The Prospective Health Assessment of Cataract Patients’ Ocular Surface (PHACO) study: the effect of dry eye

William B Trattler, Parag A Majmudar, Eric D Donnenfeld, Marguerite B McDonald, Karl G Stonecipher, Damien F Goldberg

On behalf of the PHACO Study Group

1 Center for Excellence in Eye Care, Miami, FL, USA; 2 Chicago Cornea Consultants, Chicago, IL, USA; 3 Ophthalmic Consultants of Long Island, Garden City, NY, USA; 4 Ophthalmic Consultants of Long Island, Lynbrook, NY, USA; 5 University North Carolina School of Medicine, Chapel Hill, NC, USA; 6 Wolstan & Goldberg Eye Associates, Torrance, CA, USA

Purpose: To determine the incidence and severity of dry eye as determined by the International Task Force (ITF) scale in patients being screened for cataract surgery.

Patients and methods: This was a prospective, multi-center, observational study of 136 patients, at least 55 years of age, who were scheduled to undergo cataract surgery. The primary outcome measure was the incidence of dry eye as evaluated by grade on the ITF scale and secondary outcome measures include tear break-up time (TBUT), ocular surface disease index score, corneal staining with fluorescein, conjunctival staining with lissamine green, and a patient questionnaire to evaluate symptoms of dry eye.

Results: Mean patient age was 70.7 years. A total of 73.5% of patients were Caucasian and 50% were female. Almost 60% had never complained of a foreign body sensation; only 13% complained of a foreign body sensation half or most of the time. The majority of patients (62.9%) had a TBUT ≤5 seconds, 77% of eyes had positive corneal staining and 50% of the eyes had positive central corneal staining. Eighteen percent had Schirmer’s score with anesthesia ≤5 mm.

Conclusion: The incidence of dry eye in patients scheduled to undergo cataract surgery in a real-world setting is higher than anticipated.

Keywords: cataract surgery screening, dry eye, International Task Force scale, observational study

Introduction

Despite the generally positive outcomes of cataract surgery, some patients are dissatisfied with their postoperative result due to a suboptimal refractive outcome that may be the result of unresolved issues on the ocular surface.1-3 Ongoing and increasing awareness of these issues has led to anterior segment surgeons commonly performing an array of preoperative evaluations and prescribing treatments to optimize the ocular surface and ensure the health of the cornea and retina before patients undergo cataract surgery.4 Even with the ocular surface evaluation performed preoperatively, the incidence of dry eye after phacoemulsification has been reported to be 9.8%.5 Additionally, Cho and Kim found the type of wound created during cataract surgery could exacerbate patient-reported symptoms in those previously thought to be disease-free.1

The diagnosis of dry eye can be challenging, as some studies have found that nearly 50% of dry eye patients may show no corneal staining, despite other evidence of dry eye disease (increased tear osmolarity, reduced Schirmer’s scores, or presence of dry eye symptoms).6 Earlier studies showed that dry eye symptoms, such as blurred vision, are sometimes erroneously attributed to the cataract, which may contribute to the higher postoperative incidence.7
Cataract surgery has been reported in the literature to induce dry eye and to exacerbate pre-existing dry eye.\textsuperscript{1,2,5–8,14} Treatments for postoperative dry eye have been extensively reported in the literature and include nonsteroidal anti-inflammatory drugs, topical corticosteroids, artificial tears, topical cyclosporine 0.05\%, lifitegrast, 3.0\% diquafosol, 1% carboxymethylcellulose sodium, oral lactoferrin, oral doxycycline, punctal plugs, and autologous serum, among others.\textsuperscript{2,3,10–15,24} Yet, little has been reported in the literature on the preoperative incidence of dry eye in a cataract population.

