ORIGINAL ARTICLE

Comparison of post-operative inflammation using irrigating solution with and without heparin in patients with traumatic cataract

Mahtab Haider[1], Tayyaba Gul Malik[2*]

Biomedica - Official Journal of University of Health Sciences, Lahore, Pakistan
Volume 40(4):191-196
https://doi.org/10.24911/BioMedica/5-1236

ABSTRACT

Background and objective: The role of heparin in managing post-operative inflammation has been debated. Some studies suggest that heparin can reduce inflammation by inhibiting inflammatory mediators, while others argue that its anticoagulant properties could potentially worsen the inflammation. This study was designed to compare post-operative inflammation in patients undergoing traumatic cataract surgery with and without heparin added to the irrigating solution.

Methods: This quasi-experimental study was conducted in the Department of Ophthalmology at Lahore General Hospital Lahore from April 2023 to April 2024. A total of 48 patients with traumatic cataracts were divided by consecutive sampling into two groups (24 in each). Group A underwent surgery using heparin in the irrigating solution, while Group B had surgery without it. All patients were followed up on Day 1, Week 1, and after 1 month. Post-operative intraocular reaction was documented and compared. An Independent sample *t*-test was used to compare the numeric data. The chi-square test and Fisher's exact test were used to compare post-operative inflammation.

Results: The mean age of the patients was 12.29 ± 8.33 years. On day 1, Group A showed fewer Grade 1 cells in the anterior chamber (8.3% *vs.* 20.8%), with no statistically significant differences between the two groups ($p = 0.61$). Corneal edema had minimal variation between the groups ($p = 0.77$). By day 30, Group A, however, had no corneal edema in 91% of patients, while Group B had edema in 66% of cases. Pupillary membrane formation was slightly more common (12.5% *vs.* 8.3%) in Group B on day 1.

Conclusion: The use of heparin may have a beneficial effect in reducing post-operative inflammation in traumatic cataract surgery. However, the difference between the two groups was not statistically significant.

Keywords: Heparin, traumatic cataract, post-operative inflammation, irrigation solution.

Received: 04 October 2024 **Revised date:** 26 November 2024 **Accepted:** 02 December 2024
Correspondence to: Tayyaba Gul Malik
*Professor, Department of Ophthalmology, Lahore General Hospital, Lahore, Pakistan.
Email: tayyabam@yahoo.com
Full list of author information is available at the end of the article.

Introduction

Cataract is one of the leading causes of preventable blindness worldwide.[1] One of the complications of cataract surgery is post operative inflammation which is more common in children and also in complicated cataract like traumatic cataract. Various techniques have been used to reduce post-operative inflammation and one of these is the use of heparin in the infusion during cataract surgery. Heparin is an anticoagulant, which inhibits the conversion of prothrombin to thrombin. In addition to this, it has anti-inflammatory properties.[2,3]

In his study, Vasavada VA, investigated the effects of intraocular infusion of low molecular weight heparin on reducing postoperative inflammation in pediatric patients undergoing intraocular lens (IOLs) implantation and cataract surgery. The findings did not provide a significant benefit of Heparin in terms of early postoperative inflammation. However, in cases where it was not used, there was a higher frequency of Grade 2 cells and posterior synechiae in 10% of the affected eyes.[4] In contrast, studies on both adult human and animal eyes have shown that adding heparin to the irrigating solution during cataract surgery helps reduce the disruption of the blood–aqueous barrier and aids in preventing posterior capsule opacification.[5]

Given the debatable results, this study aims to evaluate the effectiveness of heparin in controlling postoperative inflammation in patients undergoing surgery for traumatic cataracts. The data generated from this study will provide insight into the efficacy of the addition of heparin in the irrigation solution during traumatic cataract surgery.

Methods

This quasi-experimental study was conducted at the Department of Ophthalmology at Lahore General Hospital, Lahore from April 2023 to April 2024 after approval from the Institutional Ethics Committee. The sample size was calculated with a 5% level of significance, 80% power of the test, and by taking an expected percentage of inflammation with heparin as 16.7% and 50% without heparin.[3] The sample size was 24 patients in each group. The study followed the Declaration of Helsinki and patients were recruited through a non-probability purposive sampling technique. Patients more than 3 years of age with traumatic cataract (caused by blunt trauma) and without any flare for the last 6 months were recruited. Patients with ocular pathology other than cataract, or with congenital or senile cataract, bleeding tendencies or on anticoagulant or systemic anti-inflammatory drugs, or having chronic debilitating chronic illness were excluded.

