

Systematic review and case report on intraocular ointment after cataract surgery

Mwale Paul*, Zheng Yan*, Chen Xiaomin, Ke Min

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Department of Ophthalmology, Zhongnan Hospital of Wuhan University, Wuhan 430071, Hubei Province, China

* Co-first authors: Paul Mwale and Zheng Yan

Correspondence to: Ke Min. Department of Ophthalmology, Zhongnan Hospital of Wuhan University, Wuhan 430071, Hubei Province, China. keminyk@163.com

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白内障术后眼药膏进入前房的病例报告及系统评价

Mwale Paul*, 郑妍*, 陈晓敏, 柯敏

作者单位: (430071) 中国湖北省武汉市, 武汉大学中南医院眼科

*: Mwale Paul 和郑妍对本文贡献一致

作者简介: Mwale Paul, 毕业于武汉大学, 硕士研究生, 主治医师, 研究方向: 青光眼与白内障。

通讯作者: 柯敏, 毕业于武汉大学, 博士研究生, 主任医师, 教授, 研究方向: 青光眼与白内障. keminyk@163.com

摘要

眼药膏通常用于预防白内障术后感染。本研究旨在报告一例白内障术后眼药膏进入前房的罕见病例并进行系统综述。检索 PubMed、Scopus、Embase、CNKI、万方数据库、中国科技期刊数据库和中国医学期刊全文数据库, 检索时间自建库至 2023-10-30, 共收集 19 篇文献 31 例术后使用眼药膏并进入前房的病例。31 例患者年龄范围为 55 至 87 岁, 中位数为 73 岁, 男性占 45.2%, 女性占 32.3%。切口长度普遍为 3.2 毫米。大多数患者在术后 3 d 内检测到眼药膏, 无并发症 (45.2%)。最常见的眼部症状为角膜水肿和葡萄膜炎。术后早期随访非常重要。前房积液是白内障手术后罕见的并发症, 但如果不及时发现和治疗, 可能会导致严重的视力丧失。当患者主诉白内障术后眼内有异物感时, 眼科医生需要密切关注并检查眼睛, 以便尽早发现积液, 进行适当的干预并防止进一步的并发症。**关键词:** 眼药膏; 白内障手术; 毒性眼前节综合征; 角膜失代偿; 黄斑囊样水肿; 前房

Abstract

• Intraocular ointment is conventionally placed on the eye to prevent infection after cataract surgery. The purpose of this study is to report a case and conduct a systematic review of a rare occurrence of the entry of intraocular

ointment after cataract surgery. PubMed, Scopus, Embase, CNKI, WANFANG data, China Science and Technology Journal Database and Chinese Medical Journal Full-text Database were systematically searched from their commencement to 30th October 2023, and 19 literatures were screened out and 31 cases of intraocular ointment after surgery were collected. Among the 31 patients, the age of presentation ranged from 55 to 87 years with a median of 73, males accounted for 45.2% and females accounted for 32.3%. The length of the incision was generally 3.2 mm. Most of the patients detected ointment within 3 days post-operation and presented without complications (45.2%). The most common ocular manifestations were corneal edema, glaucoma and uveitis. Early postoperative follow-up is very important. Presence of anterior chamber ointment is a rare complication after cataract surgery, but it can lead to severe vision loss if not detected and treated on time. When patients complain of foreign body sensation in the eye after cataract surgery, ophthalmologists need to take a keen interest and examine the eye for early detection of ointment for appropriate intervention and prevent further complications.

• **KEYWORDS:** intraocular ointment; cataract surgery; toxic anterior segment syndrome; corneal decompensation; cystoid macular edema; anterior chamber

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INTRODUCTION

Surgical restoration of patients' vision following cataract removal is a commonly performed and highly effective procedure^[1]. Although cataract surgery brings many advantages to the patients, the risk of various complications is still a concern, and accidental entry of ocular ointment into the anterior chamber is one of the rare occurrences after cataract surgery. Despite it being uncommon, it can lead to serious complications including toxic anterior segment syndrome (TASS), secondary glaucoma, corneal decompensation and cystoid macular edema (CME)^[2-5]. Several factors such as surgical technique, the way of applying

the ocular ointment and postoperative care may influence the occurrence of complications^[6]. This case demonstrates that early postoperative review is critical for early detection of retained intraocular ointment so as to enhance effective management thereby preventing potential complications^[7]. We herein report a rare case of intraocular ointment after uneventful cataract surgery with a clear–corneal incision and review systemically all cases up to 30th October 2023 without age restrictions.

