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ORIGINAL ARTICLE

Study of the use of Heparin Sulphate injection in irrigation solution intraoperatively in cataract surgery and its effect on intraocular inflammation and cellular reaction

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ABSTRACT:

Background: Inflammation after cataract surgery is due to breakdown of the blood-aqueous barrier and release of prostaglandins which leads to cellular infiltration of the anterior chamber. The post-surgical increase in the permeability of blood-aqueous barrier appears to be related to a release of Prostaglandin E2. Postoperative inflammation continues to be a cause of patient discomfort and pain and if left untreated, it can lead to formation of synechiae, increased intraocular pressure and in some cases, suboptimal visual results secondary to cystoids macular edema. **Aim of the study:** To evaluate the effectiveness of heparin sulphate in irrigating solution in controlling inflammation following an uneventful cataract surgery with intraocular lens implantation in a large sample double blinded trial. **Materials and method:** A prospective, randomized, double blinded comparative study was carried out on 200 adult patients at a tertiary care centre. A detailed history of disease and prior treatment was taken. Atleast 5 visits were scheduled on postoperative days 1, 4, 7, 15 and 30. The cases were selected from patients who underwent uncomplicated cataract surgery with posterior chamber intraocular lens (PCIOL) implantation in the capsular bag. **Results:** We found that Heparin sulphate injection 5000 IU when injected in the irrigation solution intraoperatively leads to decrease in postoperative inflammation in the early postoperative period. Therefore injection of heparin in the irrigation solution can be considered in cases where postoperative inflammation is expected. **Conclusion:** The group treated with heparin had significantly less inflammation in the early postoperative period and thereby there was a reduced necessity of anti-inflammatory agents. If, by adding heparin in the irrigating solution leads to decreased usage of postoperative steroids then it can emerge as a useful tool in preventing steroid related complications such as rise in postoperative intraocular pressure.

Keywords: Cataract, Heparin sulphate, Postoperative inflammation, surgery.

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INTRODUCTION:

Techniques of extra capsular cataract extraction and instrumentation have improved tremendously over the past few decades. Smaller incisions, more efficient phacoemulsifiers and decreased surgical times are a few of the changes that have helped to reduce postoperative inflammation. Nevertheless, intraocular surgery is an ocular trauma, so patients do exhibit inflammation after cataract surgery which needs to be treated with an anti-inflammatory agent.

Inflammation after cataract surgery is due to breakdown of the blood-aqueous barrier and release of prostaglandins which leads to cellular infiltration of the anterior chamber. The post-surgical increase in the permeability of blood-aqueous barrier appears to be related to a release of Prostaglandin E2.[1] Postoperative inflammation continues to be a cause of patient discomfort and pain and if left untreated, it can lead to formation of synechiae, increased intraocular pressure and in some cases, suboptimal visual results secondary to cystoids macular edema.

Postoperatively, the eye is also at risk for infection. Hence it is a common practice to prescribe a topical broad spectrum antibiotic and steroid combination in the postoperative period. While the antibiotic prevents the infection, the steroid controls the inflammatory reaction. Topical corticosteroids are commonly used as a routine

postoperative medication for several weeks to reduce inflammatory reaction.[2] However, these topical steroids have many side effects including elevation in intraocular pressure, inhibition of wound healing and increased susceptibility to secondary infections.[3] Paradoxically, the topical use of dexamethasone or prednisolone can lead to acute inflammation of the anterior segment of the eye.[4]

This has led a need to research additional ways to counter postoperative increase in intraocular pressure which has no or less side-effects than the prevailing regimen of treatment or an addition with the current steroid-antibiotic combination. Recent studies have found out that heparin has anti-inflammatory and anti-proliferative effects as well as anti-coagulant properties. Animal and human studies show that adding heparin to the irrigating solution during cataract surgery results in less disturbance of the blood-aqueous barrier (BAB) and helps prevent posterior capsule opacification (PCO) postoperatively.[5-9]

