



Original Research Article

Prescribing Pattern of Antimicrobial Agents in Pelvic Inflammatory Disease at a Rural Teaching Hospital in India

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ABSTRACT

Objective: Due to scarcity of data on Antimicrobial agent prescribing pattern in Pelvic Inflammatory disease (PID) from India, this study was conducted to evaluate this prescribing practice, its cost effectiveness and compliance to Centre for Disease Control and Prevention (CDC) guidelines at a rural teaching Hospital at Kishanganj, India.

Methodology: A cross-sectional study was conducted at the Department of Gynecology & Obstetrics of MGM Medical College & LSK Hospital, Kishanganj, Bihar; for a period of one year during February 2014 to January 2015. A total of 638 prescriptions of clinically diagnosed PID cases from Outpatient Department (OPD) and Inpatient Department (IPD) were collected and analyzed in the department of Pharmacology with respect to the standards mentioned above.

Results: Average number of AMAs per prescription was 3.007. Commonest organism encountered was Chlamydia trachomatis 18(37.5%) followed by Candida albicans 14(29.17%) and Trichomonas vaginalis 11(22.92%). Majority of patients received oral Doxycycline 500(78.37%) in combination with Metronidazole followed by Ofloxacin 138(21.63%) with or without Metronidazole through oral and/or Intravenous (I.V) route. Gentamicin was prescribed in 17(2.66%) cases. Clotrimazole was prescribed topically in all patients. The average cost was INR.150.37 per OPD prescription whereas average cost of per day indoor prescription was INR.169.93 only.

Conclusion: Polypharmacy is common in such patient group and prescribing practice differs from the standard guidelines and supplemented with 100% antifungal coverage. Cost effective antibiotics were prescribed with acceptable clinical recovery. Hence, regular prescription audit and dissemination of the results to the prescribers can prevent irrational drug prescription and antimicrobial resistance in long run.

Key words: Antimicrobial Agents (AMAs), Pelvic inflammatory disease (PID), prescribing pattern, India, prescription audit

INTRODUCTION

The study of prescribing patterns of antimicrobial agents is a potential pharmacovigilance aid which helps

healthcare providers to audit and suggest modifications to avoid indiscriminate prescribing practices and development of microbial resistance.

CDC guidelines 2010 state that pelvic inflammatory disease treatment regimen should include broad spectrum AMAs coverage of likely pathogens. [1] As PID has been associated with numerous complications, [2] rational selection of AMAs is of utmost importance in these cases so that we do not invite another trouble to the patient i.e. AMAs resistance.

Due to the established fact of being polymicrobial origin, an inflated utilization of broad spectrum antimicrobials has been observed for PID treatment. [1,3]

Although data is available worldwide regarding the pattern of antimicrobial usage in PID patients, such data is relatively scarce from a developing country like India especially from the eastern part of our country. Hence, this prospective study was undertaken to understand the pattern of antibiotics usage among PID patients in rural teaching hospital of India and to estimate its cost and evaluate the compliance of usage with respect to standard treatment recommendations.

MATERIALS AND METHODS

We conducted a cross sectional study for a period of one year of February'2014 – January'2015, where data from 638 prescriptions of clinically diagnosed (both acute and chronic) PID (female) patients of sexually active age group between 15-50 years, [4-6] was collected. We visited Gynaecology & Obstetrics department both OPD and IPD and gathered data randomly twice weekly and the detailed records of demographic, clinical features & treatment instructions were noted in 'Case Record Proforma' after getting explained consent from the patients.

We incorporated only women with first attack of PID but not those with recurrent attacks or those previously on antibiotic(s) related to PID. We also did not include the females with symptoms of PID

but not satisfying the criteria mentioned above. The study was carried out with proper approval from Institutional Ethics Committee. Compilation and analysis of data were done in the Department of Pharmacology. Patients were selected randomly using computer generated randomized chart and data was tabulated in MS-excel 2007 sheets.

Descriptive statistics tools were used to describe the data. Mean was used as a measure of central tendency and Standard deviation was performed to understand the dispersion of data.