MATERIALS AND METHODS

Ethical Approval This systematic review was based on the protocol previously published on PROSPERO, we followed the check list recommendations of PRISMA 2020 as an established tool to ascertain the study quality and avoid the risk of bias. The study method and protocol was approved by the medical ethics committee of Zhongnan Hospital of Wuhan University (No.20240647). Consent to publish the report was obtained from the patient.

Eligibility Criteria We included in this systematic review full – text case reports and case series of patients with intraocular ointment after cataract surgery with no age restrictions. Patients with intraocular foreign body but not ointments or not after cataract surgery were excluded. Retrospective cohort study and letters were also excluded.

Information Sources The databases PubMed, Scopus, Embase, CNKI, WANFANG data, China Science and Technology Journal Database, and Chinese Medical Journal Full-text Database were comprehensively searched from their inception until October 30, 2023 to gather case reports and case series pertaining to intraocular ointment following anterior chamber surgery.

Search Strategy The search technique used the keywords: (ointment OR intraocular ointment) AND (cataract surgery OR cataract extraction). The search phrases were adjusted to conform to the requirements of each database. There were no limitations imposed on the publication date.

Study Selection In order to identify additional research that met the criteria for inclusion, we conducted a thorough evaluation of the reference sections of the selected articles that were included, as well as the related publications for each of those articles. The title – abstract screening and full – text screening were both carried out separately and concurrently by two reviewers in order to identify suitable articles based on the specified inclusion and exclusion criteria. Disputes were addressed through the intervention of a third reviewer to ensure that the articles included were credible and of high quality.

Data Extraction Process The data were obtained from the 28 eligible studies, which provided information on the first author’s name, year of publication, patient characteristics, treatment methods, type of ointment, length and location of incision, duration of follow–up and any resulting complications. Three reviewers conducted the data extraction procedure and

subsequently verified it for accuracy and consistency. We evaluated the potential for bias in the articles that were included by utilizing the NIH quality assessment tool for case reports. Each qualified trial underwent quality assessment conducted by one investigator and subsequently reviewed by another. Conflicts arising from data extraction and quality evaluation processes were handled by author discussions or, if needed, by involving third and fourth authors.

Statistical Analysis The collected data was cleaned, coded, and analyzed using BMI SPSS version 26. A comprehensive and qualitative analysis of the data was conducted, utilizing pooled frequencies and percentages to provide categorical variables, and medians with inter quartile ranges for continuous variable.

RESULTS

Our literature search yielded 547 citations, after removing duplicates, we remained with 432 reports to be assessed for eligibility. Totally 382 of these were excluded due to a number of reasons like unavailability of full text ($n = 22$), not correlating with intraocular ointment based on title and abstract ($n = 355$), foreign bodies in anterior chamber not being ointments ($n = 4$) and article not being a case report ($n = 1$). Finally, a total of 19 studies and 31 reports were included (Figure 1).

Our systematic review identified 31 cases of intraocular ointment but we also reported our own additional case of intraocular ointment after phacoemulsification cataract extraction surgery. The median age of patients was 73 years (range, 55–87) and 14 (45.2%) patients were male. Among all cases collected, tobramycin–dexamethasone was the most common type of intraocular ointment in 11 cases (35.5%), followed by gentamicin–betamethasone in 8 cases (25.8%). The median time for patients to detect ointment was 3 d. Intraocular ointment most commonly entered the anterior chamber through the superior surgical incision, and the length of the incision was generally 3.2 mm (Table 1).

