

## Effectiveness evaluation of Alginate Oligosaccharides antibacterial gel for bacterial vaginosis

HOU Wenjie<sup>a</sup>, HAN Lin<sup>b</sup>, LI Min<sup>a</sup>, CHEN Jie<sup>a</sup>, CHEN Youguo<sup>a\*</sup>

<sup>a</sup>Gynecology and Obstetrics Department, the First Affiliated Hospital, Soochow University, Suzhou, Jiangsu 215006, China

<sup>b</sup>Internal Medicine Department, Suzhou Kowloon Hospital, Suzhou, Jiangsu 215021, China

E-mail: [lionhoumail@hotmail.com](mailto:lionhoumail@hotmail.com)

**Abstract:** Objective: To evaluate the efficiency of Alginate Oligosaccharides antibacterial gel for bacterial vaginosis(BV). Methods: With completely randomized approach, 863 patients with BV were respectively divided into three groups including: metronidazole treatment group, Alginate Oligosaccharides antibacterial gel treatment group and combined treatment group. Result: The clinical effectiveness of three groups at the first follow-up visit was 92.3%, 94.8% and 95.5% respectively(P=0.781), it was 83.0%, 92.6% and 89.9% respectively (P=0.012) at the second follow-up visit; The incidence of adverse reaction was 17.1%, 6.2% and 15.7% respectively (P=0.006). Conclusion: Alginate Oligosaccharides antibacterial gel can effectively improve the clinical symptoms of the patients as metronidazole in treatment of bacterial vaginosis, even more it has better long-term curative effect and fewer adverse reactions, which is worthy of clinical application.

[HOU Wenjie, HAN Lin, LI Min, CHEN Jie, CHEN Youguo. **Effectiveness evaluation of Alginate Oligosaccharides antibacterial gel for bacterial vaginosis.** *Life Sci J* 2014; 11(7):528-531]. (ISSN: 1097-8135). <http://www.lifesciencesite.com>. 70

Key words: Alginate Oligosaccharides antibacterial gel; bacterial vaginosis(BV); metronidazole

### 1. Introduction

Bacterial vaginosis (BV) is a most common gynecological disease and it causes tremendous threat to women's reproductive health. BV is a syndrome of unknown cause characterized by depletion of the normal *Lactobacillus* population and an overgrowth of vaginal anaerobes, accompanied by loss of the usual vaginal acidity. *Lactobacilli* dominates the normal vaginal flora, and produces inhibitory mediators including lactic acid, H<sub>2</sub>O<sub>2</sub>, defensins and bacteriocins. When bacterial vaginosis develops the *Lactobacilli* reduce in concentration and may disappear, meanwhile there is an increased concentration of anaerobic and facultative anaerobic organisms<sup>[1]</sup>. Women with symptomatic bacterial vaginosis report an offensive, fishy-smelling discharge that is most noticeable after unprotected intercourse or at the time of menstruation<sup>[2]</sup>. By recognizing the fact that many anaerobic or facultative anaerobic bacteria are present and classical signs of inflammation are absent, the older term 'Gardnerella vaginitis' was replaced by the term 'bacterial vaginosis' in 1983. According to reports, the prevalence is 10 % to 31 % worldwide, while it is 15 % ~ 45% in China<sup>[3]</sup>.

Bacterial vaginosis is sometimes distressing and must be managed with sensitivity. Because it has a relapsing-remitting course in many women, the best treatment option has not been established. Metronidazole is a traditional optimal choice. The standard treatment for bacterial vaginosis is metronidazole, 400 mg orally 12-hourly for 5-7 days<sup>[4]</sup>. The cure rate immediately after treatment with

metronidazole is up to 95%, but after 4 weeks this declines to 80% in open-label studies and less than 70% in blinded studies. What is more, oral metronidazole is associated with nausea, a metallic taste and alcohol intolerance. Therefore, finding a safer, more effective and fewer adverse reactions alternatives is particularly urgent.

Alginate Oligosaccharides (AOS) is a low molecular weight material hydrolyzed from sodium Alginate, which constructs cell walls of brown seaweed plant. It is considerable water-solubility and structural stability<sup>[5]</sup>. Furthermore, studies found that AOS has a great number of physiological activities including antibacterial, antitumor, neuroprotective and promotion of *Lactobacilli* <sup>[6]</sup>. On the other hand, because of natural degradation, AOS is no pollution and residual<sup>[7]</sup>. This study intends to evaluate therapeutic effective of AOS antibacterial gel for BV.

