

INHIBITION OF *Neisseria gonorrhoeae* BY NIFURATEL*†

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Nifuratel (Magmilor) is a nitrofurantoin derivative which has recently become available for treatment of vaginitis due to *Trichomonas vaginalis* and *Candida albicans*. The recommended dose is one tablet (200 mg.) orally three times daily for 7 days, plus one pessary (250 mg.) for 10 successive nights.

It seems possible that this drug will be used as a panacea for vaginal discharge and it is essential to know what effect, if any, it may have on *Neisseria gonorrhoeae*.

Material and Methods

Medium

Plates of chocolate agar containing 10 per cent. horse blood and serial dilutions of nifuratel were prepared. The nifuratel was initially dissolved in dimethylformamide, but dilutions for addition to the final medium were made in distilled water, so that the final concentration of dimethylformamide in the medium was never greater than 0.1 per cent. This was necessary because a concentration of dimethylformamide of 1.8 per cent. or higher in the medium was found to inhibit the growth of *N. gonorrhoeae*.

Strains

Swabs were taken from the urethra and cervix in women, and from the urethra in men, in whom a direct film of the discharge had shown Gram-negative reniform intracellular diplococci. The swabs were sent to the laboratory in transport medium (Amies, 1967), and were received within 24 hours.

On receipt in the laboratory, the material on the swabs was suspended, as uniformly as possible, in 0.1 ml. peptone water. A standard loopful was then used to inoculate the test plates, and also control plates of chocolate agar alone and chocolate agar containing 0.1 per cent. dimethylformamide. The plates were incubated in 5 per cent. CO₂ at 36°C. for 48 hours.

Chocolate agar with 10 per cent. horse blood was used to isolate strains before and after treatment with nifuratel.

Results

The effect *in vitro* of nifuratel on *N. gonorrhoeae* was tested on 32 strains (see Table); with thirty the minimum inhibitory concentration (m.i.c.) of nifuratel was 0.5 µg./ml. or less, and with the remaining two the m.i.c. was 1.0 µg./ml.

Strains tested after primary isolation showed a similar degree of sensitivity.

Clinical Trial

Eight men with gonococcal urethritis, confirmed by culture, were given nifuratel tablets, 200–400 mg. by mouth thrice daily for 7 days, and no other treatment. Some of the cases showed marked clinical improvement, especially those treated with the larger dose, but from all of them *N. gonorrhoeae* was isolated in urethral cultures at the end of treatment.

Six women, from whom *N. gonorrhoeae* had been isolated in cultures from the cervix and in whom stained smears were also positive, were given nifuratel pessaries (250 mg.) to insert, one nightly for 1 or 2 nights; no other treatment was given. Further cultures and smears were taken from the cervix 12 to 48 hours after the insertion of the last pessary. In five of the six women *N. gonorrhoeae* could not be demonstrated in the cervical specimens taken after the use of nifuratel pessaries. In four of the six, cultures and smears from the urethra had also been positive for *N. gonorrhoeae*, and in two of them urethral specimens taken after using nifuratel pessaries failed to reveal *N. gonorrhoeae*.

Discussion

Little is known of the serum and tissue levels attained in man after oral administration of

*Received for publication October 14, 1968.

†Some of these results were included in a paper read to the MSSVD in May, 1968.

nifuratel. In view of our results of sensitivity tests *in vitro*, our failure to cure cases of gonococcal urethritis in men with oral nifuratel suggests that the dose given was insufficient to produce adequate concentrations. Possibly a higher dose might be more effective, but until the maximum safe oral dose of nifuratel has been established this cannot be investigated.

After local treatment with nifuratel pessaries, provided the patient inserts the pessaries properly, the concentration of nifuratel in the region of the cervix will probably be high. Since with all 32 strains of *N. gonorrhoeae* tested the m.i.c. of nifuratel was 1 µg./ml. or less, there is a theoretical danger that nifuratel pessaries may mask the presence of gonorrhoea; experience with six patients showed that this did in fact happen with five. Our findings indicate that nifuratel pessaries should not be used in the treatment of vaginal discharge until the possibility of gonococcal infection has been eliminated.

Summary

(1) Nifuratel in a concentration of 1 µg./ml. or less inhibited the growth of 32 strains of *N. gonorrhoeae* *in vitro*.

(2) Oral nifuratel, in a dose of 200–400 mg. thrice daily for 7 days, failed to cure gonococcal urethritis in all of the eight cases investigated in males.

(3) Nifuratel pessaries masked the presence of *N. gonorrhoeae* in the cervix in the cases of five out of

six women tested. It is advised that this treatment should not be used for vaginal discharge until the possibility of gonorrhoea has been excluded.

We are grateful to Messrs Calmic Ltd., Crewe, for a supply of nifuratel (Magmilor).

TABLE

No. of Strains of <i>N. gonorrhoeae</i>	Minimum Inhibitory Concentration Nifuratel (µg./ml.)								
	≤ 0.1	0.25	0.5	1	2.5	5	10	25	50
32	2	10	18	2	0	0	0	0	0

REFERENCE

AMIES, C. R. (1967). *Canad. J. publ. Hlth*, **58**, 296.

L'inhibition de *Neisseria gonorrhoeae* par le nifuratel

RÉSUMÉ

- (1) Le nifuratel à la concentration de 1 µg./ml. ou moins a inhibé la culture de 32 souches de *Neisseria gonorrhoeae* *in vitro*.
- (2) Le nifuratel par voie buccale à la dose de 200 à 400 mg. trois fois par jour pendant sept jours n'a pas réussi à guérir l'urétrite gonococcique chez tous les huit patients étudiés.
- (3) Les ovules au Nifuratel ont masqué la présence de *Neisseria gonorrhoeae* dans le col chez cinq des six femmes testées. Ce traitement ne devrait pas être employé tant que la possibilité de la gonococcie n'a pas été exclue.