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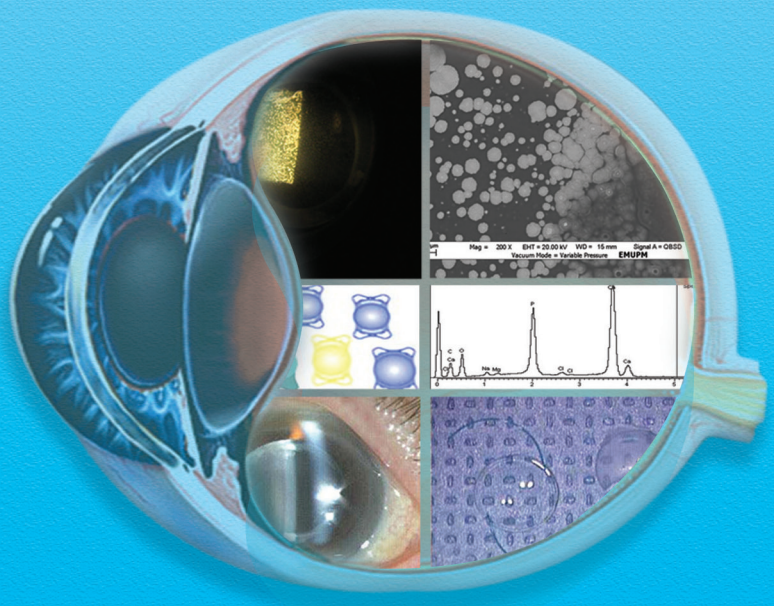
MINISTRY OF HEALTH MALAYSIA

INTRAOCULAR LENS (IOL) IMPLANTATION HYDROPHILIC ACRYLIC VERSUS HYDROPHOBIC ACRYLIC



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MINISTRY OF HEALTH MALAYSIA

Health Technology Assessment Report

INTRAOCULAR LENS (IOL) IMPLANTATION- HYDROPHILIC ACRYLIC VERSUS HYDROPHOBIC ACRYLIC

DISCLAIMER

This Health Technology Assessment has been developed from analysis, interpretation and synthesis of scientific research and/or technology assessment conducted by other organizations. It also incorporates, where available, Malaysian data, and information provided by experts to the Ministry of Health Malaysia. While effort has been made to do so, this document may not fully reflect all scientific research available. Additionally, other relevant scientific findings may have been reported since completion of the review.

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DISCLOSURE

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EXECUTIVE SUMMARY

Background

Cataract is the most prevalent ophthalmic disease and cataract surgery is a commonly performed surgery in all ophthalmology centres. Late postoperative opacification of IOL caused by dystrophic calcification requiring explantation has been reported with some hydrophilic acrylic IOL designs. This has also been encountered in a few government hospitals in Malaysia.

Technical features

Hydrophilic acrylic (hydrogel) is a soft hydrophilic material. The material used is polyhydroxyethylmethacrylate (PolyHema) with a water content varying from 18% to 30% and a refractive index of 1.47. Hydrophobic acrylics are polymers synthesised from esters of acrylic or methacrylic acid. It contains tiny amounts of water (less than 1%). Hydrophobic acrylic IOLs have a refractive index of 1.55. The hardness of the hydrophobic acrylic is temperature dependent.

Objective

To assess the safety of commonly used foldable IOLs (hydrophilic acrylic and hydrophobic acrylic IOL implants)

Methods

Electronic databases such as MEDLINE, PubMed, EBM Reviews-Cochrane Database of Systematic Reviews, EBM Reviews-Cochrane Central Register of Controlled Trials, EBM Reviews-HTA databases, FDA website and MHRA were searched. There was no limitation in the search. All relevant literature was appraised using the Critical Appraisal Skills Programme (CASP) and evidence was graded based on guidelines from U.S./ Canadian Preventive Services Task Force

Results and conclusion

There was poor to fair level of evidence to suggest that the incidence of IOL opacification affecting vision was only reported in hydrophilic acrylic IOL and not with hydrophobic acrylic IOL. IOL opacification of hydrophilic acrylic IOL was caused by deposition of calcium and phosphate on the IOL surface, or within the optic material or both (on the surface and within the IOL material) depending on the designs of the hydrophilic acrylic IOL. However, the pathophysiology of the causes of such complications have not yet been fully elucidated. Diabetic patients appeared to be more often and more severely affected by IOL opacification.

Recommendation

Based on the above review, we recommend the use of hydrophobic acrylic IOLs. Patients who had hydrophilic acrylic IOLs implantation need longer and more frequent follow-up, particularly in the presence of predisposing factors such as diabetes. In view of the absence of Medical Device Act in Malaysia, an incident reporting mechanism for IOL opacification irrespective of materials and designs need to be established to provide more information regarding IOL opacification locally.

TABLE OF CONTENTS

GLOSSARY

IOL : Intraocular lens

IOLs : Intraocular lenses

Nd:YAG : Neodymium:yttrium-aluminum-garnet

PMMA : Polymethylmethacrylate

PCO : Posterior capsule opacification

FDA : U.S. Food and Drug Administration

CSR : Cataract Surgery Registry

MDR : Medical Development Research

MHRA : Medicines and Healthcare products Regulatory Agency

MDA : Medical Devices Agency

U.S.A. : United States of America

U.K. : United Kingdom

OII : Ophthalmic Innovations International Inc

HEALTH TECHNOLOGY ASSESSMENT INTRAOCULAR LENS (IOL) IMPLANTATION- HYDROPHILIC ACRYLIC VERSUS HYDROPHOBIC ACRYLIC

1 BACKGROUND

Cataract is the most prevalent ophthalmic disease and cataract surgery is a commonly performed surgery in all ophthalmology centres. Cataract surgery has evolved over the years to modern day techniques using intraocular lens (IOL) implantation as the standard practice to improve visual outcome. IOL implantation was first introduced by Sir Harold Ridley in 1949. He was the first to successfully implant an IOL on November 29, 1949, at St Thomas' Hospital in London.[1]

The first IOL was manufactured by the Rayner company of Brighton, East Sussex, England from Perspex CQ made by ICI. The first lenses used were made of glass, they were heavy and were prone to shatter during neodymium:yttrium-aluminum-garnet (Nd: YAG) laser capsulotomy. Plastic materials were used later. The IOL did not find widespread acceptance in cataract surgery until 1970s, when further developments in lens design and surgical techniques were introduced. It usually consists of a small plastic lens with plastic side struts, called haptics, to hold the lens in place within the capsular bag inside the eye. IOLs were traditionally made of an inflexible material; polymethylmethacrylate (PMMA). With advances in small-cataract surgery and bio-material science, a variety of foldable IOL designs have been developed over the past two decades. Currently available foldable IOLs are made from silicone, hydrophobic acrylic, and hydrophilic acrylic (hydrogel) materials.[2]

Hydrophilic acrylic IOLs have been proven to be highly biocompatible, inducing less inflammatory cytologic reaction. However, late postoperative opacification caused by dystrophic calcification requiring explantation has been reported with some hydrophilic acrylic IOL designs.[2] The opacification patterns included the formation of surface deposits as well as intralenticular deposition of calcium and phosphate.[2-10] Similarly, late postoperative opacification of hydrophilic acrylic IOLs requiring explantation have also been encountered in a few government hospitals in Malaysia.

