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Ophthalmic fluorometholone-gentamicin versus ophthalmic betamethasone-gentamicin following cataract surgery

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Abstract A prospective, randomised, investigator-masked, parallel-group study was performed to compare fluorometholone-gentamicin eye drops and ointment with betamethasone-gentamicin eyedrops and ointment in the control of ocular inflammation after cataract surgery. Seventy patients (35 in each treatment group) of both sexes undergoing cataract-lens implant surgery for visually disabling cataract were enrolled in the study. The demographic and baseline parameters on day 1, the day after surgery, were similar in the two study groups. After treatment, on day 3 and day 6 post-operatively, the reduction in cells in the anterior chamber and conjunctival hyperaemia were similar in the two study groups. Both treatments were equally well-tolerated. Ophthalmic fluorometholone-gentamicin was as effective as ophthalmic betamethasone-gentamicin in the control of ocular inflammation after cataract surgery.

Key words Betamethasone-gentamicin; cataract surgery; fluorometholone-gentamicin; intra-ocular lens; ocular inflammation

Introduction Cataract extraction and intra-ocular lens (IOL) implantation, the most commonly performed ophthalmic surgical procedure, is now a very safe and predictable procedure due to modern advances like the widespread use of viscoelastics. However, this procedure is usually associated with varying degrees of post-operative inflammation and a risk of intra-ocular infection. Hence, it is common practice to use a topical steroid and antibiotic, usually as a combination eyedrop, following cataract-IOL surgery.[1]

The use of topical corticosteroids is associated with several ocular side-effects like raised intra-ocular pressure (IOP), delayed wound healing and increased risk of infections.[2] Betamethasone is a synthetic corticosteroid which is structurally similar to dexamethasone with high anti-inflammatory potency and a tendency to raise IOP.[3] Fluorometholone is a corticosteroid which has a reduced propensity for increasing IOP[4] and has been shown to be effective in controlling ocular inflammation after cataract surgery.[5]

Gentamicin is an aminoglycoside antibiotic with a broad spectrum of ac-

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tivity[6] and low bacterial resistance rates.[7] It would be of benefit to patients if a topical steroid-antibiotic combination containing fluorometholone, with its better safety profile, was found to be as effective an anti-inflammatory agent as a combination containing betamethasone, following cataract surgery. We performed a prospective, randomised, investigator-masked study to compare the efficacy, safety and local tolerance of Fluorometholone-Gentamicin (FML-Genta) combination eyedrops and ointment with that of Betamethasone-Gentamicin (Beta-Genta) combination eyedrops and ointment in the control of ocular inflammation after cataract-IOL surgery.

Materials and methods Seventy eyes of 70 patients of both sexes with visually disabling cataract and no other ocular pathology scheduled to undergo cataract-IOL surgery were included in the study. Exclusion criteria included severe systemic disease, history of intra-ocular surgery in the operative eye, concurrent medication with systemic or local anti-inflammatory drugs and known hypersensitivity to any of the components of the study medications.

The study patients were randomly allocated to one of the two treatment groups, FML-Genta (fluorometholone 0.1% and gentamicin 0.3%) or Beta-Genta (betamethasone 0.1% and gentamicin 0.3%) eyedrops and ointment respectively. They were examined one day pre-operatively and post-operatively on days 1, 3, and 6. The operation was a routine extracapsular cataract extraction and posterior chamber IOL implantation performed by a single surgeon (PDS) according to a standardised operating procedure. A subconjunctival injection of gentamicin 20 mg was given at the end of surgery. The study eyedrops were instilled three times daily and the eye ointment once every night in the operative eye from the first post-operative day, after the baseline ophthalmologic examination.

The parameters evaluated at each visit consisted of Snellen visual acuity, conjunctival hyperaemia (0-none, 1-mild, 2-moderate and 3-severe according to a standard pictorial chart), corneal oedema (presence or absence using a slit-lamp), cells in the anterior chamber (the number of cells seen in a standard oblique slit-lamp beam 3 mm long and 1 mm wide; 0-none, 1-1 to 10, 2-11 to 50 and 3-more than 50), IOP (with a slit-lamp mounted Goldmann applanation tonometer) and fundus examination (normal or abnormal using an ophthalmoscope).

A global assessment of local tolerance to the study medications was performed at the final visit by the doctor and the patient (0-poor, 1-fair, 2-good, 3-excellent).

For statistical significance testing, the following tests were used: chi-squared test (for nominal data like sex), Mann-Whitney-U-test (for ordinal data in symmetric distribution like age), Mantel-Haenszel test (for ordinal data like conjunctival hyperaemia, cells in the anterior chamber and local tolerance) and analysis of variance for visual acuity and intra-ocular pressure. A p value of <0.05 was considered statistically significant.

Results Seventy (FML-Genta 35, Beta-Genta 35) patients were enrolled in the study and randomised to one of the two treatment groups. The FML-Genta group consisted of seven males and 28 females with a mean age of 70 (SD 8) years and the Beta-Genta group consisted of nine males and 26 females with a mean age of 72 (SD 9) years. The two treatment groups were similar in all the pre-operative parameters.

