

Comparison of design of intraocular lens versus the material for PCO prevention

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Abstract

• **AIM:** To evaluate the influence of different intraocular lens (IOL) designs made of PMMA on posterior capsular opacification(PCO) and compare with foldable designs.

• **METHODS:** Phacoemulsification and IOL implantation was done in one eye of 24 New Zealand White rabbits, with IOL of two different designs (Square edged or round edge) and two different materials (PMMA or HEMA). After three months, the animals were sacrificed and enucleated. Evaluation of PCO included posterior view, migration of anterior capsular epithelial cells to the posterior capsule following epithelial-mesenchymal transition were assessed by staining the histological sections of posterior capsule by hematoxylin-eosin (HE) and Periodic acid- Schiff (PAS). The IOLs were extracted and stained with HE to evaluate the presence of adherent cells on the lens surface.

• **RESULTS:** PCO was highest with round edged rigid lens. There was no significant difference in the PCO between the square edged PMMA and square edged foldable lens.

• **CONCLUSION:** It is the design of the IOL not the material that offers protection on PCO formation.

• **KEYWORDS:** design; material of intraocular lens; posterior capsular opacification

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INTRODUCTION

The number of cataract surgeries performed annually in developing countries like India has increased to 4.8 million, and the rate of intraocular lens(IOL) implantation is 90%. It has been proposed by Vision 2020 to make IOL implantation mandatory for all cataract surgeries unless contraindicated for medical reasons^[1]. Posterior capsular opacification (PCO) is a major complication of extra capsular cataract surgery. The incidence in adults varies between 30% and 40% and in children incidence reported is 100%^[2]. The financial burden of cataract surgery is high and post operative complication like PCO adds to the existing financial burden. The current treatment of PCO i.e. Nd:YAG laser is expensive and not free from complications. Therefore, there is a strong and immediate need to explore different means to eradicate PCO.

The material and design of IOL greatly influence the incidence of PCO following cataract surgery^[3]. For an IOL, the biological compatibility depends on the cellular adhesiveness, and the lens epithelial cell (LEC) phenotype stability is the most important determining factor for IOL biocompatibility and cellular adhesiveness. This is reflected as capsular opacification. Mechanical biocompatibility is mainly determined by the fit of the haptic in the capsular bag and the shape of the optic also influences the migration of lens epithelial cells^[3].

The pathology involved is that the remaining LEC in the anterior capsule following cataract surgery undergo epithelial mesenchymal transition and migrate to the posterior capsule and secrete ground matrix leading to the opacification of posterior capsule and this leads to vision impairment.

The effective and essential step for reducing the incidence of PCO is by reducing the occurrence of Soemmering ring, this can be reduced by removing the cells that form the mass of Soemmering ring by excellent hydro dissection enhanced cortical removal of cortex, by the use of highly biocompatible IOL that reduces the stimulation of the proliferating cells. The optic barrier effect is an important method of reducing growth of cells across the visual axis. The barrier effect is best obtained by in- the- bag placement of the IOL^[4].

IOL design vs material for PCO

This study was taken up to evaluate the influence of different designs of PMMA IOL on PCO. PMMA was chosen as the material of choice considering its low cost, less support for LEC adhesiveness and more resistance to damage caused by laser treatment [2]. The study was conducted with prior permission of Institutional Animal ethics committee and by abiding by the tenets of ARVO for animal experimentation.

MATERIALS AND METHODS

Materials Phacoemulsification and IOL implantation was done by the same surgeon in one eye of 24 adult White New Zealand rabbits which were free from pre existing ocular abnormalities. The following IOLs were paired and compared: (1) Same design, different material: Comparison of Square edged PMMA lens with Square edged HEMA lens and Round edged PMMA lens with Round edged HEMA lens; (2) Same material, different design: Comparison of Square edged PMMA with round edged PMMA and Square edged HEMA with round edged HEMA; (3) All lenses were extracted at the end of study period and stained for identification of cellular adherence on the lens surface. For each study group 6 rabbits were used.

Methods

Surgical procedure Mydriasis was obtained by treatment with Phenylephrine (Ocurest eye drops® 0.12% w/v, 5mL Centaur, Pharmaceutical PVT. LTD, Mumbai, India) and tropicamide Tropicacyl® Sunways PVT LTD Ahmedabad, India) as topical instillation prior to surgery. Anti inflammatory medication flubiprofen (Flur®, Allergan, Madhya Pradesh, India) and antibiotic Ciprofloxacin (Ciplox®, Cipla, India) were instituted from 2 days prior to surgery. The animals were anesthetized with Xylazine HCL (Xylaxin® Indian immunologicals LTD, Hyderabad, India) @ 5mg/kg bd wt and Ketamine HCL (Ketamine Hydrochloride®, Vulcan Laboratories (P) LTD, Kolkata) @ 30mg/kg bd wt along with retro bulbar block with 4% lignocaine HCL. Anterior chamber was entered with a clear corneal incision with a 2.8mm keratome, this was followed by anterior capsule staining with trypan blue, continuous curvilinear capsulorhexis and hydro dissection. Phacoemulsification and aspiration of the lens was performed and IOL implantation was done with one of the following lenses, round edged rigid, square edged rigid, round edged foldable, square edged foldable. Corneal wound was repaired with 10-0 nylon. Post operative medication comprised of mydriatics, flubiprofen eye drop, ciprofloxacin eye drop and prednisolone eye drop (PDN 1% w/v, 5mL, Ophtho Remedies, India) for 15 days.

