

Incidence of and Risk Factors for Steroid-Induced Ocular Hypertension Following Cataract Surgery in 150 Patients Without Glaucoma in Cambodia: A Prospective Study

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Abstract: ***Purpose:** This study aims to report the incidence of and risk factors for steroid-induced ocular hypertension in Cambodian patients without glaucoma after cataract surgery. **Study Design:** A hospital-based prospective observational study. **Material and Methods:** This study observes the changes in postoperative intraocular pressure in 150 non-glaucomatous patients who underwent phacoemulsification or small manual incision cataract surgeries at Preah Ang Duong Hospital for the incidence of steroid-induced ocular hypertension (defined as intraocular pressure (IOP) higher than 21 mmHg) after using topical prednisolone 1% or dexamethasone 0.1% for 1 month. In addition, risk factors were analyzed. **Results:** Among 150 patients, 7 patients (4.67%) showed increased intraocular pressure during our study, among whom the younger age group (in their 40s or under), and choice of steroid use (dexamethasone 0.1%) were found to be risk factors. However, all of our steroid-induced ocular hypertension patients had their intraocular pressure notably back to normal (<21 mmHg) after 2 weeks of steroid cessation. **Conclusion:** This study shows that topical steroid could be safely used by cataract surgeons postoperatively in non-glaucomatous patients with regards to steroid-induced ocular hypertension as the risk is relatively low (4.67%) and the patients' intraocular pressure will return to normal limits upon cessation of steroid. Although some precautions should be taken with patients in their 40s or under and with a choice of steroid, dexamethasone.*

Conflict of interest: The authors declare no conflict of interest.

Keyword: Cataract, Steroid, Ocular Hypertension

1. Introduction

In 2022, the World Health Organization (WHO) reported that at least 94 million people have moderate or severe distance vision loss due to cataracts making it the second leading cause of blindness worldwide [1]. In Cambodia, the prevalence of blindness is 0.37% with uncorrected cataracts being the first leading cause of blindness, accounting for 80.4% [2]. The only existing curative treatment for cataract is cataract removal surgery.

It is reported that in 2020 alone, as many as 35,682 cataract surgeries were conducted in Cambodia, which, when uneventful, gave many Cambodian elders a second chance to perceive the world again [2]. In order to achieve a good outcome post-operatively with inflammation being controlled, topical steroids, anti-inflammatory agents, are frequently used in association with topical antibiotics. Although the use of steroid is crucial in such settings, their prolonged use could lead to increased intraocular pressure, which may then result in steroid-induced ocular hypertension or steroid-induced glaucoma [3].

Steroid-induced ocular hypertension most commonly occurs three to six weeks post-exposure to steroid; these patients are considered "steroid-responders." Studies have shown 2.8% steroid response in normal population after topical use. [4, 5]. Previous study shows around 3% of eyes that experienced an IOP elevation in the setting of steroid

use converted to steroid-induced glaucoma [6], which is a secondary open-angle glaucoma. Such complications, if they go undetected or untreated, could lead to irreversible vision loss, as one study shows IOP could remain elevated in patients being treated with steroids for up to more than four years [7].

A few risk factors for steroid response identified in previous studies were axial myopia, young age, males, pre-existing primary open angle glaucoma, a family history of glaucoma, high central corneal thickness (CCT), the potency of steroids, diabetes mellitus, and a history of connective tissue disease [8].

The main objective of this study is to report the incidence and risk factors of steroid-induced ocular hypertension in non-glaucomatous Cambodian patients after cataract surgery. The four specific objectives of the study were to (i) identify demographic characteristics of steroid-response patients, (ii) assess the incidence of steroid-induced ocular hypertension following cataract surgery, (iii) illustrate risk factors contributing to steroid response in those patients, and (iv) compare the IOP between baseline (before using steroid) and final follow-up (post-operatively).

2. Methods

This is a hospital-based prospective observational study which received ethical approval from the National Ethics

Committee for Health Research No. 073 on February 27th, 2023, with support from the Cambodian Ophthalmological Society (COS) to be conducted at the Department of Ophthalmology at Preah Ang Duong Hospital in Phnom Penh, Cambodia.

This study observed 150 patients identified by ophthalmologists as having visually disabling cataracts and needed cataract extraction surgery to restore vision and rehab the quality of life with informed consent from March 1 to August 31, 2023 at Preah Ang Duong Hospital. The patients were selected through convenience sampling. If the patients underwent cataract surgeries for both eyes within the study period, only the first eye of the patients was chosen to be studied.

The inclusion criteria include Cambodian ethnicity, age of 18 or older, patients undergoing cataract surgery alone without combining procedures, and patients with a baseline intraocular pressure of less than 21mmHg. However, patients with a past history of ocular hypertension, or any types or stages of glaucoma were excluded from the study. Likewise, any patient who underwent previous or combined intra- or extra-ocular surgeries (e.g., trabeculectomy, vitrectomy, pterygium excision, etc.), as well as complicated cataract surgeries such as posterior capsular rupture with vitreous loss, zonular dehiscence, or surgery for phacomorphic, traumatic, or pseudo-exfoliation cases, or patients unwilling to participate in this study, were all excluded. This eligibility criteria aims to exclude other causes of ocular hypertension post-cataract surgery aside from steroid-induced ocular hypertension.

