

Research Article

Probiotic Supplements do not Increase the Effectiveness of Antibiotics in the Treatment of Bacterial Vaginosis

Suplemen Probiotik tidak Meningkatkan Efektivitas Antibiotik dalam Terapi Bakterial Vaginosis

Ratnah Hamid, Eddy Tiro, Josephine Tumedia

Department of Obstetrics and Gynecology
Faculty of Medicine University of Hasanuddin/
Dr. Wahidin Sudirohusodo Hospital
Makassar

Abstract

Objective: This study aims to assess the effect of the addition of probiotic supplement to the standard therapy on the recovery of Bacterial vaginosis infection.

Methods: The research was conducted by taking samples from Obstetrics and Gynecology Department in several teaching hospitals of Faculty of Medicine, Hasanuddin University. This study was an experimental study. Consecutive sampling was conducted on 50 samples, which were then divided into two groups. Group 1 received Metronidazol therapy 2 times a day for 7 days, while group 2 received Metronidazol therapy 2 times a day supplemented with oral Probiotic of once a day for 7 days. The data were analysed by using the chi-square test.

Results: There is no significant difference in the recovery of bacterial vaginosis infection between the group that received the probiotic supplementation and the group that did not.

Conclusion: The addition of probiotic supplement to the standard therapy of BV infection does not show any significant effect.

[Indones J Obstet Gynecol 2013; 1-4: 194-8]

Keyword: bacterial vaginosis, probiotic supplement, recovery, standard therapy

Correspondence: Ratnah Hamid. BTP blok M/263, Makassar. Telephone: 0812-42209996. Email: annah_zms@yahoo.co.id

Abstrak

Tujuan: Penelitian ini bertujuan untuk menilai efek suplemen probiotik bersama terapi standar terhadap penyembuhan Bakterial vaginosis.

Metode: Penelitian ini dilakukan dengan mengambil sampel penelitian di beberapa rumah sakit pendidikan Bagian Obstetri dan Ginekologi Fakultas Kedokteran Universitas Hasanuddin. Metode penelitian yang digunakan dalam penelitian ini adalah uji klinis. Dilakukan consecutive sampling terhadap 50 sampel yang terbagi atas dua kelompok, yaitu kelompok 1 yang mendapat terapi Metronidazol oral 2 x sehari selama 7 hari, sedang kelompok 2 diberikan terapi Metronidazol 2 x sehari ditambahkan dengan Probiotik oral 1 x sehari selama 7 hari. Data dianalisis dengan menggunakan uji Chi-Square.

Hasil: Hasil penelitian ini menunjukkan tidak ada perbedaan yang signifikan dari efek penambahan probiotik pada terapi standar terhadap Bakterial vaginosis ($p > 0,05$).

Kesimpulan: Penambahan probiotik pada terapi standar tidak menunjukkan efek terhadap penyembuhan Bakterial vaginosis.

[Maj Obstet Ginekol Indones 2013; 1-4: 194-8]

Kata kunci: bacterial vaginosis, penyembuhan, suplemen probiotik, terapi standar

INTRODUCTION

Bacterial vaginosis (BV) is the most common infection in vagina. BV is also the most common cause of the abundant vaginal secret. BV could cause abnormal vaginal secret, itchy sensation and foul smell.^{1,2}

Clinical criteria used for diagnosing bacterial vaginosis is the Amsel criteria, ie vaginal pH > 4.5, the existence of a homogeneous vaginal discharge, the occurrence of fishy odor after application of KOH (potassium hydroxide) to the vaginal secret, and the presence of clue cells on microscopic examination. The diagnosis of BV is made when at least three out those four criteria are fulfilled.²

Bacterial vaginosis usually occurs due to an imbalance of the normal vaginal microorganisms population. Lactobacilli bacteria is found to be reduced while other microorganism, Gardnerella vaginalis, increase. The main therapy for Bacterial vaginosis is metronidazole 500 mg, given 2 times a day for 7 days. However, treatment with antibiotics can be followed with the incidence of recurrent Bacterial vaginosis and resistance to the antibiotic. Therefore, we need to try finding other alternatives as therapy. One of the proposed alternative is using probiotics to restore the normal population of Lactobacilli in vagina.³⁻⁵ The use of probiotics can be also used as a preventive ther-

apy against bacterial vaginosis, where probiotics can restore normal vaginal flora.⁵ Several studies have also reported that probiotics can be an alternative as a substitute for antibiotics.⁶