A systematic review and meta-analysis conducted by Cochrane Collaboration also showed significantly higher posterior capsule opacification (PCO) rates in hydrophilic acrylic (hydrogel) IOLs than with other IOL materials.[11]

In Malaysia, IOLs are introduced into the market by suppliers directly to the end users without being subjected to assessment prior to distribution. Usage is guided by whether products have U. S. Food and Drug Administration (FDA) approval or CE mark. The CE mark certifies that a product has met European Union consumer safety, health or environmental requirements.

The total number of cataract surgeries registered to the National Cataract Surgery Registry (CSR) over the years (2002 to 2007) was 71,749. It increased from 14,316 in 2002 to 22,051 in 2007. The demographic features of patients who had cataract surgery at public hospitals over 6 years (2002 to 2007) were consistent with the mean age of 64 years and slight female preponderance (ranged 50% to 52%). The proportion of patients with systemic co-morbidity increased from 56.8% in 2002 to 67.5% in 2007. The commonest was hypertension (about half), followed by Diabetes Mellitus (about one third).[12]

This systematic review was conducted following a request by the Head, Ophthalmology Service, Ministry of Health, Malaysia following reports of IOL opacification with the use of hydrophilic acrylic implants in the United States of America (U.S.A.), in the United Kingdom (U.K.) and also in three Ministry of Health Hospitals.

2 TECHNICAL FEATURES

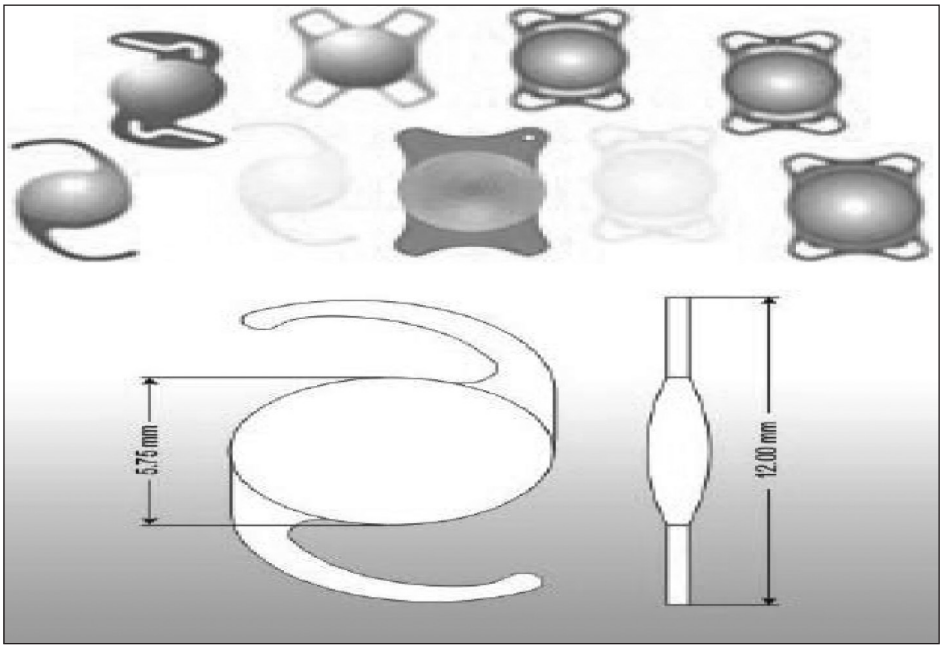
2.1. Hydrophilic acrylic IOL

Hydrophilic acrylic (hydrogel), a soft hydrophilic material developed for biomedical use has a long history of use as a biomedical material and is now used in folding IOLs. The material used is polyhydroxyethylmethacrylate (PolyHema) with a water content varying from 18% to 30% and a refractive index of 1.47. Hydrophilic acrylic (hydrogel) lenses fold and unfold faster than hydrophobic acrylic and are more controllable than silicone. Because of their water content they must be kept hydrated until implantation. Hydrophilic acrylic (hydrogel) lenses are available with a hydrophilic acrylic (hydrogel) optic of 6 mm bonded to PMMA optics and a single piece or 3 piece lens.[13] IOLs made with hydrophilic acrylic (hydrogel) polymers include the Hydroview and EasAcryl (Bausch & Lomb), Hydroflex II (Medical Development Research (MDR); Clearwater, Fla), MemoryLens (Novartis Ophthalmics), Collamer (STAAR Surgical Company), Bigbag and Stabibag (IOL Tech), and CenterFlex and Raysoft (Rayner).[14]

2.2. Hydrophobic acrylic IOL

Hydrophobic acrylic as a lens material is relatively new with FDA approval obtained in December 1994. Hydrophobic acrylics are polymers synthesised from esters of acrylic or methacrylic acid. It contains tiny amounts of water (less than 1%). Hydrophobic acrylic IOLs have a refractive index of 1.55 and the hardness of the hydrophobic acrylic is temperature dependent. The high refractive index gives acrylic lenses the lowest thickness of all available lens materials. At low temperatures the lens feels almost like PMMA and folding is facilitated by warming the lens. Hydrophobic acrylic lenses fold and unfold slowly and can be handled when wet. If the lens is too warm it becomes sticky and unfolding can be difficult. Condensations occur less frequently on hydrophobic acrylic lenses than PMMA and silicone lenses following fluid-air exchange. Present hydrophobic acrylic lens design is three-piece and single-piece, with an acrylic optic of 5.5 mm or 6.0 mm diameter and PMMA haptics.[13] IOLs made of hydrophobic acrylic polymers include the AcrySof (Alcon) and Sensar (AMO).[14]

Figure 1. Foldable hydrophobic acrylic IOL and hydrophilic acrylic IOL



3 POLICY QUESTION

Should hydrophilic acrylic IOL implants be routinely used for adult cataract surgery in Ministry of Health facilities?

4 OBJECTIVE

i. To assess the safety of commonly used foldable IOLs (hydrophilic acrylic and hydrophobic acrylic IOL implants)

5 METHODOLOGY

5.1. Literature search strategy

Electronic database were searched for published literatures pertaining to hydrophobic acrylic IOL and hydrophilic acrylic IOL opacification. The following databases were searched including MEDLINE, PubMed, EBM Reviews-Cochrane Database of Systematic Reviews, EBM Reviews-Cochrane Central Register of Controlled Trials, EBM Reviews-HTA Database, FDA website and MHRA. Additional articles were identified by reviewing the bibliographies of retrieved articles and hand-searching of journals. Google was used to search for additional web-based information. There was no limit in the search. The following search terms were used either singly or in combination: “intraocular lens”, IOL, “dystrophic calcification”, calcification, opacification, explantation, “hydrophilic acrylic”, “hydrophobic acrylic”, and “silicone contamination”.

