The Efficacy of Oral Clindamycin in the Treatment of Bacterial Vaginosis

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Abstract : *The efficacy of oral clindamycin in treating bacterial vaginosis was evaluated. In a descriptive study of 37 cases of reproductive-aged women with demonstrated clinical bacterial vaginosis on the presence of 3 out of 5 of the following signs (1) characteristically thin homogenous discharge ; (2) the vaginal pH > 4.5; (3) release of a fishy amine odor from vaginal fluid mixed with 10% KOH; (4) presence of clue cells (at least 20% of vaginal epithelial cells); (5) vaginal fluid contains few or no lactobacilli. The patients were treated with Clindamycin 600 mg per day orally for 7 days. Complete follow up was obtained one week after completion of medication. Of these 37 patients, complete response, defined as an absence of symptoms and presence of less than three clinical criteria, and partial response defined as an absence of symptoms but presence of three or more clinical criteria, were 94.5% and 5.5% respectively. Overall adverse drug reaction was 8.1% and all were mild and tolerable. Clindamycin is an alternative drug for the effective treatment of bacterial vaginosis. Its advantage over metronidazole is the absence of fetal teratogenesis during pregnancy. (Thai J Obstet Gynaecol 1994; 6: 91-99.)*

Key words : bacterial vaginosis, nonspecific vaginitis

Bacterial vaginosis (BV)is the most common cause of vaginitis among women of child-bearing age. The clinical entity is characterized by symptoms of increased amount of malodorous discharge. It is a conventional practice to diagnose BV only after excluding trichomoniase, vulvovaginal candidiasis and cervicitis, although these conditions may coexist. Amsel et al recommended clinical diagnosis basing on the presence of three or four of the following :[1] (1) characteristic homogenous white adhering discharge (2) elevation of the vaginal pH above 4.5 (3) release of a fishy amine odor from vaginal fluid mixed with 10% KOH (4) pres-

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ence of clue cells (usually representing at least 20% of vaginal epithelial cell). These simple clinical tests are inexpensive and available in most gynaecologic office. Culture of the vaginal fluid usually reveals mixed microbial flora that typically include Gardnerella vaginalis, genital Mycoplasma and anaerobic bacteria such as Peptostretococcus, Bacteroides spp. and Mobiluncus spp.[2] Recent works have shown an increased risk of chorioamnionitis and prematurity among pregnant woman with BV, and suggests that BV may be a risk factor for pelvic inflammatory disease.[3-10] Many therapeutic agents have been used to treat bacterial vaginosis with various degree of success. There were many publications on oral metronidazole which showed that it was the preferential drug for the treatment of BV because it was more effective than other drugs previously used such as; ampicillin, tetracycline or topical sulfa cream.[11,12] However, metronidazole has the disadvantage of poor patient compliance due to high adverse drug reaction and potential fetal teratogenesis during pregnancy. Clindamycin, the other antibiotic which is particularly active against anaerobic bacteria, and moderately active against G. vaginalis and M. hominis, has been used as topical cream for the treatment of BV.[13] In the study, 2% clindamycin cream applied intravaginally once daily for 7 days showed an efficacy of 93%[13] In this study, oral clindamycin was chosen to confirm the efficacy against BV since it serves an alternative to metronidazole particularly for the treatment of recurrent BV and BV during pregnancy.

Materials and Methods

From January to May 1993, 37 females, aged 24-51 years old, attended the gynaecological out patient department clinic, Songklanagarind Hospital and were diagnosed as having bacterial vaginosis (BV). Those who were pregnant, lactating, prostitutes or having a history of antibiotic therapy during the last two weeks prior to the study were excluded. They were diagnosed as BV by the presence of at least 3 out of 5 criteria in the examination of the vaginal discharge; (1) pH above 4.5 (2) thin homogenous (3) fishy odor or amine test positive (4) clue cell at least 20% of total vaginal epithelial cells and (5) scanty or absence of lactobacilli.[14-15]

All cases went through a complete history taking and physical examination with particular emphasis on confirmation of urogenital symptoms and signs characteristic of vaginitis such as abnormal increased or malodorous vaginal discharge, vulvar irritation, pelvic discomfort and painful urination. The following procedures were performed for determination of BV and exclusion of other infections. The cervix was exposed with unlubricated speculum and Pap. smear was carried out by the standard VCE method. Vaginal discharge

adhering to the speculum was examined for the mentioned characteristics. The pH was determined by indicator Litmus paper (pH ranges 3.8-5.4). The amine test was performed by the addition of a single drop of 10 percent potassium hydroxide to a fresh drop of vaginal preparation. Positive result was considered if fishy amine like odor was liberated. Another drop of vaginal discharge was mixed with one drop of normal saline on a glass slide for wet mount preparation. The wet mount showed neither Trichomonas vaginalis nor Candida spp. Clue cells are vaginal epithelial cell which have their cell border obscured by bacteria during the observation in normal saline at 400 times magnification. A less objective feature is granular appearance of cytoplasm. Gram stain may also be used to identify these cells and usually shows a large number of gram variable coccobacilli with few or absence of gram positive rod lactobacilli.

