

TREATMENT OF UNCOMPLICATED GONORRHOEA WITH A SINGLE ORAL DOSE OF DOXYCYCLINE

S. Lidén, H. Hammar, L. Hillström, J. Wallin and S. Öhman

From the Department of Dermatology, University Hospital, Uppsala, Sweden

Abstract. Two-hundred-and-fifty patients (150 men and 100 women) with uncomplicated gonorrhoea were treated with 300 mg of doxycycline in a single oral dose. Among the 247 patients returning for at least two follow-up examinations, 6 failures (2.4%) and 3 probable reinfections (1.2%) were recorded. In a retrospective control group of the same size and given a standard treatment of 2.2 MIU of penicillin, there were 2.0% failures and 2.4% probable reinfections. It is concluded that doxycycline is highly effective in cases of uncomplicated gonorrhoea. Gastrointestinal side effects were frequently observed, especially when the drug was taken on an empty stomach, but were seldom of a significant degree.

Patients with uncomplicated gonorrhoea requiring an alternative to the standard penicillin treatment form a group of considerable importance in venereological practice. Thus in some parts of the world the frequency of gonococcal strains with a decreased sensitivity to penicillin is a real medical problem; up to 100% of the strains can be less sensitive to penicillin and figures of 30-50% are high values but repeatedly reported (13).

Persons with an established or presumed allergy to penicillin make up a group in which penicillin treatment is strictly contraindicated. In different populations the frequency of penicillin hypersensitivity varies between 1 and 10% (9). The sensitizing effect of penicillin seems to vary with different modes of administration, intramuscular injections giving a higher frequency of sensitization than oral medication (12).

An ideal alternative to penicillin treatment in uncomplicated gonorrhoea should thus meet the following qualifications (among others): it should not be cross-reacting immunologically with penicillin, it should be effective in a single dose in both men and women, and it should also be effective after oral administration.

The purpose of the present investigation was to relate doxycycline, a new antibiotic of the tetracycline group, to the three qualifications listed above. Doxycycline seemed to be a suitable remedy in this context because of its good absorption from the gastrointestinal tract (4) and its long intravascular half-life giving prolonged high concentrations of the antibiotic in the serum and tissues (5).

MATERIAL AND METHODS

The investigation was carried out at the Venereal Disease Clinic of the University Hospital, Uppsala, Sweden. This clinic is the only one in the city of Uppsala, which has about 100 000 inhabitants and in addition about 25 000 university students.

During the period February to May, 1970, all patients, both men and women, with uncomplicated gonorrhoea were included in the investigation. Patients with complications from their gonorrhoea and pregnant women were excluded, however, as were also a few patients who stated that they were going to complete the follow-up examinations in other clinics.

The criterion for the diagnosis gonorrhoea was a positive culture from at least one location. Specimens were taken from the anterior urethra of men and from the urethra, cervix and rectum in women. Smears for staining with methylene blue and microscopy were also prepared and the finding of gonococci in the smears provided the indication for immediate treatment. If this positive result was not confirmed by a positive culture, the patients were excluded from the investigation. This procedure of examination was repeated at each follow-up visit. The criterion for failure of treatment or reinfection also was a positive culture. The material for culture was transported to the bacteriological laboratory in Stuart's medium and inoculated on hematin agar within, at the most, 5 hours of taking the specimens. The bacteria were cultured for 48 hours on two plates of hematin agar with "Supplement B" (Difco), one plate without antibiotics and the other with polymyxin and ristocetin. For verification, a fluorescent antibody technique was used.

streptomycin are shown. In the doxycycline group 19 patients harboured strains with a decreased sensitivity to streptomycin compared with 4 patients in the control group. Decreased sensitivity to penicillin was found in 16 strains from the control group and in 4 strains from the doxycycline group. In one of the failures in the control group, the gonococcal strain was of penicillin sensitivity group II. None of the other failures were found in patients harbouring strains with decreased sensitivity to penicillin. In the doxycycline group, however, 3 of the 6 failures occurred in patients with strains totally resistant to streptomycin (group IV).

