SINGLE-DOSE TREATMENT OF NON-SPECIFIC URETHRITIS*

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King (1964) has recently reviewed the difficulties in assessing any form of treatment in non-specific urethritis. He points out that, in the absence of any recognizable cause and with such marked variations in the severity of the condition, different criteria are required by different workers for diagnosis as well as for assessment of the cure. He goes on to state that unfortunately these criteria, the type of case, and the duration of the disease, are often not stated clearly in the reports of the numerous therapeutic trials which have been undertaken.

With these remarks we agree and would go even further in stating that in some reports the criteria required for both diagnosis and cure are not stated at all. It is with some diffidence, therefore, that we venture for the first time into this undoubtedly difficult field.

It is now more than 10 years since Lyall (1953)—at that time working in Liverpool—published his pioneer study on the combined use of streptomycin and sulphonamides in the treatment of non-specific urethritis. To an initial injection of 1 g. streptomycin he added 1 to 1.5 g. sulphathiazole four times daily for 5 days, and this has since become the standard treatment in many clinics throughout Great Britain. At the Liverpool Royal Infirmary routine treatment for many years consisted of an injection of 0.5 g. streptomycin combined with 1 g. sulphathiazole four times daily for 5 days. More recently sulphadimidine has been substituted for sulphathiazole in similar dosage.

The introduction, however, of the so-called long-acting sulphonamides offered the possibility of relief from the four-times-daily régime, which some patients find difficult to follow.

Jelinek (1959) claimed good results with the long-acting sulphonamide sulphamethoxy-pyridazine—proprietary names Lederkyn and Midicel—given by mouth for 5 days in a dose of 0.5 g. twice daily. Prebble (1962) described a trial using sulphadimethoxine—"Madribon", 1 g. stat and 1 g. nightly for 5 nights, and claimed good results. Willcox (1962) also reported satisfactory results with another long-acting preparation "Nuprin" or sulphadimethyloxazole.

A more recent addition to the long-acting sulphonamides is sulphamethoxydiazine or "Durenate". The advantage claimed for this compound is that it is less highly protein-bound than other long-acting forms and has therefore a greater degree of antibacterial activity for a given plasma concentration.

Present Study

We decided to give this compound a trial in non-specific urethritis in combination with streptomycin. A single injection of 0.5 g. streptomycin was given and two 0.5 g. tablets of "Durenate" were swallowed under supervision. No further sulphonamide was prescribed.

The trial was started in February, 1963, and completed at the end of February, 1964. Only those patients who presented with an unequivocal urethral discharge were included. The mere presence of pus threads in the urine in the absence of a demonstrable urethral discharge or the presence of pus in an early morning smear did not qualify the patient for inclusion. Gonorrhoea was excluded by stained smear, but no other investigations were undertaken before treatment. Previous treatment did not exclude a patient from the series provided that he presented with a urethral discharge.

All patients were instructed to refrain from intercourse and from alcohol, to drink liberal quantities

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of bland fluids, and to hold their urine for a minimum of 2 hours before each re-attendance. Patients were normally seen on the second or third day and at one week, 2 weeks, and 4 weeks after treatment. Whenever possible they were seen again at the end of 2 and finally at the end of 3 months.

Results

In attempting to determine what constitutes success and failure in the treatment of non-specific urethritis difficulties immediately arise. Whereas most venereologists would regard the persistence of discharge for more than 7 days or its recurrence after it had once ceased as an indication for further treatment, there is far less agreement even among venereologists working in the same department as to whether pus threads persisting in the urine at the end of one week, or for that matter at the end of 2 weeks, are an indication for further treatment. These are points which are seldom discussed in the literature of the subject.

Discarding those patients who defaulted after the initial attendance, there remained 111 cases suitable for analysis. I have attempted to analyse their status at 1 to 7 days, 7 to 14 days, and 14 to 28 days. Cases were regarded as failures at 1 to 7 days if a discharge was still present, if the urine remained hazy, or if further treatment had been given for any reason. The mere presence of urinary threads at this stage did not constitute a failure. In distinguishing between success and failure at 7 to 14 and 14 to 28 days, the criterion employed was whether additional treatment had been considered necessary by whichever venereologist saw the patient. Unfortunately, it was not possible to arrange that patients remained continually under the care of one person.

Using these very individual criteria it was found that at 1 to 7 days only five out of 111 cases (4.5 per cent.) were regarded as failures. At 7 to 14 days defaulters had reduced the numbers to 91 and failures had increased to 10.8 per cent., and at 14 to 28 days failures had increased to 23.7 per cent. of the 76 cases still remaining.

We compared these results with those in a series of 92 patients seen between July, 1962, and February, 1964, treated with 0.5 g. streptomycin and the conventional régime of 1 g. sulphadimidine four times daily for 5 days. Using identical criteria both for selection of cases and analysis of results, we found the percentages of success and failure almost identical, the failure rates at 1 to 7, 7 to 14, and 14

to 28 days being 7.6, 12.3, and 27.8 per cent. respectively (Table). The differences, which in each case favour "Durenate", are probably not statistically significant.

TABLE
PERCENTAGE FAILURE RATES AFTER 1, 2, AND 4 WEEKS

Dosage	Time since Treatment (days)		
	1-7	7-14	14-28
Streptomycin + Durenate 1 g.	4.5	10.8	23.7
Streptomycin + Sulphadimidine 20 g.	7.6	12.3	27.8

Conclusions

Because of the difficulties inherent in trials such as this, we are reluctant to make far-reaching claims; these results if accepted suggest that, in the routine treatment of non-specific urethritis, a single dose of the long-acting sulphonamide "Durenate" when combined with streptomycin can replace the conventional 4 to 5-day course of sulphonamide and produce results which are equally satisfactory.

Summary

A trial is described of sulphamethoxydiazine ("Durenate") in a single dose of 1 g. combined with streptomycin 0.5 g. in the treatment of non-specific urethritis. The results compare favourably with a series treated with 0.5 g. streptomycin and 1 g. sulphadimidine four times daily for 5 days.

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Traitement par dose unique des urétrites non-spécifiques

RÉSUMÉ

On décrit un essai de traitement des urétrites non-spécifiques par dose unique de 1 g. de sulfaméthoxydiazine "Durenate" combinée à 0,5 g. de streptomycine. La comparaison de ces résultats avec une série traitée par 0,5 g. de streptomycine et 1 g. de sulfadimidine, 4 fois par jour pendant 5 jours, montre qu'ils sont aussi satisfaisants.