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RATIONAL USE OF ANTIBIOTICS IN GYNAECOLOGY

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ABSTRACT

Data was studied for evaluating rational use of antibiotics in gynaecology department and compare the data of public Vs private hospital on all the aspects, after so many efforts done by Delhi Society of promoting rational use of drugs (DSPRUD). The concurrent study was conducted in a 1276 bedded medical college hospital in Pt. B. D. Sharma University of Health Sciences, Rohtak and Shiv Hospital, Rohtak. The study was conducted on 100 outpatients from public and private hospital on equal population. Data was analyzed by applying statistical tools. A concurrent analysis on 100 patient's prescription was done in two groups and found that 41 (41%) prescriptions were probably appropriate, 18 (18%) prescriptions were inappropriate and 41 (41%) prescriptions were empirical. Inappropriate antibiotic therapy was due to inappropriate choice of antibiotics, having no efficacy for treatment and the cost inappropriate for the therapy prescribed, i.e. $p = 0.41 > 0.05$ (significant difference). Cost is the major factor for rational use of antibiotics. Cost comparison in two groups showed significant difference i.e. $p = 0.778 > 0.05$. The study concluded that 27% of the prescriptions were irrational and 73% of the prescriptions were empirical. Irrational use of antibiotics showed significant difference, $p = 0.27 > 0.05$. Comparing the two groups shows a significant difference i.e. $p = 0.61053$ (Chi-square test). The study was highly empirical and private practioners are giving completely empirical Vs public practioners. There are more chances of inappropriate prescriptions due to unavailability of investigation.

Keywords: Ionic Gelatine, Metadoxine, microbeads, in-vitro dissolution, stability.

INTRODUCTION

In the pre-antibiotic era, infectious diseases accounted for significant morbidity and mortality [1]. Antibiotics are the most important weapons in our hands to fight the diseases. On an average, 35% of the total health budget is spent on antibiotics[2].These are among the most commonly prescribed groups of drugs in hospitals today for infectious diseases but the miracle seems to be short lived due to irrational use. World Health Organisation (WHO) estimates that more than half of all medicines are prescribed, dispensed or sold

inappropriately, and that half of all patients fail to take them correctly. Irrational use of medicines takes place due to poly-pharmacy; inappropriate use of antimicrobials, often in inadequate dosage, for non-bacterial infections; over-use of injections when oral formulations would be more appropriate; failure to prescribe in accordance with clinical guidelines; inappropriate self-medication, often of prescription-only medicines; non-adherence to dosing regimens [3]. Highly irrational prescription is due to wrong choice of antibiotics, insufficient investigation and cost ineffectiveness. The study of rational use of antibiotics seeks to monitor, evaluate and suggest modification needed to prescribe antibiotic, so as to make medical care rational and cost effective. As 52% of world population is making up by women. The study was carried out for evaluation of available data on rational use of antibiotics in the gynaecology department, evaluation of cost appropriateness in antibiotic therapy, comparative study of antibiotics usage in public hospital Vs private hospital, determination of possible indicators for inappropriate use of antibiotics. The study hypothesized that public practioners are prescribing more appropriate prescription then private practioners.

Materials and Methods:

The study was conducted over an 8 month period in a 1276 bedded medical college hospital in Pt. B. D. Sharma University of Health Sciences and private gynaecology, Shiv hospital, Rohtak. It was a concurrent analysis of 100 outpatient's antibiotic prescription in gynae patients. Fifty prescriptions were enrolled from medical college hospital patients attending gynaecology department and fifty prescriptions were from Shiv Hospital. The data was collected in data collection form and analysed by using Statistical Analysis on tabular data in Microsoft excel by considering parameters like antibiotic, date, patient's name, age, sex, disease, brand name, generic name, route, strength, frequency in a day, number of days, represcription and remarks with clinical investigation.

We used the mean, standard deviation, level of significance 5%, Univariate analysis, Student t-test, Fischer's-exact test and Chi-square (x^2) test for studying the rational use of antibiotics in gynae patients and to determine the possible indicators for inappropriateness of antimicrobial treatment.