5.2. Inclusion and exclusion criteria

Based on the policy question the following inclusion and exclusion criteria were used:-

a) Inclusion criteria:-

i. Study design : Systematic review, randomised controlled trial (RCT), cohort, case control, cross sectional, case series, case reports and experimental laboratory studies

ii. Population : Adult patient with cataract who underwent ataract surgery with implantation of IOL

iii. Interventions : Hydrophilic acrylic IOL or hydrophobic acrylic IOL

v. Comparators : No comparator or compared with other IOL such as silicone IOL or PMMA IOL

vi. Outcomes : Primary outcome:-

Adverse events such as IOL opacification

b) Exclusion criteria

Study performed in animals

The titles and abstracts of all studies were assessed for the above eligibility criteria. If it was absolutely clear from the title and / or abstract that the study was not relevant, it was excluded. If it was unclear from the available abstract and / or the title, the full text article was retrieved.

Two reviewers assessed the content of the full text articles. Disagreements were resolved by discussion.

5.3. Quality assessment strategy

The methodological quality of all the relevant full text articles retrieved was assessed using the Critical Appraisal Skills Programme (CASP) tool depending on the type of study design.[15] Quality assessment was conducted by two reviewers. Disagreements were resolved by discussion.

All full text articles related to effectiveness were graded based on guidelines from the U.S./Canadian Preventive Services Task Force (Appendix 1) [16]

5.4. Data extraction strategy

The following data were extracted:-

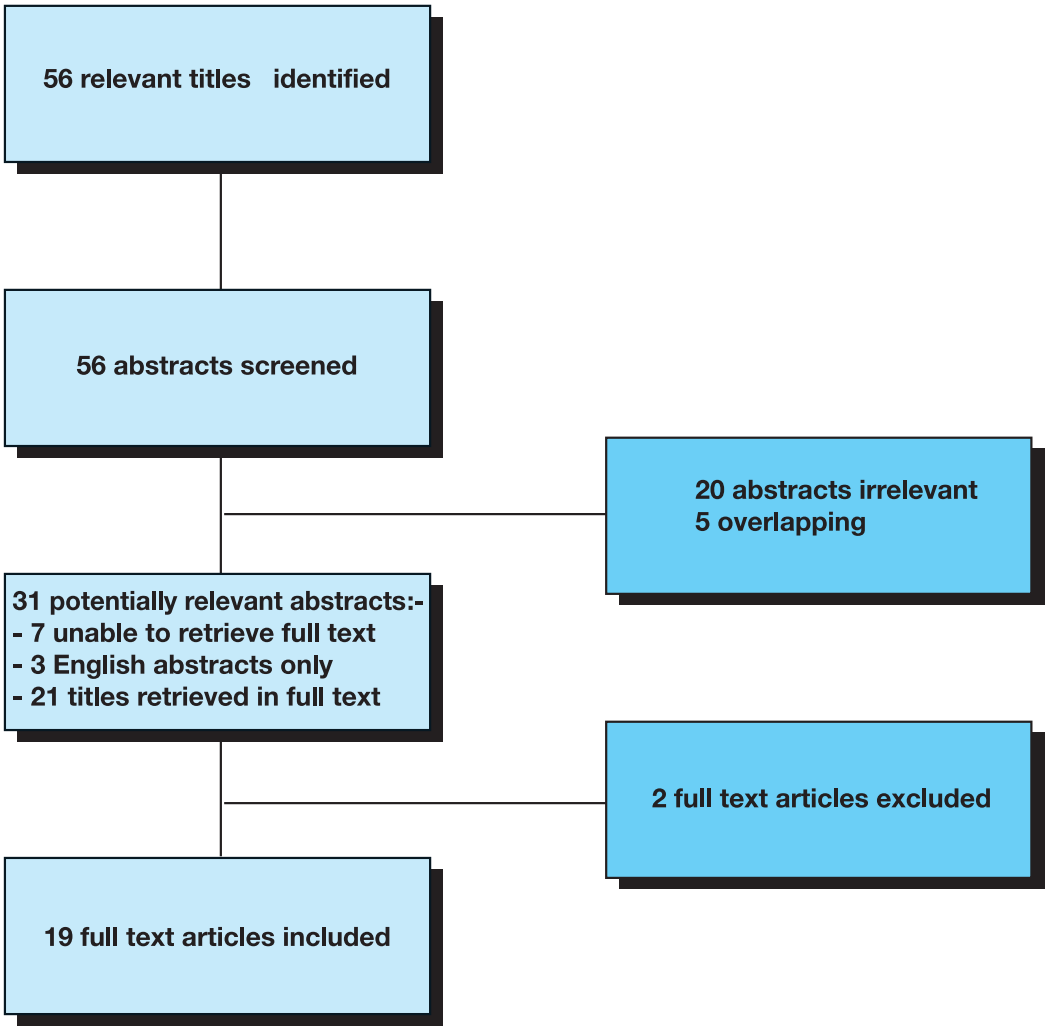
- Details of methods and study population characteristics
- Details of the interventions and comparators (if available)
- Details of individual outcomes for safety
- Data was extracted from included studies by a reviewer using a pre-designed data extraction form (evidence table as shown in Appendix 3) and checked by another reviewer. Disagreements were resolved by discussion. The extracted data were presented in evidence tables and discussed with the expert committee before deciding on the eligibility of articles to be included in this report.

6 RESULTS AND DISCUSSION

Search strategies yielded few published articles related to the safety (IOL opacification) of hydrophilic acrylic and hydrophobic acrylic IOLs. A total of 56 relevant titles were identified and 56 abstracts were screened using the inclusion and exclusion criteria. Of these, 20 abstracts were found to be irrelevant and five overlapping. Thirty-one potentially relevant abstract were attempted for retrieval. Of these, twenty-one potentially relevant articles were retrieved in full text, three were in English abstracts only and full-text for seven abstracts could not be retrieved. After reading and appraising the full text articles, nineteen articles were included as shown in Figure 2. Two full text articles were excluded based on inclusion and exclusion criteria and are listed in Appendix 4.

The articles comprised six cross sectional studies, six case series, five case reports, one laboratory experimental study, and U.S FDA approval for premarketing of hydrophilic and hydrophobic IOLs. The search did not yield any health technology assessment reports, systematic reviews or RCT related to the safety of hydrophilic and hydrophobic IOLs.