Many studies showed that the H₂O₂ produced by vaginal lactobacilli can prevent Bacterial vaginosis, although some other studies do not support this hypothesis. The use of probiotics for the prevention and treatment of infection has a strong foundation and relatively safe, especially for Bacterial Vaginosis. Side effects from the use of probiotics is rarely found, and even if found, it tends to be a mild gastrointestinal complaints.^{7,8}

In the study conducted by Falagas et al, it was reported that the use of probiotics is an effective element in the treatment and prevention of bacterial vaginosis. Study demonstrated a significant relationship between low concentrations of vaginal lactobacilli and the incidence of Bacterial vaginosis. The in-vitro study showed that certain strains of Lactobacilli can inhibit the development of *Gardnella vaginalis* in vaginal epithelium and the production of H₂O₂ and lactic acid can inhibit the growth of bacteria that can cause bacterial vaginosis.⁸

Based on this background, we found that it is necessary to conduct a clinical trial on the effects of probiotic supplementation with standard therapy in the recovery of bacterial vaginosis.

METHOD

The research was conducted by taking samples from Obstetrics and Gynecology Department in several teaching hospitals of Faculty of Medicine, Hasanuddin University. This study was an experimental study. Consecutive sampling was conducted on 50 subjects who fulfilled the inclusion criteria, which were then divided into two groups. Group 1 received Metronidazol therapy 2 times a day for 7 days, while group 2 received Metronidazol therapy 2 times a day supplemented with oral Probiotic of once a day for 7 days. The data were analysed by using the chi-square test.

RESULT

This study was performed on 50 women with complaints of vaginal discharge that met the inclusion criteria. The subjects were divided into 2 groups. Group 1 consisted of 25 patients who received standard therapy and group 2 consisted of 25 people who received standard therapy and a probiotic

supplement. The subject assignment into these two groups were performed randomly.

Characteristics of the samples include maternal age, parity, maternal education, and maternal employment. Basic characteristics of the study sample was obtained from the value of a statistical description of which is illustrated by the number of each variable, as can be seen in the Table 1.

Table 1. The Characteristic of the Subject

Variable	Metronidazole only group		Metronidazole + probiotic group	
	(n=25)	%	(n=25)	%
Age				
20 - 30	5	20	5	20
31 - 40	20	80	20	80
Parity				
0	4	16	2	8
1	5	20	1	4
2	5	20	7	28
3	2	8	4	16
≥ 4	9	36	11	44
Education				
Junior high school	5	20	4	16
Senior high school	15	60	18	72
College graduate	5	20	3	12
Occupation				
Housewife	17	68	15	60
Entrepreneur	6	24	6	24
Public officer	2	8	4	16

Table 1 shows that most subjects were in the age group of 31-40 years (80%) in both group 1 and group 2. Most subjects had given birth ≥ 4 times, as many as 9 subjects (36%) in group I and 11 subjects (44%) in group II. The majority of subjects were graduated from senior high school. The most common occupation was housewife.

Before therapy, the homogenous vaginal secret was found in all subjects in both groups. After therapy, there was only 6 people (24%) in group 1 who were still positive and 4 people (16%) in group 2 who were stil positive. Based on the statistical test, we found that there was no significant differences regarding the presence of vaginal discharge after treatment in both groups ($p > 0.05$).

From the examination of KOH test, there were 18 people (72%) tested positive in group 1 and 19 people (76%) in Group 2. Based on statistical tests of the two groups obtained p values > 0.05 , meaning that there was no significant difference in the examination of KOH test prior to therapy. After therapy, 11 subjects (61.1 %) were tested negative

Table 2. The Examination of Amsel Criteria before and after Therapy in both Group

Amsel criteria	Before therapy				p	After therapy				p
	Metronidazole+		Metronidazole +			Metronidazole +		Metronidazole +		
	n	%	n	%		n	%	n	%	
Vaginal secret										
Positive	25	100	25	100	*	6	24	4	16	0.48
Negative	0	0	0	0		19	76	21	84	
Snif (KOH) test										
Positive	18	72	19	76	0.747	7	38.90	6	31.50	0.642
Negative	7	28	6	24		11	61.10	13	68.50	
Vaginal pH										
Positive	17	68	20	80	0.333	5	29.40	9	45	0.33
Negative	8	32	5	20		12	70.60	11	55	
Clue cells										
Positive	19	76	16	64	0.424	9	47.40	6	37.50	0.557
Negative	6	24	9	36		10	52.69	10	62.50	

Note: * : No statistics are computed because variable is a constant
p: Pearson Chi-Square test

in group 1, while 13 subjects (68.5 %) were tested negative in group 2. There was no significant difference in the examination of KOH test after treatment in both groups.