Heparin sulphate added to the standard irrigating solution reduced disturbances of the blood-aqueous barrier in the early postoperative period. Studies have been conducted on various techniques such as small incision cataract surgery.[10] There seemed to be no long-term effect especially on cellular reaction, on the hydrophilic IOL surface.[11]

Pediatric cataract poses a great challenge to the surgeon in terms of postoperative inflammation as the pediatric eyes are more susceptible to inflammation. Adding heparin sulphate to the irrigating solution decreased postoperative inflammatory and fibrinoid reactions and related complication such as synechiae, pupil irregularity and IOL decentration in pediatric cataract surgery.[12]

In recent years, the operative techniques have improved and the operation has become less traumatic. The use of balanced salt solution for irrigation of the anterior chamber and use of pre-filled viscoelastics have also contributed in reducing the postoperative inflammation. As there is less postoperative inflammatory reaction and less breakdown of the blood-aqueous barrier, the need to use highly potent steroids have reduced.[6] Refined surgical techniques, smaller incision and more biocompatible intraocular lenses have contributed to this development. There is a need to evaluate the effectiveness of heparin in reducing inflammation in Indian scenario in a large sample study.

The aim of this study is to evaluate the effectiveness of heparin sulphate in irrigating solution in controlling inflammation following an uneventful cataract surgery with intraocular lens implantation in a large sample double blinded trial.

MATERIALS AND METHODS:

A prospective, randomized, double blinded comparative study was carried out on 200 adult patients at a tertiary care centre, after taking permission from the Ethics committee. An informed consent was taken from the patients prior to recruitment. Patient confidentiality was maintained and they had the right to opt out of the study at any point of time. A detailed history of disease and prior treatment was taken. Atleast 5 visits were scheduled on postoperative days 1, 4, 7, 15 and 30. The cases were selected from patients who underwent uncomplicated cataract surgery with posterior chamber intraocular lens (PCIOL) implantation in the capsular bag.

Inclusion criteria:

1. Patients with uncomplicated cataracts
2. Patients having no surgical history
3. Patients not on any systemic anti-inflammatory treatment

Exclusion criteria

1. Patients with shallow anterior chamber depth
2. Patients with ocular surface disorders and diabetes with significant retinopathy

The patients of either sex were randomly allocated to two groups A and B. Group A included 100 patients who received sample A in the irrigation fluid intraoperatively and group B included 100 patients who received sample B in the irrigation fluid intraoperatively. All patients were admitted to the hospital on the previous day of surgery. A complete history was taken to rule out any systemic illness or ocular disease and a complete ocular examination was performed. The data was entered in the case proforma and a written informed consent was taken from the patient after explaining the nature of the study and the side effects of the medications used during the study. Routine preoperative topical antibiotics were given. A routine extra capsular cataract surgery with intraocular lens implantation was performed in all the patients.

Conduction of the double blinded trial – Samples were obtained in sterile vials provided with label as Sample A or Sample B from the Department of Pharmacology and details of the samples were not available to the investigator at the time of the trial. Samples were used on the same day and the remaining drug was discarded. Sample was injected in the irrigation fluid of Ringer's lactate (fresh sample for every case) before the starting of the surgery by the investigator. The details of the sample were not provided to the surgeon. Postoperative results were noted in the proforma the nest day and on subsequent follow-up visits. 200 cases were performed. Cases which defaulted or did not come for postoperative follow-up visits were excluded from the trial. After the completion of the trial the information was sent to the Department of Pharmacology and the coding was revealed.

Assessment of postoperative inflammation – The operated eyes were examined on postoperative days 1, 4, 7, 15 and 30. During each visit the following symptoms and signs were examined:

A. Clinical symptoms suggestive of inflammation such as pain in the eye, patient discomfort and stinging.
B. Slit lamp examination to look for the clinical signs suggestive of inflammation such as evidence of cells. Grading of cells was performed with a 2mm X 1mm wide slit beam with maximal intensity and magnification. The findings were recorded as in **Tables 1 to 5** and **Fig 1 to 5**.
C. Visual acuity was checked at each postoperative visit with Snellen's chart. The data was entered in the proforma attached in the proforma attached in the appendix.