Figure 2. Flow chart of retrieval of articles used in the results



6.1. SAFETY

Various pathologic processes may lead to clinically significant opacification of the optic component of IOL manufactured from different biomaterials and in different designs. Factors such as the patient's associated conditions, the manufacturing process, the method of IOL storage, the surgical techniques and adjuvants, or a combination of these may be involved.[17]

Mamalis *et al.* in their tenth annual survey of complications associated with foldable IOLs requiring explantation or secondary intervention among members of the American Society of Cataract and Refractive Surgery and the European Society of Cataract and Refractive Surgeons in 2007, noted that the most common reason for removing the 1-piece and 3-piece hydrophilic acrylic IOLs was calcification / opacification (60%), followed by glare/optical aberrations (20%) and incorrect IOL power (20%). The authors also noted that the overall incidence of IOL opacification was less frequently seen as there are no approved hydrophilic acrylic IOLs presently in use in the United States. In contrast, the most common reason for surgical intervention or exchange of 3-piece hydrophobic acrylic IOLs was incorrect IOL power (34%), followed by dislocation/decentration (31%).[18] level II-3

6.1.1. Hydrophilic acrylic IOLs

There was retrievable evidence to show the approval for marketing of Hydroview H60M hydrophilic acrylic IOL, SC60B-OUV hydrophilic acrylic IOL and MemoryLens hydrophilic acrylic IOL by U. S. FDA.[19] However, Medicines and Healthcare products Regulatory Agency (MHRA) U.K. had received notifications related to IOL opacification due to Hydroview H60M hydrophilic acrylic IOL, Aqua-Sense hydrophilic acrylic IOL and SC60B-OUV & SC600-2 hydrophilic acrylic IOLs.[20] In February 2001, Bausch & Lomb informed their customers of an increased incidence of opacification with the Hydroview hydrophilic acrylic IOL. Studies conducted by the manufacturer have indicated that surface calcification appeared to be linked to the migration of silicone from the packaging onto the lens surface. A packaging system containing silicone was in use from December 1997 until May 2001. A total 88,527 Hydroview hydrophilic acrylic lenses were supplied to the U.K. in the silicone-containing packaging. Of these, 304 (0.3%) were reported to be explanted.[20]

Similarly, Opthalmic Innovations International Inc (OII Inc.) had also informed their customers of an increased incidence in opacification with the Aqua-Sense hydrophilic acrylic IOL and studies by the manufacturer indicated that surface calcification appeared to be linked to the migration of silicone from the packaging onto the lens surface. Of the total 868 Aqua-Sense hydrophilic acrylic IOL implanted in the U.K., 233 (27%) have been explanted. No Aqua-Sense hydrophilic acrylic IOL have been supplied in the U.K. since November 2000. Medical Devices Agency (MDA) had also received reports from seven U.K. hospitals regarding opacification of Acryflex SC60B-OUV hydrophilic acrylic IOLs in 27 patients. Nine patients had their lenses removed because of it. The manufacturer was unable to establish the cause for the opacification and had discontinued the distribution of Acryflex SC60B-OUV and SC600-2 hydrophilic acrylic IOLs in the U.K.[20] In a study by Gashau *et al.* whereby 152 SC60B-OUV hydrophilic acrylic were monitored for 5 years, he found that 98 IOLs developed opacification and 52 were exchanged.[21] level II-3

There have been established reports on IOL opacification with hydrophilic acrylic IOL which required explantation. The summary of characteristics of hydrophilic acrylic IOL opacification that required explantation is as shown in Table 1. Mackey *et al.* reported two patients who became symptomatic only three months after uneventful pharmacoemulsification and lens implantation with SC60B-OUV hydrophilic acrylic IOLs.[22 level III] Late postoperative opacification of hydrophilic acylic IOLs also occurred as described by several studies. The reported time interval between implantation and opacification of hydrophilic acrylic IOLs ranged from five months to three years.[2 level III, 23-25 level II-3, 26-27 level III]

Analyses performed on the explanted hydrophilic acrylic IOL have shown various patterns of opacification caused by the deposition of calcium and phosphate.[2, 3, 22 level III, 24 level II-3,26-28 level III] This included surface deposition as in Intraocular Optic International hydrophilic acrylic IOL, MemoryLens hydrophilic acrylic IOL, Hydroview H60M hydrophilic acrylic IOL and Stabibag hydrophilic acrylic IOL.[2-3 level III, 23-25 level II-3,27-28 level III] The deposition of calcium and phosphate was within the substance of the optic as in the SC60B-OUV hydrophilic acrylic IOL and Bigbag IOL or a combination of both (on the surface of the IOL and within the optic material) as in Aqua-Sense hydrophilic acrylic IOL.[2,3,22,26-28 level III] The overall pattern of opacification within a given IOL design (with all the lenses being manufactured from the same IOL material) was generally the same.

However, Neuhan *et al*. reported completely two different patterns of opacification even though the biomaterial used for the manufacturing of both lenses (Stabibag hydrophilic acrylic IOL and Bigbag hydrophilic acrylic IOL) was the same. Only surface deposits were observed with the Stabibag IOL, whereas the deposits were present within the optic substance in the case of Bigbag IOL. The reasons for such a different presentation of the calcified deposits remain unclear.[2 level III] Pandy *et al.* also described two different pattern of opacification of a single-piece hydrophilic acrylic (SC60B-OUV) IOL in a diabetic patient with bilateral cataract. The opacification involved both the IOL optic and the haptics in the left eye and was confined to the IOL optic in the right eye.[26 level III] In another study, Neuhan *et al.* also noted three different patterns of calcification in Biocomfold 92S hydrophilic acrylic IOL optic material. In Case 1, deposits were located in 2 non continuous parallel lines (exhibiting gaps) beneath the anterior and posterior optic surface and the haptics were free of deposits. In Case 2, the granules were located beneath the optic's anterior surfaces in the central optic region; the peripheral optic region and the haptics were free of deposits. In Case 3, a fine line of deposits was located just beneath the anterior and posterior surfaces of the entire optic and haptics. The reason for this remains unclear.[29 level III]

Studies have also found a high percentage of associated conditions such as glaucomas and diabetes in patients with hydrophilic acrylic IOL opacification. Balasubramaniam *et al.* in his cross sectional study involving hydrophilic acrylic (Hydroview IOL) implantation after cataract surgery found that 193 of 1,330 eyes had evidence of IOL opacification. Of these, 56 (4.2%) had visually significant opacification and had IOL exchange. They also found that 21.5% of diabetic eyes had IOL opacification compared with 14.3% of non diabetic eyes (P=0.06) and 20.5% of glaucomatous eyes had IOL opacification compared with 14.0% of non-glaucomatous eyes.[25] level II-3 Similarly, Neuhan *et al.* found that 53 patients (50.0%) of 106 patients with explanted MemoryLens hydrophilic acrylic IOL had positive medical history. The most frequent medical history was diabetes (25 cases; 23.5%) followed by hypertension (12 cases; 11.3%), arthritis (5 cases), renal failure (5 cases), gout (2 cases), hypercholesteremia (3 cases) and hypothyroidism (2 cases).[24] level II-3 Several other studies have also demonstrated that diabetes was found to be present in patients with hydrophilic acrylic IOL opacification that required explantation.[22] level III, [23] level II-3, [26, 28] level III.