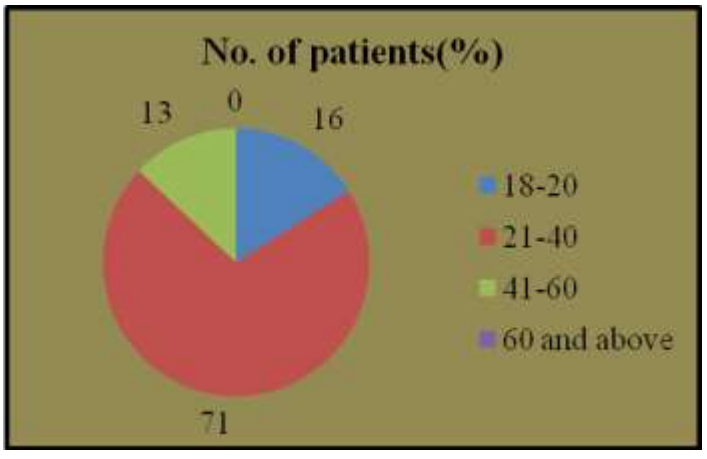
Result:

A total of 100 outpatient prescriptions in two equal groups each have 50 patients. They were distributed according to their age group and disease for evaluating them carefully as shown in table I and graph 1.

Table I: Age distribution of patients observed

Age (in years)	No. of patients (%)	Public patients (%)	Private patients (%)
18-20	16 (16)	11 (22)	5 (10)
21-40	71(71)	31 (62)	40 (80)
40-60	13 (13)	8 (16)	5 (10)
≥ 60	0 (0)	0	0

P = 0.199 > 0.05 by student t-test



Graph 1: Age distribution of patients observed

Out of 100 prescriptions, 16% were of age 18-20 years, 71% were of 21-40, 13% were of 40-60 years of age. As 13 patients were of above 40 years of age and as above 40 changes in hormones occurs, so there is need to take care of the age of patients. p = 0.199 > 0.05 (significant difference) determined by applying student t-test.

Complications with age increase on the basis of the disease so does the prescription distribution as shown in table II i.e disease distributions with age. 13 patients were having age greater than 40, three of them having Urinary tract infections (UTI), five of them have pelvic inflammatory disease (PID), one of them have Pruritis vulvae, two having pain in lower abdomen and two of them have Tinea ascaris (TA) and Post menopausal bleeding (PMB).

Table II: Disease distribution in patients according to age

Disease↓ Ages→	18-20	20-40	41-60	Total
UTI	4	29	3	36
PID	7	21	5	33
Pruritis vulvae	0	8	1	9
Cervicitis &vaginitis	3	2	0	5
Pain in lower abdomen	1	2	2	5
Oligomennorohea	1	4	0	5
Dysmennorohea	0	1	0	1
Other	0	4	2	6
Total	**16**	**71**	**13**	**100**

UTI - Urinary tract infection; PID – Pelvic Inflammatory Disease

In the study we found that UTI was the most common disease followed with PID and found the indication for the irrational use of antibiotics in individual infection in table III. Probably appropriateness of use was higher in PID compared to UTI. As the overall probability of appropriateness of the study was 31.50% as explained in table III.

Table III: Distribution of patient according to infection

Disease	No. of patients	Physical Examination	Micro-organism isolation	Other Investigation	Probably appropriate antibiotic therapy (%)
UTI	32	32	15	1	40.625
UTI(ANC)	4	4	1	0	25
PID	33	33	8	11	48.48
PV	9	9	0	0	0
Boils	1	1	0	0	0
TA	1	1	0	0	0
Pain in episectomy	1	1	0	0	0
Pain in lower abdomen	5	5	3	1	80
Cervicitis & Vaginitis	1	1	0	0	0
Cervicitis	2	1	1	0	50
Vaginitis	2	2	2	0	100
Swelling on uterus	1	1	0	0	0
PMB	1	1	1	1	100
Oligomennorohea	5	5	0	2	60
Dysmennorohea	1	1	0	0	0
IUD	1	1	0	0	0
Total	**100**	**100**	**31**	**16**	**31.50**

UTI – Urinary tract infection, UTI(ANC) – Urinary tract infection (anti-netal case), PID- Pelvic inflammatory disease, PV – Pruritis vulvae, TA – Tinea ascaris, PMB – Post menopausal bleeding, IUD – Intra uterine disease

35 samples were prescribed for microbiological investigation and 16 samples for other investigation as shown in table III. Overall, probably appropriateness of treatment was 31.50% (p= 0.31 > 0.05).