The patients were divided into two groups. Group A underwent surgery with an irrigating solution containing heparin, while Group B had surgery with a solution without heparin. Informed consent was taken from the adult patients and from the guardian/parents of minors. The sampling was done through a convenient sampling method by alternating patients between the two groups. Comprehensive preoperative eye examinations, including intraocular pressure measurements, retinal evaluations, and slit lamp tests, were conducted for each patient.

10 IU per ml of Heparin was used in the irrigating solution. In 500 ml of irrigating solution, 5000 IU of sterile heparin injection was used. 1 IU of Heparin is equal to 0.002 mg. Hence, 5000IU is equal to 10 mg in 500 ml of irrigating solution.[6] The solution was prepared within the theater under sterile conditions. A single surgeon performed all operations using the same surgical technique.

Postoperative inflammation was assessed using slit lamp biomicroscopy at each follow-up visit on the following criteria; aqueous flare and cells, corneal edema and striations, posterior synechiae, and pupillary membrane. Grading Corneal Edema (0 to 4+) was done as follows.

0	Clear cornea; no edema
1+	Mild stromal haze, no Descemet's folds
2+	Moderate stromal haze with a few Descemet's folds
3+	Marked stromal haze, multiple Descemet's folds, early epithelial bullae
4+	Severe haze, numerous folds, diffuse epithelial bullae (bullous keratopathy).

Standardization of Uveitis Nomenclature Working Group was used to measure the number of white cells in a 1 mm × 1 mm slit beam field of the anterior chamber.[7] Grading is as follows:

Grade 0.5+ (Trace cells):
- 1–5 cells per field.

Grade 1+:
- 6–15 cells per field.

Grade 2+:
- 16–25 cells per field.

Grade 3+:
- 26–50 cells per field.

Grade 4+:
- More than 50 cells per field.

Corneal edema was graded as follows:

Grade 1: Mild edema (Slight corneal cloudiness that is localized, usually just in the central area. There may be a faint haze but vision is typically not significantly affected).

Grade 2: Moderate edema (Increased cloudiness, involving a wider area of the cornea, there might be the presence of mild Descemet's folds, and vision is usually mildly affected, with some blurring).

Grade 3: Severe edema (significant cloudiness of the cornea that may involve stromal swelling, more pronounced Descemet's membrane folds, and vision is moderately to severely affected).

Grade 4: Very severe edema (extensive, diffuse corneal opacity, marked stromal thickening, and large Descemet's membrane folds or striae, vision is severely reduced).

Postoperative intraocular complications, such as fibrin formation, anterior and posterior synechiae, and pupillary membrane formation, were recorded and compared between the groups. Both groups received Dexamethasone every 2 hours, Moxifloxacin every 2 hours, and the non-steroidal inflammatory drug, Nepafenac, four times daily. In cases of pupillary membrane formation, sub-conjunctival Mydricaine (0.1 ml of atropine and adrenaline each mixed with 0.8 ml of lignocaine) was administered. Follow-up appointments were scheduled for day 1, week 1-, and 30 days post-surgery, with additional visits for cases requiring closer monitoring due to pupillary membrane formation.

Statistical analysis

Data were entered and analyzed using SPSS version 27. The numerical data were presented in the form of Mean + SD. The categorical variables were presented in the form of frequencies and percentages. An Independent sample *t*-test was used to compare the numeric data. Chi-square and Fisher's exact tests were used to compare post-operative Inflammation. A p-value < 0.05 was taken as significant.

Results

The mean age of the patients was 12.29 ± 8.33 years (3–40 years) with a mean of 11.95 ± 9.06 years and 12.83 ± 7.69 years in Group A and Group B, respectively (p 0.72). There

Table 1. *Characteristic features of Group A (Heparin) and Group B.*

		Study groups		Total *N* (%)	*p*-value*
		Group A; *N* (%)	Group B; *N* (%)		
Gender	Male	18 (75)	19 (79.2)	37 (77.1)	0.731
	Female	6 (25)	5 (20.8)	11 (22.9)	
Operated eye	Right	11 (45.8)	12 (50)	23 (47.9)	0.773
	Left	13 (54.2)	12 (50)	25 (52.1)	

*Fisher Exact Test.

