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No Cytogenetic Effects of Quinolone Treatment in Humans

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Cytogenetic effects of ciprofloxacin (500 to 2,000 mg daily) and ofloxacin (200 mg daily) were studied in lymphocytes from 31 patients treated for 1 to 10 weeks. Blood samples for cytogenetic analysis were taken before the start of treatment from all patients, after 1 week from 25 patients, and after 2, 4, 6, and 10 weeks from six patients. No chromosome-damaging effect could be demonstrated in any treatment group. The mean aberration yields for each cytogenetic parameter studied and the total number of aberrations were all normal at each sampling occasion.

Ciprofloxacin, norfloxacin, and ofloxacin are new quinolone derivatives which are structurally related to nalidixic acid but far more bactericidal; they are active against a wide range of gram-positive and gram-negative bacteria. The new 4-quinolones bind to DNA (9) and significantly increase the incorporation of [^{3}H]thymidine into the DNA of mitogen-stimulated human lymphocytes (1–3), indicating a stimulation of DNA synthesis in vitro. It has also been suggested that the quinolones may affect de novo pyrimidine biosynthesis and at high concentrations inhibit cell growth in vitro (2). A possible genotoxic effect can thus not be excluded. The present study was undertaken to investigate the cytogenetic effects of these drugs in vivo.

A total of 31 patients (16 men and 15 women) between 31 and 86 years of age (with a mean age of 67) were studied. The patients made up two groups. (i) The first group consisted of 25 ambulatory patients with complicated urinary tract infections treated for 7 days with either ciprofloxacin (Bayer) (13 patients) or ofloxacin (Hoechst) (12 patients). The 25 patients were randomly assigned at the start of the trial to either the ciprofloxacin or ofloxacin group. There was no difference between these two groups in sex, age, or duration or severity of disease. The daily dose of ciprofloxacin was 500 mg, and the daily dose of ofloxacin was 200 mg. (ii) The second group consisted of six hospitalized patients, four men and two women, with osteitis treated with 750 to 1,000 mg of ciprofloxacin twice daily for at least 10 weeks.

Blood samples for cytogenetic analysis were taken before the start of treatment from all patients, after 1 week of treatment from the first group, and after 2, 4, 6, and 10 weeks of treatment from the second group.

The blood samples were cultured for 48 h at 37°C in 10 ml of McCoy 5A medium with 20% fetal calf serum according to a standard method. Chromosome preparations were stained with Giemsa stain. One hundred metaphases from each individual and sampling occasion were analyzed on coded slides by two investigators, and the aberrations were recorded according to the ISCN nomenclature system (7). When difficulty arose in the classification of an aberration, a second opinion was sought. Such cells were never rejected, and agreement between the two observers was required before such cells were scored as normal or abnormal. The chromosome aberrations were referred to as gaps (chromatid and isochromatid gaps), breaks (chromatid breaks and acentric fragments), or exchange-type aberrations (chromatid interchanges, ring chromosomes, dicentric chromosomes, pericentric inversions, and marker chromosomes). Student's *t* test was used to analyze differences between means.

No significant differences were found in the mean yield of any aberration type or of the total number of aberrations between before and after 1 week of treatment with either ciprofloxacin or ofloxacin (Table 1). There were no differences in cytogenetic effects between the two treatment groups for any of the individual parameters or for the total number of aberrations. Neither were there any significant differences for any aberration type or combination of aberration types among the five sampling occasions for those patients who received a much higher ciprofloxacin dose (1,500 to 2,000 mg daily) for 10 weeks (Table 2). In both the short-term and long-term-treated patient groups, the mean aberration frequencies of each cytogenetic parameter studied as well as the total number of aberrations were all within the normal limits of our laboratory (4–6, 8).

The present study confirms results recently presented by Forsgren et al. (2), who found no increase in chromosome damage or DNA-strand breaks in lymphocytes incubated with up to 25 μg of ciprofloxacin per ml. Our results add the information that no chromosome-damaging effect can be observed in vivo with clinically used dosages even after long-term treatment.

TABLE 1. Structural chromosome aberrations in 13 patients treated with ciprofloxacin and 12 patients treated with ofloxacin

Patient group	Sampling time	Mean no. of structural chromosome aberrations			
		Gaps	Breaks	Exchanges	Total
Ciprofloxacin	Before treatment	2.9	2.2	0.4	5.5
	After 1 wk of treatment	1.6	2.6	0.5	4.7
Ofloxacin	Before treatment	1.8	2.5	0.7	4.9
	After 1 wk of treatment	1.8	2.1	0.7	4.6

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TABLE 2. Structural chromosome aberrations in six patients before treatment and on four occasions during treatment with 1,500 to 2,000 mg of ciprofloxacin daily

Wk of ciprofloxacin treatment	Mean no. of structural chromosome aberrations			
	Gaps	Breaks	Exchanges	Total
0	1.0	2.6	1.2	4.8
2	1.3	2.4	0.4	4.1
4	0.8	3.3	0.8	4.8
6	1.9	1.0	1.0	3.9
10	1.7	3.0	0.3	5.0

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