Safety and Efficacy of Acuvail (Ketorolac Tromethamine) Eyedrops prior and after Corneal Collagen Cross-Linking

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INTRODUCTION

Corneal collagen cross-linking (CXL) is a minimally-invasive procedure that has been increasingly performed in clinical settings to improve corneal biomechanical stability for conditions such as keratoconus. Significant post-operative discomfort is a challenge for many patients, as the corneal epithelium is debrided prior to instillation of riboflavin drops and exposure to ultraviolet light. Post-CXL pain is thought to be multifactorial; with neuropathic pain from afferent corneal nerve injury and inflammatory pain from the resultant healing process[1].

Strategies for providing postoperative analgesia for CXL include both oral medications such as acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs) and codeine, as well as topical medications such as diclofenac and ketorolac[2,3]. Currently, there are no universally accepted method of providing pain management after CXL procedures[2].

OBJECTIVE

The objective of this study is to conduct a quality improvement (QI) assessment to determine if Acuvail (Ketorolac Tromethamine) eyedrops are safe and effective for providing analgesia after CXL.

METHODS

Patients treated with CXL at Vector Eye Centre in Calgary, Alberta were given Acuvail (0.45%) eyedrops prior to the procedure and one day after the procedure. Patients were also provided with a minim of Tetracaine eyedrops and a prescription for Tylenol, Tylenol 3 with Codeine, and Celebrex to use as needed, All patients were asked to fill a pain survey on postoperative day one (POD1).

Patient responses between January 2021 to March 2022 were collected and analyzed to conduct a quality improvement (QI) assessment.

RESULTS

A total of 191 eyes (145 male) were included in this study. The average patient's age at time of CXL was 35.2 ± 12.7. No severe medical adverse events occurred.

At POD1, patients on average rated their least severe level of pain experienced as 2.32 ± 3.78 out of 10 (0 being no pain and 10 being worst pain possible) and most severe level of pain experienced as 5.58 ± 2.41 (**Table 1**).

Table 1. POD1 pain survey results for last 24 hours after CXL

	Mean	SD
Least pain (out of 10)	2.32	3.78
Worse pain (out of 10)	5.58	2.41
% Time experiencing severe pain	26.58	24.26

Patients did not report significant levels of feeling "anxious", "depressed", "frightened", or "helpless", and had minimal nausea, drowsiness, itching, and dizziness (**Figure 1**).

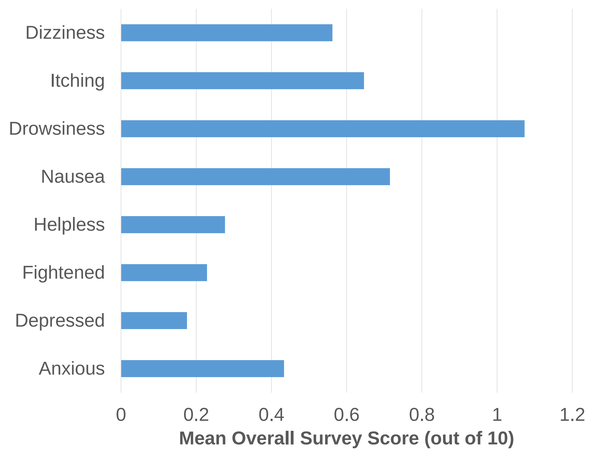

Figure 1. Average survey score (out of ten) for how much the patient experienced symptoms of "Dizziness", "Itching", "Drowsiness", and "Nausea", as well as feelings of being "Helpless", "Frightened", "Depressed", and "Anxious" 24 hours after undergoing CXL.

RESULTS

Most patients did not report a significant impact of CXL on their sleep, with an average score of 2.03 ± 3.44 for difficulty falling asleep and 1.84 ± 2.84 for staying asleep (out of 10).

Patients had access to oral Tylenol, Tylenol 3 with Codeine, and Celebrex medications as well as one minim of topical Tetracaine to use as-needed after CXL.

Overall rates of analgesia usage by POD1 is summarized in **Table 2**.

Table 2. Number of patients (out of 191) and percentage usage of supplementary analgesic medications by POD1.

	T3	Tylenol	Celebrex	Tetracaine
Usage (n)	160	16	169	160
% usage	84.77%	8.38%	88.48%	83.77%

DISCUSSION

While CXL is an effective therapy for slowing disease progression and preserving vision for keratoconus, postoperative pain remains a major issue for many patients. Previous studies indicate that younger patients may experience more severe pain than older patients[1]. CXL technique has also been shown to impact postoperative pain levels, with epithelial-on CXL treatments resulting in lower pain levels compared to epithelial-off treatments, and higher pain levels reported with accelerated CXL techniques[2,4].

Few studies have evaluated the efficacy of analgesic eyedrops for the management of postoperative pain in CXL. Pang et al. found that patients receiving pranoprofen (an NSAID) and fluorometholone eyedrops experienced significantly reduced pain compared to those who received fluorometholone alone[5]. Sameen et al. compared topical diclofenac 0.1% to topical ketorolac 0.5% eyedrops, and did not find a significant difference in postoperative pain scores between the two medications[3].

DISCUSSION

Since patients were not required to complete a pain survey before Acuvail eyedrops were added to the post-CXL analgesia regiment, our data analysis is limited by the lack of a control or comparison arm.

Nevertheless, this pilot study provides promising evidence on the efficacy and safety of Acuvail eyedrops for CXL pain management, and will be expanded on in future case control studies to compare analgesic response versus placebo and other topical medications.

CONCLUSIONS

Acuvail eye drops are well-tolerated, safe, and apparently effective at providing ocular comfort and analgesia during and after CXL treatment. Overall, patients report significant pain relief and satisfaction with their pain management when Acuvail eye drops were provided as part of a multi-modal analgesic regimen. No significant adverse events were recorded.

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