### 2. Materials and methods

#### 2.1 General Information

We randomly selected 863 patients coming to out-patient department from January 2013 to December 2013 and all of them were randomly divided into three groups including: metronidazole treatment group, AOS antibacterial gel treatment group and combined treatment group. Case inclusion criteria: (1) over 18 years old, sexual life history, except for pregnancy; (2) informed consent after clinical diagnosis of bacterial vaginosis (BV); (3) during treatment and follow-up do not sexual intercourse; (4) within one month oral drug treatment of vaginal

infections or two weeks vaginal drug using cases were excluded; (5) mixed vaginal infections and vulvovaginal candidiasis cases were excluded. Diagnostic criteria: Vaginal pH >4.5; Release of a fishy smell on addition of alkali (10% potassium hydroxide); Characteristic discharge on examination; Presence of 'clue cells' on microscopy of vaginal fluid mixed with normal saline. At least three of the four criteria must be fulfilled to make a diagnosis of bacterial vaginosis<sup>[8]</sup>.

## 2.2 Treatment

287 patients in metronidazole treatment

group undertook metronidazole(400mg orally 12-hourly for 7 days); 286 patients in AOS antibacterial gel treatment group undertook AOS antibacterial gel(3.0g daily pro vagina); 290 patients in combine treatment group undertook metronidazole(400 mg orally 12-hourly for 7 days) and AOS antibacterial gel (3.0g daily pro vagina).

## 2.3 Symptom score criteria

Clinical symptoms /signs as observed indicators including genital itching, genital pain, vaginal wall hyperemia and edema, and vaginal discharge quantity, the score criteria in Table 1.

Table 1. The symptom score criteria of BV

Symptoms / signs	0	1	2	3
Genital itching	N/A	Occasionally	Frequently	Continuous
Genital pain	N/A	Mild	Moderate	Severe
Vaginal wall hyperemia and edema	N/A	<1/3	1/3-2/3	>2/3
Vaginal discharge quantity	N/A	Slightly increased	Increased, without overflow	Increased, with overflow

## 2.4 Therapeutic effect criteria

Recovery: Clinical signs and symptoms completely disappeared, symptom score changed percentage 100%, vaginal examination pathogens disappeared, cleanliness grade I ~ II degree; Effective: Significant improvement in clinical symptoms and signs, not completely disappeared, symptom score changed percentage <100%, but  $\geq 65\%$ , vaginal examination pathogens disappeared, cleanliness grade II ~ III degree; Improved: Clinical symptoms and signs improved, 30%  $\leq$  symptom score changed percentage <60%, vaginal examination pathogens disappeared, cleanliness is more than III degree; Invalid: no improvement in clinical signs and symptoms or worsen, symptom score changed percentage <30%, the pathogen has not disappeared. Symptom score changed percentage = (pre-treatment clinical symptoms / signs points - after treatment clinical symptoms / signs Points) / pre-treatment clinical symptoms / signs points  $\times 100\%$ . Total efficiency = recovery + effective + improved. Three groups of patients came for the first follow-up visit in 7 to 14 days after treatment, and patients who were evaluated

with recovery, effective and improved would come for the second follow-up visit after menstruation or 28 to 35 day after treatment.

## 2.5 Statistical methods

We used SPSS19.0 statistical software for statistical analysis, measurement data expressed with  $\bar{x} \pm s$ , the two groups were compared using t test; between groups and within groups multiple comparison using ANOVA, count data using chi-square test. P <0.05 was considered statistically significant.

## 3. Results

### 3.1 Treatment effectiveness

Three groups of patients came for the first follow-up in 7 to 14 days after treatment, invalid patients in metronidazole treatment group, AOS antibacterial gel treatment group and combined treatment group were 22 (7.7%), 15 (5.2%) and 13 (4.5%). Total efficiency were 92.3%, 94.8% and 95.5% separately (P=0.781). Table 2 shows the data in detail.

Table 2. Comparison of clinical efficacy of different treatment groups in the first follow-up

	Recovery (%)	Effective (%)	Improved (%)	Invalid (%)	Total	$\chi^2$	P
metronidazole group	100(34.8%)	121(42.2%)	44(15.3%)	22(8.7%)	287	3.22	0.781
AOS gel group	102(35.6%)	128(44.8%)	41(14.3%)	15(5.2%)	286		
combined group	103(35.1%)	131(45.8%)	43(14.8%)	13(4.5%)	290		

AOS= Alginate Oligosaccharides

Patients who were evaluated with recovery or effective or improved would come for the second time follow-up after menstruation or 28 to 35 day after treatment, invalid patients in three groups were 45

(17.0%), 20 (7.4%) and 28 (10.1%). Total efficiency were 83.0%, 92.6% and 89.9% separately (P=0.012). Table 3 shows the data in detail.

Table 3. Comparison of clinical efficacy of different treatment groups in the second follow-up

	Recovery (%)	Effective (%)	Improved (%)	Invalid (%)	Total	$\chi^2$	P
metronidazole group	78(34.8%)	79(42.2%)	63(15.3%)	45(8.7%)	265	9.10	0.012*
AOS gel group	81(35.6%)	112(44.8%)	58(14.3%)	20(5.2%)	271		
Combine group	90(35.1%)	105(45.8%)	54(14.8%)	28(4.5%)	277		

AOS= Alginate Oligosaccharides

\* P < 0.05 difference was statistically significant

### 3.2 Comparison of adverse reactions

Adverse reactions happened on 112 cases (13.0%) totally, including nausea, mouth pain, fatigue, headache, vaginal burning sensation, metallic taste in

mouth, skin rash and secondary vulvovaginitis candidiasis. Three groups of patients with adverse events rates were 17.1%, 6.2%, 15.7%, (P = 0.006). Data detail in Table 4.

