

# Effect of heparin in the intraocular irrigating solution on postoperative inflammation in the pediatric cataract surgery

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**Purpose:** To evaluate the influence of irrigation of the anterior chamber with heparin sodium on postoperative inflammation after pediatric cataract surgery.

**Setting:** Kartal Training and Research Hospital, First Eye Clinic, Istanbul, Turkey.

**Design:** Randomized prospective double-blind study.

**Methods:** Fourteen consecutive eyes from 14 patients aged  $8.9 \pm 5.9$  years, (range 3–18 years) (group 1) and 19 eyes from 19 patients aged  $9.1 \pm 5.2$  (range 1.5–18 years) (group 2) underwent pediatric cataract surgery. Five patients in group 1 were between three and five years old. One patient was 1.5 years old and six patients in group 2 were between three and five years old. During the procedure, group 1 received anterior chamber irrigation with heparin sodium (5 IU/cc) and 1 ml of heparin sodium (concentration 10 IU/ml) added to the irrigating balanced salt solution (BSS Plus; Alcon Laboratories, Inc., Fort Worth, TX, USA) while group 2 received BSS without heparin sodium only. Cases aged under three years received anterior vitrectomy in addition to posterior capsulorrhexis. One eye received anterior vitrectomy in group 1 and two eyes received anterior vitrectomy in group 2. Cases with preoperative complications were not included in the study. Early and late postoperative inflammatory complications, including fibrin formation, anterior and posterior synechia, cyclitic and pupillary membrane formation were recorded and compared.

**Results:** Mild anterior chamber reaction was observed in three patients in Group 1, while nine cases in group 2 experienced marked anterior chamber reaction. In four of nine patients from group 2, anterior chamber reaction was severe and resulted in pupillary membrane and synechia despite treatment in the postoperative 7th day, while in all three cases in group 1, reaction disappeared by the 7th day.

**Conclusion:** Anterior chamber irrigation with heparin during pediatric cataract surgery may minimize early inflammatory reaction and decrease the number of postoperative inflammatory related complications.

**Keywords:** pediatric, cataract, surgery, inflammation

Pediatric cataract surgery may result in preoperative and postoperative complications.<sup>1</sup> Cataract surgery and other intraocular procedures have a higher incidence and more pronounced postoperative inflammatory reactions in children compared with adults.<sup>1</sup> These reactions are associated with younger age and may be affected by surgical technique, intraoperative injury to adjacent structures such as iris, presence of antecedent ocular infection, and remnants of retained cortical material.<sup>1</sup> Heparin has anti-inflammatory and antiproliferative effects in addition to its anticoagulant function,<sup>2</sup> inhibits fibrin formation after intraocular surgery, and has also been shown to inhibit fibroblast activity.<sup>3</sup>

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In this prospective study, we evaluated the influence of anterior chamber irrigation with heparin sodium on early postoperative inflammation and cellular reaction after pediatric cataract surgery.

## Patients and methods

Fourteen eyes from 14 pediatric cataract cases aged  $8.9 \pm 5.9$  years (group 1: range 3–18 years) received anterior chamber irrigation with heparin sodium (5 IU/cc) during operation and received 1 ml of heparin sodium (concentration 10 IU/ml) added to the irrigating solution of BSS (BSS Plus) whilst in 19 eyes from 19 pediatric cataract cases aged  $9.1 \pm 5.2$  (group 2: range 1.5–18 years), BSS without heparin sodium was used.

All patients had no ocular pathology other than cataract. The parents were asked to sign an informed consent for the procedure. All children underwent cataract extraction under general anesthesia by two experienced surgeons. After a 3.2-mm limbal tunnel incision was created, the anterior chamber was entered, and a continuous curvilinear capsulorhexis (CCC) was made with the Utrata forceps. The size of anterior capsulorhexis was between 5.0 mm and 5.5 mm. After the nucleus was hydrodissected, lens material was aspirated using the automated irrigation/aspiration mode of the phacoemulsifier after the hydrodissection. All cases received posterior capsulorhexis with a diameter of 3.5 mm and 4.0 mm. One eye received anterior vitrectomy in group 1 and two eyes received anterior vitrectomy in group 2. Cases aged under three years received anterior vitrectomy in addition to posterior capsulorhexis. One eye received anterior vitrectomy in group 1 and two eyes received anterior vitrectomy in group 2.

All eyes having intraocular lens (IOL) implantation received monoblock, hydrophobic foldable acrylic IOL (AcrySof MA30BA; Alcon Laboratories, Inc.). Cases with perioperative complications were not included in the study. No oral or subconjunctival steroids were used. Standardized postoperative treatment comprised prednisolone acetate 1% (Pred Forte®; Allergan, Inc., Irvine, CA, USA) eight times a day for one week followed by six times a day for the second week and tapered over six weeks, and ciprofloxacin 0.3% (Ciloxan; Alcon Laboratories, Inc.) and ketorolac 0.5% three times a day for one month. All patients were followed daily for the first three days, once a week for the first month, and at the 3rd and 6th months. At all visits, postoperative intraocular complications, including fibrin formation, anterior and posterior synechia, cyclitic and pupillary membrane formation, and posterior capsular opacification (PCO) were recorded and compared. The follow-up period after surgery was between three and 24 months

(average 9.4 months =  $\pm 7.15$ ). The Fisher's exact test was used for statistical analysis.

