Treatment of Urinary Infection with Co-Trimoxazole (Trimethoprim-Sulphamethoxazole)

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CO-TRIMOXAZOLE IS a new anti-infective agent. It is a combination of sulphamethoxazole and trimethoprim (5:1). This combination of drugs exerts a synergistic effect and is bactericidal (Darrell et al, 1968). The antibacterial action is due to blockage of successive steps in biosynthesis of folinic acid in bacteria. It possesses wide antibacterial spectrum and attains therapeutic tissue and urine concentration (B.M.J., 1969).

Toxic effects are few and trivial (Gruneberg and Kolbe, 1969; Csonka, 1969).

It has been used effectively in treating septicaemia, bacterial endocarditis, respiratory infection and gonorrhoea. Reeves et al (1969) and Grunneberg et al (1969) reported good clinical results with it in the therapy of urinary infection.

However, no comparative study of the effectiveness of co-trimoxazole has been reported from this country where the pattern and antibiotic sensitivity of the infective organisms may be different and cost of therapy is important. The present study compares the relative effectiveness of co-trimoxazole, ampicillin and sulphadimidine in the treatment of urinary infection.

Methods

Diagnosis of Infection :

The sole criterion of infection was the presence of significant bacteriuria which was defined as a bacterial count exceeding 10^5 bacteria per ml of urine in two consecutive specimens and showing the same bacterial flora on both occasions.

Presence of urinary symptoms or pyuria was considered as supportive evidence.

Bacteriological Techniques :

Urine specimen was collected early in the morning by a clean catch method in the female and in the male midstream urine was used.

Urine was cultured as soon as possible and not exceeding one hour after collection. Organisms were identified by standard techniques. Antibacterial sensitivity testing was performed by the disc diffusion method.

Criterion of Cure :

Eradication of the original organism was considered to be a cure. Urine specimens were examined and cultured on the third day of treatment and one week after completion of treatment.

Other Investigations :

These were urine for microscopy, glucose and protein; erythrocyte sedimentation rate, haemoglobin, total white cell count and differential; blood urea and liver function tests. They were done before and one week after completion of treatment.

Where indicated intravenous pyelogram and other investigations relevant to urinary infection were done.

The Trial

All patients were admitted and treated in hospital. Patients were only excluded in the following conditions; past history of drug hypersensitivity,

blood dyscrasias, hepatic and renal failure. When infective organism was found to be resistant to the drug initially allocated, a random reallocation to one of the other two remaining drugs was done.

Randomisation was achieved by drawing from sealed envelopes containing the name of drug to be used.

The dosage of co-trimoxazole (Bactrim) was two tablets twice daily (total of 320 mgm trimethoprim plus 1600 mg sulphamethoxazole), ampicillin 500 mgm 8 hourly and sulphadimidine 2 gm stat and 1 gm 6 hourly. The duration of therapy was seven days.

Results

Forty patients were admitted to and completed the trial. The groups were reasonably homogenous with respect to the age composition, sex and clinical presentation (Table I). The comparatively smaller number included in two of the three treatment groups was due to higher incidence of resistance of the infecting organisms (Table II) to sulphadimidine and ampicillin (Table III) thereby resulting in reallocation to the co-trimoxazole group.

Among the cases thus allocated, cure rate was 88.8% with co-trimoxazole, 100% with ampicillin and 33.3% with sulphadimidine. The difference observed between co-trimoxazole and sulphadimidine was statistically significant ($p < 0.05$) but not between co-trimoxazole and ampicillin.

No incidence of side-effects was reported during the trial and no significant alteration in haematological, renal and liver functions (Table IV).

