INTRAMUSCULAR INJECTION OF PROCAINE PENICILLIN COMBINED WITH ORAL ADMINISTRATION OF AMPICILLIN IN THE TREATMENT OF GONORRHOEA*

BY

H. C. GJESSING AND K. ØDEGAARD

From the Bureau of Public Health, Department of Venereal Diseases, and the National Institute of Public Health, Department of Bacteriology, Oslo, Norway

Because of the increase in strains of *N. gonorrhoeae* relatively resistant to penicillin and the subsequent rise in treatment failures (Gjessing and Ødegaard, 1964), we decided to modify our previous treatment of males (one injection of 600,000 units procaine penicillin). Neither repeated smaller doses of procaine penicillin nor administration of a single large dose seemed to give satisfactory results. Epstein (1959) had 20 per cent. failures after five daily injections of 600,000 units procaine penicillin. Willcox (1963a) found failure rates of 5 to 10 per cent. after one dose of 1·2 mega units procaine penicillin, and Rantasalo (1963) had about 9 per cent. failures when the infection was caused by strains with highly decreased sensitivity and the treatment was a single dose of 3 mega units procaine penicillin. At present the substitution of other injectable drugs for procaine penicillin cannot be recommended for routine treatment without reservation (Willcox, 1962; Laird, 1963).

From a psychological and epidemiological point of view, oral administration of drugs is open to serious objections. The method is too convenient for the patients and could lead to a general belief that gonorrhoea can be cured merely by taking tablets. There are also other objections, well expressed by Willcox (1963a): "Not only do patients vary in their powers of absorption of orally administered drugs, but those with venereal diseases are notoriously unreliable in taking their medicines at the times and in the doses required. The danger also remains that unused tablets may be reserved for self-medication at a later date or may even be sold on the 'black-market' ". Our experience is the same and it requires little imagination to see that widespread and uncontrolled oral medication could lead to chaos.

We decided, therefore, to try a combination of intramuscular injection and oral administration under supervision. It was considered advantageous to continue with 600,000 units procaine penicillin as an injection, chiefly because this has been our routine treatment for some years, and it still has a very good effect on strains sensitive to penicillin. For oral administration ampicillin was chosen. Ampicillin has a better effect *in vitro* on gonococci than the three other oral penicillins—propicillin, phenethicillin, and penicillin V (Ødegaard, 1960; 1962)—and it was suggested (Ødegaard, 1962) that it might be of value in the treatment of gonorrhoea. Willcox (1963b) showed that ampicillin is very effective in the treatment of gonorrhoea, and Alergant (1963) found that it was a suitable alternative to penicillin by injection. It was also observed that ampicillin could be used to cure patients with relapse following routine treatment with procaine penicillin (Gjessing and Ødegaard, 1964).

Material and Methods

The subjects of the trial were 500 consecutive male patients. In association with the injection of 600,000 units procaine penicillin, a single dose of 1 g. ampicillin† (four tablets, each of 0·25 g.) was swallowed under supervision, the patients being told that the tablets were only a reinforcement of the injection. This treatment has been used from December, 1962, to February, 1964. The methods of diagnosis, sensitivity testing, follow-up, and distinction between relapse and re-infection were the same as described in previous papers (Gjessing and Ødegaard, 1962a, b).

Results

A comparison between the former treatment, Series I, which is part of a previous study (Gjessing

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† Doktacillin "Astra".

TABLE

COMPARISON BETWEEN 500 PATIENTS TREATED WITH 600,000 UNITS PROCAINE PENICILLIN ONLY (SERIES I) AND 500 PATIENTS TREATED WITH BOTH 600,000 UNITS PROCAINE PENICILLIN AND 1 G. AMPICILLIN (SERIES II)

