Treatment of bacterial vaginosis with a three day course of 2% clindamycin vaginal cream: a pilot study

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Abstract

Objective—To evaluate the efficacy and safety of a 3 day course of 2% clindamycin cream in the treatment of bacterial vaginosis.

Design—A prospective, randomised, double blind, placebo controlled study.

Setting—Department of Genitourinary Medicine, Royal Liverpool University Hospital.

Subjects—55 female patients aged 18 years and over, and premenopausal, who spontaneously or after questioning complained of symptoms of bacterial vaginosis.

Results—55 patients were enrolled. 44 patients were evaluable at Visit 1 when among the 23 who received clindamycin cream bacterial vaginosis was not present in 22 (95.6%) and only one failed treatment. Of the 21 patients in the placebo group only one (4.8%) patient was cured and 20 (95.2%) were failures. Of the 17 patients evaluable at Visit 2 in the clindamycin group, bacterial vaginosis was not present in 14 (82.4%) and had recurred in three. No serious adverse events were noted in either group.

Conclusion—This pilot study provides encouraging evidence of the efficacy and safety of a 3 day course of 2% clindamycin cream in bacterial vaginosis.

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Introduction

Bacterial vaginosis (BV) is a common condition which in 1990 accounted for 33% of all cases of vaginal infections seen in genitourinary medicine (GUM) clinics in England.¹ Just how the condition is initiated remains a mystery. However, there is a shift in the vaginal flora that is, replacement of the normal *Lactobacillus*-predominant vaginal flora by vast numbers of other organisms, especially, *Gardnerella vaginalis*, obligate anaerobes and *Mycoplasma hominis*.

Currently metronidazole is considered the drug of choice. However, the condition often recurs for reasons yet unknown. Other drawbacks of metronidazole include its side effects and uncertainty about the effects of metronidazole on the foetus. The recent reports of association of BV with preterm birth,² low birth weight, postpartum endometritis³ and pelvic infection⁴ have also highlighted the

need for alternative treatment, especially in pregnant women.

Clindamycin has excellent activity against anaerobic bacteria⁵ and has been found to be effective in the treatment of BV when given orally in doses of 300 mg twice daily for 1 week⁶ and when applied intravaginally as a 2% cream twice daily for 5 days⁷ or once daily for 7 days.⁸ The incidence of systemic side effects is low as only approximately 4% of the cream is absorbed.⁹

We conducted this study to assess the efficacy and safety of a shorter course (3 days) of 2% intravaginal clindamycin for the treatment of BV in a prospective, randomised, double blind, placebo controlled trial.

Patients and methods

Premenopausal women, over 18 years of age, who either spontaneously or on questioning had symptoms suggestive of BV were included. A diagnosis of BV was made in the presence of malodorous vaginal discharge, vaginal fluid pH > 4.5, a fishy amine odour after adding 10% KOH to the vaginal fluid and clue cells in the vaginal fluid on microscopic examination. Patients were eligible only if findings on a Gram stain of vaginal discharge were consistent with BV (that is there was a marked decrease or absence of lactobacilli morphotypes and a marked increase in other Gram variable morphotypes).

Exclusion criteria were: known allergy to clindamycin, pregnancy or breast feeding, presence of an intrauterine contraceptive device, women not taking adequate contraceptive measures, history of inflammatory bowel disease or diarrhoea, symptoms suggestive of pelvic infection, genital herpes, cervical or vaginal warts, hysterectomy, history of systemic or vaginal antimicrobial therapy in the previous 2 weeks and the presence of any serious disease and infection such as chlamydia, *Trichomonas vaginalis* or candida at the base line visit. Women who were likely to menstruate within the following week were also excluded.

Clinical evaluation at each visit included a medical and sexual history, examination of the vulva, vagina, uterus and adnexa, description of vaginal discharge, determination of vaginal fluid pH, test of vaginal fluid for fishy odour after addition of 10% potassium hydroxide, smear of vaginal fluid for clue cells, gram stain of vaginal fluid, wet mount

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Table 1 The efficacy criteria

Success: (bacterial vaginosis is not present)				
1. Absence of symptoms.				
2. Gram stain negative.				
3. Clue cells absent.				
4. Normal vaginal fluid.				
5. Vaginal fluid pH < or = 4.5.				
6. Negative amine odour with KOH.				
Improved				
Criteria 1 to 3 as above BUT two or less of No. 4-6 are true.				
Failure				
BV is present based on the criteria described under 'Patients and Methods'.				
Recurrence				
Following either success or improvement at the first follow-up evaluation, BV recurred as per criteria described above.				

and culture for *T vaginalis* and culture for candida *Neisseria gonorrhoeae* and *Chlamydia trachomatis*.

After obtaining written informed consent, the patients were assigned to one of the two treatment groups in a random, double blind, 1:1 fashion. Each patient received a tube containing either 20g 2% clindamycin vaginal cream or 20g matching placebo cream and three disposable applicators. They were instructed to insert 5g of cream high into the vagina at bedtime for three consecutive nights and to return any unused cream at the next clinic attendance. The patients were to be assessed at 7 days (Visit I) and 28 days (Visit II) after the start of treatment.

The patients were requested to abstain from sexual intercourse and to avoid prolonged soaking in a bath until the first follow-up at day 7 (Visit I), after treatment.