Table 2. *Comparison of post-operative (day 1 and day 30) inflammatory changes between two groups.*

	Post-operative day 1			Post-operative day 30		
	Group A; *N* (%)	Group B; *N* (%)	*p* value	Group A; *N* (%)	Group B; *N* (%)	*p* value*
Cells in anterior chamber						
Grade 1	2 (8.3)	5 (20.8)	0.61	0	2 (8.3)	>0.99
Grade 2	3 (12.5)	4 (16.7)		0	1 (4.2)	
Grade 3	3 (12.5)	5 (20.8)		0	1 (4.2)	
Grade 4	0 (0)	2 (8.3)		0	0	
No flare	16 (66.7)	8 (33.3)		0	2 (8.3)	
Corneal edema						
Grade 1	3 (12.5)	5 (20.8)	0.77	0	5 (20.8)	>0.99
Grade 2	2 (8.3)	3 (12.5)		1 (8.3)	1 (12.5)	
Grade 3	2 (8.3)	3 (12.5)		1 (8.3)	2 (12.5)	
Grade 4	2 (8.3)	4 (16.7)		0	0	
No edema	15 (62.5)	9 (37.5)		22 (91.6)	16 (66.66)	
Pupillary membrane						
Present	2 (8.3)	3 (12.5)		0	0	
No membrane	22 (91.7)	21 (87.5)		24 (100)	24 (100)	

*Fisher Exact Test.

were 37 (77.08%) males and 11 (22.92%) females with a male-to-female ratio of 3.4:1. All eyes were quiet before surgery, and only 2 eyes had posterior synechia (one in each group). Comparison between study groups on day 1 and day 30 for corneal edema, flare, and pupillary membrane as stratified by age, gender, and operated eye showed insignificant difference ($p > 0.99$).

Table 1 presents the demographic characteristics of patients in the heparin (Group A) and control (Group B) groups. Both groups had a similar gender distribution, with around 75% of patients being males. The operated eye (right or left) was also comparable between the groups, with no significant differences in either category ($p = 0.731$ for gender and $p = 0.773$ for the operated eye).

Table 2 shows that on day 1, the Group A eyes showed fewer Grade 1 cells in the anterior chamber (8.3% *vs.* 20.8%), with no significant differences ($p = 0.61$) among the groups. Corneal edema was also similar between the two groups ($p = 0.77$). By day 30, Group A however had no anterior chamber cells or corneal edema in all cases, while the control group still had two cases of Grade 1 cells. The pupillary membrane disappeared on all cases on day 30.

There was inflammation in both groups on day 1. However, by day 30 it was improved in such a way that none of the patients showed pupillary membrane.

Discussion

The present study aimed to evaluate the effect of adding heparin to the irrigating solution during traumatic cataract surgery on early postoperative inflammation. The findings suggest that heparin use may contribute to reduced intraocular inflammation in the early postoperative period, with improved clinical outcomes observed by day 30 compared to control. However, the difference was not statistically significant. By day 30, patients in the heparin group showed better outcomes, with no anterior chamber

cells or corneal edema, while the control group still had mild inflammation and edema. Heparin also seemed to lower the frequency of pupillary membrane formation. However, the results were not statistically significant, indicating a need for further investigation.

Ocular trauma is a major contributor to vision loss, with around 1.6 million people losing their sight each year due to traumatic cataracts. Eye injuries affect roughly one-fifth of adults, with men and young individuals being the most frequently impacted. Globally, there are an estimated 55 million eye injuries annually, and developed countries report a high incidence of unilateral blindness.[8] In Pakistan, there is currently no national-level data on the prevalence and incidence of ocular trauma. However, few single-center studies from tertiary care institutions have been published, reporting variable findings. The only common finding in these studies is the age ranging from late teens to early 30s. [9,10]