Statistical analysis was done for comparing symptoms and signs of patients in group A and group B on each postoperative follow-up visit by applying Chi-square test. Graphs were plotted for each variable for group A and group B from day 1 to day 30 by taking postoperative day of follow-up on X-axis and number of patients with positive signs on the Y-axis. P value was calculated and $p<0.05$ was taken to be statistically significant.

RESULTS:-

At the end of the trial the coding was revealed by the Department of Pharmacology and which concluded that sample A contained Ringer's lactate and sample B contained Heparin sulphate solution all through the trial. As shown in **Table 1-5,** we found that Heparin sulphate injection 5000 IU when injected in the irrigation solution intraoperatively leads to decrease in postoperative inflammation in the early postoperative period. Therefore injection of heparin in the irrigation solution can be considered in cases where postoperative inflammation is expected. We did not have any case of complications such as hyphema or vitreous hemorrhage or drug related toxicity such as corneal endothelial toxicity or macular ischemia as seen with other agents.

Table 1: No. of patients with anterior chamber cells on Day 1 in Group A and Group B

Anterior Chamber Inflammation: Cells		Group A	Group B	Total
Day 1	Absent	31	49	80
		31.00 %	49.00%	40.00%
	Present	69	51	120
		69.00%	51.00%	60.00%
Total		100	100	200
		100.00%	100.00%	100.00%

Pearson Chi-square test = 0.00141, with 95% significance level the result is significant (less than 0.05).

Table 2: No. of patients with anterior chamber cells on Day 4 in Group A and Group B

Anterior Chamber Inflammation: Cells		Group A	Group B	Total
Day 4	Absent	54	71	125
		54.00 %	71.00%	62.50%
	Present	46	29	75
		46.00%	29.00%	37.50%
Total		100	100	200
		100.00%	100.00%	100.00%

Pearson Chi-square test = 0.0130, with 95% significance level the result is significant (less than 0.05).

Table 3: No. of patients with anterior chamber cells on Day 7 in Group A and Group B

Anterior Chamber Inflammation: Cells		Group A	Group B	Total
Day 7	Absent	87	90	177
		87.00 %	90.00%	88.50%
	Present	13	10	23
		13.00%	10.00%	11.50%
Total		100	100	200
		100.00%	100.00%	100.00%

Pearson Chi-square test = 0.5061, with 95% significance level the result is not significant (less than 0.05).

Table 4: No. of patients with anterior chamber cells on Day 14 in Group A and Group B

Anterior Chamber Inflammation: Cells		Group A	Group B	Total
Day 14	Absent	100	100	200
		100.00 %	100.00%	100.0%
Total		100	100	200
		100.00%	100.00%	100.00%

Pearson Chi-square test = 1.0000, with 95% significance level the result is not significant (less than 0.05).

Table 5: No. of patients with anterior chamber cells on Day 30 in Group A and Group B

Anterior Chamber Inflammation: Cells		Group A	Group B	Total
Day 30	Absent	100	100	200
		100.00 %	100.00%	100.0%
Total		100	100	200
		100.00%	100.00%	100.00%

Pearson Chi-square test = 1.0000, with 95% significance level the result is not significant (less than 0.05).

Figure 1: No. of patients with anterior chamber cells on Day 1 in Group A and Group

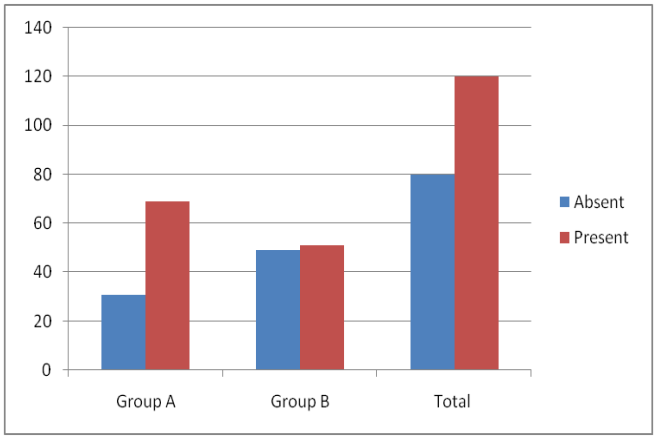


Figure 2: No. of patients with anterior chamber cells on Day 4 in Group A and Group B

