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DRUG UTILIZATION STUDY IN PELVIC INFLAMMATORY DISEASE IN A TEACHING HOSPITAL IN NORTH INDIA

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Abstract: The study was carried out in the OPD (out-Patients) of Teerthanker Mahaveer Medical college, Hospital & Research Centre, a 550-bedded teaching hospital situated in Moradabad, U.P, India. It was a prospective study and was based on medication utilization form, which has been designed on the basis of a WHO format. It contained patient particulars, diagnosis, investigations, drug details and information from the prescriber regarding the indication for prescribing agents (both topical and oral), underlying infection, duration of therapy and details of any concomitant medications. The information was compiled and analyzed in consultation with the concerned consultant. The duration of study was 12 months (January 2012 to February 2013). The study was approved by the Institutional Ethical Committee. An oral and written consent was obtained from the patients before their participation in the study. The purpose of this study was to: a. Evaluate the quality of the prescriptions in terms of the adequacy, effectivity and clarity of the information contained, and number of medicines prescribed by doctor to achieve rationale medical care b. Bring about improvement in the practical training of medical students in teaching hospitals so that better treatment policy can be outlined for the benefit of such patients, doctors and students being trained in that hospital.

Keywords: Anti microbials, PID, Drug utilization research (DUR), RCT



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INTRODUCTION

Pelvic Inflammatory Disease

Pelvic inflammatory disease (PID) implies inflammation of the upper female reproductive tract, involving the Fallopian tubes, as well as the Ovaries. As most of the PID's are due to ascending or blood-borne infection, the lesion is often bilateral, though one tube may be more affected than the other.

The failure of acute pelvic infection to resolve results in chronic tubo-ovarian masses. These masses manifest in the form of:-

Hydrosalpinx

Chronic pyosalpinx

Chronic interstitial salpingitis

Tubo ovarian cyst/abscess

Tuberculous Form

PID is an expensive public health problem. It has been estimated that the direct costs of treating PID in the U.S. exceeds billion annually. These costs do not include

the indirect costs of treating sequelae such as infertility, ectopic pregnancy & preterm birth.

The PID evaluation & Clinical health (**PEACH**) study found that use of the oral contraceptive pill (type not specified) does not reduce the risk of acquiring PID, but

that women may have less severe symptoms. It was suggested that the oral contraceptive pill may reduce the severity of inflammation and therefore mask the diagnosis of PID.

Clinical Features:

At presentation, women with PID may range from asymptomatic to seriously ill. The most common presenting complaint is lower abdominal pain.

PID is initiated by infection that ascends from the vagina and cervix causing endometritis, salpingitis, parametritis, oophoritis, tuboovarian abscess and pelvic peritonitis.

Symptoms:

The following features are suggestive of a diagnosis of PID. ^(2,3,4,5)

Lower abdominal pain(usually the most prominent symptom).

Dyspareunia – caused by pelvic masses prolapsed in the pouch of Douglas are more common complaints.

Menorrhagia, polymenorrhagia, congestive dysmenorrhoea.

Postcoital or intermenstrual bleeding.

Dysuria (pelvic inflammatory disease can occur with concurrent urethral chlamydial Infection).

Infertility results from blockage of fallopian tubes.

Nausea and vomiting (rare other than in acute infection).

Signs:

Lower abdominal tenderness which is usually bilateral.

Adnexal tenderness on bimanual vaginal examination.

Cervical motion tenderness on bimanual vaginal examination.

Rebound tenderness and guarding in some severe cases.

Mucopurulent cervical discharge and cervicitis, which may be seen on speculum examination.

Fever(>38°C).

Diagnosis:

The diagnosis of acute PID is primarily based on historical and clinical findings, but many patients may exhibit only a few or no symptoms. So, PID may be symptomatic or asymptomatic. Even when present, clinical symptoms and signs lack sensitivity and specificity (the positive predictive value of a clinical diagnosis is 65-90% compared to laparoscopic diagnosis).^(1,4,5)

Material and Methods

Empirical treatment is suggested by the Centers for Disease Control and Prevention (CDC) Sexually Transmitted Disease Management Guidelines in patients with uterine or adnexal tenderness and cervical motion tenderness, if no other etiology explains the findings. All antibiotic regimens must be effective against *C trachomatis* and *N gonorrhoeae*, as well as against gram-negative facultative organisms, anaerobes, and streptococci.