RESULTS

Of the total 638 prescriptions analyzed 19 belonged to the indoor patients **Demographic Details: (Figure: 1):** Age of the females ranged from 15 to 50 years. Eleven (1.72%) patients out of 638 were unmarried and came with acute unbearable pain and other associated signs and symptoms.

Among all the patients 72(11.29%) came with acute symptoms out of which 18(2.82%) required hospitalization and intravenous medication and rest 566(88.71%) patients were chronic cases of PID (came with history of long standing dull aching lower abdominal pain increases during menstruation). Only one patient from the chronic cases did require hospitalization due to associated urinary tract infection. Majority (55.49%) of the patients were of between 15 to 23 years age group. Mean age of the patients was 24.41 years.

Microorganisms Profile: (Figure: 2): We were able to collect investigation reports of 48(7.52%) patients only due to logistical constraints and it was observed that the commonest organism in the available reports was Chlamydia trachomatis 18(37.5%) followed by Candida albicans 14(29.17%), Trichomonas vaginalis 11(22.92%), Neisseria gonorrhoeae 4(8.33%) &

miscellaneous [E coli] 1(2.08%) respectively.

Antimicrobial Regimens Used : In the out patients department the antimicrobials prescribed were tablet Ofloxacin(400mg) once daily; or tablet Ofloxacin (400mg) once daily with tablet Metronidazole (400mg) thrice daily; or tablet Doxycycline (100mg) twice daily in conjunction with tablet Metronidazole(400mg) thrice daily. The duration of each therapy was 14 days respectively. (Table: 1)

For the admitted patients prescribed antimicrobials were Injection Ofloxacin (400mg) intravenously (I.V) twice daily with Injection Metronidazole (500mg) infusion intravenously thrice daily; or Doxycycline (100mg) orally twice daily along with Injection Metronidazole(500mg) I.V thrice daily along with Injection Gentamicin (80mg) I.V twice daily; or Ofloxacin (400mg) I.V twice daily with Metronidazole (500mg) I.V thrice daily and

Gentamicin (80mg) I.V twice daily for the first 48 hours and then switch to oral medications depending on the clinical improvement of the patient. Clotrimazole was prescribed (in the form of vaginal pessary tablets) to all 638 cases (one strip containing 6 tablets prescribed per vaginally for 6 days). (Table: 2)

Classes of Amas Prescribed: Average number of AMAs per prescription was 3.007. Commonest class of systemic antibiotic prescribed was Tetracyclines (doxycycline) whereas topical antifungal was prescribed to all the patients.

Cost Of Treatment: The average cost (as per the medicines available in local pharmacy) is Rs.150.37 (Rs = Indian rupees) per OPD prescription (fourteen days duration) whereas average per day cost of indoor AMAs prescriptions is Rs.169.93. As clotrimazole was given to all patients, cost of it was included in each regimen cost.

Table 1: Regimens, prescriptions and their costs (OPD)

| OPD Regimens | Number of Prescriptions | percentage of Prescriptions | Total number of AMAs prescribed | Approximate Total Cost (Rs.) Per Prescription [for 14days AMAs] |
|---|-------------------------|-----------------------------|---------------------------------|---|
| REGIMEN-A Tab.Ofloxacin(400mg) once daily | 8 | 1.25 | 8x2=16 | 156 |
| REGIMEN-B Tab.Ofloxacin(400mg) once daily and Tab. Metronidazole (400mg) thrice daily | 122 | 19.12 | 122x3=366 | 205.98 |
| REGIMEN-C Tab. Doxycycline (100mg) twice daily & Tab. Metronidazole(400mg) thrice daily | 489 | 76.65 | 489x3=1467 | 136.41 |
| Total number of AMAs prescribed | | | 1849 | |

Table 2: Regimens, prescriptions and their costs (IPD)

| IPD Regimens | No.of Prescriptions | % of Prescriptions | Total no. of AMAs prescribed | Approximate Total Cost Per Day (Rs.) |
|--|---------------------|--------------------|------------------------------|--------------------------------------|
| REGIMEN-A Ofloxacin(400mg) I.V twice daily and Metronidazole(500mg) I.V thrice daily | 6 | 0.94 | 6x3=18 | 308.18 |
| REGIMEN-B Doxycycline(100mg) P.O twice daily and Metronidazole(500mg) I.V thrice daily & Gentamicin(80mg) I.V twice daily | 11 | 1.72 | 11x4=44 | 66.47 |
| REGIMEN-C Ofloxacin(400mg) I.V twice daily plus Metronidazole(500mg) I.V thrice daily & Gentamicin(80mg) I.V twice daily | 2 | 0.31 | 2x4=8 | 324.18 |
| Total number of AMAs prescribed | | | 70 | |