	Series I					Series II				
Minimum Inhibitory Concentration of Penicillin G (units/ml.)	Patients (No.)	Followed up		Gc. neg.	Not followed up	Patients (No.)	Followed up		Gc. neg.	Not followed up
		Gc. positive					Gc. positive			
		Relapse	Re-infection				Relapse	Re-infection		
Less Sensitive:										
1.0	23	17	0	4	2	24	1	0	14	9
0.5	66 } 169	24 } 50	0	26	16	78 } 207	6 } 15	1	51	20
0.25	54 } (33.8%)	6 } (29.6%)	0	38	10	81 } (41.4%)	7 } (7.2%)	6	44	24
0.125	26 }	3 }	2	13	8	24 }	1 }	1	15	7
Sensitive:										
0.06	49	0	4	27	18	36	0	2	22	12
0.03	163 } 331	5 } 8	9	116	33	173 } 293	0 } 0	8	126	39
≤ 0.015	119 } (66.2%)	3 } (2.4%)	6	82	28	84 } (58.6%)	0 }	3	54	27
Totals ..	500	58 (11.6%)	21	306	115	500	15 (3%)	21	326	138

and Ødegaard, 1964), and the present treatment, Series II, is shown in the Table. In patients treated with both procaine penicillin and ampicillin, 15 failures (3 per cent.) were observed. All these failures occurred among the 207 patients infected with gonococci with decreased sensitivity to penicillin G (minimum inhibitory concentration ≥ 0.125 units/ml.), giving a relapse rate of 7.2 per cent. in this group. Among the 500 patients treated with procaine penicillin only, there were 58 cases of relapse (11.6 per cent.); 29.6 per cent. among the 169 patients with gonococci of decreased sensitivity, and 2.4 per cent. among patients infected with gonococci with a minimum inhibitory concentration of penicillin G of less than 0.125 units/ml.

Discussion

Whereas exclusively oral administration of drugs in the treatment of venereal diseases is open to serious objections, this is not the case when the orally administered drug is given in one dose under supervision and together with an injection. The two drugs used in this way in the present investigation (procaine penicillin G and ampicillin), both being penicillins, may provide the patient with a dose of penicillin which is equivalent to an amount normally requiring two injections.

The 3 per cent. failure rate in this series is about one-fourth of that in the series where the treatment was one injection of 600,000 units procaine penicillin only, and, though low, it could perhaps be further lowered by increasing the dose of procaine penicillin.

Willcox (1963b) had a failure rate of 12 per cent. in 199 patients treated with a single dose of ampicillin (0.5 to 2 g.). He found no real advantage in increasing the dose of ampicillin above a single dose of 0.5

g. Alergant (1963) had a failure rate of 5 per cent. in 200 cases treated with a single dose of 1 g. ampicillin.

It is however difficult to compare statistics. The number of patients treated and followed are not always sufficient. Further, the number of relatively resistant gonococci may vary from one investigation to another. It is evident that many other schedules of treatment may be used. At present we are trying a combination of one injection of 600,000 units procaine penicillin with 0.5 g. chloramphenicol by mouth.

Summary

In 500 males with gonorrhoea treated with one injection of 600,000 units procaine penicillin combined with a single dose of 1 g. ampicillin (four tablets, each of 0.25 g.) there were 15 failures (3 per cent.).

From a psychological and epidemiological point of view, injection is the method of choice. Exclusively oral administration of drugs as routine treatment is open to serious objections. As long as no injectable drug is discovered which is in every respect better than procaine penicillin it is therefore considered preferable to combine an injection of procaine penicillin with supervised oral administration of other drugs.

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Traitement de la gonococcie par intramusculaire de pénicilline procaine associée à un traitement oral d'ampicilline

RÉSUMÉ

Dans 500 cas de gonococcie chez des patients mâles, traités par une piqûre de 600,000 unités de procaine

pénicilline et une dose unique de 1 g. d'ampicilline (4 comprimés de 0,25 g.) il y eut 15 échecs (soit 3%).

Du-point de vue psychologique et épidémiologique le traitement par piqûre est la méthode de choix. Un traitement basé uniquement sur l'administration orale de médicaments est sujet à de sérieuses critiques. Tant qu'on n'a pas découvert de médicaments par piqûre supérieurs en tous points à la pénicilline procaine, il est préférable d'associer une piqûre de cette dernière à l'administration contrôlée d'autres médicaments par voie orale.