Each cataract surgery was conducted by different surgeons under local anesthesia, mainly retrobulbar block, and with either a standard phacoemulsification procedure or a standard manual small incision cataract surgery. Immediately after surgery, oral paracetamol (500 mg) was routinely prescribed to the patient three times per day.

The patients' intraocular pressure (IOP) was measured by an iCare tonometer preoperatively for baseline, and postoperative day 1, week 1, month 1, and month 1.5 (optional). Three measurements are made each time, and the average of the three measurements was recorded for analysis.

Other variable measures were: (i) demographic data, including age, gender, and residence; (ii) clinical data, such as visual acuity (VA), axial length, types of cataract; (iii) therapeutic data, including types of cataract surgery or any intraoperative complications, and types of steroid used and dosage. The VA, IOP, and dosage of steroid use were recorded at each follow-up on day 1, week 1, month 1, and month 1.5 (optional).

The outcome variable is the incidence of steroid-induced ocular hypertension, which is defined as an increase in intraocular pressure above 21 mmHg.

Once steroid-induced ocular hypertension patients were identified, risk factors were analyzed based on their

collected data, including age, gender, axial length, types of cataract surgery, and type of steroid use.

Statistical Analysis

All patient data was recorded and analyzed on Microsoft Excel version 16.16.27. Descriptive statistics such as mean, standard deviation, median, and percentage were used. The independent variables for analysis were age, axial length, types of surgery, types of steroid use, and gender. A paired t-test or Wilcoxon-Signed rank test was used for the association of categorical and numerical variables, while a chi-square or Fisher exact test was also used for the association of categorical variables. P value of less than 0.05 was considered statistically significant.

3.Results

A total population of 207 patients' data was initially collected for the study, but among them, 57 eyes did not meet the eligibility criteria resulting in only **150 patients' eyes** being included for analysis. Among the excluded participants,

- 24 patients' eyes had a pre-existing history of glaucoma and/or a previous steroid response.
- 18 patients' eyes had intraoperative complications such as posterior capsular rupture (14), vitreous loss (13), and zonular dehiscence (4).
- 2 patients did not consent to be part of the study.
- 13 patients' eyes underwent or had a history of combined procedures such as scleral fix IOL (5), combined trabeculectomy (1), and previous pterygium excision (7).

The mean age of the studied 150 patients was 63.9 ± 10.48 years old (range: 23-86) among whom 56% (84) were female and 44% (66) were male. The laterality ratio is 1:1 between the right and left eyes. The mean axial length of the studied eyes was 23.64 ± 1.2 mm.

Table 1: Baseline Characteristics

Mean age (range)	
Gender	
Female	66 (44%)
Male	84 (56%)
Laterality	
Right	75 (50%)
Left	75 (50%)
Mean axial length	23.64 ± 1.2 mm

Patients' visual acuity was measured with a tumbling E-chart at 3 meters, but the results were converted to LogMar for data analysis. A statistically significant difference was seen pre- and post-operatively.

Table 2: Comparison of median visual acuity (LogMar)

Visual Acuity (Median, IQR)	
Baseline	Final Follow Up
1.80	0.30
(0.88-2.30)	(0.18-0.48)
-	p-value* is < .00001

Among the studied group, 107 patients (71.33%) underwent phacoemulsification, and only 43 patients (28.67%) underwent small incision cataract surgery based on surgeon preference, as well as grading and types of cataract. After the cataract surgery, we observed two main types of post-operative topical steroid usage prescribed by surgeons: (i) Topical Prednisolone 1% in 143 patients (95.3%) and (ii) Topical Dexamethasone 0.1% in 7 patients

only (4.7%). All the patients followed a protocol of 2 hourly (day 1 to week 1), 3 hourly (week 1 to week 2), 4 times per day (week 2 to month 1) and stopped at month 1 unless anterior chamber inflammation persisted.

During follow-up, the mean changes of intraocular pressure among the patients were significant at week 1 (12.09 ± 3.85 mmHg) and at month 1 (12.06 ± 3.68 mmHg).

Table 3: Mean intraocular pressure (LogMar) at each follow-up

Intraocular Pressure (Mean ± SD)			
Baseline	Day 1	Week 1	Month 1
12.83 ± 3.59	13.02 ± 5.22	12.09 ± 3.85	12.06 ± 3.68
P value*	0.441829	0.01423	0.01033

At each follow-up, patients with intraocular pressure higher than 21 mmHg were: 11 patients (7.3%) at day 1, 3 patients (2%) at week 1, 5 patients (3.33%) at month 1, and 2 patients (1.33%) at month 1.5. Three of the ocular hypertension patients at month 1 persisted from week 1. Increases of intraocular pressure on postoperative day 1 were not analyzed as steroid response due to many other temporary causes of high IOP, such as incomplete viscoelastic removal, over-forming of the anterior chamber, microhyphema. As a result, the total number of steroid-induced ocular hypertension cases post-cataract surgery in our study is 7 (4.67%).