Table 1. Summary of Characteristics of Opacification of Hydrophilic Acrylic IOLs

Authors	No. of lens explanted	IOL trade name /model	Time interval between implantation and opacification	Pattern of opacification	Composition of deposits causing opacification	Associated conditions
Mackey *et al.* 2003	2 lenses	SC60B-OUV	3 months	Within the optic and extension into the haptic	Calcium	Type II diabetes ; N=2
Neuhan *et al.* 2006	1 lens (1 case)	Stabibag	7 months	Lens surface (anterior and posterior optic surfaces)	Calcium and phosphate	Hypercholesterolaemia, coronary heart disease, post operatively :- - intracameral fibrinous reaction, secondary glaucoma, fililiform keratitis
	1 lens (1 case)	Bigbag IOL	21 months	Within the optic	Calcium, phosphate, sulphur and sodium	Hypertension, post operatively:- - transient corneal oedema, fibrin in anterior chamber, secondary glaucoma
Apple *et al.* 2001	6 lenses	Hydroview H60M	Not mentioned	Lens surface (anterior and posterior optic surfaces)	Calcium and phosphate	Cardiovascular disease, N=2 Diabetes, N=2
	9 lenses	SC60B-OUV	24 months	Within the optic	Calcium	Diabetes, N=2
Oner *et al.* 2002	3 lenses	Intraocular Optical International	6.3±1.5 months (range; 5 to 8 months)	Lens surface	Not analysed	Insulin dependent diabetes and on renal dialysis; N=2
Neuhan *et al.* 2004	106 lenses	MemoryLens	25.8±11.9 months	Lens surface (anterior and posterior optic surfaces)	Calcium and phosphate	Diabetes; N=25, Hypertension; N=12, Renal failure; N=5, Gout; N=2, Hyper--cholesterolaemia N=3 Hypothyroidism; N=2
Balasubramaniam *et al.*2006	56 lenses	Hydroview H60M	3 years	Lens surface (anterior and posterior optic surfaces)	Not mentioned	Diabetes; N=93 eyes Glaucoma; N=156 eyes
Pandy *et al.* 2002	2 lenses in one diabetic patient (bilateral cataract)	SC60B-OUV	Left eye - 20 months Right eye – 11 months	Left eye- within the optic and haptic Right eye- within the optic	Calcium and phosphate	Diabetes
Toboada *et al.* 2007	7 lenses	5 SC60B-OUV 1 Aqua-Sense 1 Hydroview H60M	1-3 years	Within the optic- Lens surface (anterior and posterior optic surfaces)	Calcium and phosphorus salts	More frequent among diabetic patients
Werner *et al.* 2007	40 lenses	20 Memory Lens	Not mentioned	Lens surface (anterior and posterior optic surfaces)	Calcium and phosphate	Diabetes; N=8 hypertension; N=5 hyperthyroidism; N=1 gout; N=1 arthritis; N=1 glaucoma; N=4 macular hole; N=1
		10 SC60B-OUV		Within the optic		Diabetes; N=2 macular pucker; N=1
		10 Aqua-Sense		Within the optic, haptic and lens surface		Diabetes; N=4 hypertension; N=4 asthma; N=1 age-related macular degeneration; N=2 macular pucker/ retinal detachment; N=1

Patient factors related to some kind of metabolic imbalance or breakdown of blood-aqueous barrier in combination with other factors have also been implicated. Kim *et al.* in their cross-sectional study compared the levels of calcium and phosphorus in aqueous humour and serum of non-diabetics and diabetics to investigate the basis for the increased incidence of late opacification of hydrophilic acrylic IOL in diabetic patients. They found that the level of phosphorus in the aqueous humour and serum of diabetics was significantly increased, especially in diabetics with proliferative diabetic retinopathy. They concluded that it may be related to hydrophilic acrylic IOL opacification.[30 level II-3] Nakome *et al.* in a concentration-change experiment, whereby the calcium and phosphate concentration levels were changed, found that hydrophilic acrylic IOL (Hydroview H60M) had significantly higher amounts of calcified deposits than IOL of other materials ($P<0.01$), indicating that hydrophilic acrylic IOL easily accumulate calcified deposits in the body when the concentration of calcium, phosphate, and albumin in the aqueous humour fluctuate as a result of blood-barrier breakdown.[31 level III]

Mattova *et al.* in another cross sectional study reported that opacification of the hydrophilic acrylic MemoryLens U940A was caused by premature consumption of the UV absorber in the polymer component of the IOLs optic, with subsequent degradation of the polymer.[32 level II-3]

6.1.2. Hydrophobic acrylic IOLs

There was retrievable evidence to show the approval for marketing of AcrySof (Alcon) hydrophobic acrylic IOL and Sensar (AMO) hydrophobic acrylic IOL by U. S. FDA.[19]

There was no report on hydrophobic acrylic IOL opacification caused by calcium and phosphorus deposition requiring explantation. However, glistenings (visible water vacuoles) have been reported in single-piece AcrySof (models SA60 and SN60; Alcon) hydrophobic acrylic IOL. Waite A *et al.* found that neither size, density, nor severity index (size and density) correlated with visual acuity, glare testing or wavefront analysis results. High spatial resolution contrast acuity and progress over time had a borderline correlation with severity index ($P=0.06$) and ($P=0.04$).[33 level II-3] Glistenings were thought to be caused by microvacuole formation within the lens polymer as the temperature exceeded the glass transition temperature. Water from the anterior chamber was able to enter these vacuoles and cause glistenings. They disappeared when the IOL dehydrated or dried.[23]

Iwase T and Sugiyama K reported a case in which the optic of a single-piece AcrySof acrylic (SA60AT, Alcon) IOL became opacified in a 64 years old man who had triple procedure of vitrectomy, phacoemulsification and IOL implantation for cataract and a dense vitreous haemorrhage in the left eye. The IOL was clear on the day after surgery, but by the third day, a dusty haze was observed on the surface due to the presence of numerous, small brown corpuscles. Analysis of the explanted IOL indicated the presence of proteinaceous material but there was no calcium on the surface of the lens. They concluded that early post-operative opacification of the single-piece hydrophobic acrylic SA60AT IOL might occur in combined cataract and vitreous surgery, even in eyes in which the posterior capsule is intact and there is no operative complication.[34 level III]

The surface of the hydrophilic acrylic IOL is subject to opacification as a result of calcium phosphate deposition, whereby limiting the patient's visual outcome, and in some cases necessitating explantation. In this review, the safety of hydrophilic acrylic IOL and hydrophobic acrylic IOL was sought by searching databases in combination with cross-reference. There was no systematic review, health technology assessment report or RCT retrieved. Therefore, this systematic review included studies which were of poor to fair level of evidence. From this review, calcification of the hydrophilic acrylic IOL is relatively a serious complication, but the conditions leading to its appearance and the pathophysiology have not yet been fully elucidated. Ophthalmologists should be very careful in the choice of the intraocular lens to implant, particularly if the patient is diabetic.

The estimated cost of hydrophilic acrylic IOL is comparable to hydrophobic acrylic IOL. However, taking the incidence of hydrophilic acrylic IOL opacification into consideration, the use of hydrophilic acrylic IOL maybe more costly to the patients and to the service providers should explantation and IOL exchange be necessary.