Regimen used in Chronic PID includes:
(EML)

- Doxycycline
- Clindamycin plus gentamycin,
- Ampicillin
- Metronidazole
- Ofloxacin
- Ornidazole
- Sulbactam plus doxycycline
- Ceftriaxone or cefoxitin plus doxycycline⁽⁷⁾

Outpatient Regimens- i.m. ceftriaxone 250mg stat. or i.m. cefoxitin 2g stat. with oral probenecid 1g followed by :

oral doxycycline 100mg BD plus metronidazole 400mg BD for 14 days

Grade A (Ib)(11-15) oral ofloxacin 200mg BD **plus** oral metronidazole 400mg BD for 14 days Grade A (Ib)^(9,16)

Inpatient Regimens

- i.v. cefoxitin 2g TID plus i.v. doxycycline 100mg BD (oral doxycycline may be used if tolerated) followed by:

oral doxycycline 100mg BD plus oral metronidazole 400mg BD for a total of 14 days Grade A (Ib)^(8,9)

- i.v. clindamycin 900mg TID plus i.v. gentamicin (2mg/kg loading dose followed by:

1.5mg/kg TID [a single daily dose of 7mg/kg may be substituted]) followed by: either oral clindamycin 450mg QID for 14 days or oral doxycycline 100mg BD plus

Oral metronidazole 400mg BD for 14 days Grade A (Ib) Gentamicin levels need to be monitored if this regimen is used.

Alternative Regimens

- i.v. ofloxacin 400mg BD(10) plus i.v. metronidazole 500mg TID for 14 days Grade B (III)⁽¹⁷⁾
- i.v. ciprofloxacin 200mg BD **plus** i.v. (or oral) doxycycline 100mg BD **plus** i.v. metronidazole 500mg TID for 14 days Grade B (III)¹⁴

Antibiotic regimens used for pelvic inflammatory disease in primary care are unsuitable for pregnant or lactating women.

Drug Utilization:

According to WHO, drug utilisation has been defined as the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences.⁽¹⁸⁾

The primary purpose of DUR is to enhance the quality of drug therapy. Due to limited resources, identifying non-efficient pharmacological treatment among PID patient is of increasing importance. Drug utilization research is useful for evaluating physician prescribing patterns. Data from this type of work can be linked to the measures of morbidity, in order to explore the efficacy and toxicity of different therapies. Drug utilisation studies of agents other than those used to treat PID can estimate concomitant conditions.

The purpose of this study was to:

- a. Evaluate the quality of the prescriptions in terms of the adequacy, effectivity and clarity of the information contained, and number of medicines prescribed by doctor to achieve rationale medical care
- b. Bring about improvement in the practical training of medical students in teaching hospitals so that better treatment policy can be outlined for the

benefit of such patients, doctors and students being trained in that hospital.

The present study is a prospective, cross sectional analysis of Prescription pattern of Antimicrobial Drugs in cases of Chronic Pelvic Inflammatory Disease, which included all prescriptions of CPID patients admitted in Gynaecology outpatient ward of Teerthanker Mahaveer Medical College Hospital & Research Centre, Moradabad, UP.

Prescriptions of the outdoor patients receiving antimicrobial drugs in the department of Gynaecology were collected and analyzed for drug utilization studies & in this analysis, we investigated the agents used in the treatment regimen. The information was collected from the patients attending the outpatient department through a random sample method.

Regimen used in Chronic PID includes:
(EML)

- Doxycycline
- Clindamycin plus gentamicin,
- Ampicillin
- Metronidazole
- Ofloxacin
- Ornidazole
- Sulbactam plus doxycycline

➤ Ceftriaxone or cefoxitin plus doxycycline

World Health Organisation-based prescription-auditing proforma was used for data collection. The study was carried out in the OPD(out-Patients) of Teerthanker Mahaveer Medical college, Hospital & Research Centre, a 550-bedded teaching hospital situated in Moradabad, U.P, India.

