5% cefuroxime as an alternative to 5% cefazolin in the treatment of Gram-positive bacterial keratitis

Sir,

5% cefazolin recommended for treating Gram-positive bacterial keratitis (GPBK)[1] has been the mainstay of therapy for decades. In 2017, cefazolin sodium injection, from which the topical preparation was constituted, became unavailable in India. This inconvenienced treating GPBK, as a recent study[2] had reported an increase in fluoroquinolone resistance in Gram-positive bacteria in India, which meant that fourth-generation fluoroquinolones were less effective. While fluoroquinolone monotherapy is popular among ophthalmologists, cornea specialists still prefer fortified antibiotic combination to treat severe infections.[3] Left with little choice, we began using 5% cefuroxime, a second-generation cephalosporin. Cefuroxime-gentamicin has been reported to be equivalent to cefazolin-tobramycin or moxifloxacin in treating bacterial keratitis in one study[4] and ofloxacin in another study.[5] However, topical cefuroxime is not widely used in India like cefazolin.

We retrospectively reviewed medical records of 21 consecutive patients with GPBK treated with 5% cefuroxime from November 2017 to January 2018 and compared the outcome with another cohort of 54 consecutive patients with GPBK treated with 5% cefazolin from April to August 2017. The Institute Ethics Committee approval was taken for the study.

Both groups exhibited similar baseline characteristics [Table 1], except for the higher proportion of males in the cefazolin-treated group ($P = 0.04$). There was no statistically significant difference in outcome, resolution time, or posttreatment visual acuity

Table 1: Comparison between patients with bacterial keratitis treated with 5% cefuroxime* (Group A) and 5% cefazolin† (Group B)

Parameters	Group A (*n*=21)	Group B (*n*=54)	Two-tailed *P* value
Gender			
Male	9 (42.9)	37 (68.5)	0.04‡
Female	12 (57.1)	17 (31.5)	
Mean age (years)	47.5±22.7	45.1±20.8	0.66§
Mean symptom duration (days)	10±5.8	10.4±12.6	0.86§
Mean LogMAR visual acuity‖	1.76±0.78	1.63±0.91	0.56§
Mean size of ulcer (mm^2)	18.1±12.7	13.1±13.8	0.15§
Depth of ulceration			
Full thickness	10 (47.6)	20 (37)	0.4‡
Anterior stromal	11 (52.4)	34 (63)	
Hypopyon	12 (57.1)	27 (50)	0.58‡
Perforation/threat to perforation	4 (19)	5 (9.3)	0.24‡
Culture¶			
Streptococcus pneumoniae	12 (57.1)	34 (63)	0.65‡
Streptococcus pyogenes	2 (9.5)	3 (5.5)	
Staphylococcus aureus	4 (19)	13 (24.1)	
Bacillus spp.	2 (9.5)	0	
Staphylococcus epidermidis	1 (4.8)	1 (1.9)	
Corynebacterium diphtheriae	1 (4.8)	3 (5.5)	

*5% cefuroxime was prepared by dissolving two vials of cefuroxime sodium IP 250 mg (Cetil®, Lupin Ltd., Mumbai) in 2 ml of sterile water for injection each, and then adding 4 ml of this solution to 6 ml of artificial tears (Tears Plus® eye drop, Allergan India Pvt. Ltd., Bengaluru), †5% cefazolin was prepared by dissolving cefazolin sodium IP 500 mg (Reflin®, Ranbaxy Lab. Ltd., Gurugram) in 2 ml of sterile water for injection and then adding this solution to 8 ml of artificial tears. The dosing schedule of these topical antibiotics and other adjunct medications was as per standard guidelines[1], ‡*Z*-test for proportion, §Unpaired Student *t*-test, ‖Visual acuity could not be measured in one eye in Group A and two eyes in Group B, ¶One patient had polymicrobial infection in Group A, hence total number of isolates is 22. LogMAR: Log of the minimum angle of resolution

Table 2: Outcome in patients with bacterial keratitis treated with 5% cefuroxime (Group A) and 5% cefazolin (Group B)

Parameters	Group A (*n*=21)	Group B (*n*=54)	Two-tailed *P* value
Treatment outcome			
Healed	14 (66.6)	36 (66.7)	1.0*
Perforated	1 (4.8)	2 (3.7)	
Lost to follow-up	6 (28.6)	16 (29.6)	
Mean time to resolution in days	30.5±19.4	28.5±25.4	0.78†
Mean final corrected LogMAR distant visual acuity‡	1.61±0.89	1.32±0.98	0.3†

**Z*-test for proportion, †Unpaired Student *t*-test, ‡Visual acuity could not be measured in one eye in Group A and two eyes in Group B. LogMAR: Log of the minimum angle of resolution

between the two groups [Table 2]. 5% cefuroxime topical preparation remained stable for 5–7 days in room temperature, and no ocular toxicity was seen.

There are limitations in our study. This is not a randomized control trial, with a head-to-head comparison of cefuroxime and cefazolin, but a comparison with a historical cohort of patients treated with cefazolin. While such a trial would be desirable, in this case, the unavailability of cefazolin makes it impossible to carry out such a study. This study's intention is only to inform ophthalmologists of the potential of cefuroxime to be a viable and safe alternative to cefazolin, and drugs like vancomycin can be held in reserve. Larger controlled trials comparing cefuroxime to vancomycin or fourth-generation fluoroquinolones are required to support our findings. As these trials take considerably more time and resources, we believe that in the interim, our findings should provide useful direction in treating GPBK in India.

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Conflicts of interest

There are no conflicts of interest.

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