There were methodological limitations in this study. Most of the studies were cross sectional studies, case series and case reports, therefore, the assessment of the methodological quality of these studies using CASP assessment tool was not possible due to limitations in the CASP checklist itself. Although every effort has been made to retrieve full text articles, there were seven articles which the authors failed to retrieve their full text.

7 CONCLUSION

Opacification of the IOL is a serious complication of IOL implantation following cataract surgery. The following conclusions are drawn:-

i. There was poor to fair level of evidence to suggest that the incidence of IOL opacification affecting vision was only reported in hydrophilic acrylic IOL and not with hydrophobic acrylic IOL

ii. IOL opacification of hydrophilic acrylic IOL was caused by deposition of calcium and phosphate on the IOL surface, or within the optic material or both (on the surface and within the IOL material) depending on the designs of the hydrophilic acrylic IOL. However, the pathophysiology of the causes of such complications have not yet been fully elucidated

iii. Diabetic patients appeared to be more often and more severely affected by IOL opacification

8 RECOMMENDATION

Since IOL opacification can cause significant morbidity to patients as well as cost and medico-legal implications, a guide to the choice of IOL should be made available.

Based on the above review;

i. We recommend the use of hydrophobic acrylic IOLs

ii. Patients who had hydrophilic acrylic IOLs implantation need longer and more frequent follow-up, particularly in the presence of predisposing factors such as diabetes

iii. In view of the absence of Medical Device Act in Malaysia, an incident reporting mechanism for IOL opacification irrespective of materials and designs need to be established to provide more information regarding IOL opacification locally

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Appendices

APPENDIX 1

HIERACHY OF EVIDENCE FOR EFFECTIVENESS STUDIES DESIGNATION OF LEVELS OF EVIDENCE

I Evidence obtained from at least one properly designed randomized controlled trial.

II-I Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III Opinions or respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

SOURCE: US/CANADIAN PREVENTIVE SERVICES TASK FORCE (Harris 2001)

APPENDIX 2

HEALTH TECHNOLOGY ASSESSMENT (HTA) PROTOCOL INTRAOCULAR LENS (IOL) IMPLANTATION- HYDROPHILIC ACRYLIC VERSUS HYDROPHOBIC ACRYLIC

1 BACKGROUND INFORMATION

Cataract is the most prevalent ophthalmic disease and cataract surgery is a commonly performed surgery in all ophthalmic practice. Cataract surgery has evolved over the years to modern day techniques with intraocular lens (IOL) implantation as the standard practice to improve visual outcome. IOL implantation was first introduced by Sir Harold Ridley in 1949. He was the first to successfully implant an IOL on November 29, 1949, at St Thomas' Hospital at London.

The first IOL was manufactured by the Rayner company of Brighton, East Sussex, England from Perspex CQ made by ICI. The first lenses used were made of glass, they were heavy and were prone to shatter during neodymium:yttrium-aluminum-garnet (Nd: YAG) laser capsulotomy. Plastic materials were used later. The IOL did not find widespread acceptance in cataract surgery until 1970s, when further developments in lens design and surgical techniques were introduced. It usually consists of a small plastic lens with plastic side struts, called haptics, to hold the lens in place within the capsular bag inside the eye. IOLs were traditionally made of an inflexible material; polymethylmethacrylate (PMMA). With advances in small-cataract surgery and bio-material science, a variety of foldable IOL designs have been developed over the past two decades. Currently available foldable IOLs are made from silicone, hydrophobic acrylic, and hydrophilic acrylic (hydrogel) materials.

Hydrophilic acrylic IOLs have been proven to be highly biocompatible, inducing less inflammatory cytologic reaction. However, late postoperative opacification caused by dystrophic calcification requiring explantation has been reported with some hydrophilic acrylic IOL designs. The opacification patterns included the formation of surface deposits as well as intralenticular deposition of calcium and phosphate. Similarly, late postoperative opacification of hydrophilic acrylic IOLs requiring explantation have also been encountered in a few government hospitals in Malaysia.

In Malaysia, IOLs are introduced into the market by suppliers directly to the end users. There is no mechanism whereby these IOLs are subject to review prior to distribution. Usage is guided by whether products have U. S. Food and Drug Administration (FDA) approval/CE mark. Since IOL opacification can cause significant morbidity to patients as well as cost and medico-legal implications to Ministry of Health, a guide to choice of IOL should be made available.

The total number of cataract surgery registered to National Cataract Surgery Registry (CSR) over the years (2002 to 2007) was 71,749. It increased from 14,316 in 2002 to 22,051 in 20007. The demographic features of patients who had cataract surgery at public hospitals over 6 years (2002 to 2007) were consistent with the man age of 64 years and slight female preponderance (ranged 50% to 52%). The proportion of patients with systemic co-morbidity increased from 56.8% in 2002 to 67.5% in 2007. The commonest was hypertension (about half), followed by Diabetes Mellitus (about one third).

This systematic review was conducted following a request by a Senior Consultant Ophthalmologist, Selayang Hospital following reports of IOL opacification with the use of hydrophilic acrylic implants in the United States of America, in the United Kingdom and also in Selayang Hospital.

2 POLICY QUESTION

Should hydrophilic acrylic IOL implants be routinely used for adult cataract surgery in Ministry of Health Facilities?

3 OBJECTIVE /AIM

i. To assess the safety of commonly used foldable IOLs (hydrophilic acrylic and hydrophobic acrylic IOL implants)

4 METHODOLOGY

4.1. Search strategy

Electronic database will be searched for published literatures pertaining to hydrophobic acrylic and hydrophilic acrylic IOL implantation. The following sources will be searched:-

i. Databases as follows MEDLINE, PubMed, EBM Reviews-Cochrane Database of Systematic Reviews, EBM Reviews-Cochrane Central Register of Controlled Trials, EBM Reviews-HTA Database, FDA website and MHRA

ii. Google will be used to search for additional web-based information.

iii. Additional articles will be identified from reviewing the bibliographies of retrieved articles.

4.2. Inclusion and exclusion criteria

Inclusion criteria

i. Study design : Systematic review, randomised controlled trial (RCT), cohort, case control, cross sectional, case series, case reports and experimental laboratory studies

ii. Population : Adult patient with cataract who underwent cataract surgery with implantation of IOL

iii. Interventions : Hydrophilic acrylic IOL or hydrophobic acrylic IOL

v. Comparators : No comparator or compared with other IOL such as silicone IOL or PMMA IOL

vi. Outcomes : Primary outcome:-
Adverse events such as IOL opacification

Exclusion criteria

Study performed in animals.

Based on these inclusion criteria, study selection will be carried out independently by two reviewers. Disagreements will be resolved by discussion.

4.3. Data extraction strategy

The following data will be extracted:

- Details of methods and study population characteristics
- Details of the intervention and comparator
- Details of individual outcomes for safety

Data will be extracted from included studies by a reviewer using a pre-designed data extraction form and checked by another reviewer. Disagreements will be resolved by discussion.

4.4. Quality assessment strategy

The methodological quality of all the relevant articles retrieved will be assessed using Critical Appraisal Skills Programme (CASP) depending on the type of study design. Quality assessment will be conducted by a reviewer and checked by second reviewer.