One of the complications of ocular trauma is traumatic cataract. Inflammation after traumatic cataract surgery has a significant role in the delayed recovery of vision. Increased inflammatory response in the eyes increases the likelihood of secondary problems, such as cystoid macular edema, which may or may not result in irreversible blindness.[6] Furthermore, eyes that have an inflammatory response are more likely to have delayed postoperative problems such as posterior capsular opacification. Over half a century after the first intraocular lens was implanted, ongoing research aims to make the IOL more biocompatible and minimize postoperative inflammation. To address the inflammation caused by surgical trauma, various techniques have been used including reducing the time of surgery, lesser uveal manipulation, less phaco power, microincision cataract surgery, and use of specific lenses. [11,12]

Heparin-coated IOL usage has been investigated to control post-operative inflammation.[13] Heparin contains properties that are both anti-inflammatory and anti-proliferative. Apart from its anticoagulant properties, heparin has been shown to impede the development of fibrin during ophthalmic surgery and to suppress fibroblast activity.[14] Some studies suggest that eyes with heparin-coated lenses experience reduced inflammation. However, one of the primary challenges of using these intraocular lenses is their cost. Moreover, research indicates that heparinized intraocular infusion can decrease postoperative inflammation following cataract surgery.[15]

The effect of Heparin was also studied on posterior capsular opacification. Nema et al. [16] evaluated the effect of posterior capsular opacification and postoperative inflammatory response in relation to low-molecular-weight heparin infusion with square-edge IOL. Their study demonstrated that heparin infusion with square-edge IOL implantation is both safe and effective in high-risk patients, reducing the incidence of posterior capsular opacification and postoperative inflammation without causing significant adverse effects.[16]

Krall et al. [17] conducted a study to assess flare and cell intensity in the anterior chamber after uneventful cataract surgery, focusing on the effectiveness of heparin-surface-modified hydrophobic acrylic intraocular lenses compared to uncoated IOLs. The results indicated that the heparin-surface-modified IOL significantly reduced the inflammatory response in the early postoperative phase, leading to a quicker resolution of inflammation symptoms.[17] Following this, another study conducted by Krall et al. [17] also reports the frequency of posterior capsule opacification in both uncoated and hydrophobic acrylic heparin-surface-modified IOLs 1 year after implantation. While the findings revealed a reduction in flare on the first postoperative day with the heparin-surface-modified IOL, there were no statistically significant differences in posterior capsule opacification between the two types of lenses after 1 year.[18]

Safi and Rahimi [19] compared the use of heparin versus no heparin in pediatric cataract surgery, demonstrating its potential to significantly reduce postoperative inflammation in children.[19] In this study, the heparin-irrigated group showed lower complication rates, including posterior capsule opacification in 28%, posterior synechiae in 14%, and hyphaema in 14%. In contrast, a group without heparin had a higher rate of occlusive pupil formation, observed in 75% of eyes. Earlier, Ozkurt et al. [20] had investigated the effects of heparin sodium irrigation in the anterior chamber following pediatric cataract surgery. His findings suggested that adding heparin to the irrigating balanced salt solution helped prevent inflammatory complications after the procedure. Mild anterior chamber reaction was noted in three patients from the heparin group, all of which resolved by the seventh postoperative day. In contrast, nine patients in non-heparin Group 2 exhibited marked anterior chamber reaction; in four of these cases, the inflammation was severe, leading to pupillary membrane formation and synechiae despite treatment. Their results were compared on the seventh day but in our study the follow up continued for 1 month. [20]

A local study from Sindh evaluated the effects of heparin sodium irrigation in the anterior chamber on cellular responses and early postoperative inflammation after cataract surgery in adult patients. Mild anterior chamber reaction was observed in only four patients in the heparin group, while nine cases of the non-heparin group experienced marked anterior chamber reaction. The researchers found that adding heparin sodium to the irrigating solution appeared safe, promising, and effective method for preventing the development of posterior capsule opacification and reducing

early postoperative inflammatory responses following cataract surgery.[5] In another study, implantation of Heparin-coated lenses resulted in the lower aqueous flare on day one, postoperative week one, and on the third month but there was no statistically significant difference (p = 0.11) at later follow up.[21] The study results are quite similar to our results with the difference that we added heparin in the irrigating solution instead of implantin heparin coated lenses.

