

Original Article

Benefits of probiotic treatment in cases of bad obstetric history (BOH) and for prevention of post IVF pregnancy complications

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Abstract

Objectives: To study the benefits of probiotics (application of urogenital probiotic strains, Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri RC-14) in cases of bad obstetric history (BOH) while preventing the post IVF pregnancy complications. **Methods:** This study was carried out from January 2006 to July 2007. The study groups of 70 pregnant women were treated with probiotics (application of urogenital probiotic strains, Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri RC – 14) along with treatment for infertility; and were compared with similar number of 70 cases from control group who were not given probiotics but were treated for infertility earlier i.e. before January 2006. **Results:** The control group witnessed 44 cases (63%) that delivered successfully and fetal loss in 26 cases (37%). From the study group 56 cases (80%) delivered successfully, while 14 cases (20%) suffered fetal loss. The ratios suggest that the rate of delivery and fetal loss in the study group is statistically significant (P value is 0.0031) when compared with that of the control group. **Conclusions:** Probiotics (application of urogenital strains Lactobacillus rhamnosus GR – 1 and Lactobacillus reuteri RC-14) has a definite role to play in cases of BOH. It helps in improving the vaginal flora by restoring the lactobacillus colonies and vaginal pH, thereby removing the anaerobic bacteria. It also prevents ascending infection, improves vaginal mucosal immunity and helps in safe deliveries.

Key words: urogenital probiotics, bad obstetric history, bacterial vaginosis.

Introduction

The commonest cause of leucorrhoea in women worldwide is bacterial vaginosis, secondary to poor personal hygiene. This condition is associated with infertility and also fetal wastages like missed abortion, spontaneous abortion^{1,2,4}, preterm delivery¹⁻³ and increased incidence of neonatal mortality and morbidity.

Infection occurs in spite of the natural defense mechanism present in the vulva, vagina, cervix and uterus; the natural protection in the vulva being the secretion of the apocrine gland (undecylenic acid) which is fungicidal and the closure of the introitus by the labia which protects the genital tract above. The vagina protects itself by its acidic pH, stratified columnar epithelium, gram positive anaerobic lactobacillus, antibodies produced by the mucosal immune response as also by the apposition of the anterior and posterior wall. The cervical mucous plug and the periodic shedding of the surface endometrium, during menstruation act as bacteriolytics. Bacterial vaginosis is said to occur when any of the natural protective mechanism is breached apart from hormonal changes and promiscuity. In spite of the above facts, pathogenesis and sequelae, there is still lacunae in the

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etiology of bacterial vaginosis and its repeated recurrence in the same individual.

Methods

The study groups of 70 subjects treated with probiotics were compared with similar number of 70 cases from retrospective control group who were not given probiotics. All the cases in the study group as well as the control group were treated for infertility. A detailed history was taken from all the cases of both the groups. The history included age and years of married life and a detailed history of BOH and interventions in the past. The study group consisted 10 cases of chronic leucorrhoea, 10 with pre-term labor, 20 with severe BOH and 30 who undergone cervical cerclage. In the control group there were 16 cases with chronic leucorrhoea, 28 with preterm labor, 24 with severe BOH and two who had undergone cervical cerclage (refer to table 1), establishing the fact that the two groups were statistically comparable. Z-test has been used for testing the significant difference between the ratios. These cases were followed by diagnostic laparoscopy for tubal patency and pelvic pathology after taking a vaginal swab for gram staining (Nugent scoring) to study the bacterial flora. The wet preparation of swab specimen was subjected to gram staining for identification of gram positive bacillus. Infertile patients were treated with a course of antibiotics to eliminate Chlamydia and Mycoplasma. Serology for HIV, HbsAg and STS was included. The period of treatment for infertility in the study group and control group varied from three months to five years. The positive pregnancies were taken during January 2006 – July 2007 with retrospective

comparison. The case of BOH included chronic leucorrhoea, premature labor, repeated pregnancy loss, and cervical os incompetence, for which cerclage was performed at 15-16 weeks of gestation. All the subjects in the trial group were given a probiotic of choice, in a dose of two capsules OD in the first 30 days followed by one capsule OD for the next 30 days with informed consent. The treatment of infertility in both the groups varied from diagnostic laparoscopy to male seminal analysis and induction of ovulation followed by IUI or IVF.