4.5. Methods of analysis / synthesis

Data on safety will be presented in tabulated format with narrative summaries. A decision on whether to pool efficacy, safety and accuracy outcomes will be taken following the updated search and based on clinical and statistical heterogeneity and the range of outcome measures reported. Data will be pooled using fixed effect model unless statistical heterogeneity between studies is found, in which case random effect model will be used.

5. Report writing

APPENDIX 3

Evidence Table : Safety
Question : Do Hydrophilic acrylic IOLs or Hydrophobic acrylic IOLs prone to IOL opacification?

Bibliographic Citation	1. Neuhan IM, Stoduka P, Werner L *et al.* Two opacification patterns of the same hydrophilic acrylic polymer; Case reports and clinicopathological correlation. J Cataract Refractive Surgery. 2006;32 May:879-886
Study Type / Methodology	Case report : Aim of study was to present 2 cases of hydrophilic acrylic IOLs (Stabibag and Bigbag) that had to be explanted because of late opacification of their optic component. Case 1. - After the operation the patient had an intracameral fibrinous reaction, secondary glaucoma and filiform keratitis requiring corneal abrasion. 7 months after surgery the best corrected visual acuity (BCVA) had dropped to hand movements because of IOL opacification and the IOL was explanted and analysed. Case 2. - Postoperatively the patient had transient corneal oedema and fibrin noted in the anterior chamber, and secondary glaucoma. 21 months after surgery, decreased visual acuity in the left eye to hand movements and secondary cataract in the left eye. Homogenous white opacification of the optical component of the IOL was noted. The IOL was explanted from the left eye, 22 months postoperatively and analysed. After gross, microscopic, and histochemical analyses to confirm the presence of deposits, the lenses underwent scanning electron microscopy (SEM) on the surface and sagittal optic section. Energy dispersive x-ray spectroscopy (EDS) for elemental composition, peformed on the surface deposits, control area and within the optic substance .
LE	III
Number of patients and patient characteristics	Case 1 - 78 year old woman who had an uneventful cataract surgery and implantation of a Stabibag IOL in the right eye. Had medical history of hypercholesterolaemia and coronary heart disease. Associated conditions in the right eye included pseudoexfoliation and history of penetrating trauma with hypopyon in 2001. Case 2 - 61 year old woman with bilateral high myopia, cataract, and history of uveitis in the left eye had an uneventful phacoemulsification with the implantation of the Bigbag IOL in left eye. The only general disease noted was arterial hypertension.
Intervention	(Stabibag and Bigbag IOLs, Ioltech) – are both 1-piece foldable hydrophilic IOL designs manufactured from the same methymethacrylate/hydroxyethylmethacrylate copolymer with an incorporated ultraviolet blocker and same surface treatment. Lenses only differ in size and shape.
Comparison	

Length of follow up	
Outcome measures / Effect size	Stabibag IOL - Gross evaluation showed white discolouration, especially at 1 side of the optic and the corresponding haptic. Gross and microscopic analysis showed that the external surface of the lens was covered with multiple fine granules. These deposits were present on both the optic surfaces around the edges as well as the haptics. Staining of the internal surface of the sagittal optic cut of the lens was negative. SEM analysis confirmed the presence of granular deposits over the optic surface and absence of granules within the substance of the optic. EDS performed on the surface deposits showed the presence of calcium and phosphate peaks. Bigbag IOL - Had milky opacification of the central 5.0 mm of its optic with transparent haptic component.Gross and microscopic analysis showed that the optic surface and haptics of the IOL were almost free of any deposit. However, there were multiple small granular structures within the central 5.0 mm of the IOL optic. Edges and the haptics appeared clear. Analysis of the cut section (sagittal view) of the lens optic showed multiple granules of variable sizes in the region beneath the external anterior surface of the IOL. SEM analysis showed the presence of the granules in the intermediate region beneath the anterior surface. EDS performed precisely on the deposits in the same section showed the presence of calcium, phosphate, sulphur and sodium peaks. Peaks of carbon and oxygen, normal components of the hydrophilic acrylic material used for the manufacture of this IOL design were also present in the control area. **Authors conclusions** Pathologic analyses of the explanted IOLs were consistent with dystrophic calcification leading to optic opacification but the pattern was different between the two IOL designs manufactured from the same polymer. Further investigations will be necessary to clarify the mechanism of calcification of these IOL designs. Patient related factors might have been responsible for this complication
General Comments	

Evidence Table : Safety
Question : Do Hydrophilic acrylic IOLs or Hydrophobic acrylic IOLs prone to IOL opacification?

Bibliographic Citation	2. Apple DJ, Werner L. Complication of cataract and refractive surgery: a clinicopathological documentation. TR. Am. Ophth. Soc. 2001;99: 95-109.
Study Type / Methodology	Case series Aim of the study was to present selected complications of keratorefractive and phakic intraocular lens (IOL) surgery and a series of IOLs that required explantation because of various postimplantation opacification of the IOL optic. Explanted IOLs from cases in which postimplantation opacification of the IOL optic had occurred were studied. Included 6 Bausch and Lomb (B&L) Hydroview H60M designs and 9 Medical Development Research (MDR) SC60B-OUV designs The analysis was performed in Centre for Research on Ocular Therapeutics and Biodevices, Storm Eye Institute, Medical University of South Carolina, Charleston. Analysis performed included gross and light microscopic evaluation, histochemical staining, electron microscopy, and energy-dispersive spectroscopy.
LE	III
Number of patients and patient characteristics	**6 Hydroview lenses.** - 2 women - 4 men Age of the patients at the time of explantation ranged from 70 to 85 years. - 2 diabetics - 2 cordiovascular diseases - 2 healthy (Lenses explanted in Australia (1), in Sweden (4) and in Canada (1). All lenses were explanted at least 1 year after the primary procedure. **9 SC60B-OUV lenses** Age of the patients at the time of explantation ranged from 62 to 77 years (70.28 ±.5.76) - 2 diabetics Lens explanted – 14 to 29 months postoperatively (24.42 ± 5.12)
Intervention	6 Bausch and Lomb (B&L) Hydroview H60M designs and 9 Medical Development Research (MDR) SC60B-OUV designs
Comparison	Hydroview explanted due to IOL malposition
Length of follow up	
Outcome measures / Effect size	**Hydroview H60M design.** - Surface calcification, the deposits occurred on both the anterior and posterior IOL optic surfaces, but not the haptics. Staining of the control Hydroview lens was negative EDS performed on the deposits demonstrated the presence of peaks of calcium and phosphate. **SC60B-OUV designs** - Diffusion of calcium into the substance of the optic of hydrophilic "acrylic" SC60B-OUV IOL design sometimes leading to total opacification of the IOL optic and its haptics. EDS performed precisely on the deposits revealed the presence of calcium peaks.
General Comments	

Evidence Table : Safety
Question : Do Hydrophilic acrylic IOLs or Hydrophobic acrylic IOLs prone to IOL opacification?