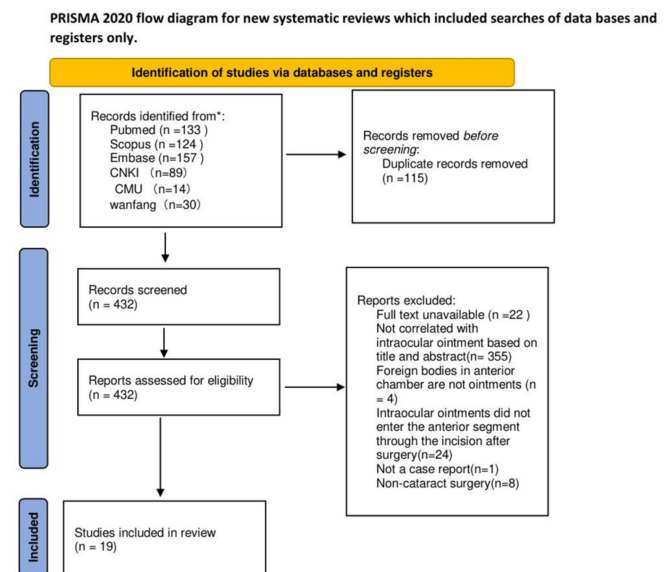


Figure 1 PRISMA flow diagram of systematic review.

14 patients who had intraocular ointment detected after cataract surgery did not exhibit ocular complications (45.2%), the median duration for ointment removal stood at 6 d. Among the patients who presented with ocular complications, the most common ones were corneal edema (5/31 cases) and uveitis (4/31 cases; Table 2). In addition, there were 4 cases of CME and 3 cases of decreased corneal endothelial cell. Patients with complications due to retained intraocular ointment displayed a significantly prolonged duration for ointment removal compared to those without complications (Table 3).

Case report A 61-year-old woman who had undergone an event free phacoemulsification cataract extraction in the right eye with placement of an artificial lens (multi-focal 1 piece-IOL, ZMB00, Johnson & Johnson Surgical Vision, Inc.) was reviewed post-operatively the following day in our in-patient department. The eye examination before discharge was normal, and the telephone call follow-up one day after discharge reported no complaints. Before being discharged from the hospital, the patient was given tobramycin dexamethasone eye ointment and drops (Tobradex®, Texas, Alcon) to use once before going to bed and four times daily in the operated eye respectively. On another scheduled review

one week later in the out-patient department, the patient complained of blurred vision and a foreign body sensation in the operated eye. The best corrected visual acuity (BCVA) was 20/40 OD and intraocular pressure (IOP) was 10 mmHg. A round oily globule was seen around the corneal incision at 12 o'clock (superiorly) on slit-lamp examination (Figure 2A). No evident conjunctival congestion or corneal edema was seen. Upon inquiry regarding the application of ocular ointment for post-operative infection prevention, the patient disclosed that she repeatedly applied pressure and rubbed the eye after instilling the medication which potentially resulted in the ointment entering the anterior chamber through the corneal incision. The macular thickness, optic disc and the central corneal thickness (CCT) on optical coherence tomography (OCT) were normal. There was no significant difference in corneal endothelial cell density before and after surgery respectively. Under local anesthesia, anterior chamber was washed and globule removed under the microscope with a balanced saline solution (BSS plus*) using an irrigation-aspiration cannula. After surgery, patient's BCVA improved to 20/20 OD and IOP was 12 mmHg. Blurry vision and foreign body sensation disappeared. On slit-lamp examination, the anterior chamber became normal and clear (Figure 2B).

Table 1 Summary of patients' characteristics and clinical features

Parameters	Cases
Age [$M(P_{25}, P_{75})$, years]	73 (66.5, 77)
Sex (n, %)	
Male	14 (45.2%)
Female	10 (32.3%)
NA	7 (22.6%)
Type of ointment (n, %)	
Tobramycin-dexamethasone	11 (35.5%)
Gentamicin-betamethasone	8 (25.8%)
Chloramphenicol	2 (6.5%)
Dexamethasone-neomycin-polymyxin B	2 (6.5%)
framycetin sulphate	2 (6.5%)
Bacitracin zinc-neomycin	1 (3.2%)
Ofloxacin	1 (3.2%)
Petrolatum	1 (3.2%)
Detected time [$M(P_{25}, P_{75})$, d]	3 (1, 30)
Incision length [$M(P_{25}, P_{75})$, mm]	3.2 (3.0, 3.2)

NA: Not applicable.