From the examination of vaginal pH, there were 17 subjects (68%) tested positive in group 1 and 20 subjects (80%) tested positive in group 2. Then after therapy 12 subjects (70.6%) were tested negative in group 1 and 11 subjects (55%) were negative. Based on statistical tests found no significant differences in the pH of the vaginal examination after therapy in both groups with $p > 0.05$

From the examination of clue cells, there were 19 subjects (76%) tested positive in group 1 and 16 subjects (64%) in group 2. After therapy there were 10 people (52.6%) tested negative in group 1, and 10 subjects (62.5%) in group 2 . Then the obtained value of the test statistic $p > 0.05$ means that there is no significant difference in the examination of vaginal clue cells after treatment in both groups.

Table 3. Bacterial Vaginosis after Therapy in both Groups

Groups	Result				Total	p	
	Cured		Not cured				
	n	%	n	%			
Metronidazole	19	76	6	24	25	100	0.747
Metronidazole+ probiotic	18	72	7	28	25	100	

Note: p: Pearson Chi-Square test

Table 3 shows that 19 subjects (76%) were cured in group 1 and 18 people (72%) were cured in group 2. From statistical tests using Pearson Chi-Square test, it was found that there was no significant difference between the two groups ($p > 0.05$).

DISCUSSION

Bacterial vaginosis (BV) is the most common infection in vagina. BV is also the most common cause of the abundant vaginal secret.^{1,2} We performed a clinical trial comparing the use of metronidazole only and metronidazole supplemented by probiotic in the management of bacterial vaginosis.

In this study, most subjects were in the age group of 31-40 years (80%) in both groups. Several previous studies reported that Bacterial vaginosis is more common in younger women.⁹ Meanwhile, another study showed that the risk of bacterial vaginosis increases with increasing age.¹⁰ Our study's finding was similar to the later study. This may be associated with the lower estrogen levels at this age. Decreased levels of estrogen causes an increase in vaginal pH, so this condition is not optimal for the development of Lactobacillus sp, a normal vaginal flora , but very conducive to the growth of microorganisms that cause bacterial vaginosis.¹⁰

Most subjects had given birth ≥ 4 times in both treatment groups . Research conducted by P. Bhalla and A. Kaushika in 1994 found a significant rela-

tionship between the incidence of bacterial vaginosis with higher parity.¹¹ Meanwhile, in 2004 a study by multivariate analysis found that there was no relationship between the incidence of bacterial vaginosis and parity.¹²

The majority of subjects were graduated from senior high school. The most common occupation was housewife. Both of these variables are related to the socio-economic level. Research conducted by Tamonud Modak et al in 2011 found that all subjects with bacterial vaginosis were from a low socioeconomic level.¹³ It could be explained that the subjects with lower socioeconomic had a low awareness in personal and environmental hygiene, thus more susceptible to infection.

Bacterial vaginosis usually occurs due to an imbalance of the normal vaginal microorganisms population. Lactobacilli bacteria is found to be reduced while other microorganism, Gardnerella vaginalis, increase. The main therapy for Bacterial vaginosis is metronidazole 500 mg, given 2 times a day for 7 days. However, treatment with antibiotics can be followed with the incidence of recurrent Bacterial vaginosis and resistance to the antibiotic. Therefore, we need to try finding other alternatives as therapy. One of the proposed alternative is using probiotics to restore the normal population of Lactobacilli in vagina.³⁻⁵

The goal of probiotic therapy in addition to standard therapy is to restore the normal balance of vaginal microorganisms populations, which contains probiotics lactobacilli required by normal vaginal ecosystem. Research conducted by Gabriela Lilies et al showed that probiotic supplementation therapy may increase the effectiveness in the management of Bacterial vaginosis.¹⁴

The result of homogeneity examination towards both group based on the amsel criteria before therapy showed that both groups were homogenous population with $p > 0.05$.

The influence of probiotic supplementation in the standard therapy were reassessed after 7 day of therapy. The reassessment included vaginal secret examination, Sniff test, vaginal pH examination and the examination for the presence of clue cells.

The statistical analysis towards all criteria after therapy showed that there was no significant difference in both groups. There was no difference either in the overall recovery of subjects in both groups.