A recent rare case report describes a 67-year-old male with recurrent conjunctival granuloma after multiple excisions following cataract surgery. The combination treatment of plasmin activator, heparin, cortisone, and cyclosporine effectively prevented the recurrence of ligneous conjunctivitis.[22] This study clearly signifies the important role played by heparin in reducing inflammation not only in intraocular surgery but in extraocular diseases too.

Limitation of study

The study has few limitations. The sample size may not be large enough to draw definitive conclusions about the efficacy of heparin in reducing post-operative inflammation. The quasi-experimental nature of the study limits the ability to establish causality. Additionally, the follow-up duration (1 month) may be insufficient to capture the long-term effects of heparin on post-operative inflammation and other potential complications. Factors such as the severity of cataract, surgical technique, and patient demographics were not controlled, which could influence inflammation outcomes. Although some trends were observed, the lack of statistically significant differences (e.g., p-values of 0.61 and 0.77) suggests that the findings may not be clinically relevant. Addressing these limitations in future research could enhance the reliability and validity of findings regarding the role of heparin in post-operative inflammation management.

Conclusion

The use of heparin in the irrigation solution in patients undergoing traumatic cataract surgery may have a beneficial effect in reducing post-operative inflammation by decreasing the post-operative flare, infiltration by inflammatory cells, and pupillary membrane formation. However, the difference with the non-heparin irrigation solution was not statistically significant.

Acknowledgment

The authors would like to acknowledge the staff of the Ophthalmology Department of Lahore General Hospital Lahore, for their support during the conduct of the study.

List of Abbreviations

IOL Intraocular lens

Conflict of interest

None to declare.

Grant support and financial disclosure

None to disclose.

Author's contribution

MH: Study design, data collection, drafting of manuscript, critical intellectual input.

TGM: Concept and design of study, data analysis, drafting of manuscript, crtical intellectual input, and revising.

ALL Authors: Approval and responsibility of the final version of the manuscript to be published.

Ethics approval

The study was approved by the Institutional Review Board of the Lahore General Hospital, Lahore, Pakistan vide Letter No:00/139//22 dated 21/04/22.

Authors ' Details

Mahtab Haider[1], Tayyaba Gul Malik[2]

1. Postgraduate Resident, MS (Ophthalmology) Lahore General Hospital, Lahore, Pakistan
2. Professor, Department of Ophthalmology, Lahore General Hospital, Lahore, Pakistan

References

1. Naidoo K, Kempen JH, Gichuhi S, Braithwaite T, Casson RJ, Cicinelli MV, et al. Vision Loss Expert Group of the Global Burden of Disease Study. Prevalence and causes of vision loss in sub-Saharan Africa in 2015: magnitude, temporal trends and projections. Br J Ophthalmol. 2020;104(12):1658–68. https://doi.org/10.1136/bjophthalmol-2019-315217
2. Lever R, Page CP. Non-anticoagulant effects of heparin: an overview. Handb Exp Pharmacol. 2012;(207):281–305. https://doi.org/10.1007/978-3-642-23056-1_12
3. Caça I, Sahin A, Cingü AK, Ari S, Alakuş F, Cinar Y. Effect of low molecular weight heparin (enoxaparin) on congenital cataract surgery. Int J Ophthalmol. 2012;5(5):596–9. https://doi.org/10.3980/j.issn.2222-3959.2012.05.10
4. Vasavada VA, Praveen MR, Shah SK, Trivedi RH, Vasavada AR. Anti-inflammatory effect of low-molecular-weight heparin in pediatric cataract surgery: a randomized clinical trial. Am J Ophthalmol. 2012;154(2):252–8.e4. https://doi.org/10.1016/j.ajo.2012.02.021
5. Yousif H, Chohan A, Ahsan M. Effect of heparin on post-operative inflammation after cataract surgery in diabetics. Indo Am J P Sci. 2021;8(1):1–5. https://zenodo.org/record/4437827
6. Ganekal S, Dorairaj S, Ganekal V. Effect of heparin sodium on postoperative inflammation after adult cataract surgery. Indian J Clin Exp Ophthalmol. 2021;7(4):699–702. https://www.ijceo.org/html-article/15575
7. Trusko B, Thorne J, Jabs D, Belfort R, Dick A, Gangaputra S, et al. Standardization of Uveitis Nomenclature (SUN) Project. The Standardization of Uveitis Nomenclature (SUN) Project. Development of a clinical evidence base utilizing informatics tools and techniques. Methods Inf Med. 2013;52(3):259–65. https://doi.org/10.3414/ME12-01-0063