The patients were diagnosed as having BV when examination of the vaginal discharge consisted of three or more criteria mentioned earlier. Recruited patients were given clindamycin 600 mg per day orally for seven days. Patients were advised to abstain from sexual intercourse until first follow up one week after complete treatment, in their nonmenstrual period.

Complete response was noted by the absence of symptoms and presence of less than three criteria in the examination of vaginal discharge whereas absence of symptoms with presence of three or more criteria were categorized as partial response. No response cases were those who had both symptoms and three or more of the criteria as mentioned above.

Results

Of the 37 recruited patients, all had complete dose of medication and there was no loss follow up. The mean age of patients entering the study was 34.86 years old. Most of them were government officials and house-wives. (Table 1)

Pre and post treatment symptoms were shown in Fig. 1. Abnormal increased amount of vaginal discharge, offensive odor were the prominent symptoms while pruritus was much less frequent. There were

Table 1 ***Demographic characteristic of studied patients***

Mean age	**34.6 years**
Occupation	
Government official	16 (43.2%)
House-wives	9 (24.3%)
Agriculture	2 (5.4%)
Trained worker	4 (10.8%)
Others	6 (16.2%)
Contraception	method
No contraception	10 (27%)
Condom	1 (2.7%)
Pill	2 (5.4%)
IUD	2 (5.4%)
DMPA	2 (5.4%)
Vasectomy	4 (10.8%)
Tubal sterilization	6 (43.2%)

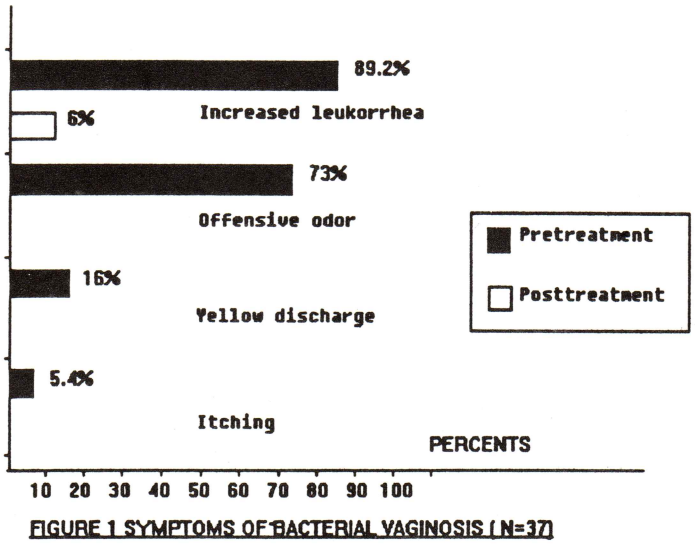


Fig. 1 compares the symptoms of bacterial vaginosis pre and post treatment.

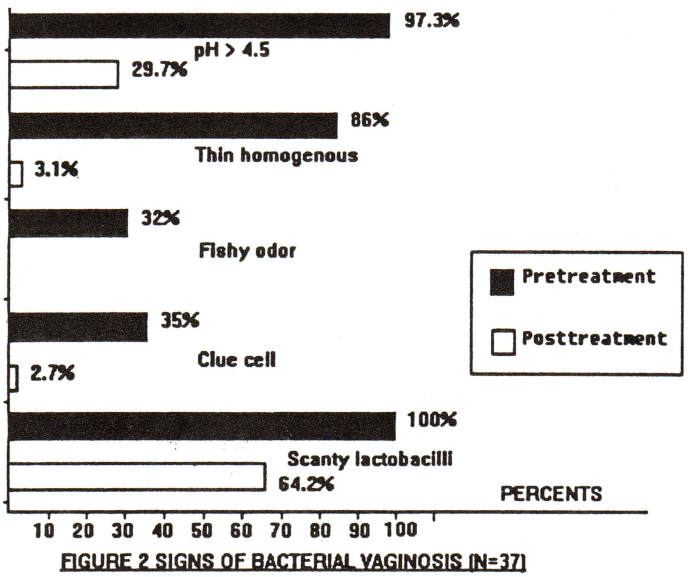


Fig. 2 compares the signs of bacterial vaginosis pre and post treatment.

no symptoms of dysuria or vaginal sores. After treatment, each symptom improved or disappeared. Changes in the characteristics of vaginal secretion before and after treatment are presented in Fig. 2.

With regard to the number of criteria during pre and post treatment (Table 2), it was noted that patients who had three or more criteria decreased from 100% to 5.4% after treatment. Complete response

Table 2 *Results of treatment, considering the number of criteria for diagnosis of bacterial vaginosis*

No. of criteria	Clindamycin treatment (N=37) Pre	Post
5	24 (64.9%)	0
4	13 (35.1%)	0
3	0	2 (5.4%)
3 or more	37 (100%)	2 (5.4%)
2	0	7 (18.9%)
1	0	18 (48.6%)
0	0	10 (27.1%)
Less than 3	0	35 (94.5%)

Table 3 *Results of treatment, considering response of treatment*

Response group	No. of patients (%)
Complete response	35 (94.5%)
Partial response	2 (5.5%)
No response	0

Table 4 *Adverse drug reactions of clindamycin.*

Nausea	1 (2.7%)
Vomiting	0
Dizziness	1 (2.7)
Others	2 (5.4%)

*One patient may have more than one adverse effect

94.5% complete response while partial response was 5.5%

Table 4 presents the adverse drug reactions of clindamycin found in 8.1% of the patients as follow nausea (5.4%), dizziness (5.4%), metallic taste (5.4%) and palpitation (5.4). All of them were minor and transient.