This result is consistent with the research conducted by Katarina Eriksson et al. which found that there was no significant difference in the recovery rates between treatment with only antibiotic and antibiotic supplemented with probiotic.¹⁵ But in research conducted by Liliior et al, it was showed that treatment with probiotic supplements can increase the effectiveness of management on bacterial vaginosis.¹⁴ Similarly, the study by Valentine Marcone also found that probiotics can significantly increase the effectiveness of antibiotic therapy.¹⁶

CONCLUSION

Addition of probiotic supplements do not increase the effectiveness of antibiotics in the treatment of bacterial vaginosis.

REFERENCES

1. Phillip Hay. Bacterial Vaginosis. *J Pediat Obstet Gynaecol*. 2002; 36-40.
2. David A, Eschenbach M. Screening, Diagnosis and Management of Bacterial Vaginosis. *Management of STDs in Family Planning Settings*. 1999; 13:71-5.
3. Roberta B. Ness, Kevin E. Kip, Sharon L. Hillier, David E. Soper, Carol A. Stamm, Richard L. Sweet, et al. A Cluster Analysis of Bacterial Vaginosis-associated Microflora and Pelvic Inflammatory Disease. *Am J Epidemiol*. 2005; 162: 585-90.
4. Catriona S. Bradshaw, Anna N. Morton, Jane Hocking, Suzanne M. Garland, Margaret B. Morris, Lorna M. Moss, et al. High Recurrence Rates of Bacterial Vaginosis over the Course of 12 Months after Oral Metronidazole Therapy and Factors Associated with Recurrence. *J Infect Diseases*. 2006; 193: 1478-86.
5. Abiola C Senok, Hans Verstraelen, Marleen Temmerman, Giuseppe A Botta. Probiotics for the treatment of bacterial vaginosis. *Cochrane Database of Systematic Reviews*. 2009.
6. T. Iannitti, B. Palmieri. Therapeutical use of probiotic formulations in clinical practice. *Clin Nut*. 2010;701-25.
7. Sarah Cribby, Michelle Taylor, Gregor Reid. Vaginal Microbiota and the Use of Probiotics. *Interdisciplinary Perspectives on Infectious Diseases*. 2008:1-9.
8. M. E. Falagas, G. I. Betsi, S. Athanasiou. Probiotics for the treatment of women with bacterial vaginosis. *Clin Microbiol Infect*. 2006; 13:657-64.
9. Seblewongiel Ayenalem, Lukman Yusuf, Mogessie Ashenafi. Lactic Acid Bacterial Vaginosis among Outpatients in Addis Ababa. *Journal Ethiop Health Dev*. 2010; 24:198-204.
10. Dwiana Ocviyanti, Yeva Rosana, Shanty Olivia, Ferry Darmawan. Risk factors for bacterial vaginosis among Indonesian women. *Med J Indones*. 2010;19:130-5.
11. P Bhalla, A Kaushika. Epidemiological and microbiological correlates of bacterial vaginosis. *Indian J Dermatol Venereol Leprol*. 1994;60:8-14.

12. Shimano S, Nishikawa A, Sonoda T, Kudo R. Analysis of the prevalence of bacterial vaginosis and Chlamydia trachomatis infection in 6083 pregnant women at a hospital in Otaru, Japan. *J Obstet Gynecol Res.* 2004; 30:230-6.
13. Tamonud Modak, Preeti Arora, Charan Agnes, Raja Ray, Se-banti Goswami, Prमित Ghosh, et al. Diagnosis of bacterial vaginosis in cases of abnormal vaginal discharge: comparison of clinical and microbiological criteria. *J Infect Dev Ctries.* 2011; 5:353-60.
14. Gabriela Lilius MD, Cristina Farcas MD, Violeta Sapira MD, Dragos Doicescu MD, Iulian Bratu MD. Probiotics - a complementary therapeutic necessity in non-specific vaginitis. *Practica Medicală.* 2012; 25:63-5.
15. Katarina Eriksson, Bodil Carlsson, Urban Forsum, P-G Larsson. A Double-blind Treatment Study of Bacterial Vaginosis with Normal Vaginal Lactobacilli after an Open Treatment with Vaginal Clindamycin Ovules. *Acta Derm Venereol.* 2005; 85:42-6.
16. Valentina Marcone, Ettore Calzolari, Marco Bertini. Effectiveness of vaginal administration of Lactobacillus rhamnosus following conventional metronidazole therapy: how to lower the rate of bacterial vaginosis recurrences. *New microbiologica.* March 2008; 31:429-33.