Dose and duration of antibiotics were evaluated by studying the pharmacokinetic of prescribed antibiotics. Pharmacokinetic parameters considered for evaluating dose and duration Antibiotics prescribed was appropriate on the basis of pharmacokinetic parameters. All the prescriptions have antibiotic prescribed with accurate dose, duration and route.

118 antibiotics were prescribed. Out of them, 113 (95.7%) antibiotics were prescribed orally and 5 (4.23%) antibiotics prescribed were intramuscular (IM), p = 0.0423 for IM route is statistically significant. In table IV we found that the p = 0.053 (Fischer's exact test) was nearly significant for intramuscular therapy. The use of IM antibiotics was significant as they have clinical value higher than the oral therapy and reduces the cost of the treatment.

Table IV: Route of antibiotics prescribed in both groups

		Public	Private	Total
Route	**Oral**	62	51	113
	IM	5	0	5
Total		67	51	118

P= 0.053 (Fischer's test)
IM – Intra muscular

Cost evaluation of antibiotics was done by evaluating the marketed product and the range was evaluated by applying mean ± S.D. to evaluate the appropriateness of antibiotics as shown in table V.

Table V: Cost Evaluation of marketed antibiotics

Antibiotic	Cost Mean ± S.D.
Ofloxacin (200mg)	44.89±13.70
Ofloxacin (200mg) and Ornidazole (400mg)	68.4± 14.8
Doxycycline (100mg)	29.79± 19.97
Cefixime (200mg)	125± 86.58
Ciprofloxacin (500mg) and tinidazole (600mg)	73±17
Azithromycin (250mg)	109± 56
Norfloxacin (400mg) and Tinidazole (600mg)	50± 13
Norfloxacin (400mg) and Metronidazole (500mg)	54±5
Ofloxacin (400mg)	85± 42.60
Norfloxacin (400mg)	26.93± 17.23
Inj. Ceftriaxone (250mg)	29.8± 11
Cefadroxil (250mg)	33.7± 11.7
Ciprofloxacin (500mg)	54± 13.9
Amoxicillin (500mg)	63.45± 20.79
Ampicillin (500mg)	54.5± 10.8
Levofloxacin (500mg)	75.5± 33.5
Azithromycin (1000mg)	84.62± 6.23
Cefixime (400mg)	176 ± 109

Most frequently prescribed antibiotics during the study were ofloxacin (200 mg), ofloxacin (200 mg) with ornidazole (400 mg) and doxycycline (100 mg) in the gynaecology outpatients. Cefixime (400 mg) and ceftriaxone (250 mg) were the most rationally prescribed antibiotics and followed by norfloxacin (400 mg) with metronidazole (500 mg) - (80%) and doxycycline (100 mg) - (76.4%) as shown in table VI.

The table VII above shows that approximately 41 (41%) prescriptions were probably appropriate, 18 (18%) prescriptions were

inappropriate and 41 (41%) prescriptions were empirical.