The degree of conjunctival hyperaemia during the study period is shown in Table 1. It may be seen that the reduction in conjunctival hyperaemia was similar in the two study groups. Similarly, the reduction in the severity of cells in the anterior chamber (Table 2) was similar in the two study groups. There was no statistically significant difference between the two treatment groups in the other clinical parameters evaluated – visual acuity, corneal oedema, IOP and fundus examination.

There was no statistically significant difference between the two treatment groups for local tolerance assessment by the doctor (FML-Genta mean grade 2.2, SD 0.3; Beta-Genta 2.2, SD 0.2; p=0.2) or the patient (FML-Genta mean 2.0, SD 0.3; Beta-Genta 2.2, SD 0.4; p=0.2).

The key efficacy variable in this study was cells in the anterior chamber which was graded on a 0 to 3, 4-point scale. The clinically significant difference between the two treatment groups for this variable was specified as 0.5. The standard deviation of this variable was 0.5 on day 3 post-operatively and 0.35 on day 6 post-operatively. Given the total sample size of 70 patients, this study had a power of >90% to detect a clinically significant difference of 0.5 (in the grading of cells in the anterior chamber) between the two treatment groups if such a difference really existed. This study also had a similar degree of power (>90%) to detect clinically significant differences (specified as 0.5) between the two treatment groups for the other variables evaluated (conjunctival hyperaemia, local tolerance, etc.) all of which were graded on a 0 to 3, 4-point scale.

There were three adverse events during the study – two patients on FML-Genta complained of a slight and transient stinging sensation on instillation while one patient on Beta-Genta had to be withdrawn from the study due to increased intra-ocular inflammation.

Discussion In spite of the increasing use of topical NSAIDs (non-steroidal anti-inflammatory drugs) to control inflammation after cataract surgery, topical corticosteroids continue to be widely used for this purpose. As regards the reduction of risk of intra-ocular infection after cataract surgery, various practices have been adopted for this purpose. These include pre-operative topical antibiotics, intra-operative topical or intra-ocular antibiotics and at the end of surgery, antibiotics are administered subconjunctivally or

TABLE 1. The severity of conjunctival hyperaemia.

Post-operative day	*Mean (standard deviation)*		*'p' value*
	FML-Genta	Beta-Genta	
1	1.5 (0.5)	1.6 (0.5)	0.71
3	1.3 (0.5)	1.4 (0.5)	0.38
6	1.1 (0.3)	1.0 (0.3)	0.92

TABLE 2. The grading of cells in the anterior chamber.

Post-operative day	*Mean (standard deviation)*		*'p' value*
	FML-Genta	Beta-Genta	
1	1.6 (0.6)	1.7 (0.6)	0.74
3	1.1 (0.5)	1.2 (0.5)	0.61
6	0.9 (0.3)	1.0 (0.4)	0.85

through the use of collagen shields. However, one of the most widely adopted practices is probably the administration of a topical antibiotic post-operatively, usually in combination with a corticosteroid. These combinations include dexamethasone-tobramycin, dexamethasone-gentamycin, dexamethasone-chloramphenicol, dexamethasone-neomycin-polymyxin, betamethasone-gentamycin, betamethasone-neomycin and fluorometholone-neomycin.

In this study we found FML-Genta to be as effective as Beta-Genta in controlling post-operative conjunctival hyperaemia and intra-ocular inflammation as assessed by cells in the anterior chamber. Although betamethasone is clinically perceived to be more potent than fluorometholone, particularly for the management of intra-ocular inflammation, it is apparent that the degree of ocular inflammation induced by modern extracapsular cataract surgery is as well-controlled by ophthalmic FML-Genta as by ophthalmic Beta-Genta. Also, both the study treatments were equally well-tolerated as assessed both by the doctor and the patient. These observations are consistent with that of Van Endt *et al.*[8] who found that FML-Genta eye drops were as effective and well-tolerated as Maxitrol® (a combination of dexamethasone 0.1%, neomycin 0.35% and polymyxin-B 10,000 IU/ml) eyedrops in controlling inflammation after cataract surgery. Thus, while FML-Genta was as effective and as well-tolerated as Beta-Genta in this study, it did not demonstrate any advantages. However, the use of steroid-antibiotic combinations like FML-Genta after cataract surgery has theoretical advantages over the use of steroid-antibiotic combinations containing potent steroids like betamethasone and dexamethasone in terms of reduced risk of steroid-related side-effects, particularly raised intraocular pressure. It is possible that FML-Genta would have demonstrated its lesser tendency to raise intraocular pressure compared with Beta-Genta if the follow-up period in this study had been extended to, for example, four to six weeks.

In conclusion, this study demonstrates that ophthalmic fluorometholone-gentamicin is as effective and well-tolerated as ophthalmic betamethasone-gentamicin in the control of ocular inflammation after cataract surgery.

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