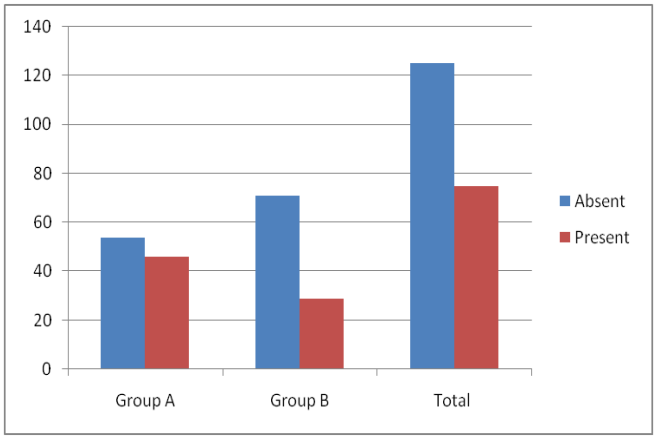


Figure 3: No. of patients with anterior chamber cells on Day 7 in Group A and Group B

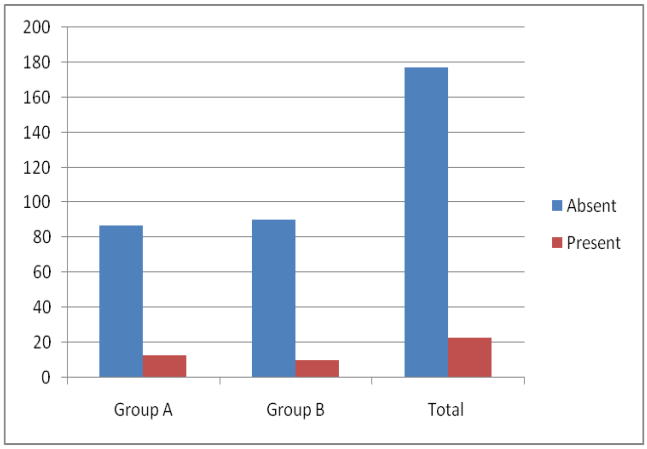


Figure 4: No. of patients with anterior chamber cells on Day 14 in Group A and Group B

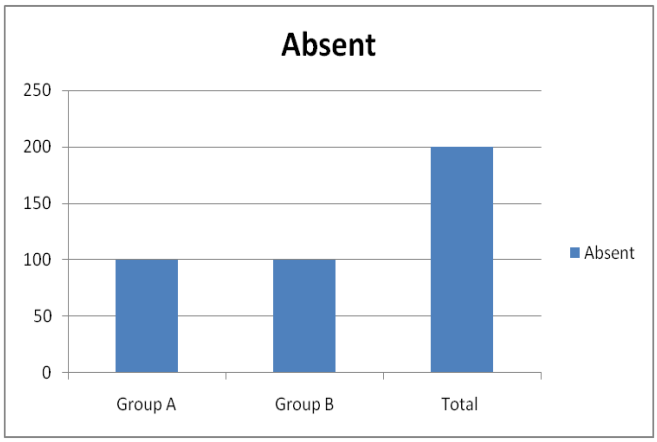
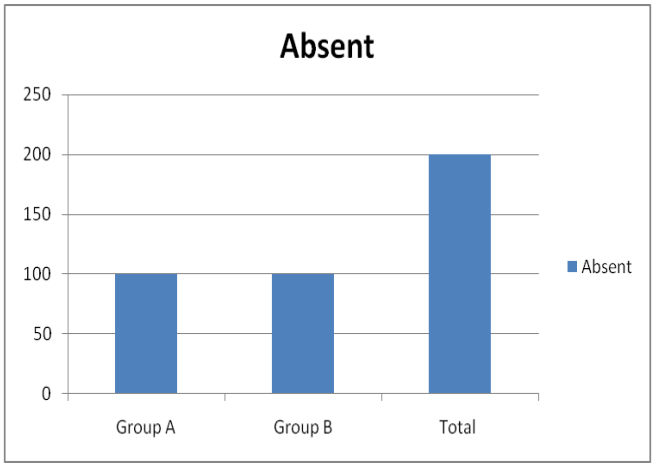


