RIFAMPICIN (RIMACTANE(R) CIBA) IN ACUTE GONORRHOEA

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Curtis and Wilkinson (1958) were the first to report on the emergence of strains of gonococci relatively insensitive to penicillin. Later, these were confirmed by other workers throughout the world. The clinicians very soon overcame this insensitiveness by increasing the dose of penicillin, but the "single-session" limit of penicillin therapy have already been reached at least in some countries. The resistance to streptomycin has already achieved a high percentage of treatment failures and it is considered that by 1971 the failure rate may reach 85.8% with 1 gm. of this antibiotic (Willcox et al. 1968).

Fortunately for us, the discovery of drugs against gonococci is still keeping pace with the increasing resistance and unfortunately imparting a sense of complacency in planning and execution of "anti-gonorrhoea measures".

Rifampicin is one such group obtained semi-synthetically from the primary substance produced by Streptomyces mediterranei. It has been shown to be active in vivo and in vitro against many Gram-positive and Gram-negative organisms including Mycobacterium tuberculosis (Rifampicin-S. V. Maggi et al. 1966), Mycobacterium leprae (Rees et al. 1970), against some viruses (Leading article, B.M.J. 1969a).

Rifampicin is known to act by inhibiting bacterial RNA synthesis. It acts on DNA-dependant enzyme RNA synthetase but it has no action on human RNA synthetase enzyme and as such on the synthesis of RNA in mammalian cells.

Cobbold et al. (1968), Fuga and Gentili (1968), and Willcox et al. (1968) have shown that the drug is active in gonorrhoea and although it imparts orange-red colour to urine yet with no other side effects. It has no effect on Dark field examinations of patients infected with early syphilis (Fuga, et al, 1968). Serum concentrations (as supplied by the manufacturers) after a single dose of 900 mg have been shown to be as high as 27.2 ug/ml at 2 hours; 15.44 at 8 hrs., and 8.33 at 12 hrs. even the level 1.64 ug/ml noted at 24 hrs. is in excess of MIC in vitro for gonococci. Phillips et al. (1970) listed 12 antibiotics and drugs in order of in vitro effectiveness (MIC for N. gonorrhoeae) as follows: penicillin, erythromycin, rifampicin, tetracycline, doxycycline, gentamicin, kanamycin, streptomycin, clindamycin, lincomycin, sulphamethoxazole and trimethoprim.

Material andmethods

This trial was given in 50 cases selected at random at the VD Clinic, Medical College Hospitals, Calcutta. Priority was given to those living or working near the clinic for ease of follow-up. The entire trial was done by the same investigators for selection, assessment and follow-up to eliminate any personal variation. The capsules were given on an empty stomach

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(approx. 4 hrs. after breakfast) in the clinic under personal supervision of the clinician. Efforts were made to follow-up the case after 24 hours, 3, 7, 14 and 21 days followed by a prostatic smear examination. Other tests of cure in urethritis cases were rigidly followed as a routine. Special tests were done in some cases viz., haemoglobin estimation, total and differential count of WBCs, estimation of total protein with albumin and globulin ratio, thymol turbidity and S.G.P.T. tests. Cultures of the discharge were done in some of the cases. The special tests and culture were done in pre and post-treatment periods to evaluate any possible toxicity and persistence of the Organism. Every patient was advised to withhold alcohol till advised.

Results

An analysis of the clinical data obtained is given below (details have been omitted for brevity):

Out of 50 cases 47 patients completed treatment and follow-up. Three cases defaulted. Out of these 47, five were females and 42 males.

The average age was 26.1 years (range was 17 to 42 years). Eleven patients had no occupation.

Of the total number of cases, 34 patients gave no previous history of venereal diseases and 16 patients had venereal anamnesis. Of the 16 patients, 6 had previous history of gonorrhoea which had been treated successfully. Seven patients had doubtful infections and 3 had other diseases than gonorrhoea.

The patients were put into two main groups according to their bodyweight. Group one patients weighing 120 lbs. or below had 600 mg (4 caps) of the drug. Out of 30 cases in this group four failed to respond. In group two patients weighing more than 120 lbs. had 900 mg. (6 caps) each. In this group there were 2 failures. The patients who failed to respond with 4 capsules within seven days were subsequently given 6 capsules statim (repeat dose) without any result. Total failures were six.

The average duration of the discharge in all the cases before treatment was 6.1 days (range 1-7 days). The discharge stopped after treatment within an average of 2.2 days, range being 1–7 days.

Of the 47 cases in this study, 41 cases were clinically cured (87.2%) while bacteriological cure rate was 40 (85.1%) and 6 cases failed (12.8%). The bacteriological examination was not done in one patient, hence this discrepancy.

Discussion

Rangiah[11] reported satisfactory result in 25 out of 38 cases of acute gonococcal urethritis treated with Rimactane. Yawalkar et al.[18] gave a trial of Rifampicin 30 cases with 93 3% cure. Previous trials as cited by him Cobbold et al.[3] Ciaula et al.[2] Califano[1] and Migliano (1968) gave a cure rate from 88.8% to 100% with single oral dose of 900 mg. Willcox (1970) compared a failure of 11.9% (900 mg of Rifampicin) with 28.6% (Proc. penicillin 2 4 m.u. by inj.). In this study a failure rate of 12.8% has been obtained with single dose of Rifampicin given according to the weight of the patient. Unpublished data of the work done in this clinic shows failures with single dose of inj. proc. penicillin G (aqueous) 1.5 m.u. with cryst. penicillin G 0.5 m.u. in 2%–these 2% cases were cured with another single dose on 4th day.

In one case successfully treated with Rimactane during the follow-up period, a penile sore appeared exactly after 2 months of taking Rimactane. This was diagnosed as "chancre" and was subsequently treated with benzathine penicillin. It corroborates the findings of Ciaula and Rantuccio[2] Fuga and Gentili[5].

The treatment failures were retreated with a repeat dose of 900 mg of Rifampicin but "once a failure always a failure." No side-reaction was observed in any patient except "red" urine. Laboratory investigations revealed normal data in pre and post-treatment periods.

Whether Rifampicin will also be active against viruses of Herpes progenitalis or warts is not yet known as none in this series had these concomittant infections.

The failure rate in this series (12.8%) has been calculated at the end of 3 weeks' follow-up. In all of our failure cases, the failure was obvious within first week (6th day usually) therefore according to Curtis and Wilkinson[4] postulation they were recurrences and not re-infection. Secondly, as stated earlier even a repeat dose of 900 mg did not help contrary to the report of Califano[1].

Conclusions

In conclusion, the points emerged out that Rifampicin (Rimactane) is a new drug for the treatment of acute gonococcal urethritis, potent, with no "masking of syphilis" having a good tolerability and particularly useful in cases of penicillin-sensitive cases. It has also the advantage of "single-session" therapy.

Addendum

Since the manuscript of this article has been prepared, the 3 drop-outs as mentioned above reported, and were found to be clinically and bacteriologically cured. Therefore out of the total of 50 cases put under this trial only 6 cases failed (12%).

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