Evaluation for PCO formation was done by routine examination with slit lamp biomicroscope or under the operating microscope as required. All animals survived till

Table 1 PCO scores for each type of lens based on visual assessment of gross pathology

| Round PMMA (A) | Square edged PMMA (B) | Round HEMA © | Square edged HEMA (D) |
|----------------|-----------------------|--------------|-----------------------|
| 3.67±0.21 | 1±0.26* | 3.5±0.22 | 0.83±0.30# |

Data is expressed as Mean ± SE, * $P < 0.05$ vs A, # $P < 0.05$ vs C; but $P > 0.05$ C vs A & D vs B.

the end, at the end of study period of 3 months the animals were sacrificed and enucleated and the eyes ($n=6$) from each group were preserved in neutral buffered formalin.

Gross pathology and histology The enucleated and preserved eyes were sectioned at the equator. The gross evaluation from behind using the Miyake-Apple posterior photographic technique revealed the degree of opacification of the posterior capsule. Following gross examination from behind (Figure 1) and gradation for opacity of posterior capsule, the posterior capsule was removed for histopathology. The evaluation for PCO was done on the basis of opacification of the posterior capsule as observed from posterior view (Miyake Apple) and histology, PCO was graded with a score of 0-4 (0=completely transparent, 1=clear, 2=mild, 3=moderate, 4=severe) 0=posterior capsule completely free from cells, 1=clear, no visible proliferative tissue on the peripheral or central capsule; 2=mild, proliferative tissue only in the periphery; 3=moderate, sparse proliferative tissue on the peripheral and central capsules; and 4=severe, dense, diffuse, and thick opacification on the entire capsule, depending on the increasing degree of opacification as observed grossly, it was supported by results of histopathology of the posterior capsules.

The entire study on histological investigation of posterior capsule and whole lens were done in blind fashion in another center. Routine histological procedures for HE and PAS staining were done for posterior capsules. The IOLs were extracted and collected in 10% neutral formalin for whole lens staining. The IOLs were stained with HE observed under light microscope for presence of lens epithelial cells adherence on the IOL surface.

Statistical Analysis The statistical analysis for PCO gradation (Table 1) was done by two ways ANOVA.

RESULTS

Table 1 shows the grades of PCO formation with different types of IOL. The evaluation was done on the basis of opacity of the posterior capsule as observed from posterior view (Figure 1). There was no significant difference in the PCO formation between the groups having same design i.e. Square edged PMMA vs Square edged HEMA, or between Round edged PMMA vs round HEMA.

The results of same material but different designs showed significant difference, square edged PMMA showed significantly less PCO vs Round edged PMMA lens, and

