

Ceftriaxone diffusion from blood to aqueous humour in man

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SUMMARY Ceftriaxone penetrates into the aqueous humour in man. The interaction of indomethacin on the disposition of ceftriaxone appeared to be time-dependent. Indomethacin delayed ceftriaxone penetration into, but enhanced its persistence in, the aqueous humour, permitting a period of antibiophylaxis covering the required time for surgical treatment.

Ceftriaxone (Rocephin), a third generation cephalosporin, is widely used in ophthalmological surgery to prevent postoperative infections. It is active against a wide variety of pathogens, and its long terminal half-life permits a single preoperative intravenous administration. Although highly protein-bound (more than 90%), ceftriaxone shows good penetration of cerebrospinal fluid and eye.^{1,2} It is well known that indomethacin, a prostaglandin synthesis inhibitor, interacts with several drugs—epinephrine, ceftazidime, timolol.³⁻⁵ In this trial we studied the intraocular kinetics of ceftriaxone and the influence of indomethacin administration.

Patients and methods

Forty eight patients, 15 male and 33 female, ranging in age from 28 to 89 years (mean 72, SD 11), who had had cataract extractions were included in this study. They had no history of allergy to β -lactam antibiotics. All the operated eyes were free from infection and inflammation. The patients received 2 g of ceftriaxone during a 10-minute infusion. They were divided into two groups of 24 each. Group 1 received ceftriaxone alone, group 2 ceftriaxone and intrarectal indomethacin (100 mg) the day before surgery. Local anaesthesia was with a lidocaine-etidocaine mixture, and sedation was by flunitrazepam and phenoperidin.

Biochemical tests on all the patients gave normal results and protein levels were within the normal range. Blood and aqueous humour (0.1 ml collected

by anterior chamber paracentesis) samples were collected 30 minutes, and 1, 2, and 3 hours after the end of ceftriaxone infusion from six patients at each time for each group. Blood samples were centrifuged after collection, and plasma was removed and stored with aqueous humour (AH) at -20°C before assay. The samples were assayed by specific high liquid performance chromatography.⁶

Data were compared by Student's *t* test and were expressed as mean and SE of mean.

Results

The concentrations of ceftriaxone in plasma and aqueous humour are shown in Tables 1 and 2 for the two groups of patients. The ceftriaxone plasma levels obtained in both groups of patients were in the same range as those reported.⁶

The penetration kinetics of ceftriaxone in aqueous humour were faster in group 1 than in group 2. Furthermore, we found a statistical difference between the two groups for plasma and aqueous humour ceftriaxone levels two hours after the end of

Table 1 Ceftriaxone plasma concentrations: ceftriaxone alone (CA) and ceftriaxone plus indomethacin (CI)

Time (hour)	Plasma $\mu\text{g/ml}$ CA	Plasma $\mu\text{g/ml}$ CI
0.5	215 (36)	193 (38) NS
1.0	205 (41)	176 (15) NS
2.0	194 (19)	158 (18) S
3.0	152 (21)	154 (18) NS

Each value is the mean (SE) for six patients. NS=not significant. S=significant ($p<0.01$).

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Table 2 Ceftriaxone aqueous humour concentrations: ceftriaxone alone (CA) and ceftriaxone plus indomethacin (CI)

Time (hour)	Aqueous humour µg/ml CA	Aqueous humour µg/ml CI
0.5	ND	ND
1.0	6.0 (3.2)	ND
2.0	1.0 (0.7)	3.1 (2.2) S
3.0	ND	2.1 (4.2) S

Each value is the mean (SE) for six patients. ND=below limit of detection. NS=not significant. S=significant ($p<0.01$).

the antibiotic infusions: higher plasma concentrations and lower aqueous humour levels in group 1 and the contrary for group 2. Three hours after infusion the statistical difference was only in the aqueous humour.

Discussion

The spectrum of ceftriaxone is similar to that of the other cephalosporins. The main difference is its long plasma half-life.⁷ It is well known that ceftriaxone crosses the blood-brain and blood-ocular barriers, and prolonged aqueous humour levels are probably related to its prolonged plasma levels.²

Indomethacin seems to interfere with ceftriaxone. This interference involves ceftriaxone plasma and aqueous humour kinetics (levels and persistence).

The synergistic influence of both drugs is interest-

ing because it permits a longer antibioprophyllaxis for anterior chamber surgery. Furthermore indomethacin, either systemic or topical, may have a protective effect against cystoid macular oedema following cataract extraction.⁸

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