Table I
Clinical Features of Patients Admitted to the Trial

	Co-moxazole No	Ampi-cillin No	Sulpha-dimidine No
No. of patients completing study	27	7	6
Age: 10 – 40 years	10	2	3
40 – 60 years	6	3	2
60 years	11	2	1
Females	26	7	5
Patients with urinary symptoms	13	3	5
Past history of urinary infection	14	2	1
Recognisable predisposing cause	5	2	3

Table II
Comparison of Infecting Organisms in the Three Treatment Group

Organisms	Co-trimoxazole	Ampicillin	Sulphadimidine	Total
E. Coli	7	3	1	11
Coliform	18	3	5	26
Proteus	0	1	0	1
Staph. Pyogenes	1	0	0	1
Pseudomonas	1	0	0	1
Total	27	7	6	40

Table III
Antibiotic Senstitivity of all Infecting Organisms on Initial Isolation

	No. of Organisms Tested	% Sensitivity
Ampicillin	40	57.5
Co-trimoxazole	40	90.5
Sulphadimidine	40	40.0
Nitrofurantoin	37	97.3
Kanamycin	19	68.4
Cephaloridine	15	66.7

Discussion

The overall results show that in the treatment of urinary infection due to susceptible organisms, co-trimoxazole and ampicillin were superior to sulphadimidine. These findings are in agreement with those of Reeves *et al* (1964) and Gruneberg *et al* (1969).

The three cases of failure to respond to co-trimoxazole were due to organisms acquiring resistance during therapy. However Brumfitt et al (1972) found no evidence that trimethoprim caused resistance of the organism responsible for the urinary infection.

No toxic effect occurred during the trial. The incidence of toxic effects of co-trimoxazole reported were few and these were rashes (Reeves et al, 1969), thrombocytopenia (Hanley, 1969), aplastic anaemia (Allison et al, 1969), and poor response to specific haematinic therapy in patients with megaloblastic anaemia (Chanarin et al, 1972). Therefore, the use of the drug is contraindicated in megaloblastic anaemia, aplastic anaemia and thrombocytopenic purpura.

Table IV
Haematological and Biochemical Data
(mean values)

	Bacterium			Ampicillin			Sulphadimidine		
	No.	Before	After	No.	Before	After	No.	Before	After
ESR	17	58.7±7.4	69.4±8.3	6	63.2±17.7	65.0±16.7	2	*	*
Haemoglobin	23	11.4±0.84	11.7±0.42	6	10.9±0.8	11.3±1.34	2	12.65	13.3
Total white cells	24	10,189.5±965	8,462.5±474	6	8,566.7±3,909	9,050±2,836.3	2	13450	7550
Blood Urea	20	49.2±7.6	63.2±14.4	5	38 ±7.7	39.4±5.4		*	*
Bilirubin	18	0.98±0.3	0.53±0.05	5	0.92±0.5	0.8±0.4		*	*
SGPT	16	14.6±7.6	8.75±2.1	5	6.0±1.3	7.8±2.3		*	*
SGOT	17	13.5±2.1	18.9±3.0	5	12.8±1.4	16.2±2.3		*	*

*not done

V
Results of Treatment

	Cured		Failed		Total
	No.	%	No.	%	
Co-trimoxazole	24	88.9	3	11.1	27
Ampicillin	7	100.0	0	0	7
Sulphadimidine	2	33.3	4	66.7	6
Total	33	82.5	7	17.5	40

In view of the high incidence of infecting organisms in urinary infections resistant to sulphadimidine (56%) in this country, the place of sulphonamide as the drug of first choice in treatment of urinary infection (Today's Drugs, B.M.J. 1970) should be reappraised.

Both co-trimoxazole and ampicillin achieved highly acceptable cure rates among susceptible organisms. The advantage of the former apparently lies in this that more organisms are sensitive to it – an important consideration to the practitioner who has limited access to sensitivity testing. Co-trimoxazole is also less expensive per unit course of treatment.

Summary

The therapeutic efficiency of co-trimoxazole used in the treatment of urinary infection was evaluated by comparing it with ampicillin and sulphadimidine.

Forty patients entered the trial. The sole criterion of infection was a bacterial count exceeding 10^5 bacteria per ml of urine in two consecutive specimens. Allocation to treatment group was at random. The duration of chemotherapy was seven days.

The cure rate effected by co-trimoxazole and ampicillin was comparable and superior to sulphadimidine. No toxic effects were reported in the trial.

Acknowledgement

We are grateful to Dr. H. O. Wong, Department of Medicine, University Hospital, for allowing us to study the patients under her care. We also wish to thank Messrs F. Hoffman-La Roche Ltd. for their supply of co-trimoxazole (Bactrim) used in this study and Miss Y. K. Pavee for typing the manuscript.

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