8. Okoye GS, Gurnani B. Traumatic cataract. 2023 Aug 27. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2024.
9. Karamat B, Azhar J. Frequency and characteristics of ocular trauma in a tertiary care hospital in Lodhran. Pak J Ophthalmol. 2019;34(2):116–21. https://doi.org/10.36351/pjo.v34i2.953
10. Jamil AZ, Bahoo MLA. Visual outcome of ocular trauma presenting in a tertiary care hospital in Sahiwal. Pak J Ophthalmol. 2020;36(2):130–5. https://doi.org/10.36351/pjo.v36i2.987
11. Hansen NC, Erichsen JH, Holm LM, Kessel L. Corneal thickness and anterior chamber flare after cataract surgery: a randomized controlled trial comparing five regimens for anti-inflammatory prophylaxis. Clin Ophthalmol. 2021;15:2835–45. https://doi.org/10.2147/OPTH.S312350
12. Sawa M. Laser flare-cell photometer: principle and significance in clinical and basic ophthalmology. Jpn J Ophthalmol. 2017;61(1):21–42. https://doi.org/10.1007/s10384-016-0488-3
13. Huang Q, Cheng GP, Chiu K, Wang GQ. Surface modification of intraocular lenses. Chin Med J (Engl). 2016;129(2):206–14. https://doi.org/10.4103/0366-6999.173496
14. Luo C, Wang H, Chen X, Xu J, Yin H, Yao K. Recent advances of intraocular lens materials and surface modification in cataract surgery. Front Bioeng Biotechnol. 2022;10:913383. https://doi.org/10.3389/fbioe.2022.913383
15. Bayramlar H, Totan Y, Borazan M. Heparin in the intraocular irrigating solution in pediatric cataract surgery. J Cataract Refract Surg. 2004;30(10):2163–9. https://doi.org/10.1016/j.jcrs.2004.07.003
16. Nema K, Hussain S. Low molecular weight heparin in intraocular infusion in high risk group cataract surgery—minimizes inflammatory reaction and prevents posterior capsular opacification. J Med Sci Clin Res. 2018;6(7):777–86. https://doi.org/10.18535/jmscr/v6i7.130
17. Krall EM, Arlt EM, Jell G, Strohmaier C, Bachernegg A, Emesz M, et al. Intraindividual aqueous flare comparison after implantation of hydrophobic intraocular lenses with or without a heparin-coated surface. J Cataract Refract Surg. 2014;40(8):1363–70. https://doi.org/10.1016/j.jcrs.2013.11.043
18. Krall EM, Arlt EM, Jell G, Strohmaier C, Moussa S, Dexl AK. Prospective randomized intraindividual comparison of posterior capsule opacification after implantation of an IOL with and without heparin surface modification. J Refract Surg. 2015;31(7):466–72. https://doi.org/10.3928/1081597X-20150623-05
19. Safi AB, Rahimi I. Heparin sodium uses in children's cataract surgery. Int J Res Biol Pharm. 2019;5(9):16–23. https://doi.org/10.53555/bp.v5i9.1102
20. Ozkurt YB, Taşkiran A, Erdogan N, Kandemir B, Doğan OK. Effect of heparin in the intraocular irrigating solution on postoperative inflammation in the pediatric cataract surgery. Clin Ophthalmol. 2009;3:363–5. https://doi.org/10.2147/opth.s5127
21. Kumari D, Simakurthy S, Sharma N, Titiyal J, Kumar A, Chawla R, et al. Comparison of clinical outcomes of implantation of foldable hydrophobic acrylic intraocular lens with and without heparin surface modification in Indian diabetic patients. Cureus. 2024;16(3):e56855. https://doi.org/10.7759/cureus.56855
22. Maamri A, Zemova E, Moslemani K, Flockerzi F, Seitz B. Recurrent ligneous conjunctivitis after cataract surgery in a 67-year-old male patient: a case report. BMC Ophthalmol. 2022;22(1):103. https://doi.org/10.1186/s12886-022-02329-7