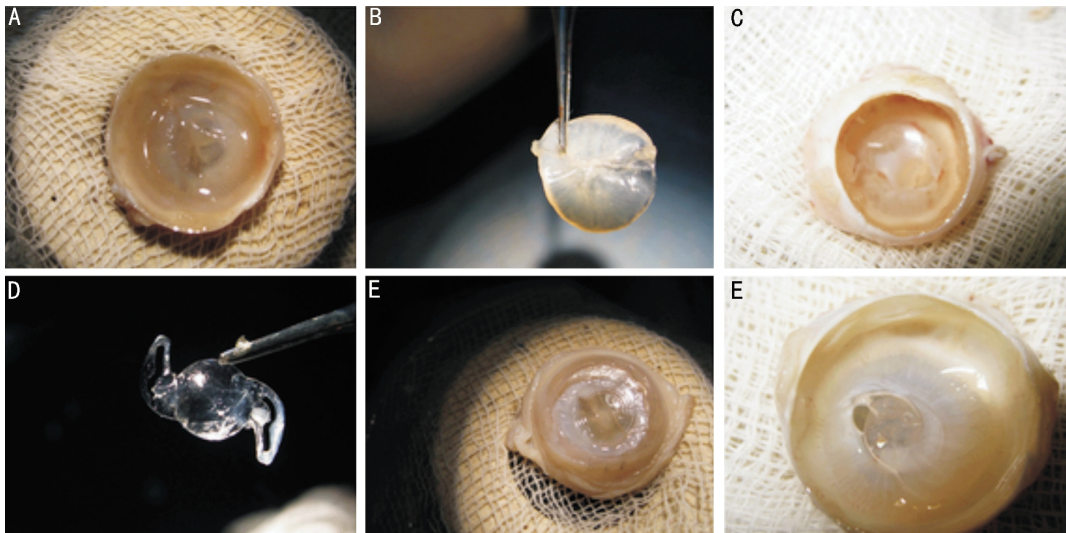


Figure 1 Gross photographs of pseudophakic rabbit globes obtained following enucleation, posterior view (Miyake Apple View photographic technique) A: Round edged rigid lens, PCO grade 4; B: Posterior capsule from round edged rigid IOL; C: Round edged foldable lens, PCO grade 3; D: The explanted round edged foldable lens shows membranous posterior capsule attached to the haptics and optic; E: Square edged rigid lens, PCO grade 1; F: Square edged foldable lens PCO grade 0.

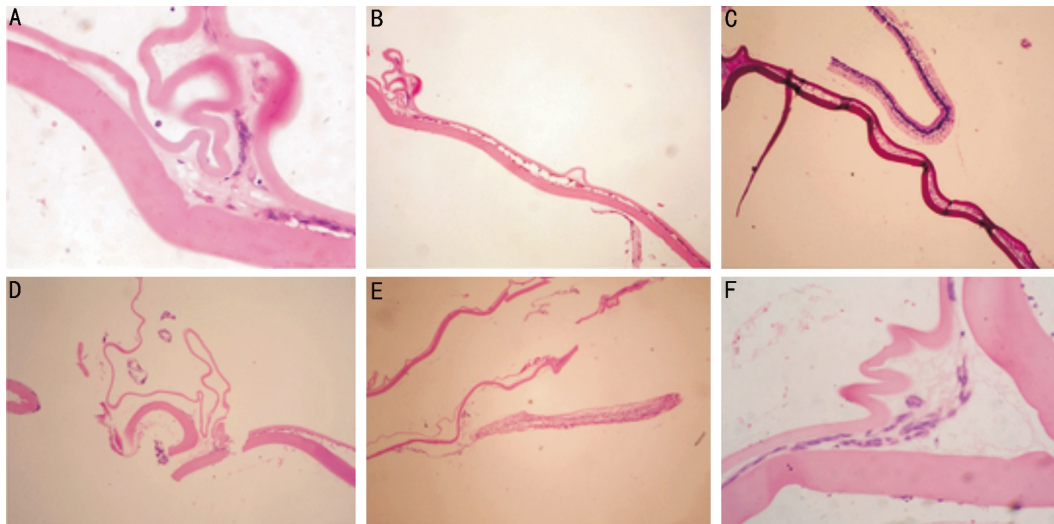


Figure 2 shows the histological sections of posterior capsule from eyes implanted with different intraocular lens A & B: Posterior capsular fibrosis in eyes implanted round edged rigid lens (HE: A 20x; B:10x); C: Section of capsular bag from eyes implanted with round edged foldable lens shows extracellular matrix deposition between anterior and posterior capsule (PAS: 10x); D, Posterior capsule from eyes implanted with square edge rigid lens shows monolayer of lens epithelial cells(LECs), with some areas free LECs (HE 10x); E & F: Posterior capsule from eyes implanted square edged foldable lens shows capsular bag with minimum cellular proliferation (E:10x; F: 20x).

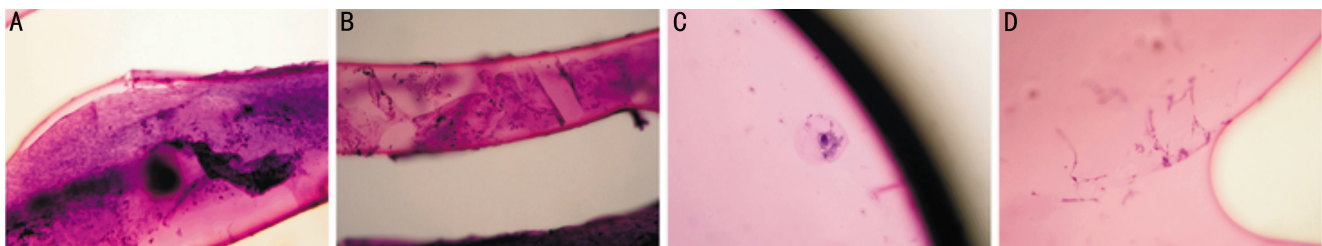


Figure 3 Histological observation of hematoxylin and eosin stained whole IOLs, 3 months post surgery, revealed extensive cellular (macrophages, fibroblasts, and foreign body giant cells) deposition on the surface of round edged PMMA (A) and round edged foldable lens HEMA (B), whereas minimum cellular deposits were observed on the Square edged PMMA lens (C) and Square edged HEMA lens (D).

square edged HEMA showed significantly less PCO *vs* round edged HEMA less (Table 1, Figure 2). Moreover, the surface of the PMMA and HEMA IOL showed presence of

LEC adherent on the surface there was presence of LEC distribution both in the central and peripheral optic portion of the both type of lens (Figure 3).