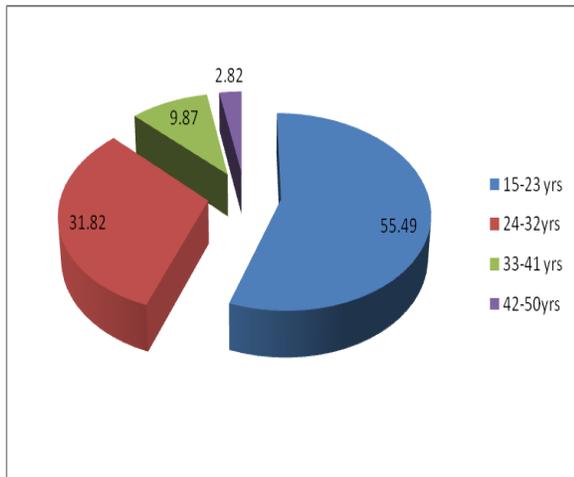


Figure 1. Demographic profile of patients

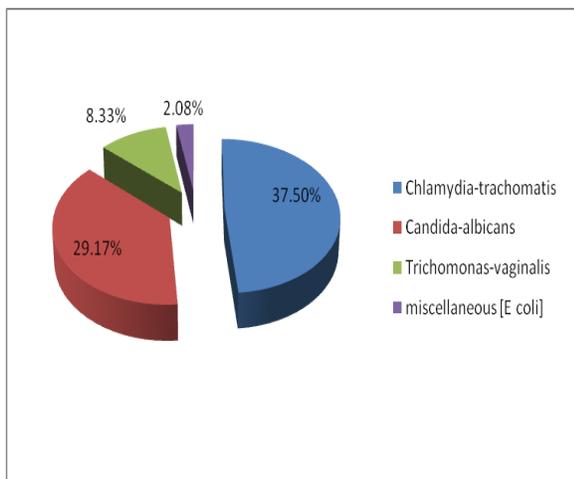


Figure 2. Microorganisms' profile

DISCUSSION

This cross-sectional study conducted in a rural hospital of India, where it was observed that the mean age of the patients with PID was 24.41 years which differs from the average age of presentation (31.68 years) of similar patients studied in North India by Sharma S, et al. [7]

In the present study the average number of antimicrobials prescribed was 3.007 whereas it was 2.52 in Sharma S, et al's study. [7]

We also observed in our survey that antimicrobial agents were prescribed empirically following the syndromic approach; to avoid pelvic inflammatory

disease induced probable complications and such trend were also seen in Sharma S, et al's study. [7] It was evidenced by Agarwal et al in their study from Northern India in 2004 that chance of over treatment for PID was only 16% if we follow empiric therapeutic approach. [8]

It was observed in the available investigation reports that Chlamydia trachomatis was the commonest pathogen 18 (37.5%) followed by Candida albicans 14 (29.17%), Trichomonas vaginalis 11 (22.92%), Neisseria gonorrhoeae 4 (8.33%) & miscellaneous [E coli] 1 (2.08%) respectively. In a study done by Saini et al in North India, [9] E coli was found as predominant isolate (33.2%) whereas in our study it was the least found organism (2.08%).

Doxycycline (as shown in tables 1 & 2) was prescribed with metronidazole to provide coverage against Chlamydia trachomatis and anaerobes, respectively. Saini et al recommended doxycycline against C. trachomatis in their study. [9] Though the CDC recommendations 2010 stated that parenteral cephalosporin single dose in the OPD regimen should be included and third generation cephalosporins were again suggested by Saini et al. [9] to cover N. gonorrhoea but in our study it was found that cephalosporins were not prescribed at all. The possible reason for such prescribing behaviour could be preference of the prescriber to select a cheaper drug like Doxycycline as our hospital caters mainly to the poor rural population. It is interesting to note that Doxycycline therapy achieved the similar clinical cure rate as observed in a study done by Malhotra et al in PID patients (91%) with the same regimen. [10] A study published from United States of America has also suggested routine inclusion of Tetracycline in the treatment regimen of PID to give protection for Chlamydia trachomatis. [11] Hence, we can conclude that

Doxycycline appears as a cost effective therapeutic option for the rural patients.