At Visit I, any new symptoms, adverse events, sexual history, administration of medication and concurrent use of other agents was noted. Thereafter, clinical examination and base line tests were repeated. The second follow-up at 28 days (Visit II) after completion of therapy included a similar assessment.

The patients were considered to be evaluable at Visit I if they used the medication as described in the protocol, and had not received any other antibiotics or antifungals (topical or systemic), and had not menstruated within 72 hours of the last application of the protocol therapy. The efficacy criteria are defined in table 1.

Statistical analysis for comparison of cure, improvement, recurrence and failure rates between the two groups was done by Fisher's exact test and was considered to be statistically significant at a p value of <0.05.

Results

Fifty-five women were enrolled, 45 completed the protocol, 24 in Clindamycin Group and 21 in Placebo Group. Comparison of the two groups for age,

Table 3 Outcome of clindamycin versus placebo at Visit II

Group	Success	Improve	Failure/ Recurrence	Total
Clindamycin	12	2	3	17
Placebo	-	-	3	3

weight, menstrual cycle, parity, number of abortions, bowel habits, history of previous infections or previous episodes of BV and methods of contraception, did not yield any significant differences.

Table 2 lists the treatment outcomes at Visit 1 when 44 patients were evaluable. The overall success together with improvement rate was 96.6% (22/23) with clindamycin and this was highly significant when compared with the placebo group (p < 0.001). Symptomatic candidal vulvovaginitis requiring treatment was seen in one patient in the clindamycin group. Diarrhoea was reported by one patient in each group. However, both the patients with diarrhoea recovered without any residual effects and did not need any treatment.

In the Clindamycin Group, *C trachomatis* was isolated from the endocervical swabs of three patients who were accordingly treated for chlamydia infection (with tetracycline) at the follow-up Visit I. The one patient with persistent BV received a course of metronidazole tablets. A further two patients defaulted. After excluding all these patients, 17 were evaluable at follow-up Visit II. Success or improvement was noted in 14 (82.4%) while BV recurred in three (table 3). Of the three patients treated for chlamydia infection and one retreated for persistent BV at the follow-up Visit I, three (including the one retreated for persistent BV) returned at the follow-up Visit II and all were considered cured.

In the Placebo Group, of the 20 with persistent BV, 16 had symptoms of whom five were also found to be infected with *C trachomatis*. These five cases were, therefore, treated for chlamydia (with tetracycline) as well as persistent BV (with metronidazole) at follow-up Visit I. All of the remaining 11 received a course of metronidazole tablets. A further two patients (including one success at Visit I) defaulted. After excluding all these patients, only three patients (asymptomatic at Visit I) were evaluable at follow-up Visit II, and they had by then begun to re-experience malodorous vaginal discharge. Results of wet film and gram stain of the vaginal material were once again consistent with the presence of BV (table 3). Of the 16 patients retreated at the follow-up Visit I, eight returned at the follow-up Visit II, seven were considered cured and one patient who had received tetracycline and metronidazole, although asymptomatic, showed evidence of BV.

Discussion

Various treatment regimens, both oral and topical, have been used for BV. At present the United States Center for Disease Control

Table 2 Outcome of clindamycin versus placebo at Visit I

Group	Success	Improve	Failure	Total
Clindamycin	16	6	1	23
Placebo	1	-	20	21

recommends metronidazole, 500mg orally twice daily for 1 week.¹⁰ (Because of metronidazole formulation, the dose in Great Britain is 400mg, twice daily). However, the possibility of side effects necessitates search for an alternative to metronidazole, especially for use in early pregnancy.

Clindamycin has been shown to be effective in the treatment of this condition. In a study by Greaves *et al*⁶ oral clindamycin (300 mg twice daily for one week) was shown to be effective in 94% of patients with BV. However, 16% of patients had adverse effects, although these did not necessitate discontinuation of therapy.

Two recent placebo controlled studies have demonstrated the efficacy of topical intravaginal clindamycin in BV. In a dose ranging study by Livengood *et al*,⁷ where 2% clindamycin was compared with 0.1% and 1% concentrations of the cream and used twice daily for 5 days, 93–94% cure rates were achieved. Hillier *et al*,⁵ also examined the efficacy of 0.1%, 1% and 2% concentrations of clindamycin applied intravaginally once daily for 7 days. While persistent cure was noted in 94% of patients who used 2% clindamycin, the efficacy of the lower concentration creams had dropped to 71% at one month.

Five grammes of 2% clindamycin vaginal cream daily for one week has been compared with oral metronidazole, 500mg twice a day, in two recent studies.^{8,11} Andres *et al*,¹¹ reported cure or improvement rates of 97% with clindamycin and 83% with metronidazole at one week. This difference was not statistically significant. Schmitt *et al*,⁸ found a 72% cure rate with clindamycin and 87% with metronidazole at one week (difference not significant) and 61% in each group after one month.

The present study demonstrates that a 3 day course of 5 grammes of 2% clindamycin cream applied vaginally once daily has similar cure rates as a five or a seven day course referred to above. It is also comparable with treatment with metronidazole, and, pending further proof of its efficacy and its safety in pregnancy, is likely to become the preferred treatment in pregnant women. No serious adverse side effects were noted with its use. Other advantages are topical treatment and possibly better patient compliance due to the short course of treatment.

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