Type of Study

It is a prospective study and is based on medication utilization form, which has been designed on the basis of a WHO format. It contained patient particulars, diagnosis, investigations, drug details and information from the prescriber regarding the indication for prescribing agents (both topical and oral), underlying infection, duration of therapy and details of any concomitant medications. The information was compiled and analyzed in consultation with the concerned consultant.

Study Population

A total of 100 patients were enrolled on the basis of inclusion and exclusion criteria. All the patients using antimicrobials, irrespective of age, including pregnancy and lactating patients were studied. However, patients who were not treated with antibacterial or were unable to comply due to mental retardation or drug addiction etc were excluded.

The present study followed some WHO/INRUD indicators, in addition to some other useful indicators. The outcome measures included average age range of patients, types of infections, average number of antibacterials per prescription, concomitant drug used, comparison of antibacterials prescribed generic versus brand name, mode of administration, drugs from Essential list.

Method of Collection of Data

Data of patients matching inclusion criteria was recorded only. Data like age, diagnosis, ongoing treatment was recorded from case record of patients.

Identity of patient was to be kept confidential.

Data was coded, computed and analyzed using SPSS Version 13.

Core Indicators:

Prescribing Indicators:

Average number of drugs per visit.

Percentage of visits with an antibiotic prescribed.

Percentage of drugs prescribed by generic name .

Percentage of drug prescribed from essential drug list formulary.

Percentage of encounters with an injection prescribed.

Patient care indicators:

Patient's knowledge of correct dosage was found by dividing the number of patients who can adequately report the dosage schedule for all drugs, by the total number of patients interviewed, multiplied by 100.

Facility Indicators:

Availability of copy of Essential drug list formulation

Availability of key drugs

Data was to be further analysed as under:

Age wise distribution.

Average no. of Antimicrobials prescribed.

Average no. of concomitants prescribed.

Percentage of Antimicrobials prescribed.

Percentage of encounters with an injection prescribed.

Percentage of drugs prescribed by generic name.

Percentage of drug prescribed from Essential drug list formulary.

In the prospective study 100 patients visited the outpatient Gynaecology department of Teerthanker Mahaveer Medical College and Research Centre, Moradabad over a period of 12 months. A total of 100 prescriptions were analysed

during the 12 months study period. All of the 100 patients were female patients.

The maximum numbers of female patients suffering from Chronic PID were from the age group of 21-40 years (n=86), least of the patients fall under age group of 0-20 years (n=4) while none of the patients were there in age group of 61-80 yrs. **(Table-1)**

The total no. of drugs which were prescribed to the patient was 470. Each patient on an average was prescribed 5 drugs per prescription. A total of 100 people were prescribed one or more antibiotic during the study period. Out of 470 of total drugs, 252 were antibiotics.

During the study, it was observed that the most commonly prescribed Antibacterials were Antifungals (Imidazoles and Triazoles) (n=71, P=28.17 %) followed by Doxycyclines (n=46, P=18.25%), Antiamoebics (n=44, P=17.46), Quinolones (n=38, P=15.07 %), Anthelmintics (n=22, P=8.73 %), Macrolides (n=15, P=5.95%), β -Lactams (n=10, P=3.96%), Urinary antiseptics and Urinary Alkalizers were the least prescribed class (n=6, P=2.38%). The most commonly used agents of these

classes, i.e., Antifungals was Imidazoles (clotrimazole or clotrimazole with Tinidazole and Clindamycin) n=44 and Triazoles (Fluconazole or Fluconazole with ornidazole and Azithromycin) n=27. The combination of Antifungals with Antiamoebics and macrolides was the most prescribed combination while combination of quinolones with β -Lactam was least prescribed. **(Table-2)**

In the concomitant medications Antacids and supplementary drugs were mostly prescribed (n=68, P=31.19%) followed by NSAIDs (n=35, P=16.05%), Antiemetics (n=32, P=14.05%). Sedatives were the least prescribed class (n=15, P=6.88%). **(Table-3)**