Figure 5: No. of patients with anterior chamber cells on Day 30 in Group A and Group B



DISCUSSION:

In recent years, the operative techniques for cataract surgery have improved and the operation has become less traumatic. As there is less postoperative inflammatory reaction and less breakdown of the blood-aqueous barrier, the need to use highly potent steroids has reduced. Refined surgical techniques, smaller incision and more biocompatible intraocular lenses have contributed to this development.

Since their introduction into ocular therapy, corticosteroids have been the gold standard in the control of inflammation following cataract surgery. However these topical corticosteroids have many side effects including elevation of intraocular pressure, inhibition of wound healing and facilitation of infections. Hence there is a need to use alternative drugs.

The most promising drug which has been proved to decrease post operative inflammation is Heparin sulphate used intraoperatively in the irrigation solution of Ringer's lactate. We found our results to be at par with the European or Asian studies. Many studies have been done to prove the effect on animal as well as in human eyes which have found promising results in decreasing post-operative inflammation and cellular reaction.

1. **Anterior chamber inflammation: cells-**
   Anterior chamber cells are primarily lymphocytes and neutrophils and are an indirect measure of the inflammatory reaction of the iris and ciliary body. They represent the index of the activity of the inflammation. Persistence of cells for a long time after cataract surgery may increase the risk of inflammatory complications and worsen the prognosis after cataract surgery. It is important to monitor the cells during the acute stage of inflammation. The reduction of cellularity may indicate an early response to the therapy and a lack of response may dictate a change in therapy.

   The incidence of cells in the anterior chamber in our study was observed to be low in group B and group A had a high incidence of postoperative inflammation on day 1, 4 and 7. On day 1 p=0.0141, on day 3 p=0.0130 in group A and B respectively. This difference was statistically significant. On day 7, p=0.5061 in group A and group B respectively. This difference was not statistically significant. Patients in both groups did not have cells in the anterior chamber on day 15 and 30. Group B was effective in controlling the anterior chamber inflammation in the early postoperative period. Studies conducted by Kohnen, et al and Dick B on effect of heparin in irrigating solution on inflammation following small incision cataract surgery suggest that heparin sulphate added to the infusion solution during small incision cataract surgery reduced inflammation in the early postoperative period.[37] Thus the results of our study are in agreement with all the previous studies.

2. **Anterior chamber inflammation: flare-**
   When the slit beam is obliquely aimed across the anterior chamber, the ability to visualize the path of the beam is termed as 'flare.' A beam of 2mm*1mm and high intensity illumination is used to look for the flare. Presence of flare is due to increased protein content in the anterior chamber and is a manifestation of a breakdown of the blood-aqueous barrier. The amount of light scattering is proportional to the concentration of protein in the solution and an increased flare indicates increased protein concentration in the anterior chamber and indirectly indicates a more severe inflammation.

   In our study, the incidence of flare in the anterior chamber was less in group B on postoperative day 1 (p=0.0000) in group A and group B respectively. On day 4, the incidence of flare was less in group B p=0.0004. This difference was statistically significant. On day 7, the incidence of flare was p=0.6634. This difference was not statistically significant. On day 15, the incidence of flare was p=0.6135. This difference was not statistically significant. Though none of the patients had cells in the anterior chamber after day 15, group B was effective in controlling early anterior chamber inflammation.