Table VI: Frequency of antibiotics prescribed in the study

No.	Antibiotic	n (%)	Probably appropriate therapy (%)	Empirical antibiotic therapy (%)	Cost Appropriate (%)	Empirical therapy (%)
1	Oflox (200mg)	14 (11.86)	1 (7.14)	13 (92.85)	14(100)	0 (0)
2	Oflox (200mg) and ornidazole (400mg)	22 (18.64)	6 (27.27)	16 (72.72)	22(100)	0 (0)
3	Doxy (100mg)	17 (14.4)	13 (76.4)	1(5.88)	17(100)	0 (0)
4	Cefixime (200mg)	4 (3.38)	2 (50)	1 (50)	4 (100)	2 (50)
5	Ciproflox (500mg) and tinidazole (600mg)	9 (7.62)	8 (88.88)	0 (0)	0 (0)	0(0)
6	Azithro (250mg)	2 (1.69)	1 (50)	0 (0)	2 (100)	1 (50)
7	Norflox (400mg) and Tinidazole (600mg)	1 (0.84)	0 (0)	0 (0)	0 (0)	0 (0)
8	Norflox (400mg) and Metro (500mg)	5 (4.23)	4 (80)	1 (20)	5(100)	4 (80)
9	Oflox (400mg)	3 (2.54)	0 (0)	3 (100)	3 (100)	0 (0)
10	Norflox (400mg)	4 (3.38)	3 (75)	0 (0)	2 (50)	2 (50)
11	Inj.Ceftriaxone (250mg)	5 (4.23)	5 (100)	0 (0)	5 (100)	5 (100)
12	Cefadroxil (250mg)	2 (1.69)	1 (50)	0 (0)	2 (100)	1 (50)
13	Ciproflox (500mg)	3 (2.54)	0 (0)	2 (66.66)	3 (100)	0 (0)
14	Amox (500mg)	5 (4.23)	1 (20)	4 (80)	5 (100)	1 (20)
15	Ampicillin (500mg)	1 (0.84)	0 (0)	1 (100)	1 (100)	0 (0)
16	Levoflox (500mg)	1 (0.84)	0 (0)	1 (100)	1 (0)	0 (0)
17	Azithro (1000mg)	16 (13.55)	4 (25)	12 (75)	16 (100)	4 (25)
18	Cefixime (400mg)	4 (3.38)	4 (100)	0 (0)	4 (100)	4 (100)

Inappropriate antibiotic therapy was due to inappropriate choice of antibiotics, having no efficacy for treatment and the cost inappropriate for the therapy prescribed, i.e. p = 0.41 > 0.05(significant difference).

Table VII: Antibiotic therapy evaluation

	Probably Appropriate (%)	Inappropriate (%)	Empirical (%)
Total (100Prescriptions)	41 (41)	18 (18)	41 (41)
Public (50 prescriptions)	41 (82)	6 (12)	3 (6)
Private (50 prescriptions)	0 (0)	12 (24)	38 (76)

P = 0.41 > 0.05 by Fischer's test

P = 0.5391 > 0.05 by chi-square test

In empirical therapy, treatment is only based on the physical examination having no clinical investigation and antimicrobial sensitivity. Probably appropriate is that in which treatment is only based on the clinical investigation and has no antimicrobial sensitivity. Comparisons between two groups was significant different i.e. 0.5391 (Chi-square test).

Table VIII shows that 37 (31.35%) antibiotics prescribed were by generic name and 81 (68.64%) antibiotics prescribed were by brand name. Out of the 67 antibiotics prescribed in public hospital group, 36 (53.73%) antibiotics were by generic name and 31 (46.27%) antibiotics prescribed were by brand name. As 51 antibiotics were prescribed in private hospital group, out of them 1 (1.96%) antibiotic prescribed was by generic name and 50 (98.04%) prescribed were by brand name. Significance value of brand name i.e. p = 0.68 > 0.05 shows significant different.

Table VIII: Antibiotics prescribed

	Generic	Brand	Total
Public	36	31	67
Private	1	50	51
Total	37	81	118

P = 0.68 > 0.05 by fischer's test

As the cost is the major factor for rational use of antibiotics. Cost effectiveness was evaluated on the basis of table 6. 78% of antibiotics were cost effective and appropriate and 22% of antibiotics were inappropriate. Cost evaluation was done by evaluating the mean ± S.D. of antibiotics prescribed. Cost comparison in two group was not significant, i.e. p = 0.778 > 0.05, significant difference summarized by applying chi-square test in table IX.