Out of Total 252 antibiotics prescribed all antibiotics were given orally, no parenteral administration. There was a high prevalence of empiric treatment with orally administered antibiotics in this study. The average no. of Antibacterial agents prescribed per patient per course was found to be 4.70. It was observed that out of 470 drugs which were prescribed to the patient none of drugs were in generic form. All drugs were prescribed from Essential Drug List. **(Table-4)**

Table 1: Age wise distribution of patient:

Age(yrs)	No. of patients	Total No. of Patients
0-20	4	4
21-40	86	86
41-60	10	10
61-80	0	0
Total	100	100

Table 2: Antimicrobials prescribed in Gynaecology department

Class	Antibacterial Agents(Combinations)	No. of Agents Prescribed	Consumption (%)
B-Lactams	Amoxicillin + Clavulanate	4	3.96
Semisynthetic Aminopenicillins	Cefuroxime	2	
Cephalosporins	Cefixime or Cefixime + Ofloxacin	2	
Quinolones		2	

Fluoroquinolones	Ofloxacin		
	+	36	15.07
	Ornidazole		
	Or		
	Ofloxacin		
	+	(2)	
Macrolides	Cefixime		
	Azithromycin	15	5.95
	+		
	Ornidazole		
	+		
	Fluconazole		
Broad spectrum antibiotics	Doxycycline	46	18.25
Antifungals	Clotrimazole		
Imidazoles	or		
	Clotrimazole	6	28.17
	+		
	Tinidazole	38	
	+		
	Clindamycin		
Triazoles	Fluconazole		
	Or		
	Fluconazole		
	+	25	
	Ornidazole		
	+		
	Azithromycin	(2)	

Antiamoebics	Ornidazole +Ofloxacin	(36)	17.46
	Or		
	Ornidazole + Fluconazole		
	+ Azithromycin	(2)	
Antiprotozoal	Povidone-Iodine	6	
Anthelminics	Metronidazole	22	8.73
Urinary Antiseptics	Nitrofurantoin	4	2.38
Urinary Alkalizer		2	
	Grand Total	252	100 %

Table 3: Concomitant drugs used:

Class	No. of agents Prescribed	Consumption (%)
Antacids	68	31.19%
Antiemetics	32	14.67%
NSAIDs	35	16.05%
Sedatives	15	6.88%
Supplementary drugs	68	31.19%
Total	218	100%

Table 4: Prescribing Indicators:

Average no. of Drugs per prescription	4.70
<hr/>	
Prevalance of Use	
Total no. of prescription	100
Total no. of AMAs	252
Mean no. of AMAs	2.52
Percentage of drugs prescribed by generic name	0% (None of drug was given with generic name)
Percentage of drugs prescribed from EML	100% (All drugs were prescribed from EML only)
No. of encounters resulting in prescription of an injection (parental)	no parenteral antibiotic was prescribed

Discussion

Antibiotics were once considered 'miracle drugs' and have been used for decades to effectively treat a variety of bacterial infections. Unfortunately, widespread use and misuse worldwide have led to the emergence of 'super bugs' and other drug-resistant bacteria. Unnecessary use of antibiotics has also given rise to an increased risk of side effects, high costs and effects requiring medical attention.

Quality of life can be improved by enhancing standards of medical treatment at all levels of the health care delivery system. Setting standards and assessing the quality of care through performance review should become part of everyday clinical practice. The study of prescribing patterns seeks to monitor, evaluate and suggest modifications in practitioners'

prescribing habits so as to make medical care rational and cost effective.

Drug Utilization:

In our Study, the most commonly prescribed Antibacterials were Antifungals (Imidazoles and Triazoles) (28.17 %) followed by Doxycyclines (18.25%), The combination of Antifungals with Antiamoebics and macrolides was the most prescribed combination. In the concomitant medications Antacids and supplementary drugs were mostly prescribed (n=68,P=31.19%) followed by NSAIDs (16.05%).

Adapted from Clinical Evidence

A Clinical Evidence review (search date May 2005) considered antibiotic treatments for pelvic inflammatory disease.

No systematic reviews or randomized controlled trials (RCTs) that compared empirical treatment with treatment guided by test results were identified. However, the author commented that observational evidence (from one case-control study involving 76 cases and 367 controls) suggests that fertility may be impaired by delaying treatment for 3 days or more (odds ratio 2.6, 95% CI 1.2 to 5.9).

