COMPARATIVE EVALUATION OF AMPICILLIN AND TRIMETHOPRIM-SULFAMOXOLE COMBINATION IN GONORRHOEA

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Summary

Fifty men suffering from uncomplicated gonococcal urethritis were treated alternatively either with 1,280 mg of trimethoprim (TMP) and 6,400 mg of Sulfamoxole (SDMO) (SUPRISTOL, 16 tablets) orally in two equally divided doses taken at a 12-hour interval, or with a single dose of 3.5 gm of ampicillin with 1 gm of probenecid (AMP-PBD). The cure rate in TMP-SDMO regimen was 79%, while that in AMP-PBD regimen was 95.7%. Sensitivity of the organism was tested to penicillin, ampicillin and TMP-SDMO. Toxic effects of the drugs were studied.

Introduction

Penicillin remains the most popular drug in the treatment of gonorrhoea since its discovery. Betalactamase producing gonococci pose a real threat to the treatment in the future, even with increasing doses of penicillin or with its derivatives. There is an urgent need to find out an alternative antibiotic/chemotherapy to cope up with the situation. Many workers have tried trimethoprim-sulfamethoxazole combination in various dose schedules in gonorrhoea patients with encouraging results. They have given the treatment for more than one day, which carries an inherent drawback of patient default and consequent failure. One day regimen is advisable in STDs clinics. So we conducted one day treatment schedule of TMP-SDMO (SUPRISTOL R) and compared it with the ampicillin plus probenecid regimen recommended by the U.S. Public Health Service[1].

Male patients suffering from uncomplicated gonococcal urethritis attending the skin and V.D. Clinic of the University Hospital, Banaras Hindu University, Varanasi, were admitted to the

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study. In every case urethral smear was made and stained by Gram's technique. The discharge was cultured on Chacko-Nair Medium[2] and incubated for 48 hours at 36°C in a candle jar. Blood VDRL was done for every patient.

Patients were given alternatively either TMP-SDMO or AMP-PBD. In the case of TMP-SDMO regimen, 8 tablets were given to the patient with the instruction to take all of them at 9.00 p.m. at his residence and to attend the Out-patient Department on the following morning at 9.00 a.m. for the second similar dose. In the case of AMP-PBD regimen, 1 gm of probenecid and 3.5 gm of ampicillin was administered orally as a single dose in the hospital. Patients were advised not to consume alcohol and to refrain from sexual intercourse. They were asked to attend the hospital for follow up on third and seventh day. In the case of TMP-SDMO regimen, total and differential white cell count, Hb%, ESR, serum proteins, serum alkaline phosphatase, SGOT and SGPT were done. On each follow up visit, patients were questioned about the progress and were clinically examined. Urethral smears were taken and Gram stained on each visit and culture was done on seventh day. Any case which showed smear or culture positivity on any follow up visit was classified as treatment failure. Those patients who had failed to return even once within seven days of registration were excluded from statistical analysis. Post-gonococcal urethritis was diagnosed if a urethral discharge showed atleast 10 leukocytes per field of microscopy using a $\times 100$ objective.

The culture plates were examined for oxidase positive colonies after 48 hours of incubation. The typical oxidase positive colonies were taken out with platinum loop and spread out uniformly over the fresh Chacko-Nair culture medium. The sensitivity discs of penicillin in the strengths of 0.1, 0.5, 1.0 and 10 units/ml, ampicillin discs in the strengths of 0.1, 0.5, 1.0 and 10 μg/ml and TMP-SDMO discs supplied by the manufacturers of the drug were planted over the media. The plates were incubated as before and examined after 48 hours for the zone of inhibition. A zone of inhibition of more than 20 mm was considered as criteria for the sensitivity of the organism to the penicillin and ampicillin and a zone of more than 16 mm was considered as sensitive in case of TMP-SDMO.

Results

Of the 25 patients treated with TMP–SDMO, 24 had follow up, out of them 19 were cured (79%). In the case of AMP–PBD regimen, 23 out of 25 patients were followed up. In this group 22 were cured (95.7%). The results are shown in Table-1. Five patients who failed in the TMP–SDMO

TABLE 1

Results of Treatment

Regimen	No. Treated	No. Followed up	No. of Failures	Success		PGU
				No.	%	
TMP–SDMO	25	24	5	19	79.0	1
AMP–PBD	25	23	1	22	95.7	2

P>0.9 P value was calculated by the X^2 tests.
PGU – Post gonococcal urethritis.

TABLE 2
Sensitivity of Gonococci In Vitro

MIC	No. of Strains Sensitive	Percentage of Strains
Penicillin in units / ml		
0.1	14	35.0
0.5	30	75.0
1.0	34	85.0
Ampicillin in ug / ml		
0.1	17	42.5
0.5	32	80.0
1.0	37	92.5
TMP-SDMO 7.5 mcg/ml (1.25 mcg TMP and 6.25 mcg SDMO)	34	85.0

Total number of strains tested 40.
All strains were highly sensitive to 10 units/ml of penicillin and 10 ug/ml of ampicillin.