Results

All the subjects in the study group had wet vaginal preparation and gram staining for bacterial vaginosis done on days 0, 15, 30 and 60. All the subjects were given urogenital probiotic stains Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri RC-14 for three months and the results were studied. The study included a wet smear preparation of vaginal flora every 15 days to see the difference followed by successful childbirth. In the study group a gradual increase in the numbers of gram positive bacillus was observed on the smears done on days 15, 30 and 60 (please refer to table 2). The vaginal smear taken every 15 days showed a vast difference from anaerobic bacteria to normal vaginal flora. Thus there was a shift in vaginal pH from alkaline to normal acidic pH, whereas in the control group all the cases showed 85% gram negative rods. In the study group 56 cases (80%) had successful delivery and 14 cases (20%) ended in fetal loss. In the control group 44 cases (63%) delivered, and 26 cases (37%) experienced fetal loss (please refer to table 3).

Table 1. Outcomes based on the risk factor.

S.No.	Risk factor	Study group		Control group		P-value
		No. of cases	%	No. of cases	%	
1	Chronic leucorrhoea	10 (8)	80%	16 (8)	75%	0.432 ^a
2	Preterm labor	10 (6)	60%	28 (18)	64%	0.323 ^b
3	Severe BOH	20 (16)	80%	24 (12)	50%	0.07 ^c
4	After os tightening	30 (26)	87%	2 (2)	100%	-
	Total	70 (56)	80%	70 (44)	63%	

Figures in parenthesis represent the risk count

^aNot significant, ^bNot significant, ^cNot significant

Table 2. Nugent scoring outcome of the study group.

Number of subjects	Days	Gram positive bacteria	Gram negative bacteria
n=70	Day 0	33%	67%
	Day 15	51%	49%
	Day 30	77%	23%
	Day 60	93%	7%

Table 3. Pregnancy outcome between the study group and the control group.

Pregnancy outcome	Study group	Control group	P value		
	No. of cases	%	No. of cases	%	
Delivered	56	80%	44	63%	0.0031 ^a
Expelled (Fetal loss)	14	20%	26	37%	0.0031 ^b

^{a,b} Significant

Chi-square test was used to test the difference between the proportions of pregnancy outcome in the study group and control group. The proportion between delivery rates of the patients who were treated with probiotics is statistically higher than that in the patients who were not treated with probiotics. ($\chi^2=4.24$, $p<0.05$).

Backward conditional logistic regression was performed to identify the significant factor which is responsible for pregnancy outcome. The probiotic treatment plays a significant role factor for pregnancy outcome. (AOR =2.721, 95% C.I. (1.232, 6.011)). The study has more than 80% power. Maternal age, paternal age, age of the husband, duration of marriage and risk factors such as chronic leucorrhea, preterm labor, severe BOH and after the case of os tightening are not found to be significant.

Discussion

Bacterial vaginosis, a polymicrobial condition, decreases the concentration of Lactobacillus and vaginal acidity, leading to an increase in the concentration of vaginal microorganisms. There are a multitude of organisms involved apart from the commonest infection of Chlamydia and Mycoplasma, like gardnerella, bacteriocides, peptostreptococcus and trichomonas. The incidence of vaginitis varies in different populations at different periods of their

reproductive life, promiscuity and associated diseases like diabetes mellitus. At our centre, we generally initiate our infertility therapy with an antibiotic course for the couple in order to eliminate basic urogenital pathogens. This by itself has promoted conception. With the advent of drug resistance / microbial resistance and inappropriate hygienic measures, pregnancy losses have been on the rise despite preventive therapy. In such circumstances a drug which would help modify the existing flora and also prevent any ascending infections is a boon. In our trial, there were no adverse effects experienced by the patients or any drug related malformations to the fetus. We are still continuing to use the above mentioned probiotics in the indicated groups and would perhaps be able to publish wider data soon.

Conclusion

It is well known that the lower genital tract harbors plenty of bacteria which become pathogenic as the body resistance is lost. This definitely leads to infertility, fetal wastage and premature labor. Our study proves that probiotics used in selected cases brings back the normal vaginal epithelium thereby increasing the resistance to pathogenic bacteria and preventing fetal loss. We have now further included probiotics to patients with bad obstetrics history (BOH) and early pregnancy with

threatened abortion. Every patient who undergoes cervical os tightening has probiotics added for three months.

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