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Assessment of the effect of cyclosporine-A 0.05% emulsion on the ocular surface and corneal sensation following cataract surgery

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ABSTRACT

Aim: To assess the effect of cyclosporine-A (CsA) 0.05% ophthalmic emulsion on corneal sensation and ocular surface problems following cataract surgery.
Design: Prospective, randomized, double masked clinical trial.
Methods: Consecutive case series of patients attending for bilateral cataract surgery. Subject's eyes were randomized to receive either topical CsA or carboxymethylcellulose 0.5% (CMC) eye drops twice daily for one month following routine cataract surgery. Subjective and objective assessments were performed pre-operatively, one week, and one month after surgery. Primary safety parameters included best spectacle-corrected visual acuity and incidence of adverse events. Objective assessments included tests of tear film (osmolarity, tear break-up time, and Schirmer's type-I test), ocular surface staining, corneal sensitivity and a subjective assessment: ocular surface disease index (OSDI) questionnaire.
Results: 30 subjects (60 eyes) were recruited. At one month following cataract surgery, osmolarity, ocular surface staining, TBUT, Schirmer's results showed a greater improvement after CsA drops compared to CMC and this was statistically significant for all measures ($p < 0.05$). All corneal sensation measurements were reduced after one week and one month. Eyes receiving CsA had higher recovery of corneal sensation at both time points post operatively and this was statistically significant at one month. OSDI questionnaire results did not show a statistically significant difference between the two eyes.
Conclusions: CsA is effective and safe in the management of ocular surface problems after cataract surgery and allows faster recovery of corneal sensation. This recovery of sensation may be relevant to the improvement in ocular surface problems in all patients.

1. Introduction

Recent advances in ophthalmology, in particular those relating to cataract surgery have led to an increasing focus on the qualitative outcomes of cataract surgery. Measurement of patient's satisfaction after cataract surgery now includes not only the visual outcomes but also ocular comfort and the patient's experience of surgery [1].

The occurrence of dry eye in the first few months following cataract surgery has been frequently reported [2,3]. Several factors could exacerbate a dry eye condition or lead to a new transient status of dry eye in patients following cataract surgery including disruption of corneal nerves [4], ocular surface toxicity from topical ophthalmic medications [5,6], and the surgical procedure itself [7]. Khanal et al. described a deterioration in corneal sensitivity and tear physiology immediately after small incision cataract surgery, which does not return to preoperative levels until three months postoperatively, whereas the tear function recovers within one month [3]. Lyne has also demonstrated anaesthesia in the upper half of the cornea even after one year [8].

Suboptimal visual outcomes in the period immediately after cataract surgery (particularly with premium intraocular lenses) are

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sometimes felt to be related to a dry ocular surface and tear film instability with the presence of superficial corneal punctate erosions [2].

Topical cyclosporine-A (CsA) is an immunomodulator and anti-inflammatory agent. It is a fungal peptide which inhibits expression of various immune mediators such as Interleukin (IL) 2, IL-4 and Interferon (IFN) gamma, and through interaction with T cells inhibits lymphocyte proliferation [9]. In doing so CsA may well protect the goblet cell, a key player in providing a healthy ocular surface [10]. Studies have confirmed increased numbers of goblet cell in patients using topical CsA [11]. CsA has been shown to improve dry eye symptoms by restoring the tear film equilibrium and volume in dry eye patients [12].

The aim of this study was to assess the safety and efficacy of topical CsA ophthalmic emulsion used after cataract surgery to improve the ocular surface and hence surgical outcomes, and also to explore the possibility of CsA accelerating the recovery of corneal sensation.

2. Materials and methods

Full ethical approval was obtained from the University of Ulster and procedures carried out were in accordance with the ethical standards of the local Research Ethics Committee and with the Declaration of Helsinki.

A prospective, randomized, double masked, single-centre clinical trial recruited a consecutive case series of 30 subjects attending a tertiary referral eye centre for bilateral cataract surgery. Subjects included adults with cataract with normal lid position and closure and no known ocular disease. Informed consent was obtained from all subjects after discussion of the risks and possible consequences of the study.

A thorough history was taken to ensure that any subject with potential contra-indications to the study medication was excluded. Those with ocular surface disease, systemic or an ocular disorder that could possibly interfere with the interpretation of study results, prior usage of CsA or a systemic or topical steroidal or non- steroidal anti-inflammatory drugs during the previous 90 days before surgery, or had complicated surgery were also excluded from the study.