We hypothesized that the incidence of pre-existing dry eye disease in patients who are scheduled to undergo cataract surgery is higher than previously thought based on the published literature. The Prospective Health Assessment of Cataract Patients’ Ocular Surface (PHACO) study sought to determine the incidence of dry eye and its severity (as determined by the International Task Force [ITF] scale)\textsuperscript{25} in patients undergoing cataract surgery and to assess the signs and symptoms of dry eye in this patient population.

\textbf{Patients and methods}

This was a prospective, multicenter, observational study of 143 consecutive patients at least 55 years of age scheduled to undergo standard phacoemulsification cataract surgery in one or two eyes at one of nine clinical sites in the US and Canada. Exclusion criteria included any previous intraocular surgery in the previous 3 months before enrollment; subjects without visually significant cataract, corneal laser vision correction surgery in either eye in the previous year; previous lid surgery within 3 months; and use of topical antibiotics, topical nonsteroidal anti-inflammatory drugs, or topical steroid in either eye. Those subjects who had recently initiated topical cyclosporine 0.05\% use for dry eye were excluded from study testing, but were asked to complete a questionnaire about medication use and any additional dry eye treatments (ie, warm compresses). Although lifitegrast is currently approved for the treatment of both signs and symptoms of dry eye, that pharmacologic treatment was not approved in the US at the time of this study.

Preoperatively, all eligible subjects underwent ocular surface testing in both eyes that included tear break-up time (TBUT), corneal and conjunctival staining (with fluorescein and lissamine green, respectively) according to the National Eye Institute (NEI) grid,\textsuperscript{26} Schirmer’s score evaluation with anesthesia,\textsuperscript{7} Ocular Surface Disease Index (index range from 0–100),\textsuperscript{28,29} and a patient questionnaire to assess dry eye symptoms (if any). For the purposes of this study, a TBUT > 5 seconds considered highly likely of dry eye symptoms.

In this study, corneal staining was evaluated under cobalt blue illumination 2.5–3 minutes after fluorescein instillation and conjunctival staining was performed 2.5–3 minutes after 10 \(\mu\)L of a 1% sodium lissamine green dye was instilled. Both of these followed the NEI scale.\textsuperscript{26}

Written consent to publish their data was obtained from all patients prior to being enrolled in the study. This research was approved by the Institutional Review Board Company, Inc. (Buena Park, CA, USA). As this was an observational study, it was not powered to determine statistical significance. Similarly, there was no control arm as all subjects were pre-determined to have visually significant cataract. All analyses were descriptive in nature and used StatView Software (SAS Institute, Cary, NC, USA).

\textbf{Results}

\textbf{Patient demographics}

There were 143 patients (286 eyes) scheduled to undergo routine cataract surgery who met the initial inclusion criteria. The mean age of the patients was \(70.7 \pm 7.8\) years (range: 54.5–87.9 years). Seven patients (4.9\%) were using topical cyclosporine 0.05\% at the time of presentation and were excluded from this analysis. Among the remaining 136 patients (272 eyes) included in this analysis, there were 100 Caucasian patients (73.5\%), 15 Hispanic patients (11.0\%), 11 Asian patients (8.1\%), five black patients (3.7\%), and five who identified their race as “other” (3.7\%).

Thirty patients (22.1\%) had received a prior diagnosis of dry eye but were not on prescription or over-the-counter treatments; 68 patients (50\%) were male. If the previously excluded seven patients who were using topical cyclosporine 0.05\% had been included in this analysis, the percentage of patients with a previous diagnosis of dry eye would increase to 25.9\%.

The incidence of dry eye as evaluated by the ITF\textsuperscript{25} level included 34 patients (25\%) at level 0 and 39 patients (28.7\%) at level 3 (Table 1).