The study has concluded that the 0% of the prescriptions was rational, 27% of the prescriptions were irrational and 73% of the prescriptions were empirical. Irrational use of antibiotics was significant different, p = 0.27 > 0.05 as shown in table X and graph 2. The study shows that the 30% of public prescription were irrational and 70% of them were empirical and in the private hospital there was no prescription which was rational, 24% were irrational and 76% were empirical. Comparing the two groups shows a significant difference i.e. p = 0.61053 (Chi-square test).

Table IX: Cost evaluation of prescribed antibiotics

	Appropriate cost (%)	Inappropriate cost (%)
Total	78 (78)	22 (22)
Public	38 (76)	12 (22)
Private	40 (80)	10 (20)

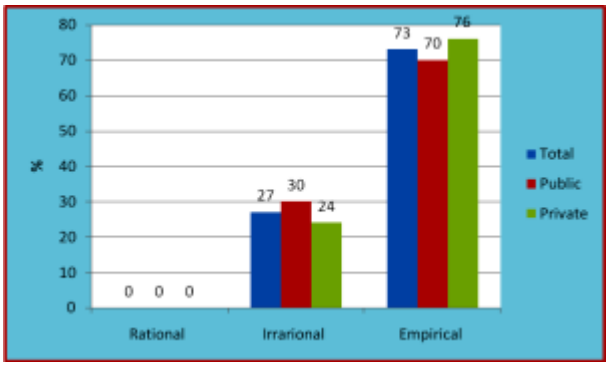
p = 0.778 > 0.05 by chi-square test

Table X: Rational antibiotic therapy:

	Rational (%)	Irrarional (%)	Empirical (%)
Total	0 (0)	27 (27)	73 (73)
Public	0 (0)	15 (30)	35 (70)
Private	0	12 (24)	38 (76)

p = 0.27 > 0.05 by fischer's test

p = 0.61053 > 0.05 by chi–square test



Graph 2: Rational antibiotic therapy

Univariate analysis of indicators for appropriate antibiotic therapy revealed that age distribution group patient received the 35% chance of receiving appropriate therapy. Indicators were identified with which appropriateness of treatment could be determined i.e. age, disease, clinical investigations, route, strength, antibiotic drug, cost appropriateness. In patients of 18-20 years, 43.75% have chance of receiving appropriate therapy, compared to 30.98% patients of 21-40 years and 30.76 % patients of 41-60 years. In patient of 18-20 age group, 6.23% inappropriate due to cost ineffectiveness, 4.22% of patients in 21-40 age group and 30.76% of patients in 41-60 age group. Probablity of appropriate treatment varied among the diseases, with a range of 0 - 100% as shown in table III. Probablity of appropriate prescription among the antibiotics is 0-100% (Table IV- VII).

Inappropriate use of antibiotics is the major cause for the irrational use of antibiotics. In the study, 4 prescriptions having the re-prescription and have no significance for the treatment i.e. there was no indication for the re-prescription of antibiotics and has no clinical evaluation for their use.

In 20 prescriptions, cost was inappropriate i.e. cost of treatment was higher than range. It was major causing factor for inappropriate use of antibiotics.

In 17 prescriptions, the inappropriate use of antibiotics was due to improper choice of antibiotics i.e. there was no benefit of antibiotic in any case in the indication as shown in table XI.

Table XI: Indication for inappropriate use of antibiotic therapy

Inappropriate indication	No. of Patients
Overuse or re-prescription	4
Cost ineffective	20
Antibiotic Inappropriate	17

The study has shown that the use of antibiotics was highly empirical. Irrational prescriptions were 27% and empirical prescriptions were 73%. Irrational prescribing is a problem that is difficult to counter[4]. However, prevention is possible. There is some evidence that interventions such as short problem-based training course in pharmacotherapy and rational use focused workshops can improve antibiotic use [5]. There is an urgent need to implement training initiatives, with support from public sources to ensure that there is no conflict of interest, to improve prescription behavior of practitioners in India and ensure that patients received evidence-based, cost-effective treatments for their health problems.