Table 2 Summary of complications

Complications	Cases (n, %)	Duration of removed ointment [$M(P_{25}, P_{75})$, d]
Uncomplicated cases	14 (45.2%)	6 (0, 67.5)
Uveitis	4 (12.9%)	755 (520, 802)
Cystoid macular edema	4 (12.9%)	810 (210.8, 952.5)
Decreased corneal endothelial cell	3 (9.7%)	210 (6, 450)
Corneal edema	5 (16.1%)	165 (60.5, 815)
Glaucoma	3 (9.7%)	7 (6, 180)

Table 3 Relationship between ointment type, detection period, intervention and complications

Year	Author	Age	Sex	Ointment type	Ointment detected after surgery (d)	Incision length (mm)	Incision location	Follow-up (mo)	Ointment removed after surgery (d)	Complications
2003	Riedl <i>et al</i> ^[2]	72	Male	Bacitracin zinc-neomycin	180	NA	Temporal	12	180	Chronic uveitis and glaucoma
2004	Garzoni <i>et al</i> ^[4]	74	Male	Gentamicin	1	5.0	NA	35	1020	Glaucoma
2006	Wong and Bank ^[6]	70	Male	Chloramphenicol	60	3.0	Superior	12	75	Nil
2006	Chew <i>et al</i> ^[9]	55	Male	Tobramycin-dexamethasone	540	3.0	Superotemporal, sutured	24	810	Uveitis
2006	Werner <i>et al</i> ^[16]	86	Female	Gentamicin-betamethasone	10	3.2	Superior	NA	120	Corneal edema
		75	Female	Gentamicin-betamethasone	5	3.2	Superior	NA	90	Nil
		63	Female	Gentamicin-betamethasone	7	3.2	Superior	NA	7	Glaucoma, corneal edema
		75	Male	Gentamicin-betamethasone	1	3.2	Superior	NA	45	Nil
		87	Male	Gentamicin-betamethasone	1	3.2	Superior	NA	60	Nil
		74	Female	Gentamicin-betamethasone	60	3.2	Superior	NA	165	Corneal edema
		72	Female	Gentamicin-betamethasone	5	3.2	Superior	NA	6	Glaucoma, corneal edema
		73	Female	Gentamicin-betamethasone	1	3.2	Superior	NA	6	Nil
2006	Humayun <i>et al</i> ^[19]	NA	NA	Tobramycin-dexamethasone	1	5.2	Temporal	33	0	Nil
		NA	NA	Tobramycin-dexamethasone	1	5.2	Temporal	46	0	Nil
		NA	NA	Tobramycin-dexamethasone	1	3.2	Temporal	41	0	Nil
		NA	NA	Tobramycin-dexamethasone	1	3.2	Temporal	13	0	Nil
2009	Wong <i>et al</i> ^[7]	77	Female	Dexamethasone-neomycin-polymyxin B	730	3.0	Superior	NA	730	Corneal edema, uveitis
2010	Ugurbas and Akova ^[5]	65	Female	Tobramycin	30	3.0	Nasal	1	780	Uveitis, CME
2011	Shukla <i>et al</i> ^[10]	79	Male	Petrolatum	7	NA	NA	60	840	CME
2014	Cetinkaya <i>et al</i> ^[17]	62	Male	Tobramycin-dexamethasone	1	3.2	Superior	6	1	Nil
2015	Mansour <i>et al</i> ^[18]	84	NA	Tobramycin-dexamethasone	21	NA	NA	NA	21	Vision loss, CME
		82	Female	Tobramycin-dexamethasone	1	NA	NA	NA	900	Vision loss, corneal edema
2018	Kudo <i>et al</i> ^[3]	63	Male	Ofloxacin	450	2.0	Superior	NA	450	Uveitis, CME, decreased corneal endothelial cell density
2018	Sanders <i>et al</i> ^[15]	74	Male	Neomycin-polymyxin-dexamethasone	990	NA	NA	9	990	CME
2022	Mohamed-Noriega <i>et al</i> ^[11]	71	Male	Tobramycin-dexamethasone	1	3.0	Temporal	84	210	A decreased corneal endothelial cell density and TASS (uveitis)
2023	Lin and Si ^[12]	62	Male	Tobramycin-dexamethasone	1	NA	NA	NA	6	A decreased corneal endothelial cell density

NA; Not applicable; CME; Cystoidmacular edema; TASS; Toxic anterior segment syndrome.