3. **Pigments/fibrin over intraocular lens-**
   Inflammation is often accompanied by the release of pigments and deposition of fibrin over the intraocular lens. The inflammatory mediators promote clotting, fibroblast proliferation and fibrin deposition. A transitory deposit of a fibrin-like material in the anterior chamber following extra capsular cataract extraction and intraocular lens (IOL) implantation is

described by Walinder, et al. The reaction appears in the early postoperative period in an otherwise quiet eye and the signs varied from a few threads in the pupil area to a dense pupillary membrane in front of the IOL. The deposits disappear one day to three weeks postoperatively, usually without any remnants.

In our study, the incidence of flare in the anterior chamber was less in group B on postoperative day 1 (p=0.0123). On day 4, the incidence of flare was less in group B (p-0.0034). This difference was statistically significant. On day 7 the incidence of flare was p=0.1238. This difference was not statistically significant. On day 15, the incidence of flare was p=1.0000. This difference was not statistically significant. Though none of the patients had cells in the anterior chamber after day 15, group B was effective in controlling early anterior chamber inflammation.

4. **Cystoid macular edema (CME)-**

Pseudophakic cystoid macular edema (CME) following cataract surgery is an important complication after cataract surgery and may be responsible for suboptimal vision after cataract surgery and may be responsible for suboptimal vision after cataract surgery. It can occur even after an uneventful cataract surgery. The reported incidence of CME after cataract surgery varies from 10 to 20%. The incidence is low within the first postoperative week and peaks around 4 to 6 weeks after surgery. In our study, none of the patients developed cystoids macular edema till the 14th day post-operative. Incidence after 15th day was 0.6785 which is not statistically significant with a confidence level of 95%. Cystoid macular edema was diagnosed using slit-lamp biomicroscopy using a +90D lens. None of the studies have suggested role of heparin in controlling the incidence of cystoid macular edema.

5. **Other complications-**

It has been reported that in occasional cases there has been incidence of hyphema or hemorrhage in the post-operative period due to the use of heparin in the irrigating solution.[20] But in our study all the patients had good control of inflammation without any incidence of hemorrhage or hyphema.

CONCLUSION:-

As in today's world with the advances in the technology there is a growing expectation for a perfect and normal eye postoperatively and so, by introducing heparin as a routine addition in the irrigating solution may aid by reducing postoperative inflammation in routine cataract cases. The group treated with heparin had significantly less inflammation in the early postoperative period and thereby there was a reduced necessity of anti-inflammatory agents. If, by adding heparin in the irrigating solution leads to decreased usage of postoperative steroids then it can emerge as a useful tool in preventing steroid related complications such as rise in postoperative intraocular pressure. We recommend studies exploring postoperative anti-inflammatory regimen to be given in eyes infused with heparin as, if we are able to achieve a good postoperative anti-inflammatory status, the use of steroids can be substituted with NSAIDs. Only further studies are necessary to explore this subject. Also, by reducing the need for postoperative anti-inflammatory drops due to the use of heparin intraoperatively we can reduce the financial burden of buying costly anti-inflammatory drugs which will be very helpful in the Indian scenario where the majority of cataract surgeries are performed in camp setting or on people belonging to low socio-economic strata.

We also conclude that heparin is safe to be used in normal general population. Heparin has no direct role in reducing the incidence of cystoid macular edema but it may indirectly help reduce the incidence by reducing overall inflammation of the eye. There is no ethnic or geographic variation in the effect of heparin in controlling postoperative inflammation.

We recommend further studies to evaluate the role of heparin in pediatric cataract, confirmed cases of uveitis and also phacomorphic glaucomas in an Indian setup.