No RCTs comparing antibiotics with placebo or no treatment were found, probably because there is agreement that antibiotics are effective in women with PID, and that studies would therefore be unethical.

Two systematic reviews discussed in Clinical Evidence looked at the effects of different antibiotic regimens to treat PID.

The first review combined observational studies and RCTs and looked at 21 studies in 1992, with an update in 1997 that included 26 studies (n = 1925).

Antibiotics were found to be effective in relieving the symptoms experienced with PID. Clinical and microbiological cure rates ranged from 88–100%. The oral metronidazole and doxycycline regimen performed less well.

However, there were methodological problems with the review. From the data presented, it was not possible for Clinical Evidence to determine which of the included studies were RCTs. It appears that the included studies were of low power and differences in disease severity between studies may have affected the comparison of the efficacy of different treatments.

Table 5.

Cure rates for the antibiotic treatment of acute pelvic inflammatory disease: Aggregated data from a systematic review of randomized controlled trials and case series.

Outpatient drug regimen	Number Of studies	Number Of women	Cure rate (%)	Microbiological cure rate (%)
Clinical Cefoxitin (IM) + probenecid + doxycycline	3	219	89	93
Ofloxacin	2	165	95	100

Co-amoxiclav	1	35	100	100
Sulbactam/ampicillin	1	36	70	70
Ceftriaxone (IM) + doxycycline	1	64	95	100
Ciprofloxacin + clindamycin	1	67		94

❖ The second review (search date 2004, 34 RCTs, n = 3548) found limited evidence for treatment efficacy. All antibiotic regimens had high clinical and microbiological response rates (90–100%), with no significant difference between them.

- There were also methodological problems with this review. Trial quality was reported to be poor and, in addition, the review made no distinction between intravenous and oral treatment, or distinctions on the basis of disease severity.

Conclusion

The present study on antibiotic use on first time patients conducted in the Gynecology department at our university hospitals, under the circumstances tested, provides six characteristics of antibiotic prescribing:

(1) In the majority of cases treatment was empirical, with antibiotic prescription based on a clinical suspicion of infection without objective criteria of infection.

(2) Most of these drugs were prescribed using brand names.

Use of high cost broad spectrum antibiotics when the cheaper generic drug would have sufficed doesn't encourage compliance and this can lead to resistance.

(3) All antibiotics were administered orally and parenteral administration never occurred. The excessive use of injectables in developing countries is very common. However, interestingly no parenteral antibiotic was prescribed during this study and this may be reflective of an improvement in this aspect of prescribing pattern as opposed to previous excessive use of injections by some physicians who hold the erroneous belief that injections are more effective and offer better patient satisfaction.

(4) Aminoglycosides were not encountered at all in this study and this may be due to the fact that they are mainly available in parenteral forms. More so, being an outpatient centre, it may not be convenient and would not ensure

compliance if the patient is placed on such medication which would require that they return for treatment repeatedly especially when there are available alternatives.

(5) The average number of drugs per prescription is an important index of a prescription audit such as this study. It is preferable to keep the number of drugs per prescription as low as possible to minimize risk of interactions, development of bacterial resistance, and hospital costs.

(6) Most of the drugs prescribed were drugs in the essential drug list however.

This study did not however look at co-prescribed drugs and hospital costs but concentrated on prescribed antibiotics.

The findings of this study suggest that there was minimal difference between defined recommendations in standard treatment guidelines and the clinical use of antimicrobial agents. Establishing an appropriate and restrictive guide for antibiotic was therefore be a high aim and priority to this hospital.

A standard treatment guideline should be established in the hospital for antibiotic prescription and a drug utilization program should be setup alongside as a means of checking the practices of physicians on a regular basis.

Antibiotic resistance among pathogenic microorganisms is a matter of worldwide concern. Selective pressures by antimicrobial drugs are by far the most

important driving force for the development of such resistance. Prevention and control of the spread of antibiotic-resistant organisms will require increased adherence to basic infection control policies and procedures, incorporation of antimicrobial resistance strategies into institutional goals and development of a plan to deal with patients colonized with resistant organisms.

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