Discussion

Bacterial vaginosis resulted from the replacement of the normal vaginal flora with mixed flora consisting of Gardnerella vaginalis, anaerobics and Mycoplasma hominis. Since vaginal inflammation is not a feature of this infection the term "vaginosis" has replaced "vaginitis". We did not attempt to diagnosis BV based on bacterial isolation because it was not practical and might not be correct and also a variety of other bacteria in addition to G. vaginalis are important in this type of vaginal infection. Moreover, G. vaginalis can be recovered from up to 58% of those without clinical criteria for BV and can be found 6-63% in asymptomatic healthy women.[9,16-17] A positive culture in the absence of composite clinical signs of BV should not be used as a basis of therapy.[18] In this study, composite clinical criteria for

diagnosis of BV, recommended by Amsel and modified by Holmes were used in stead.[11]

Several regimen trials have shown that 5-nitroimidazole ánd its derivatives taken orally are effective for the treatment of BV. The two most common are 500 mg twice daily for 7 days and 2 grams as a single dose. The 7-day course has been associated with higher cure rates (79%-89%) in each of five studies in comparison with the single 2-gram dose (47%-85%).[18] The common adverse drug reactions include nausea, vomiting, anorexia, metallic taste in mouth, dizziness, and darkening of urine were reported to range from 2.6-26%.[19-22] Various skin rashes are less common, and the patients should not take metronidazole together with alcoholic beverages since the combination may produce disulfiram-like effects. Others reported the cure rate of 86% with less adverse drug reactions(8%) when a single dose of tinidazole was used.[23-24] Chandeying et al reported 3 different regimens of nimorazole with clinical efficacy ranged from 70% to 90%.[15] Although the efficacy of metronidazole is unquestioned, the toxicity of the drug has been brought into concern. Questions of mutagenicity and carcinogenicity remain unanswered. Use of metronidazole in pregnant women is generally not recommended[25] and the drug is contraindicated in first trimester of pregnancy and puerperium. Beta lactam antibiotics such as ampicillin, amoxicillin are effective against G. vaginalis however, resistant beta-lactamase-producing strains of one or more species of Prevotella or Porphyromona may be present in BV. Amoxicillin in combination with clavulonic acid have been used successfully but the beta-lactam agent has the disadvantage of destroying vaginal lactobacilli, already reduced in bacterial vaginosis, and may delay repopulation of the vagina with these organisms. These factors may be responsible for the low cure rate with the average of only 60% in the treatment of BV with ampicillin.[11,20,27-30] Hence, they do not appear to be effective for such treatment. Other antibiotics that are currently used include ciprofloxacin, cephalexin, tetracyclin and erythromycin. These drugs are less effective.[20,31] Erythromycin is less effective because macrolide antibiotics are not effective in acid pH of the vagina, therefore a study of the efficacy of oral clindamycin was done. The results of this study confirmed the clinical efficacy of clindamycin (600 mg. per day orally for 7 days) against BV. Treatment with clindamycin yielded complete response and partial response rate of 94.5% and 5.5% respectively. The efficacy was comparable to that reported by Lossick and Greaves.[32,33] It causes few side effects and well-tolerated by the patients. Clindamycin therapy could be particularly useful in the treatment of BV during pregnancy, in metronidazole treatment failure, and metronidazole intolerant cases. However, clindamycin is not

free from problems; it has been associated with pseudomembranous colitis.[34] The incidence of this side effect of clindamycin is unclear, but the reasonable estimate is about 0.01-1%.[35] None of the patients in our study developed colitis. Although we are not aware of any patients developing pseudomembranous colitis during the period of follow-up, we cannot be certain that this complication does not occur later, because we did not follow patients for more than two weeks after therapy. We believe that patients taking clindamycin should be informed about the possibility of bloody diarrhea and advised to discontinue the medication in such condition.

Summary

A descriptive study of the treatment of bacterial vaginosis was carried out in 37 reproductive-aged women. The patients were treated with clindamycin 600 mg per day orally for 7 days. Complete follow up was obtained one week after completion of medication. Of these 37 patients, the complete response, defined as absence of symptoms and presence of less than three clinical criteria, and partial response, defined as absence of symptoms but presence of three or more clinical criteria, were 94.5% and 5.5% respectively. Overall adverse drug reactions were 8.1% and all were minor as well as well-tolerated. Clindamycin is another effective drug for the treatment of bacterial vaginosis. Its advantage over metronidazole is in the absence of fetal teratogenesis in pregnant women.

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