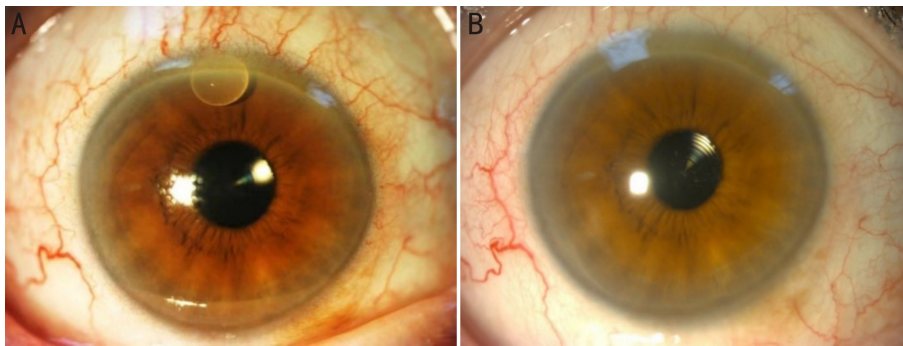


Figure 2 An eye post cataract surgery before and after removal of the inadvertent ointment. A: An oily globule (ointment) seen at 12 o'clock; B: A clear anterior chamber after removal of the ointment.

Thereafter, the patient was discharged, given education on ocular hygiene and instructed the proper way to use ocular medication. One month later, the patient came for follow-up review. The BCVA was maintained at 20/20 OD and IOP was 10 mmHg. The endothelial cell count, central macular thickness, corneal endothelial cell count were also stable. The patient was followed up by telephone again 3 mo later, and she said that there was no discomfort in the eye.

DISCUSSION

Phacoemulsification is a commonly used surgical technique for treating cataracts that is used in clinical practice of ophthalmology and leads to improvement of patients' visual acuity^[8]. While it is uncommon, the accidental entry of eye ointment into the anterior segment after cataract surgery can lead to serious complications if not promptly detected and removed^[9]. This paper presents a complete systematic evaluation of previous cases of intraocular ointment retention, making it the first of its kind.

Presence of intraocular ointment in the anterior chamber can lead to a number of complications including corneal endothelial thinning^[10], corneal edema, macular edema, uveitis, secondary glaucoma and others that can negatively affect visual acuity^[11]. Among the 31 cases we collected, 5 patients had corneal edema, accounting for 16.1% of all cases. Due to the fact that the ointment that entered the anterior chamber from the incision and was a foreign material, it caused aseptic inflammation upon contact with the corneal endothelium. Additionally, 4 patients had macular edema, postoperative CME following intraocular lens implantation was caused by increased retinal capillary permeability and loss of blood brain barrier due to release of inflammatory mediators^[12]. Four patients presented with uveitis, which resulted in chronic endophthalmitis due to the presence of eye ointment in their anterior chamber for more than 6 mo^[13-14]. Three cases presented with secondary glaucoma, as the ocular ointment occupied the anterior chamber space, obstructed aqueous circulation, and caused inflammation involving anterior chamber, trabecular meshwork and Schlemm's

canal^[15].

Following a systematic analysis of a series of collected cases, the issue of "time" emerged as a crucial factor in the occurrence of complications after ointment entry in anterior chamber. The time frame between the postoperative discovery of ointment in the anterior chamber and its removal plays an important role in determining the severity of complications^[16]. We collected 31 patients and found that the median time for eye ointment to enter the anterior chamber was 3 d, which is consistent with our analysis of the time when eye ointment enters the anterior through a corneal incision. This suggests that application of ointment following transparent corneal cataract surgery may result in its entry because the self-sealing wounds are unstable^[17]. Previous research has shown a corneal incision epithelialization time of 3 d for patients. The prompt management of intraocular ointment after its discovery is very crucial^[18]. Patients presenting with macular edema had a median ointment removal time of 810 d, and prolonged removal time exacerbated the severity of chronic intraocular inflammation, leading to serious postoperative complications. In patients with uveitis, the median ointment removal time was 755 d, while those developing complications associated with a decrease in corneal endothelial density had a median removal time of 210 d. Interestingly, patients without complications had a median removal time of 6 d only. Therefore, we consider that early detection and treatment can ensure that the patient has no complications. As we reported in this case, the patient underwent a thorough eye examination at discharge without any problems. However, a week postoperatively, an ointment globule was detected floating above the anterior chamber during a follow-up examination. Immediate anterior chamber irrigation was promptly arranged upon diagnosis, preventing the occurrence of complications. In addition, the type of eye ointment used by patients also has an important role about the occurrence of these complications^[19]. Among the reported cases, various ointments such as Tobramycin-dexamethasone, Gentamicin-betamethasone, Chloramphenicol, framycetin sulfate and