The subjective side effects encountered were all of gastrointestinal origin. Twelve of the first 25 patients who were given the doxycycline without a previous light meal experienced either nausea (9 patients) or vomiting (3 patients). Among the other 225 patients 35 (16%) had some nausea or abdominal pain, mostly of a very mild degree and 4% vomited. Four patients vomited only half an hour after taking the capsules; nevertheless, their gonorrhoea was cured.

DISCUSSION

The figures regarding the efficiency of various forms of treatment often vary within wide limits in different reports. No doubt a considerable part of this variation is due to differences in criteria for diagnosis and healing as well as differences in sensitivity of the gonococcal strains to antibiotics and in the social structure of the group of patients treated. Hence the results of new forms of treatment should be compared with the results of an established therapy, all variables other than the treatment being kept as constant as possible. The retrospective control material of the present investigation differs to some extent from the doxycycline-treated material with respect to the pattern of sensitivity of the gonococcal strains. In other respects the two groups are comparable. The fact that 3 of the 6 failures in the doxycycline group occurred in patients with gonococci totally resistant to streptomycin is worthy of note and deserves further observance.

The failure rates both in the doxycycline and in the penicillin-treated groups were of the same magnitude, i.e. about 2%. This result of the penicillin treatment is in agreement with the

figures given in a recent Swedish report (10). Thus, treatment with a single oral dose of 300 mg of doxycycline is comparable to a single injection of a mixture of 1 megaunit of short-acting crystalline penicillin and 1.2 megaunits of moderately long-acting procaine penicillin in this material.

Only a few reports on treatment of gonorrhoea with doxycycline have been published hitherto. Failure rates of 6% (7) and 3.7% (1) were recorded in two series consisting of male patients only. In another investigation doxycycline treatment of patients of both sexes having strains with decreased sensitivity to penicillin resulted in a failure rate of 17% (7 out of 41 patients) (8).

Of the 100 women in the present series 34 had rectal gonorrhoea. All these patients except one were cured by doxycycline, as also was the one man with rectal gonorrhoea. The woman who was not cured after the first treatment was certainly reinfected repeatedly, as she admitted having intercourse with her partner, who was not yet treated, and later repeated courses of both penicillin and tetracycline hydrochloride were unsuccessful despite an entirely benign sensitivity pattern of her gonococci. The result indicates that no special or additional doxycycline treatment is required in cases of rectal gonorrhoea. The material is too small, however, to permit any definite conclusions.

The results of other single session oral treatments are summarized in some recent articles (2, 6, 11, 13, 14). The rates of failure vary between 0% and 72%. The significance of these figures, of course, also varies owing to the factors mentioned in the beginning of the discussion and to variations in the numbers of patients treated. As a rule, no control series are available in the investigations quoted. With due regard paid to these circumstances, doxycycline seems to be comparable to the most efficient remedies known for oral single session treatment of uncomplicated gonorrhoea in both men and women.

Side effects of the doxycycline treatment, consisting of gastrointestinal disturbances, occurred despite the light meal preceding the intake of the capsules. Actual vomiting (9 patients) did not impair the therapeutic results, however. This supports the previous findings of a rapid absorption of the substance from the gastrointestinal tract (4). The nausea and/or gastric pain were regarded as insignificant by most of the 35 patients having

these symptoms and therefore we do not consider them as factors limiting the use of doxycycline in a large single dose. A smaller dose of 200 mg has been tried, but found to give unsatisfactory results (7).

When summarizing the results in relation to the three demands given in the introduction it can be concluded that all of them are fulfilled, except for the fact that the large single dose needed is less well tolerated by some patients. However, doxycycline would seem to be a suitable alternative treatment in cases of penicillin hypersensitivity. In the case of decreased penicillin sensitivity of the gonococci, our material does not permit any conclusions. In this context, however, the report of Lassus (8) indicating that doxycycline does not give uniformly good results in this situation, must be kept in mind.

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S. Lidén, M.D.
Department of Dermatology
University Hospital
S-750 14 Uppsala
Sweden