Using the NEI scale to assess corneal staining,\textsuperscript{7} 61 patients (44.9\%) had a corneal staining score of \(\geq 1\). These same

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|}
\hline
\textbf{ITF level} & \textbf{Number of patients} & \textbf{Percentage of cohort} \\
\hline
0 & 34 & 25 \\
1 & 27 & 19.9 \\
2 & 36 & 26.5 \\
3 & 39 & 28.7 \\
4 & 0 & 0 \\
\hline
\end{tabular}
\caption{Incidence of dry eye as evaluated by ITF}
\end{table}

\textbf{Abbreviation: ITF, International Task Force.}
patients had a cumulative score of $\leq 1$ (on a scale of 1–4) in burning/stinging, foreign body sensation, dryness, and pain/soreness.

Similarly, the mean ($\pm$ standard deviation) TBUT score was 4.95$\pm$2.5 seconds (range 0–15 seconds); 171 eyes (62.9%) had TBUT scores of $\leq 5$ seconds; 58 eyes (21.3%) had Schirmer’s scores of $\leq 5$ mm (mean 12.4$\pm$7.3 mm; range 0–35 mm); and 209 eyes (76.8%) had positive fluorescein corneal staining scores (mean 4.3$\pm$3.5; range 0–15), with 136 eyes (50%) also showing positive central staining. The mean lissamine staining score was 0.92$\pm$0.61, with a range of 0–2.8 (Table 2).

**Subjective analyses**

All patients (N=136) completed a dry eye signs and symptoms questionnaire (Table S1). Patients were allowed to provide more than one response to each question. The majority (94/136; 69.1%) reported no stinging and burning. Eighty-six patients (63.2%) were never affected by the symptom of dryness; 80 patients (58.8%) reported no foreign body sensation; 73 patients (53.7%) reported no itching; 53 patients (39%) reported no sensitivity to light; 107 patients (78.7%) reported no dryness; 80 patients (58.8%) reported no foreign body sensation; 50 patients (36.8%) reported no blurred vision and productivity on a daily basis, most reported missing 0–2 hours of work weekly due to health problems and the majority reported their health problems did not affect work productivity or daily activities.

**Discussion**

In our observational study, fewer than 25% of patients had been previously diagnosed with dry eye when they presented for cataract surgery, yet 30% reported at least occasional symptoms (Table S1). Our results add to the literature findings of diagnosed dry eye prevalence rates between 3.5% and 33.7%.

Dry eye is already considered both underdiagnosed and undertreated, and our findings support that belief. It is now well accepted that people affected by dry eye are often more symptomatic than clinical tests may indicate, and in our study, almost 45% had a corneal staining score of at least 1, but a cumulative score of $\leq 1$ in traditionally reported subjective symptoms of dry eye including burning/stinging, foreign body sensation, dryness, and pain/soreness. This suggests that somewhere between 15% and 20% of our study population would have eluded the diagnosis of dry eye suspect/confirmed dry eye had they not presented for cataract surgery evaluation.

When patients were asked about their employment and productivity on a daily basis, most reported missing

### Table 2 TBUT, Schirmer’s score, and staining scores

<table>
<thead>
<tr>
<th>Testing method</th>
<th>Number of eyes</th>
<th>Percentage of eyes</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBUT (N=268)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\leq 5$ seconds</td>
<td>171</td>
<td>62.9</td>
</tr>
<tr>
<td>$&gt;5$ seconds</td>
<td>97</td>
<td>35.6</td>
</tr>
<tr>
<td>Missing</td>
<td>4</td>
<td>1.5</td>
</tr>
<tr>
<td>Schirmer’s scores (N=272)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\leq 5$ mm</td>
<td>58</td>
<td>21.3</td>
</tr>
<tr>
<td>$\leq 10$ mm</td>
<td>214</td>
<td>78.7</td>
</tr>
<tr>
<td>Corneal staining (fluorescein) (N=271)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>209</td>
<td>76.8</td>
</tr>
<tr>
<td>Negative</td>
<td>62</td>
<td>22.8</td>
</tr>
<tr>
<td>Missing</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>Central staining (fluorescein) (N=271)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>136</td>
<td>50</td>
</tr>
<tr>
<td>Negative</td>
<td>135</td>
<td>49.6</td>
</tr>
<tr>
<td>Missing</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>Conjunctival staining (lissamine) (N=271)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>0.92</td>
<td></td>
</tr>
<tr>
<td>Standard deviation</td>
<td>0.61</td>
<td></td>
</tr>
<tr>
<td>Minimum</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Maximum</td>
<td>2.8</td>
<td></td>
</tr>
</tbody>
</table>

