NALIDIXIC ACID IN THE TREATMENT OF URINARY TRACT INFECTIONS

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'Nalidixic acid' is a new naphthyridine derivative,[1] unrelated to either antibiotics or sulphonamide compounds, which has shown bacteriostatic activity against a large range of Gram-negative organisms causing urinary tract infection.

Clinical Tolerance in Humans

Human volunteers showed excellent tolerance to daily oral medication with sustained dose of 8 G/day for 180 successive days.[1] No significant alterations occurred in blood pressure, heart rate, haemoglobin level, blood cell picture, urinalysis and alkaline phosphatase.

Subsequent authors, Slade,[2] Lishman and Swinney,[3] Ward-McQuaid *et al.*[4] and Barlow,[5] report very few side-effects of a mild transient character, confirming by microscopy that no renal damage occurred.

Pregnancy Tests in Animals and Humans

High oral doses to both pregnant rats and monkeys showed no untoward effects upon mother or offspring,[1] while 4 pregnant human patients at 16 - 34 weeks' gestation had normal deliveries of healthy babies.[5]

Bacteriostatic Action

Nalidixic acid is absorbed from the gastro-intestinal tract and excreted in concentration by the kidneys with excellent antibacterial activity in the urine.[1] Single-dose oral medication was evident 4 hours afterwards with bacteriostatic activity detectable even at 24 hours. Correlation between clinical response and disc test sensitivity has been good.

Treatment

Ten patients were treated with nalidixic acid for urinary tract infections; two after ureter transplants.

Of these, 4 had infection with a single organism, *E. coli*, 2 with *N. gonorrhoea*, 1 with *Klebsiella* (with contaminant of *Strep. faecalis*); 1 (ureter transplant) with double infections of *Proteus* and *Pseudomonas*, 1 with *E. coli* and *Aerobacter*, and 1 (ureter transplant) with multiple infections of *Klebsiella*, *Aerobacter* and *Proteus*

The most common organism against which the drug was used was *E. coli*, 5 patients having this causative organism, one combined with *Aerobacter aerogenes*.

Results

Clinical cures were effected with sterile urine obtained from the 5th day to the 11th day after commencement of treatment. Single *E. coli* infections responded soonest with sterile urine — 5th - 6th - 8th days. Double and multiple infections of *Klebsiella*, *E. coli*, *Aerobacter*, *Proteus* and *Pseudomonas* responded with sterile urine on the 8th - 10th day. One *N. gonorrhoea* responded with vaginal smears negative on the 11th day.

TABLE I. ANALYSIS OF ORGANISMS PRESENT

Patients infected	(a) *Gram-negative*						(b) *Gram-positive*	
	Klebsiella pneumoniae 1	*Escherichia coli* 2	*Aerobacter aerogenes* 3	*Proteus vulgaris* 4	*Pseudomonas aeruginosa* 5	*N. gonorrhoea* 6	*Strepto-coccus faecalis* 7	*Total organisms incriminated*
1	+						+	2
4		+						1
1		+	+					2
1 (transplant)	+		+	+				3
1 (transplant)				+	+			2
2						+		1
10	2	2	2	2	1	1	1	—

TABLE II. RESULTS OF ALL PATIENTS TREATED

No.	*Condition*	*Urine culture*	*Dose (1 tab 500 mg.)*	*Period*	*Results*
1. F	Cystitis	*Klebsiella* *Strep. faecalis**	1 *q.i.d.*	10 days	Cured—urine sterile 8th day
2. F	Cystitis	*E. coli*	1 *q.i.d.*	10 days	Cured—urine sterile 10th day
3. F‡	Cystitis	*E. coli* *Aerobacter*	1 *q.i.d.*	10 days	Cured—urine sterile 10th day
4. F	Cystitis	*E. coli*	1 *t.d.s.*	7 days	Cured—urine sterile 8th day
5. F	Cystitis	*E. coli*	1 *q.i.d.*	10 days	Cured—urine sterile 5th day
6. F	Cystitis	*E. coli*	1 *t.d.s.*	10 days	Cured—urine sterile 6th day
7. M†	Gonorrhoea	*N. gonorrhoeae*	1 *q.i.d.*	10 days	Failure smears throughout
8. F	Gonorrhoea	*N. gonorrhoeae*	11 *q.i.d.*	10 days	Cured—negative vaginal smear 11th day
9. F	Ureter transplant postop. infection	*Klebsiella* *P. vulgaris* *Aer. aerogenes*	11 *q.i.d.*	10 days	Cured—urine sterile 10th day
10. F§	Ureter transplant postop. infection	*P. vulgaris* *Ps. aeruginosa* (second infection)	11 *t.d.s.* 11 *q.i.d.* (chloramphenicol administered and cure effected)	8 days 10 days	Cured—urine sterile after 3rd day

**Strep. faecalis* a contaminant, apparently also affected by treatment.
‡Organisms previously resistant to treatment with long-acting sulphonamides.
†Very resistant case, previously unsuccessfully treated with (1) penicillin (2) erythromycin (3) 'albamycin' and (4) pen. streptomycin.
§Second infection after initial cure effected.

Of the 2 remaining cases, 1 with *N. gonorrhoea* failed to respond, with urethral smears remaining constantly positive even through 4 previous courses of different antibiotics, received as outpatient; the other case (ureter transplant) with double postoperative infections of *Proteus* and *Pseudomonas* responded with sterile urine on the 3rd day after treatment, but these were again present in the urine several days after this. This patient subsequently responded to treatment with chloramphenicol.

The following interesting observations were made:

(*a*) A Gram-positive contaminant, *Strep. faecalis*, in one case disappeared from the urine during treatment with nalidixic acid.

(*b*) In one case with double infection of *E. coli* and *Aerobacter aerogenes* these responded to treatment with sterile urine obtained on the 10th day, despite remaining resistant to previous treatment with long-acting sulphonamides.

(*c*) Although *Monilias* are fairly common here, no *Monilias* were seen in urine of patients after treatment with nalidixic acid.

Dosage

Standard dosage adopted was 500 mg. *q.i.d.* or *t.d.s.* for 10 days with a total dose of 15 - 20 G.

Tolerance

The course of treatment for all patients was trouble-free and uncomplicated.

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