Subjects were randomized, via a computer-generated randomization schedule, into two treatment groups. The first group received topical CsA 0.05% ophthalmic emulsion (Restasis®, Allergan Inc., Irvine, CA) twice daily for one month following surgery in the first eye undergoing cataract surgery. The second group used carboxymethylcellulose 0.5% (CMC) preservative free (Refresh Plus®, Allergan Inc., Irvine, CA) drops on the same regimen following cataract surgery in the first eye to be operated. After a minimum of two months, the second eye of each subject underwent cataract surgery and received the other drop i.e. if first eye had received CsA then the second eye had CMC; and vice versa.

In both groups, subjects used CsA or CMC in addition to the standard postoperative treatment. Both Restasis® and Refresh Plus® look the same and have similar vials and the drugs labelling was masked in both groups.

All patients underwent standard small incision cataract surgery by the same surgeon, whereby the corneal incision was made in the

Table 1
Outcomes comparing all parameters between the CMC eyes and CsA eyes.

	Parameter	CMC (Mean ± SD)	CsA (Mean ± SD)	*P*-value
Pre-op	BSCVA (LogMAR)	0.8 ± 0.6	0.6 ± 0.5	0.17
	Osmolarity (mOsmol/L)	304.6 ± 20.2	306.6 ± 19.1	0.06
	TBUT (seconds)	7.1 ± 4.3	7.3 ± 4.5	0.87
	Staining	0.3 ± 0.5	0.4 ± 0.6	0.66
	Schirmer's 1 Test (mm)	17.0 ± 8.1	15.3 ± 6.7	0.26
	Sensation Central (mm)	4.4 ± 1.2	4.3 ± 1.1	0.71
	Sensation Q1 (mm)	4.2 ± 1.2	4.0 ± 1.2	0.54
	Sensation Q2 (mm)	4.4 ± 1.1	4.2 ± 1.3	0.49
	Sensation Q3 (mm)	4.4 ± 1.1	4.3 ± 1.3	0.51
	Sensation Q4 (mm)	4.3 ± 1.2	4.2 ± 1.2	0.59
	OSDI	38.7 ± 13.2	40.3 ± 12.3	0.17
One week post-op	Osmolarity (mOsmol/L)	318.6 ± 22.7	300.6 ± 13.7	<0.01*
	TBUT (seconds)	5.8 ± 3.1	8.3 ± 3.2	0.01*
	Staining	0.6 ± 0.9	0.2 ± 0.4	0.04*
	Schirmer's 1 Test (mm)	14.1 ± 5.9	17.6 ± 5.0	<0.01*
	Sensation Central (mm)	3.5 ± 1.5	3.6 ± 1.3	0.70
	Sensation Q1 (mm)	2.0 ± 1.3	2.5 ± 1.5	0.26
	Sensation Q2 (mm)	3.7 ± 1.2	3.4 ± 1.6	0.49
	Sensation Q3 (mm)	4.1 ± 1.1	4.2 ± 1.1	0.63
	Sensation Q4 (mm)	4.0 ± 1.1	4.1 ± 0.9	0.81
One month post-op	BSCVA (LogMAR)	0.3 ± 0.4	0.2 ± 0.4	0.49
	Osmolarity (mOsmol/L)	312.3 ± 24.1	298.7 ± 20.7	0.01*
	TBUT (seconds)	7.4 ± 3.9	9.6 ± 4.1	0.02*
	Staining	0.9 ± 1.3	0.3 ± 0.7	0.04*
	Schirmer's 1 Test (mm)	15.6 ± 7.7	20.0 ± 6.8	0.02*
	Sensation Central (mm)	3.5 ± 1.2	4.1 ± 1.1	0.03*
	Sensation Q1 (mm)	2.2 ± 1.3	2.9 ± 1.2	0.03*
	Sensation Q2 (mm)	3.5 ± 1.0	4.2 ± 0.9	0.01*
	Sensation Q3 (mm)	4.2 ± 1.1	4.1 ± 1.2	0.73
	Sensation Q4 (mm)	4.2 ± 1.1	4.2 ± 1.2	0.80
	OSDI	19.1 ± 16.6	13.6 ± 15.4	0.17

CMC: Carboxymethylcellulose.
CsA: Cyclosporine-A.
BSCVA: Best Spectacle Corrected Visual Acuity.
Corneal sensation was measured in all four quadrants (Q1 superotemporal, Q2 superonasal, Q3 inferotemporal, and Q4 inferonasal) and the centre of the cornea (central).
Corneal surgical incision was at the10 o'clock position (Q1).
OSDI: Ocular Surface Disease Index.
SD: Standard deviation.
* Denotes significance at $p < 0.05$.