**Note:** Not all patients completed all preoperative corneal testing. Abbreviation: TBUT, tear break-up time.
undergo these evaluations before being cleared for cataract surgery. We also did not include age-matched control subjects, as this study was designed to be observational and not interventional. These decisions may have skewed our results in that our patient population was older and more likely to have dry eye. However, we attempted to compensate for that by eliminating patients who were already diagnosed with dry eye and were on a prescription treatment from our analysis. It is interesting to note, however, that only seven patients were actively being treated, although substantially more (n=30) had been previously diagnosed, adding to our supposition that if dry eye is not being actively screened for in this patient population, it may be overlooked altogether. Although the study had strict exclusion criteria to eliminate other disorders and known treatments that are associated with dry eye or its treatment (such as topical steroid use), we did not exclude patients who used antihistamines, antidepressants, or anticholinergic drugs because the literature has shown that while the latter may have an association with dry eye, different drugs within those classes may alleviate, exacerbate, or have no effect on dry eye.\textsuperscript{58–63} It was not the purpose of this study to determine the cause of dry eye, just to ascertain its presence.

The evaluations were conducted at a time when newer diagnostic modalities such as tear osmolarity and methods to detect the presence of inflammatory markers were not available. It is possible that the true incidence of dry eye might have been even higher had those modalities been included in the overall assessment. Finally, as an observational study, it is subject to all the potential biases inherent with these types of evaluations.

However, this study also has numerous strengths. Enrolled patients had already undergone extensive preoperative assessment, both of their cataract and of their overall ocular health, consistent with commonly used cataract assessment parameters. As such, patients with known dry eye or presumed dry eye that may be the result of glaucoma medication use, or disorders such as meibomian gland dysfunction, chronic conjunctivitis, or trichiasis, would have been excluded from our analysis. To our knowledge, this is the first study to evaluate preoperative levels of dry eye in a real-world cataract population, regardless of a previous diagnosis or lack thereof. We encourage further exploration on our findings, especially as they may relate to potential cataract surgery outcomes.

Conclusion
The percentage of prospective cataract patients who have signs or symptoms of dry eye continues to be underreported; increased awareness should lead to careful monitoring of the patient’s ocular health both before and after surgery.

Acknowledgments
This study was funded by an unrestricted grant from Allergan. Members of the PHACO study group are consultants to Allergan. EDD, MBM, KGS, DFG, and WBT are also consultants to Shire. Michelle Dalton, ELS, provided medical writing and editing; this support was funded by an unrestricted grant from Allergan, Irvine, CA, USA.

This paper was presented in part at the American Society of Cataract & Refractive Surgery annual meetings in 2011 (San Diego, CA; March 25–29) and 2012 (Chicago, IL, April 20–24).

Members of the PHACO Study Group: Damien F Goldberg, MD; Chaz Reilly, MD; Mark Packer, MD; Parag A Majmudar, MD; Eric D Donnenfeld, MD; Marguerite B McDonald, MD, FACS; Karl G Stonecipher, MD; Jon Vukich, MD; Gregg Berdy, MD; Ranjan Malahotra, MD; and William B Trattler, MD.

Author contributions
WBT, PAM, EDD, MBM, KGS, and DFG conducted the study; WBT, PAM, EDD, MBM, KGS, and DFG analyzed data and revised the paper; and WBT, PAM, EDD, MBM, KGS, and DFG reviewed and approved the manuscript.