regimen were later successfully treated with AMP-PBD regimen. The patient who failed to AMP-PBD regimen was successfully treated with TMP-SDMO regimen. One in the former and two in the latter regimen developed post-gonococcal urethritis. Both regimens were well tolerated by the patients. TMP-SDMO did not exhibit any adverse effect on hemopoiesis or hepatic functions. As regards the sensitivity of the organism to penicillin, ampicillin and TMP-SDMO, 14 strains (35%) were sensitive to 0.1 unit per ml of penicillin and 30 strains (75%) were sensitive to 0.5 unit per ml of penicillin. Six strains required more than 1.0 unit per ml of penicillin for the inhibition of the growth. As regards sensitivity to ampicillin, 17 strains (42.5%) were sensitive to 0.1 ug per ml., 32 strains (80%) were sensitive to 1.0 ug per ml of ampicillin for inhibition of their growth in vitro. In case of TMP-SDMO 34 strains (85%) were sensitive to standard disc of TMP-SDMO supplied. The sensitivity of the organisms is shown in Table-2.

Discussion

In the present study though TMP-SDMO regimen apparently cured less number of patients (79%) as compared to that of AMP-PBD regimen (95.5%), the difference was not significant statistically ($P > 0.9$). Arya et al[3] in Uganda got 65% of success in their patients treated with 4 tablets of trimethoprim-sulfamethoxazole (TMP-SMZ) twice a day for one day. Elliot et al[4] compared TMP-SMZ treatment with 2 doses of 6 tablets 12 hourly with U.S. Public Health recommended regimen of penicillin plus probenecid, and found that TMP-SMZ was significantly less effective (19% failure) than penicillin plus probenecid (4% failure). The lack of significance in our study may be due to small number of cases we treated. But the multiple dose regimen of TMP-SMZ given over two to five days by some workers yielded better results than single day regimen. Csonka[5] treated 180 men with gonorrhoea with various doses of TMP-SMZ. The highest cure rate (95.6%) was found after a 4 days course of the drug with a daily dose of 3 tablets twice a day. Carroll and Nicol[6] with a single dose regimen of 4 tablets daily for 5 days obtained a cure rate of 95.5%. Rodin and Seth[7] used 4 tablets one a day for 5 days and achieved 100% cure. Above results suggest that certain concentrations of TMP-SDMO in serum must be achieved and maintained for a critical period of

time to eradicate gonococcal infection. The minimal duration of time that such levels need to be maintained in the blood is yet to de determined. It is quite possible that by increasing the duration of treatment we may get a better response with the same dosage.

As regards the in vitro sensitivity, all of 40 strains were sensitive to 10 units per ml of penicillin and 10 ug/ml of ampicillin, indicating the absence of betalactamase producing gonococci (W.H.O.Report)[8]. There was no significant difference between penicillin and ampicillin in regards to sensitivity of the organism in vitro except in the cases of 0.1 unit/ml of penicillin and 0.1 ug/ml of ampicillin, where ampicillin inhibited more number of strains ($P < 0.01$). In case of TMP-SDMO the number of strains inhibited was equal to the number of strains inhibited by 1.0 unit/ml of penicillin. One patient who had a insensitive strain in vitro to TMP-SDMO responded successfully to the TMP-SDMO regimen in vivo. One strain which failed to AMP-PBD regimen whose MIC was more than 1.0 ug/ml of ampicillin was sensitive to TMP-SDMO disc. Patient harbouring this strain responded to TMP-SDMO regimen.

In view of the larger number of treatment failures with TMP-SDMO regimen, it is not advisable to use this as routine treatment for gonorrhoea. This regimen may give better results if the same dosage is given over a longer period than one day. Further studies of such regimen is necessary so that an alternative to penicillin regimen can be advised to patients liable to hypersensitivity reactions to penicillin and those infected with resistant strains of gonococci.

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References :

1. US Department of Health, Education and Welfare. Gonorrhoea-CDC Recommended treatment schedule, 1974. Public Health Service, Center for Disease Control, Atlanta, Georgia 30333.

2. Chacko CW: and Nair GM : A new convenient egg-enriched medium for the cultural diagnosis of gonorrhoea. Ind J Derm Vener Lep 1966, 32 : 41-51.

3. Arya OP, Pearson CH, Saroj K Rao and Blowers R: Treatment of gonorrhoea with Trimethoprim - Sulphamethoxazole in Uganda. Brit J Vener Dis. 1970, 46 : 214-216.

4. Elliott NC, Reynold G, Thornsberry C, Kellogg DS, Jaffe HW, Brown DT, Amstrong J and Rein MF: Treatment of gonorrhoea with Trimethoprim - Sulfamethoxazole. J Inf Dis 1977, 135 : 939-943.

5. Csonka CW: Therapeutic trial of some genital infections with Trimethoprim-Sulphamethoxazole. Post-grad Med J 1969 ; 45 Supp (Nov : 77-80.

6. Carroll BRT, and Nicol CS : TMP-SMZ in the treatment of non-gonococcal urethritis and gonorrhoea. Brit J Vener Dis 1970 ; 46 : 31-33.

7. Rodin P and Seth AD : Treatment of gonorrhoea with co-trimoxazole, procaine penicillin alone and procaine penicillin plus probenecid. Brit J Vener Dis 1972 ; 48 : 517-521.

8. World Health Organization. Report of a WHO Scientific Group. Neisseria gonorrhoeae and gonococcal infections. Technical Report Series 616 ; WHO Geneva 1978. 138.