REFERENCES:-

1. Kremer M, Baikoff G, Charbonnel B. The release of prostaglandins in human aqueous humour following intraocular surgery. Effect of indomethacin. Prostaglandins, 1982 May;23(5):695-702.
2. Ableson MB, Butrus S. Corticosteroids in Ophthalmic practice. In: Albert DM, Jacobiec FA, Gragoudas ES, Power SM, Robinson NL, editors. Principles and practice of Ophthalmology. 2nd ed. Philadelphia: W.B. Saunders Company; 2000.p.258-65.
3. Havener WH. Corticosteroid therapy. In: Ocular pharmacology. 3rd ed. St. Louis: CV Mosby; 1974.p.343-95.
4. Sapir-Picchadze R, Blumenthal EZ. Steroid induced glaucoma. Harefuah. 2003 Feb; 142(2):137-40,157.
5. Nelson RM, Cecconi O, Roberts WG, et al. Heparin oligosaccharides bind L- and P-selectin and inhibit acute inflammation. Blood 1993; 82:3253-3258.
6. Reilly CF, Fritze LMS, Rosenberg RD. Heparin inhibition of smooth muscle cell proliferation: a cellular site of action. J Cell Physiol 1986; 129:11-19.
7. Del Vecchio PJ, Bizios R, Holleran LA, et al. Inhibition of human sclera fibroblast proliferation with heparin. Invest Ophthalmol Vis Sci 1988; 29:1272-1276.
8. Ekre HP, Naparstek Y, Lider O, et al. Anti-inflammatory effects of heparin and its derivatives: inhibition of complement and lymphocyte migration. Adv Exp Med Biol 1992; 313:329-340.
9. Zaturinsky B, Naveh N, Saks D, Solomon AS. Prevention of posterior capsular opacification by cryolysis and the use of