## Results

The two groups were comparable in age and distribution of sex (Student *t*-test  $p > 0.05$ ). There were no statistically significant differences between the two groups. Table 1 shows preoperative and postoperative patient data in groups 1 and 2. Mild anterior chamber reaction was observed in only three patients in group 1, while nine cases of group 2 experienced marked anterior chamber reaction. In four of nine patients from group 2, anterior chamber reaction was severe which resulted in pupillary membrane and synechia, despite treatment on the postoperative 7th day (Table 2).

In two of these four cases, synechiotomy was performed as a second surgical procedure. In the long-term follow up in two cases from group 2, pupillary irregularity was reported. It was seen that anterior chamber reaction disappeared in all three cases of group 1 on the 7th day and pupillary irregularity was not reported in any of these cases. Hyphema or intraocular hemorrhage due to heparin were not reported in any cases in both groups. Differences found between the group 1 and the group 2 could have occurred by chance or because of the small size of the studied population.

## Discussion

The pathogenesis of postoperative fibrinoid inflammation is unknown. Any defect in the blood–aqueous barrier (BAB), possibly due to intraocular inflammation, preoperative high intraocular pressure (IOP), or excessive eye manipulation during surgery may lead to a disturbance in the coagulation and fibrinolytic pathway.<sup>4</sup>

A tendency towards increased postoperative inflammation in children is well recognized.<sup>5</sup> Intraocular inflammation manifests itself as increased cells and flare, inflammatory precipitates on the IOL and the endothelium, formation of synechia, and inflammatory cyclitic membranes.<sup>1</sup> The fibrinoid reaction after pediatric cataract surgery is caused by the breakdown of the immature BAB and insufficient trabecular meshwork

**Table 1** Postoperative complications after cataract surgery

Characteristics	Group 1 (14 eyes)	Group 2 (19 eyes)	Statistical difference
Gender (M:F)	6:8	9:10	$P = 1.0000$
Cells in anterior chamber $> 10$	3	9	$P = 0.1604$
Fibrin in anterior chamber	0	4	$P = 0.1192$
Pupillary membrane and anterior synechiae	0	4	$P = 0.1192$

**Table 2** Posterior capsular opacification

	Group 1 (n = 14)	Group 2 (n = 19)	Statistical difference
1st week	0	0	
1st month	0	1	P = 1.0000
3rd month	1	2	P = 1.0000
6th month	1	4	P = 0.3662

fibrinolytic activity.<sup>6</sup> Secondary complications of severe fibrinoid reaction include papillary membrane and opacification of the anterior hyaloid face.<sup>6</sup> Therefore, measures that may prevent or decrease inflammation in these eyes deserve consideration.<sup>7</sup> In addition to its well-known anticoagulant activity, heparin has anti-inflammatory and antiproliferative properties.<sup>6</sup> Heparin inhibits fibrin formation after intraocular surgery and has also been shown to inhibit fibroblast activity.<sup>3</sup>

Due to its antithrombin effect, heparin inhibits fibrin formation by accelerating the control mechanisms for thrombin and activated X-factor.<sup>8</sup>

Previous studies elucidate several mechanisms through which heparin may inhibit inflammation including induction of apoptosis in human peripheral blood neutrophils, inhibition of the complement activation and lymphocyte migration, L- and P-selectin, adhesion-molecule support of the initial attachment of leukocytes to the vessel wall at the inflammation site, neutrophil chemotaxis, and generation of refractive oxygen species by mononuclear and polymorphonuclear leukocytes.<sup>1,4,6</sup> Another useful adjunct for the prevention of membrane formation over the IOL optic is the use of a heparin-coated IOL.

In our study of pediatric cataract surgery, addition of heparin to the irrigating BSS prevented postoperative inflammatory complications. In this study it was shown that in heparin sodium-added group 1 patients, early postoperative inflammatory reactions were rare. Bayramlar and colleagues<sup>6</sup> concluded that the addition of heparin to the irrigating solution during surgery decreases postoperative fibrinoid reaction and late inflammatory complications.

The incidence of PCO after pediatric cataract surgery has been reported as high as 95.8%.<sup>9</sup> Several studies demonstrated the antiproliferative effect of heparin on lens epithelial cells

and its additive effect to prevent PCO in children. In our study, in the 6th month, PCO was reported in only one case from group 1 and in four cases from group 4.

Hyphema, which can be seen during surgery due to heparin irrigation, was not seen in our study. However, this risk can also be diminished by using low molecular weight heparin.<sup>8</sup> Iverson and colleagues suggest that fragmin, at a concentration of 5 IU/mL, lowers the risk of hemorrhage during vitreoretinal and lensectomy surgeries.<sup>10</sup>

Our results suggest that adding heparin sodium to the irrigating solution seems to be a safe, effective, and promising method to prevent early postoperative inflammatory reactions and PCO formation in the long term after pediatric cataract surgery.

## Disclosure

The authors report no conflicts of interest in this work.

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