

A Prospective Study Of Comparison Of Efficacy Of Two Combination Treatment Regimens In Syndromic Treatment Of Pelvic Inflammatory Disease

J Sharma, C Chanana, S Mittal, U Raina

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Abstract

Aim: The aim of the study was to compare the efficacy and safety of two combination regimens in the syndromic management of pelvic inflammatory disease (PID).

Methods: One hundred and eight non pregnant women presenting with symptoms of pelvic inflammatory disease (PID) like abnormal vaginal discharge with lower abdominal pain with or without fever and diagnosed as PID on clinical examination were enrolled in one of the two treatment regimens as a syndromic treatment. No investigations were performed to cut the cost, and to avoid loss of patients on follow-up. Fifty-two women (Group I) and their partners were prescribed a course of doxycycline (100 mg) twice daily with metronidazole (400 mg) thrice daily for seven days. Fifty-six women (Group II) and their partners were prescribed a combination kit containing 150 mg fluconazole, 2gm secnidazole and 1 gm azithromycin (FAS-3 kit, Lyka) with advice to take azithromycin on empty stomach, while other 3 tablets after food. All women in both groups were seen after one week for relief of symptoms and after one month for any recurrence.

Results: The mean age was 29.2 yrs and 28.5 yrs and mean parity was 2.7 and 3.0 respectively in the two groups. The symptomatic relief was observed in 92.3% and 94.6% cases respectively in Groups I & II. No relief was observed in 4 patients in each group. Recurrence was seen in 1 case in each of the two groups. Most women tolerated both the treatments well with no major side effect in any case. Most of the women tolerated the treatment well with minor side effects. Treatment cost was similar in the two groups being (approx Rupees 85) in Group II and (approx Rupees 75) in Group I.

Conclusions: Both treatment groups were reasonably effective and safe in the syndromic approach for lower genital infections. The combination kit with azithromycin, secnidazole and fluconazole was better tolerated and was more convenient to take and may be routinely recommended in all cases of pelvic inflammatory disease as a cost effective, safe and effective strategy.

INTRODUCTION

The general term pelvic inflammatory disease has been used to describe infection of the uterus and fallopian tubes usually occurring following ascent of bacteria present in the cervix and presents with history of abnormal vaginal discharge, fever and adnexal tenderness requiring microbiological studies on cervical smear or diagnostic laparoscopy for the diagnosis.^{1,2,3} In 2002, the Center for Disease Control (CDC) published recommendations for the treatment of pelvic inflammatory disease based on current knowledge of the etiology of pelvic inflammatory disease and of the antimicrobial activity of available antibiotic.³ The World

Health Organisation (WHO) has also promulgated new treatment guidelines.⁴ Out-patient treatment of pelvic inflammatory diseases with cefoxitin and doxycycline or clindamycin with amikacin or gentamicin has been used with equally good results after microbiological testing.^{5,7} Symptomatic management has been advocated in the developing countries for the management of STDs and PID using clinical algorithms based on symptoms and signs to select patients who should receive antimicrobial therapy.⁸ Syndromic management is not only more feasible in many resource poor settings than laboratory based management, but has the advantage of immediate treatment, avoidance of

the costs associated with laboratory tests and assurance of treatment for those who are actually infected. STD syndrome packets have been developed to improve syndromic management of STDs in developing countries.^{9,10,11}

Gynecologists often prescribe combination of antibiotics of their choice from their clinical experience, which may not cover the microsurgical flora adequately. There is a real need of performing prospective randomized controlled study to see whether Syndromic approach using various antibiotic combination in general use are effective and safe in clinical setting. We conducted a prospective study to compare the safety and efficacy of the commonly used antibiotic regimens in the clinical syndromic management of PID in our outpatient setting.

MATERIAL AND METHODS

A total of 108 non pregnant women (47 from one hospital, and 61 from a second hospital) who presented to the outpatient department with symptoms of pelvic inflammatory disease like abnormal vaginal discharge, lower abdominal pain with or without fever were enrolled in this prospective randomized controlled trial. These patients were assigned to either of the two groups by a computer-generated randomization. Women with previous history of PID or STD, those having intrauterine contraceptive devices in situ and women with multiple sexual partners were excluded from the study population.

The detailed history of type and colour of discharge, pruritis vulvae, any vaginal pain, any abdominal pain with or without fever or any other complaint was taken from all the patients. Speculum and bimanual examination were performed to look for the type of discharge, its consistency, colour, smell and any hyperemic area on vulva and vagina. Condition of cervix and vagina and for site, size, consistency of uterus and cervix and for any tenderness or masses in the fornices.

No investigations were performed to cut the cost and to avoid loss of patients on follow-up. After seeking ethical clearance from both the hospitals the women were divided in two groups.

- Group I: - Fifty-two women and their partners were prescribed a course of doxycycline (100 mg) twice daily and metronidazole (400 mg) thrice daily.
- Group II: - Fifty-six women were prescribed a

combination kit of fluconazole (150mg), azithromycin (1gm) and secnidazole (2gm) (FAS-3 kit, Lyka) as a single dose therapy with advice to take azithromycin on empty stomach and other 3 tablets after food.

All women in both groups were seen after one week for relief of symptoms and after one month for any recurrence. Any side effects were noted. The data were analyzed to determine similarities and differences in the two groups.