DISCUSSION

In spite of the growing popularity of cataract surgery it is difficult to ignore that blindness due to PCO still remains a major post operative complication of following cataract surgery. The three major contributory factors towards PCO formation are patient factor (age, incidence is younger patients, associated ocular disorders), surgery related factors include (hydrodissection and complete cortical clean up, size of capsulorhexis should be slightly smaller than the optic of IOL, proper in the bag fixation of the IOL). The other factors contributing to PCO formation are choice IOL materials, IOL designs^[2]. The only modality for treatment of PCO, Nd: YAG laser is expensive and not readily available so it poses yet another financial burden for the health care system. It is therefore realized that there is an utmost need to find means to eradicate PCO.

It is now mandatory to implant an IOL following cataract surgery as per the directives of Vision 2020. It was felt that the contribution of an IOL towards PCO formation should be studied further to establish low cost effective IOL for prevention of PCO for the benefit of millions of beneficiaries of cataract surgery in developing countries.

Numerous studies are underway which aim at better understanding whether it is IOL material or design that is more important in PCO prevention. In our results we have found that the square edged IOL showed significantly lower PCO than the round edged IOL. There was no difference in the PCO formation between the rigid and foldable lens designs, which may signify that the properties materials of lens material i.e. PMMA and HEMA did not differ in biocompatibility in respect of PCO formation.

Many other studies have also revealed that the design of the IOL contributed more significantly to the PCO formation than the material of the IOL. Nishi *et al*^[5], compared sharp edged hydrophobic acrylic (AcrySof) IOL with round optic edge PMMA IOL, there was inhibition of LEC migration in the sharp edged optic whereas in the round optic edge LECs could freely migrate into the posterior capsule center^[6]. Sharp optic edge manufactured from different materials showed similar prevention for PCO^[6,7].

Gagandeep *et al*^[8] showed that the implantation of square edged PMMA and hydrophobic acrylic lens had similar outcome on PCO in pediatric cataract surgery and square edged PMMA lens has a significant cost advantage over hydrophobic acrylic lens. Hence the results support our findings that the preventive effect of IOL on PCO is largely dependent on sharp edge optic design.

Although concept of biocompatibility remains controversial, it is accepted that for determining the biological biocompatibility of an IOL, cellular adhesiveness resulting

from activation of the compliment system and the degree of adhesion of macrophages and related cells and LECs are important factors. The phenotypic stability of the LECs is the most important determinant. The mechanical biocompatibility depends on the shape of the optic and the fit of the haptic loop inside the capsular bag^[3]. The result of cellular adhesiveness for LEC did not vary between the two materials PMMA and HEMA in our study, variable adhesiveness of macrophages to an IOL which was highest in hydrogel IOL followed by PMMA, hydrophobic acrylic IOL and least in silicon^[3], Ravalico *et al*^[9] reported cellular adhesion to poly HEMA is less than any other types of IOL. Studies on biocompatibility of IOLs in absence of surgical and host factor concluded that all IOLs induced some amount of leukocyte chemotaxis, chemotactic activity was significantly higher in acrylic and silicone IOLs compared to the PMMA lenses^[10], so PMMA may be considered safe as IOL material. On the other hand, *in vivo* studies from animal and human experimentation show macrophagic and cellular adhesion and matrix accumulation are less on silicon IOL as compared to PMMA, but this does not indicate less fibrotic reaction on the capsule^[3], so this phenomenon may suggest that silicon is less biocompatible and incites more EMT among the LECs on the anterior capsule leading to fibrosis. As there is variation in the results for assessment of biocompatibility of the IOL material as a determinant of PCO, We feel more studies are required to understand the response of the cytokines to each type of material in vivo and the assessment of EMT of the LECs in response to different lens material would perhaps be more appropriate to decide if the material of the IOL actually contribute significantly for anterior capsular and PCO.

Presently our results corroborates with the vast body of literature which clearly state that the design of the IOL may significantly contribute to PCO reduction, we suggest that square edged PMMA IOL may be good choice for IOL, which would be inexpensive, resistant to laser treatment, and may reduce the incidence of PCO. The drawback of our work is that we have not included the modern IOL material acrylic in our study, the reason being its high price and availability amongst for the major population of patients for cataract surgery in developing countries.

We conclude PMMA Square edged has advantage over foldable round edged lens; hence it could be a good option for providing low cost IOL implantation following cataract surgery.

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