heparinized irrigating solution during extra capsular lens extraction in rabbits. Ophthalmic Surg 1990; 21:431-434.
10. Kohnen T, Dick B, Hessemer V, et al. Effect of heparin in the irrigating solution small incision cataract surgery. J Cataract Refract Surg 1998.
11. Kruger A, Amon M, Abela-Formanek C, et al. Effect of heparin in the irrigating solution on postoperative inflammation and cellular reaction on the intraocular lens surface. J Cataract Refract Surg 2002; 28:87-92.
12. Dada T, Dada VK, Sharma N, Vajpayee RB. Primary posterior capsulorhexis with optic capyure and intracameral heparin in pediatric cataract surgery. Clin Exp Ophthalmol 2000; 28:361-363.
13. Gabelt BA, Kaufman PL. Aqueous humor hydrodynamics. In: Kaufman PL, Albert A, editors. Adler's Physiology of the eye. 10th ed. USA: Mosby; 2003.p.246-7.
14. Jaffe NS. Cataract Surgery and its complications. 6th ed. St. Louis: Mosby; 1997.p.384-7.
15. Mamalis N, Edelhauser HF, Dawson DG, Chew J, LeBoyer RM, Werner L. Toxic anterior segment syndrome. J Cataract Refract Surg. 2006 Feb; 32(2):324-33.
16. Holland SP, Morck DW, Lee TL. Update on toxic anterior segment syndrome. Curr Opin Ophthalmol. 2007 Feb; 18(1):4-8.
17. Quinn CJ: Cystoid macular edema. Optom Clin. (1996)5(1):111-130.
18. European pharmacopoeia 5.0
19. Dallas L. Rabenstein Advance Article on the web of Chemistry, University of California, Riverside, CA 92521 USA.
20. Humphries DE, Wong GW, Friend DS, Gurish MF, Qui WT, Huang C, Sharpe AH, Stevens RL. Nature, 1999,400,769.
21. Forsberg E, Pejler G, Ringvall M, Lunderius C, Tomasini-Johansson B, Kusche-Gullberg M, Eriksson I, Ledin J, Hellman L, Kjellen L. Nature, 1999,400,773.
22. Bourin MC, Lindahl U. Biochem J, 1993,289,313.
23. Bjork I, Olson ST, Shore JD. In: Heparin: chemical and biological properties, clinical applications, ed. D.A. Lane and U. Lindahl, CRC Press, Inc., Boca Raton, FL,1989.p.229.
24. Kojima T, Leone CW, Marchildon GA, Marcum JA, Rosenberg RD. J. Biol. Chem., 1992,267,4859.
25. Rosenberg RD. Fed. Proc. Fed. Am. Soc. Exp. Biol., 1977,36,10.
26. Bjork I, Lindahl U. Mol. Cell. Biochem., 1982,48,161.
27. Bjork I, Lindahl U. Mol. Cell. Biochem., 1982,48,161A.
28. Rezaie AR, Olson ST. Biochemistry, 2000,39,12083.
29. Timothy G Murrey, Walter. Collagen shield heparin delivery for prevention of postoperative fibrin. Arch ophthalmology; Vol 108, January 1990.
30. Addicks EM, Quigley HA, Green WR, Robin AL. Histological characteristics of filtering blebs in glaucomatous eyes. Arch Ophthalmol. 1983 101:795-798.
31. Van Buskirk EM. Cysts of Tenon's capsule following filtration surgery. Am J Ophthalmol 1982; 94:522-525.
32. Kruger A, Amon M. Effect of heparin in irrigating solution on postoperative inflammation and cellular reaction on intraocular lens surface. J Cataract Refract Surg. Vol 28, January 2002.
33. Manaster J, Chezar J, Shurtz-Swirski R, et al. Heparin induces apoptosis in human peripheral blood neutrophils. Br J Haematol 1996; 94:48-52.
34. Dandona P, Qutob T, Hamouda W, et al. Heparin inhibits active oxygen species generation by polymorphonuclear and mononuclear leucocytes. Thromb Res 1999; 96:437-443.
35. Schwartz CF, Kilgore KS, Homeister JW, et al. Increased rat cardiac allograft survival by the glycosaminoglycan pentosan polysulfate. J Surg Res 1999; 86:24-28.
36. Ekre HP, Naparstek Y, Lider O, et al. Anti-inflammatory effects of heparin and its derivatives: inhibition of complement and of lymphocyte migration. Adv Exp Med Biol 1992; 313:329-340.
37. Kohnen T, et al. Effect of heparin in irrigating solution on inflammation following small incision cataract surgery. Journal of Cataract and Refractive Surgery. Vol.24, No.2, P.247-243.
38. Trocme SD, Li H. Effect of Heparin-Surface-Modified Intraocular lenses on postoperative inflammation after Phacoemulsification. American Academy of Ophthalmology. Vol.107, No.6, June 2000.
39. Abela-Formanek C, Amon M. Inflammation after implantation of hydrophilic acrylic or silicone intraocular lenses in eyes with cataract and uveitis. J Cataract Refract Surg. Vol.28, July 2002-3350(02)01324-4.
40. Mester U, Strauss M. Biocompatibility and blood-aqueous barrier impairment in at-risk eyes with heparin-surface-modified or unmodified lenses. J Cataract Refract Surg. 1998 Mar; 24(3):380-4.
41. Jones NP. Fuch's heterochromic uveitis: an update, Surv Ophthalmol. 1993 Jan-Feb; 37(4):253-72.
42. Bayramiar H, Totan Y. Heparin in the intraocular irrigating solution in pediatric cataract surgery. J Cataract Refract Surg. Vol.30, October 2004;2169.
43. Ozkurt YB, Taskiran A. Effect of heparin in the intraocular irrigating solution on postoperative inflammation in the pediatric cataract surgery. Clinical Ophthalmology 2009:3,363-365.
44. Mehta JS, Adams GG. r-TPA following pediatric cataract surgery. Br J Ophthalmol. 2000;84:983-986.
45. Lundvall A, Zetterstrom C. Cataract extraction and intraocular lens implantation in children with uveitis. Br J Ophthalmol 2000;8:791-793.
46. Manners TD, Turner DP. Heparinised intraocular infusion and bacterial contamination in cataract surgery. Br J Ophthalmol. 81(11):949-952, November 1997.

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