Discussion:

This study was one of the first of its kind to be reported from the Pt. B. D. Sharma University of Health Sciences, Rohtak, has highlighted the use of antibiotics in gynaecology department. Much concern about use of antibiotics has been voiced in the last two decades. It is repeatedly noted that 30-60% of antibiotics use is inappropriate, with consequent waste of resources [6]. Many hospitals have attempted the guidelines to solve these problems. Drug use evaluation has been shown to complement these efforts and provide valuable information on actual drug use. Cost-evaluation of antibiotics is a point – prevalence or retrospective analysis.

The purpose of current study was to determine the overall use of antibiotics in gynaecology outpatients, indications for use, route, utilization of clinical microbiological laboratory, appropriateness of antibiotic, cost evaluation and rational use of antibiotics. This study determines the actual status of use of antibiotics in the public Vs private hospital.

The first part of the study determines the appropriateness of antibiotic therapy. Antibiotics prescribed were 41% probably appropriate, 18% inappropriate and 41% empirical as shown in table VII. Significant difference was noted between public practitioner and private practitioner on all parameters and there has no evidence based explanations for these differences.

The second finding of study evaluates the cost effectiveness. 78% of antibiotics prescribed were cost effective and 22% antibiotics were cost ineffective. Significant difference was noted between both groups and reason for the cost inappropriateness was that the practitioner prescribing antibiotics was based on the antibiotics brand name. At other times the reason was improper use of antibiotics which increased the cost of treatment as shown in table VIII & IX.

The third finding evaluates the comparison between the two groups. As shown in table X, the public practitioners were prescribing the antibiotics more appropriate Vs the private practitioners and the study is highly empirical. But by statistical analysis there is difference in the both groups that is they are statistically different, $p = 0.61$.

Last finding in the study indicates inappropriate therapy. As in table XI, the overuse of antibiotics has led to their inappropriateness, inappropriate indication that is no investigation, cost ineffective and inappropriate choice of antibiotics. In most of the prescriptions, inappropriate therapy was due to clinically irrelevant indication.

In gynaecology, the irrational and empirical use of antibiotics is mainly to avoid clinical investigation and culture sensitivity test as far as possible. This was done to keep the patient bill low and mainly observed in private prescriptions. In public hospital, it's due to cost-ineffective, improper use of antibiotics and due to avoidance of culture sensitivity.

The principal limitation of this study was that it was done in only one private hospital for comparison of public Vs private patients and may not be representative of antibiotic use across the state. Another limitation is lack of microbial investigation, thus it is possible that difference between public and private practitioners may not reflect true differences between empirical and probably appropriate therapy. Another limitation is that the antibiotics prescribed are brand prescription by which the cost of antibiotics has increased and it can produce the difference between cost of public practitioner Vs private practitioners and

the leading cause for irrational use of antibiotics.

Univariate analysis revealed at least six indicators for appropriateness of treatment: age, disease, clinical investigations, route, strength, antibiotic drug, cost appropriateness, $p > 0.05$. These variables may be universal or hospital-specific; hence, the enormous use of antibiotics concluded that each hospital needs to conduct its own audits in order to assess hospital-specific indicators of (in) appropriateness. The obtained information should serve as a teaching tool to improve antibiotics use by physicians in gynaecology outpatients. In addition, these assessments provide information about the cost inappropriateness.

This study suggests the importance of continued and improved supervision and ongoing education of physicians pertaining optimal antibiotic use[7]. There is need of timely inspection for the appropriateness of antibiotic use. This study concluded that study was highly empirical and private practioners are giving completely empirical Vs public practioners.

Conclusion: The study has concluded that the 0% of the prescriptions was rational, 27% of the prescriptions were irrational and 73% of the prescriptions were empirical. Irrational use of antibiotics was significant different, $p = 0.27 > 0.05$. It shows that study was highly empirical and private practioners are giving completely empirical Vs public practioners. There are more chances of inappropriate prescriptions due to unavailability of investigation. This suggests that there is need of supervision, timely inspection and ongoing education of all practitioners for pertaining optimal antibiotic use.

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