Oral Ofloxacin with or without Metronidazole was the other regimen prescribed in this study population which is in contrast to the previous studies where intravenous Ofloxacin twice daily followed by an oral regimen of 10-14days has been reported to provide almost cent percent cure from both Chlamydia and Gonococcal PID. [12,13]

According to the CDC'2010 guidelines; regimens should contain adequate coverage against *N. gonorrhoeae* and *C. trachomatis* for acute PID. In fact, anaerobic bacteria have been isolated (13-78) % from the upper genital tract of women with acute PID. [14-21] Hence, therapy with anaerobic coverage is being routinely followed at our Hospital.

In the current study it was found that Gentamicin was prescribed in patients requiring hospitalization with suspected or proven urinary tract infection. Similar findings were reported by Saini et al, where the researchers found good response to gentamicin to provide coverage against gram negative aerobic bacilli. [9] Clotrimazole was prescribed to all patients in the form of vaginal pessary once daily for six days. Probable reason being high rate of infection with *Candida albicans*. Azoles like Clotrimazole are the agent of first choice for *Candida albicans* in PID. [22,23]

Cost of regimens used at our hospital were more than the costs compared in three regimens in the Malhotra et al's RCT, [10] where patients in the first and third groups received ciprofloxacin with tinidazole and doxycycline with metronidazole for a period of 7 days respectively and the second group received only a single kit of fluconazole, azithromycin and secnidazole. Yet our estimated cost for 14 days OPD-treatment is much lesser than the regimens that would include cephalosporins or penicillins as the

services offered primarily to the rural population. Parenteral AMAs were prescribed in the indoor prescriptions (except Doxycycline which is available in oral form) for a variable period of acute phase of infection, then they were switched over to oral medications accordingly. Hence in case of IPD only per day cost of AMA prescriptions was computed.

The prescribing practice was categorized in three ways with reference to compliance to the CDC guidelines, in a multiyear cross section study conducted by Sish TY, et al in the United States of America. [24] According to that study the prescriptions following any of the CDC regimens fell under fully compliant or adherent category, those having at least part of the CDC regimen in their practice were partially compliant and non-compliant category did not follow anything from the CDC guidelines. On the basis of this categorization we may conclude that our antimicrobials' prescribing practice is partially compliant to the suggested regimen in CDC'2010.

Our study had few limitations. It was a monocentric study and performed over a limited time period (1year only) hence the trend observed cannot be extrapolated to the entire country. However this being a pilot study from a rural teaching Hospital in Eastern India; our study is an attempt to understand the current prescribing practice among rural prescribers in PID in India.

CONCLUSION

This study revealed that polypharmacy is common in such patient group which is quite justified as the disease concerned itself is polymicrobial origin. Prescribing practice differs from the standard guidelines and it is supplemented with an antifungal coverage in all cases. Cost effective antibiotics were prescribed with an acceptable clinical recovery.

Indiscriminate use of antibiotics results in an inflated health risk that too with a high treatment cost. Hence there is a dire need of regular prescription audit in clinical practice and dissemination of the audit results to the prescribers at frequent intervals in the form of regional newsletters can prevent irrational drug prescription. This study clearly signifies the development of standard treatment guidelines for common disease like PID in the rural health care centres of the country taking equal consideration of the local microbiological flora as well as the socio-economic standards of the catering population.

What is new about this study?

- Pilot study from a rural teaching Hospital of eastern India
- Prescribing practice in rural population was analyzed
- Sensitivity of *Candida albicans* infection in PID found high
- Physicians got satisfactory clinical response with cost effective Doxycycline therapy than the costly cephalosporins / penicillins, which lead to less usage of beta-lactam antibiotics
- Cost per prescription of AMAs therapy in PID (both OPD and IPD) has been highlighted for the first time from India

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