RESULTS

There were 52 women in Group I and 56 women in Group II. The range and mean of age and parity in the two groups is shown in Table I and were similar in the two groups. The symptoms were abnormal vaginal discharge, vaginal or lower abdominal pain and fever in most of the women. Cervical and or adnexal tenderness was observed in 48 (92.3%) cases in Group I and 54 (96.4%) cases in Group II. The socio economic status was low or middle class in all cases and is shown in Table I. The efficacy of two treatments regimens and side effects are shown Table II. There was symptomatic relief in 48 (92.3%) cases in Group I and in 53 (94.6%) cases in Group II. Recurrence was seen in one case in each group over a period of one month. No major side effects or anaphylaxis was seen in any patients in either group. Minor side effects seen were metallic taste in 20 (38.4%) and 6 (10.7%) women, nausea in 6 (11.5%) and 3 (5.3%) in the two groups respectively. The cost of the treatment was almost equal in the two groups being Rs. 70 in group I and Rs. 85 in group II.

Figure 1

Table 1: Characteristics of women in the two groups.

	Group I (No)	Percentage	Group II (No)	Percentage
Number of women	52	100	56	100
Range of age (Yrs)	20-43		19-41	
Mean age (Yrs)	29.2		28.5	
Parity				
Range	0-6		0-7	
Mean	2.7		3.0	
Socioeconomic Status				
Middle Class	21	40.4	25	44.6
Lower Class	31	59.6	31	55.4
Symptoms				
Abnormal Vaginal Discharge	52	100	56	100
Fever	12	23	11	19.6
Lower abdominal pain	49	94.2	54	96.4
Cervical and or adnexal tenderness	48	92.3	54	96.4

Figure 2

Table 2: Efficacy of two treatment regimes in the two groups

Characteristic	Group I (N-37) No.	Percentage	Group II (N-35) No.	Percentage	P Value
Symptomatic relief	52	92.3	53	94.6	0.45 Not Significant
No relief	4	7.6	4	7.1	0.2 Not Significant
Recurrence	1	2	1	1.7	Not Significant
Side effects					
Metallic taste	20	38.4	6	10.7	0.03 Significant
Nausea	6	11.5	3	5.3	0.09
Diarrhoea	0		0		
Abdominal Pain	0		0		
Anaphylaxis	0		0		
Cost	Rs. 70		Rs. 85		

DISCUSSION

The results of present study depict a cure rate of 92.3% and 94.6% respectively for the two different antibiotic combinations, which were similar. The minor side effects were more common in doxycycline and metronidazole group than in the combination kit.

The traditional approach to the diagnosis and management of a presumed pelvic inflammatory disease is through laboratory diagnosis to determine the etiological agent., Although the approach is scientific, it is expensive in terms of diagnostics and laboratory infrastructure maintenance, and it delays the diagnosis and treatment. Unfortunately the majority of victims of STDs live in developing countries, especially Africa and Asia, where laboratory facilities for diagnosis are not available at a health center or dispensary

level. Even where laboratories do exist, quality controls to validate them are often lacking. To address these limitations, WHO developed and recommended appropriate patient management strategies based on the syndromic approach, which is especially suitable for developing countries like India.¹²

The syndromic approach to STD case management is based on the identification of a relatively constant combination of symptoms and signs (Syndrome) and on knowledge of the most common causative organisms of these syndromes and their antimicrobial susceptibility. The syndromic approach not only finds application in the developing countries, but has also been widely used in the industrialized countries for the management of pelvic inflammatory disease. The advantages of such management are expedited care, treatment at the first visit, cost saving by avoiding expensive laboratory tests, increased client satisfaction and no risk of losing the patient to follow up before starting treatment. The main disadvantage is the cost of over diagnosis and over treatment when multiple antimicrobials are given to the patient with no infection and also there is a potential for developing antibiotic resistance.

Various studies have confirmed the cost effectiveness of the syndromic approach in pelvic inflammatory disease.^{13,14,15} Combination antimicrobial therapies like cefoxitin and doxycycline or gentamycin - clindamycin have been used and found to be effective in the management of^{5,6,7} Ciprofloxacin with metronidazole or tinidazole has been found to be effective and well tolerated and treatment was successful in 97% cases.¹⁶ Oral clindamycin and ciprofloxacin versus intramuscular cefotriaxone and oral doxycycline have been used very safely and effectively in out patient treatment of mild to moderate pelvic inflammatory disease.¹⁶ Our results confirm the cost effectiveness of a syndromic approach for suspected pelvic inflammatory disease. Both the treatment combinations had equal efficacy and cost but the combination kit with fluconazole, azithromycin and secnidazole was better tolerated and was more convenient to take.

To conclude, syndromic management of genital infection appears to be a cost-effective proposition in Indian communities. Both the treatments were equally effective in control of pelvic inflammatory disease with statistically similar side effects in the two regimens.

CORRESPONDENCE TO

Dr. Charu Chanana 91, Pocket B, Sukhdev Vihar, New Delhi 110025 India Ph-091-11-26314656 E-mail: charuchanana@rediffmail.com

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Author Information

J. B. Sharma

Assistant Professor, Department of Obstetrics & Gynecology, All India Institute of Medical Sciences

Charu Chanana

Registrar, Department of Obstetrics & Gynecology, All India Institute of Medical Sciences

Suneeta Mittal

Professor and Head, Department of Obstetrics & Gynecology, All India Institute of Medical Sciences

Usha Raina

Chief Medical Officer, Department of Obstetrics & Gynecology, Lok Nayak Hospital