Table 1**).

The respiratory distress syndrome was lower in the second group (40.0%) than in the first group (56.7%). However, this difference was not statistically significant (P=0.19) (**Table 2**). In addition, neonatal sepsis in the second group (20.0%) was lower than that in the first group (26.7%). Nevertheless, this difference was not statistically significant (P=0.76) (**Table 3**).

Table 1: Complications of the study population in different groups.

	groups	Mean	Std. Deviation	F	Sig. (2-tailed)
Prepregnancy body mass index (BMI) [kg/m², median (range)]	Group 1	25.02	2.13	4.46	0.93
	Group 2	27.24	1.45		
Age (year)	Group 1	28.70	5.39	1.04	0.62
	Group 2	29.33	4.53		
Apgar score; 1 minutes	Group 1	7.96	0.99	1.29	0.02
	Group 2	8.23	0.93		
Apgar score; 5 minutes	Group 1	9.46	0.93	2.47	0.01
	Group 2	9.73	0.78		
Weight of the newborn (gr)	Group 1	2170.33	380.74	0.009	0.33
	Group 2	2268.33	396.11		
Hospitalization in NICU (day)	Group 1	10.73	4.79	15.19	0.02
	Group 2	7.96	1.91		
Duration of hospitalization after intervention (days)	Group 1	1.18	2.04	0.32	0.001
	Group 2	2.85	1.22		
Gestational age (week)	Group 1	30.53	2.16	0.17	0.21
	Group 2	29.88	1.87		
Age of delivery (week)	Group 1	31.71	2.80	0.99	0.09
	Group 2	32.73	1.76		

Group 1: PPROM+antibiotic therapy. Group 2: PPROM+antibiotic therapy+vaginal probiotic.

Independent Samples Test. P value less than 0.05 was considered significant level.

BMI: Body Mass Index. NICU: Newborn Intensive Care Unit

Table 2: Percentage of respiratory distress syndrome in the study groups.

	Respiratory distress syndrome		No	Yes	total	Value	Asymptotic Significance (2-sided)
group	Group 1	Count	13	17	30		
		% within group	43.3%	56.7%	100.0%		
	Group 1	Count	18	12	30		
		% within group	60.0%	40.0%	100.0%		
Total		Count	31	29	60	1.66	0.19
		% within group	51.7%	48.3%	100.0%		

Group 1: PPROM+antibiotic therapy. Group 2: PPROM+antibiotic therapy+vaginal probiotic.

Chi-Square Tests. P value less than 0.05 was considered significant level.

Table 3: Percentage of newborn sepsis in the study groups.

	Newborn sepsis		No	Yes	Total	Value	Asymptotic Significance (2-sided)
Group	Group 1	Count	22	8	30		
		% within group	73.3%	26.7%	100.0%		
	Group 2	Count	24	6	30		
		% within group	80.0%	20.0%	100.0%		
Total		Count	46	14	60	0.37	0.76
		% within group	76.7%	23.3%	100.0%		

Group 1: PPROM+antibiotic therapy. Group 2: PPROM+antibiotic therapy+vaginal probiotic.

Chi-Square Tests. P value less than 0.05 was considered significant level.

Discussion

The results showed that vaginal probiotic administration combined with antibiotic treatment in mothers with PPROM can be effective in delaying delivery and reducing the duration of NICU hospitalization. The Apgar scores at 1 and 5 minutes as well as the infant weight at birth were higher in the probiotic group.

In our study, the gestational age at delivery and the latency period were higher in the study group than in the control group. Delaying the time between PPROM and delivery is a key to reducing the complications of pregnancy and perinatal mortality. Therefore, it seems that increasing this period can help the management of PPROM [11]. In the study of Baldacci *et al*., the vaginal infusion of probiotic supplements increased the delivery gestational age compared to the group receiving routine treatment [12]. Our results showed that the administration of probiotics increased the Apgar scores 1 and 5 minutes after birth. PPROM is one of the most common complications in pregnant women and can affect the infant Apgar score [13-15]. Our results showed that the administration of probiotics increased the weight of newborns compared with the control group. The reason for this weight gain was the delay in delivery, providing more time for the fetus to develop [16]. Kavak et al. reported that the weight of the newborns in women with PPROM who were given both probiotics and antibiotics was higher than that of women who were only given antibiotics [17]. In the current study, there was a statistically significant difference between the two groups in terms of NICU hospitalization after delivery so that the duration of hospitalization in the NICU was shorter in the group that was given probiotics. Related to the previous study the premature rupture of membranes (PROM) increases the risk of neonatal complications by up to 75%. In addition, a prolonged NICU hospitalization is associated with adverse outcomes for the infant. Similar to our results, Afrasiabi reported that there was a significant relationship between the infant's length of NICU hospitalization and maternal PROM [18]. In addition, the results related to respiratory distress syndrome and neonatal sepsis did not have a statistically significant difference between the two studied groups.

Conclusions

One of the most important challenges in obstetrics and gynecology is the prevention of preterm birth. The administration of antibiotics in pregnant women may cause another disorder in the mother and fetus. Therefore, the study of effective alternative therapies with fewer side effects (such as probiotics) can be valuable in improving perinatal outcomes in women with PPROM. The results of this study showed that the administration of vaginal probiotics in PPROM patients may be effective in delaying childbirth and reducing neonatal complications.

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Conflict of Interest Statement

The authors declare that they have no competing interests.

Authors' Contributions

Fereshteh Kahvazi, Nasrin Soufizadeh, Shamsi Zare, Fariba Seyedoshohadaei, Khaled Rahmani, and Kaveh Rahimi participated in the study design, methodological issues, analysis, interpretation of the study, and writing of manuscript.

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