Disclosure
None of the authors have a financial interest in any product mentioned, but all are consultants to Allergan. In addition, EDD, MBM, KGS, and WBT are consultants to Shire. The authors report no other conflicts of interest in this paper.

References


### Table S1 Dry eye signs and symptoms

**Parameter evaluated** | **n** | **%**
--- | --- | ---
**Stinging and burning**
Frequency
None of the time | 94 | 69.1
Some of the time | 32 | 23.5
Half of the time | 4 | 2.9
Most of the time | 4 | 2.9
All of the time | 2 | 1.5
How bothered by each symptom? (0=not at all; 4=extremely)
0 | 90 | 69.2
1 | 19 | 14.6
2 | 13 | 10.0
3 | 5 | 3.8
4 | 3 | 2.3
**Dryness**
Frequency
None of the time | 86 | 63.2
Some of the time | 29 | 21.3
Half of the time | 11 | 8.1
Most of the time | 6 | 4.4
All of the time | 4 | 2.9
How bothered by each symptom? (0=not at all; 4=extremely)
0 | 82 | 63.6
1 | 23 | 17.8
2 | 13 | 10.1
3 | 6 | 4.7
4 | 3 | 2.3
**Foreign body sensation**
Frequency
None of the time | 80 | 59.3
Some of the time | 38 | 28.1
Half of the time | 4 | 3.0
Most of the time | 10 | 7.4
All of the time | 3 | 2.2
How bothered by each symptom? (0=not at all; 4=extremely)
0 | 75 | 58.1
1 | 34 | 26.4
2 | 8 | 6.2
3 | 8 | 6.2
4 | 4 | 3.1
**Itching**
Frequency
None of the time | 73 | 54.1
Some of the time | 47 | 34.8
Half of the time | 12 | 8.9
Most of the time | 1 | 0.7
All of the time | 2 | 1.5
How bothered by each symptom? (0=not at all; 4=extremely)
0 | 72 | 55.0
1 | 33 | 25.2
2 | 19 | 14.5
3 | 2 | 1.5
4 | 5 | 3.8

**Note:** Not all eligible patients (N=136) answered every question.

### Table S1 (Continued)

<table>
<thead>
<tr>
<th>Parameter evaluated</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
</table>
| **Sensitivity to light**
Frequency
None of the time | 53 | 39.6
Some of the time | 40 | 29.9
Half of the time | 11 | 8.2
Most of the time | 13 | 9.7
All of the time | 17 | 12.7
How bothered by each symptom? (0=not at all; 4=extremely)
0 | 50 | 38.5
1 | 35 | 26.9
2 | 26 | 20.0
3 | 8 | 6.2
4 | 11 | 8.5
| **Painful/sore**
Frequency
None of the time | 107 | 78.7
Some of the time | 21 | 15.4
Half of the time | 5 | 3.7
Most of the time | 1 | 0.7
All of the time | 2 | 1.5
How bothered by each symptom? (0=not at all; 4=extremely)
0 | 103 | 79.2
1 | 11 | 8.5
2 | 10 | 7.7
3 | 3 | 2.3
4 | 3 | 2.3
| **Blurred vision**
Frequency
None of the time | 46 | 34.1
Some of the time | 50 | 37.0
Half of the time | 11 | 8.1
Most of the time | 14 | 10.4
All of the time | 14 | 10.4
How bothered by each symptom? (0=not at all; 4=extremely)
0 | 44 | 33.6
1 | 28 | 21.4
2 | 30 | 22.9
3 | 14 | 10.7
4 | 15 | 11.5
| **Tired/fatigued eyes**
Frequency
None of the time | 65 | 47.8
Some of the time | 51 | 37.5
Half of the time | 9 | 6.6
Most of the time | 7 | 5.1
All of the time | 4 | 2.9
How bothered by each symptom? (0=not at all; 4=extremely)
0 | 67 | 50.8
1 | 31 | 23.5
2 | 21 | 15.9
3 | 8 | 6.1
4 | 5 | 3.8