Table 4. Comparison of adverse reactions in different treatment groups

	Total	Adverse reaction cases(%)	$\chi^2$	P
metronidazole group	287	49(17.1%)	17.96	0.006*
AOS gel group	290	18(6.2%)		
combined group	286	45(15.7%)		

AOS= Alginate Oligosaccharides

\* P < 0.05 difference was statistically significant

## 4. Discussions

The results of this study show that at the first follow-up visit the total efficiency of AOS antibacterial gel treatment group was 94.8%, there is no significant difference between the metronidazole treatment group and combined treatment group, indicating that AOS antibacterial gel have the same effect with metronidazole in BV. Sikorska<sup>[9]</sup> and other studies have also confirmed that AOS has strongly antibacterial activity. They extract sodium Alginate from fresh seaweed, and observed to see if AOS would affect on the growth of *Escherichia coli* and *Staphylococcus* in vitro. The results showed that AOS inhibited them in vitro and there was a positive correlation between the concentration of AOS and inhibition. At the second follow-up visit total efficiency dropped to 83.0% in metronidazole treatment group, while it was 89.9% and 92.6% respectively in AOS antibacterial gel treatment group and combined treatment group. The result indicated that AOS has a more durable effect and lower recurrence rate than metronidazole. We suppose AOS plays a role in long-term cure and reduces recurrence effectively by reducing pH in vagina and strengthening Lactobacillus restored, furthermore suppressing anaerobic growth. Li Miao<sup>[10]</sup> also confirmed AOS can significantly shorten the adaptation period of bifidobacteria and promote its proliferation.

Furthermore, since there is no pharmaceutical ingredients, AOS antibacterial gel has advantages of non-toxic, non-irritating, non-allergenic and safe to use. Incidence of adverse reactions in AOS antibacterial gel treatment group is 6.2%, it was significantly lower than metronidazole group (17.1%) and combined treatment group (15.7%), and no case stopped treatment for adverse reaction. The result illustrates that patient have better compliance to undertake alginate AOS antibacterial gel.

In summary, AOS antibacterial gel can effectively improve the clinical symptoms of the patients as metronidazole in treatment of bacterial vaginosis, even more it has better long-term curative effect and fewer adverse reactions. It is worthy for microecological therapy and clinical application.

## 5. Acknowledgments

We are grateful to YU Jing MD. for the effort in the revision process of the manuscript.

### Corresponding Author:

CHEN Youguo

Address: 188# Shizi Street, Gusu District, Suzhou, Jiangsu, China; Telephone: 0086-15850157677.

E-mail: [lionhoumail@hotmail.com](mailto:lionhoumail@hotmail.com);

**References**

- [1] P. Hay. Bacterial vaginosis[J]. VAGINAL INFECTIONS, 2010, 38 (6) : 281-285.
- [2] J. S. Huppert, E. A. Hesse, M. C. Bernard. Accuracy and Trust of Self-Testing for Bacterial Vaginosis[J]. Journal of Adolescent Health, 2012, 51 (4) : 400-405.
- [3] C. Kenyon, R. Colebunders, T. Crucitti. The global epidemiology of bacterial vaginosis: a systematic review[J]. American Journal of Obstetrics and Gynecology, 2013, 209 (6) : 505-523.
- [4] J. M. Marrazzo. Interpreting the epidemiology and natural history of bacterial vaginosis: Are we still confused?[J]. Anaerobe, 2011, 17 (4) : 186-190.
- [5] J. Courtois. Oligosaccharides from land plants and algae: production and applications in therapeutics and biotechnology[J]. Curr Opin Microbiol, 2009, 12 (3) : 261-273.
- [6] X. Qiang, C. YongLie, W. QianBing. Health benefit application of functional oligosaccharides[J]. Carbohydrate Polymers, 2009, 77 (3) : 435-441.
- [7] J. Fernebro. Fighting bacterial infections-future treatment options[J]. Drug Resist Updat, 2011, 14 (2) : 125-139.
- [8] J. A. Simoes, M. G. Discacciati, E. M. Brolazo. Clinical diagnosis of bacterial vaginosis[J]. International Journal of Gynecology & Obstetrics, 2006, 94 (1) : 28-32.
- [9] H. Sikorska, W. Smoragiewicz. Role of probiotics in the prevention and treatment of meticillin-resistant Staphylococcus aureus infections[J]. Int J Antimicrob Agents, 2013, 42 (6) : 475-481.
- [10] L. Miao. Effects of Alginate Derived Oligosaccharide on the Growth of Bifidobacterium in vitro[J]. Food Res Development, 2008, 11: 16-19.

5/4/2014