Based on the type of steroid used, 2 in 7 steroid responders were in the dexamethasone group. 28.6% of patients who were on dexamethasone 0.1% showed increased IOP compared to only 3.4% in prednisolone group. No other significant difference was seen in types of surgery, gender, or axial length in this study.

The 7 patients were continued to be observed with steroid therapy continued. Three patients received temporary antiglaucoma medications during observation as 1 patient had intraocular pressure of more than 30 mmHg, and 2 other patients had a persistent rise in IOP for more than two weeks while on steroid therapy. However, all of our steroid responders had their IOP return to less than 21 mmHg within 2 weeks of cessation of steroid use.

4. Discussion

Topical steroid use is necessary for inflammatory control after cataract surgery and is usually required for up to one month. However, steroids are also known to be predisposing factors for ocular hypertension and could lead to steroid-induced glaucoma if undetected. Previous studies showed the incidence of intraocular pressure increases post-cataract surgery due to steroid use to be from 2.1% to 12% although there is variation in the definition of steroid response, types of steroid used, and frequency of usage from study to study as shown in Table 4. [9-11, 14]. Our study shows that 7 of 150 (4.67 %) non-glaucomatous patients demonstrated increases of intraocular pressure of more than 21mmHg in response to steroid uses post-cataract surgery. David F. et al. found an incidence of only 2.37% in steroid response from Prednisolone 1%, but steroid response was defined differently from our study as intraocular pressure of more than 25% from baseline and a minimum of 28 mmHg, or a decrease of 25% in intraocular pressure after stopping steroid [9].

All patients were categorized by age group. The most prevalent age group of cataract patients falls between the ages between 60 and 69. However, 4 out of 7 steroid-induced ocular hypertension patients (57%) were in the 40-49 age group, and is equal to 30% of patients in this age group.

The steroid-induced ocular hypertension patients in this study exhibit certain common characteristics, such the use of dexamethasone, and the majority of our steroid responders were in the younger age group among the study sample, specifically in their 4th decade. Younger age as risk factors correlates well with previous studies such as by David F et al [9].

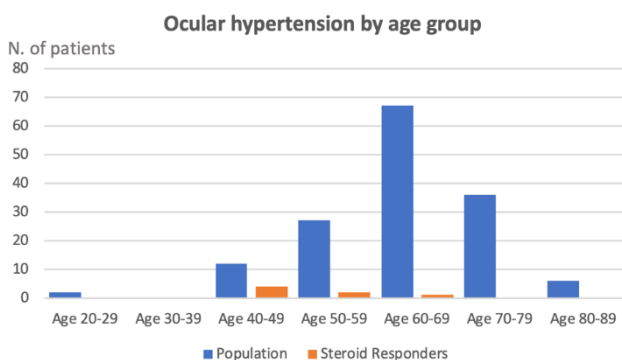


Figure 1: Comparative age distribution

Despite a few patients requiring temporary antiglaucoma medications while on steroid therapy, all patients with steroid responses in this study had their intraocular pressure decreased to less than 21 mmHg within 2 weeks of cessation of steroid therapy.

Table 4: Comparison with previous studies

Authors	Country	Year	Sample	Steroid	Freq.	Responder	Definition
Our study	Cambodia	2023	150	Pred. Dexa.	1x8 1x6 1x4	4.67%	IOP > 21 mmHg after three readings
David F. et al	USA	2011	1642	Pred.	1x3 1x2	39 (2.37%)	IOP > 25% from BL (min 28 mmHg) or < 25% after stop
Karine D. et al	USA	2021	472	Pred.	1x4	10 (2.1%)	IOP > 50% from BL
Sachit M. et al	India	2021	150	Dexa. Pred. Diflu.	1x4 6w	2 (W1) 1 (W3)	IOP > 21 mmHg after two readings

Note: Pred. = Prednisolone, Dexa. = Dexamethasone, Diflu. = Difluprednate, IOP = Intraocular Pressure, BL = Baseline

In summary, this is the first study to be conducted on this topic in Cambodian population. The sample size is relatively weighted, comparable to previous similar research. Additionally, eligibility criteria strictly excluded other risk factors of ocular hypertension, which enabled the authors to identify the incidence and risk factors of steroid-induced ocular hypertension post-cataract surgery more accurately in the study population.

There are a few limitations to this study. First of all, it is a single-center study; however, it took place in one of the biggest eye centers in the country. In addition, IOP measurement in this study was done with an iCare tonometer due to convenience and availability, but the average of three measurements were taken for better accuracy. Lastly, there were more patients who were on prednisolone 1% than dexamethasone 0.1% due to availability as well as the surgeons' preference. It is recommended that future research explore patients using dexamethasone 0.1% with a larger sample size.

5. Conclusions

Topical steroids could be safely used by cataract surgeons postoperatively in non-glaucomatous patients. The risk of developing steroid-induced ocular hypertension is relatively low, and the patients' intraocular pressure was observed to return to its normal limit upon cessation of steroid. Although some precautions should be taken with patients in their 40s or younger and with the use of dexamethasone as a postoperative topical steroid.

Conflict of Interest

The authors declare no conflicts of interest.

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