dexamethasone – neomycin – polymyxinB were identified. Notably, tobramycin – dexamethasone was implicated in 11 cases, possibly due to its widespread postoperative usage with Gentamicin–betamethasone, at 8 cases. The accidental entry of ointment into the eye was first reported in 1965, where the ointment remained in the anterior chamber of two patients for 18 and 3 years respectively, without adverse effects. Subsequent investigations involved injecting various common ointment carriers into rabbit eyes to observe the occurrence of corneal edema, uveitis, or glaucoma. The researchers found that all ointment matrices greater than 0.1 mL induced severe reactions. Furthermore, in cases of small amounts of ointment, the composition of the matrix influenced the severity of ocular complications^[20]. One case report detailed a patient who experienced TASS^[21–22] postoperatively due to the migration of Tobramycin – dexamethasone into the anterior chamber. This resulted in a decrease in endothelial cell density, and timely ointment removal prevented further declines, maintaining stability. However, direct contact between ointment and corneal endothelium can lead to vision loss, corneal edema, and inflammation, potentially causing chronic CME^[23]. Some patients are asymptomatic, as seen in the case we have presented. Despite this being the case, ointment moves in the anterior chamber freely with the position of the head which causes it to touch all the structures of the anterior chamber, including endothelium, trabecular meshwork angle as well as the iris. This lack of obvious symptoms in our case could be attributed to early postoperative follow-up, facilitating the prompt detection of ointment and timely intervention^[24].

A comprehensive ocular examination by ophthalmologists is crucial for the early detection of intraocular ointment. On slit-lamp and anterior segment photography, the presence of ointment can be observed as spherical droplets adhering to the intraocular lens or as floating globules within the anterior chamber. These globules may change position with alterations in patient positioning. Patients experiencing complications from intraocular ointment tend to be generally older, resulting in insufficient exposure of the corneal edge during eye examinations. The floating of ointment above the eyes during a seated position can lead to the oversight of some cases. Additionally, the assessment of wound apposition under a slit lamp is crucial, enabling an early evaluation of the patient's current condition and facilitating timely personalized interventions, such as replacing ointment with eye drops, to prevent potential complications^[25]. Different types of intraocular lenses (IOLs) used post cataract surgery can easily opacify and cause blurred vision in the patient^[26–27]. In our article, we have instead illustrated how different types of ointment used post cataract surgery can be a contributing

factor to the blurry vision (complication) in an event that it accidentally finds itself into the anterior chamber, and this can include IOL opacification in some cases where the ointment touches the artificially implanted lens. A study conducted by Zhang *et al*^[28] which involved 3 811 eyes divided in two groups of 2 397 and 1 414 respectively, proved that there was no need to use eye ointment after cataract surgery as there was no significant difference in post surgical infections between those patients that used eye ointment and those that did not use the ointment.

CONCLUSION

Anterior chamber ointment is a rare complication after cataract surgery, but it can lead to complications if not detected and treated on time. Patient education before discharge, early post-operative review and rigorous procedure can avoid this occurrence. And our systematic review has provided an updated summary of the reported cases. It is therefore important that ophthalmologists avoid using ointment as a post-operative treatment in cataract surgery routinely and switch to only using drops.

Conflicts of Interest: Paul M, None; Zheng Y, None; Chen XM, None; Ke M, None.

Authors' contributions: Paul M and Zheng Y wrote the manuscript and worked on all the figures and tables; Chen XM and Ke M reviewed the manuscript.

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