AN EVALUATION OF METRONIDAZOLE (FIAGYL) IN THE PREVENTION AND TREATMENT OF SEPSIS FOLLOWING GYNAECOLOGICAL SURGERY

by

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Introduction

Anaerobic bacteria were first described by Pasteur in 1861 and recognised as human pathogen by Veillon and Zuber in 1894. Anaerobes are the normal microbial flora of the vagina and cervix of healthy women. Until recently, hospital infections were believed to be entirely due to aerobic organisms such as *Pseudomonas aeruginosa, B. Proteus, Klebsiella, Staphylococci* and *E. coli.* The role of anaerobic organisms in sepsis following surgical procedures of the female genital tract is well established now. Only during the last decade, techniques for growing and identifying facultative anaerobes have been perfected and are available widely. Bacteroides and anaerobic cocci are the predominant anaerobes constituting a large portion of the normal vaginal flora. When the local resistance of the tissues is lowered or when there is loss of blood, tissue damage or a breach in the mucosa of genital tract, these microorganisms invade the tissues and produce infection. Antimicrobial agents such as chloramphenicol and clindamycin were used for the treatment of such infections. Recent reports have shown that metronidazole is highly effective against a wide range of anaerobic bacteria.

We report here our observations with metronidazole (FLAGYL) in the prevention and treatment of sepsis following gynaecological surgery.

Material and Methods

This study was carried out in the Department of Obstetrics and Gynaecology, Institute of Maternal and Child Health, Medical College, Calicut. Fifty patients admitted for prolapse of the uterus during the period August 1979 to May 1980 formed the material for the study. Fifty patients treated during the period January 1979 to July 1979 for similar complaints formed the control Group. Routine clinical evaluation and investigations were carried out in all the patients prior to surgery. Patients in the control group were given crystalline penicillin, 10 mega units, every six hours and streptomycin ½ gm. twice daily for 5 days during the immediate post-operative period. Patients in the trial group were given metronidazole in addition to the above antibiotics. During the first 48 hours after operation, metronidazole (1 gm.) was given either as a retention enema every 12 hours or as a rectal suppository every 8 hours. From

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the 3rd post-operative day, metronidazole 400 mg. was given orally, thrice daily upto the 10th post-operative day. High vaginal swabs were taken for culture preoperatively and on the 10th post-operative day. Due to technical difficulties aerobic and anaerobic cultures could be done only in 20 patients in the trial Group.

Results

The results of our study are given in the accompanying Tables.

The two treatment groups were well matched for age, type of operation and other extraneous variables (Tables I and II $p < .01$). On the fifth post-operative day, 54% of patients in the control group had pyrexia compared with 34% of the trial group (Table III). Complications have been significantly absent in more number of cases in the trial group ($p = .05$). There is an apparent difference between the control group and trial groups in that 10% of the control group developed severe wound infection compared with only 6% of the metronidazole group. As far as the post-operative bed occupancy is concerned, majority of the patients in the trial group (92%) got discharged between the 11th and 14th days as against 78% of the control group (Table IV $p < .005$).

TABLE I
Age Distribution

Age	Trial Group	Control Group
25-35 years	8	6
36-45 years	11	13
46-55 years	18	19
56-65 years	8	10
66 and above	5	2
Total	50	50

TABLE II
Type of Operation

Operation	Trial Group	Control Group
Ward Mayo	47	47
Fothergill	1	1
Anterior colporrhaphy	1	1
Complete perineal tear repair	1	1
	50	50

TABLE III
Post-Operative Complications

Complications	Trial Group	Control Group
Nil	33	23
Mild infection (Temperature 100-101°F)	14	19
Severe infection (Temperature above 101°F)	3	8

TABLE IV

No. of days	Trial Group	Control Group
11-14	46	39
15-20	4	11
	50	50

Discussion

Genital prolapse is a common gynaecological complaint requiring surgery. Most of the patients are in the perimenopausal or post-menopausal age groups. Chronic respiratory infection, hypertension and diabetes mellitus frequently complicate these patients. Introduction of antibiotics, improvements in anaesthetic techniques and facilities for blood transfusion etc. have reduced the mortality and morbidity

in geriatric gynaecological surgery. In spite of adopting strict aseptic precautions and using antibiotics prophylactically, post-operative sepsis still continues to be a common complication. A good percentage of post-operative infection is now considered to be due to non-sporing anaerobic bacteria of endogenous origin. The anaerobes that are commonly encountered are usually resistant to the conventional antibiotics like penicillin, streptomycin, tetracycline etc. Drugs like chloramphenicol, lincomycin and clindamycin are effective against anaerobic bacteria, but the severe toxic reactions and emergence of resistant strains of organisms to these drugs limit their clinical use. Metronidazole, a well established amoebicidal agent, was first shown to be effective against anaerobic bacteria by Davies *et al* (1964). Subsequently its value in the prevention and treatment of anaerobic infections has been well established by various investigators (Study Group 1974, 1975), Nalini *et al* (1978), Mitra *et al* (1978), Sen (1978) and Hakim *et al* (1978).

In this study two almost identical groups of patients undergoing vaginal operations for prolapse were selected. Analysis of the two groups showed that metronidazole given as suppositories, or retention enema during the first 48 hours post-operatively followed by 400 mg. orally thrice daily, reduced post-operative complications and minimised post-operative hospital stay. Infections of severe nature were seen only in 3 patients of the trial group compared to 8 patients of the control group. The crucial period for antibiotic prophylaxis is the 4 hour immediately following contamination of the tissues (Burke 1979). Since metronidazole suppositories and retention enema are absorbed rather slowly, effective blood level may not have been reached for some 8-10 hours after administration, as a result of which the drug was not probably available to the tissues at the crucial period. We now feel that the infection rate in the trial group would have been further reduced had we started on prophylactic medication before surgery. Incidence of mild infection was also significantly less in the trial group.

E. coli was the commonest aerobic organism grown on culture both pre- and post-operatively (Table V). Metronidazole obviously has no effect on this pathogen. Pre-operative anaerobic culture was positive in 12 of the 20 patients studied (Table VI). But post-operative cultures were negative in all these patients after metronidazole therapy. None of the patients had any difficulty in tolerating the drug regime and there were no untoward side-effects.

TABLE V
Bacteria Isolated on Aerobic Culture

Organism	No. of cases
E. coli	20
Klebsiella	7
Gram positive cocci	5
Proteus	4

TABLE VI
Bacteria Isolated on Anaerobic Culture

Organism	No. of cases
Gram positive cocci	10
Bacteroides	1
Gram negative bacilli	1
No organism	8
Total	20

Summary

Fifty patients received metronidazole during the immediate post-operative

period in addition to antibiotics and another fifty patients received antibiotics only. Post-operative infection and bed occupancy were significantly less in the metronidazole group. Only four patients in the metronidazole group had a prolonged hospital stay as against eleven in the antibiotic group. Better prophylaxis can be achieved by administering metronidazole before operation than during the early post-operative period. Metronidazole is effective against anaerobic organisms and well tolerated by our patients.

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