Bibliographic Citation	3. Mackey TA, Werner L, Soliman MM *et al.* Opacification of two Hydrophilic acrylic intraocular lenses 3 months after implantation. Ophthalmic Surgery, Lasers & Imaging. 2003;34(3): 197-202
Study Type / Methodology	Case reports Aim of the study was to report clinical, pathologic, histochemical, ultrastructural, and spectroscopic analyses of explanted hydrophilic acrylic intraocular lens (IOLs) obtained from 2 patients who had early visual disturbances caused by postoperative opacification of the lens optic. Two hydrophilic IOLs were explanted from patients with decreased visual acuity. The patients became symptomatic 3 months after uneventful phacoemulsification and kens implantation. IOL optic opacification was associated with a fine granularity within the substance of the lens optic. The lenses were explanted at 13 months (case 1) and 14 months (case 2) The IOLs were examined by gross and light microscopy. Full-thickness cut sections of the optics were stained with 1% alizarin red. Some sections were submitted for scanning electron microscopy(SEM) and energy dispersive x-ray spectroscopy (EDS). The two lenses analysed in the study were implanted and explanted by the same surgeon in Egypt.
LE	III
Number of patients and patient characteristics	2 patient (2 lenses) Two women (62 years old in case 1 and 65 years old in case 2) had diabetes but no other known systemic or ocular conditions.
Intervention	Hydrophilic acrylic (SC60B-OCV lens)
Comparison	
Length of follow up	
Outcome measures / Effect size	Microscopic analysis revealed the presence of multiple fine, granular deposits of variable sizes within the optics of the lenses distributed in a line parallel to the anterior and posterior curvatures of the optic, with a clear zone just beneath the optics' surface. Extension of the opacification into the haptics of the IOLs could also be observed. The deposits stained positive with alizarin red. Energy disperse x-ray spectroscopy of the internal substance of the IOLs also demonstrated the presence of calcium within the deposits. **Authors conclusions.** This is the first clinicopathologic report of optic and haptic opacification occurring with this hydrophilic acrylic IOL model only 3 months postoperatively. Further studies on the other similar cases with this lens should be done to determine the incidence and possible mechanism of this phenomena.
General Comments	

Evidence Table : Safety
Question : Do Hydrophilic acrylic IOLs or Hydrophobic acrylic IOLs prone to IOL opacification?

Bibliographic Citation	4. Oner HF, Durak I, Saatci OA. Late postoperative opacification of a Hydrophilic acrylic intraocular lens. Ophtalmic Surgery and Lasers. 2002;33(4):304-308.
Study Type / Methodology	Case series Aim of the study was to evaluate the incidence of postoperative opacification of hydrophilic acrylic intraocular lenses (IOLs) and discuss surgical management. Seventy-two eyes of 72 consecutive patients who received the same type of hydrophilic acrylic IOL (Intraocular Optical International, I.O.I, California, USA) after uneventful phacoemulsification were evaluated retrospectively. Study performed at Dokuz Eylul University, Turkey between February 2000 and October 2000. Systemic status, follow-up time, recognition time of IOL opacification, time lapse between implantation and explantation, and surgical technique during explantation were reported.
LE	II-3
Number of patients and patient characteristics	72 consecutive patients who received the same type of hydrophilic acrylic IOL (Intraocular Optical International, I.O.I, California, USA) 42 men and 30 women. Mean age was 65.9 years (range: 53 to 78 years).
Intervention	Hydrophilic acrylic IOL (Intraocular Optical International, I.O.I, California, USA)
Comparison	
Length of follow up	Mean follow-up of patients was 10.4±3.2 months (range: 6-13 months)
Outcome measures / Effect size	There were 37 diabetic patients of whom 29 were on antidiabetics and 8 were on insulin therapy. Two of the diabetic patients were on renal dialysis because of diabetic nephropathy. Seventeen of diabetic patients had prior panretinal photocoagulation, 10 had focal macular laser treatment preoperatively. 29 had systemic hypertension and 32 had no significant systemic disease. IOL opacification was noted in 3 patients (4.1%). Two had insulin dependent diabetes mellitus and both are on renal dialysis, whereas one had no systemic disease. Time lapse between implantation and first recognition of opacification was 6.3±1.5 months (range; 5 to 8 months). Time lapse between implantation and explantation was 8.0 ±2.0 months (range: 6 to 10 months). In all cases, hydrophilic acrylic IOLs were exchanged with AcrySof® IOL and no further opacification occurred after lens exchange. **Authors conclusions.** Use caution on implantation of hydrophilic acrylic IOLs because late opacification is a serious complication requiring further surgery.
General Comments	

Evidence Table : Safety
Question : Do Hydrophilic acrylic IOLs or Hydrophobic acrylic IOLs prone to IOL opacification?

Bibliographic Citation	5. Neuhan IM, Werner L, Izak AM *et al.* Late postoperative opacification of a Hydrophilic acrylic (Hydrogel) intraocular lens. A clinicopathological analysis of 106 explants. Ophthalmology. 2004;111: 2094-2101.
Study Type / Methodology	Case series Aim of the study was to report clinical, pathologic, histochemical, ultrastructural, and spectroscopic analyses of MemoryLens intraocular lens (IOLs) explanted from patients who had visual disturbances caused by postoperative opacification of the lens optic. The explanted IOLs were submitted to the John A. Moran Eye Centre, University of Utah, Salt Lake City, Utah. They were examined under light microscopy, histochemically and with scanning electron microscopy (SEM) equipped with an energy dispersive x-ray spectroscopy detector with light element capabilities (EDS)
LE	II-3
Number of patients and patient characteristics	A total of 106 hydrophilic acrylic IOLs of the same design explanted from 106 different patients. All patients had decreased visual acuity at presentation approximately 2 years after cataract surgery, associated with a whitish fine granularity on the topical surfaces of the IOLs. 34 male and 69 female patients, 3 no information on gender. Mean age at the time of cataract surgery with IOL implantation was 71± 11 years (range, 40 to 91 years)
Intervention	MemoryLens (CIBA Vision, Duluth, GA), a 3-piece foldable hydrophilic acrylic IOL with a refractive index of 1.473.
Comparison	One Memory Lens explanted because of decentration
Length of follow up	
Outcome measures / Effect size	Distribution, structure and composition of deposits causing opacification of their optic components. Explanted lenses were submitted from various countries including USA (82 cases), Germany (22 cases), Italy (1 case) and Switzerland (1 case). Positive medical history in 53 patients (50.0%), most frequently diabetes (25 cases; 23.5%), hypertension (12 cases, 11.3%) arthritis (5 cases), renal failure (5 cases), gout (2 cases), hypercholesteremia (3 cases), and hypothyroidism (2 cases). For 22.6% of the patients (n=24), there was no significant past medical history and for 27.3% of the patients (n=29), unable to obtain information regarding past medical history. Most of the lens had been implanted in 1999 and 2000. The average interval between lens implantation and opacification was 25.8 ±11.9 months. Microscopic analysis revealed the presence of multiple fine, granular deposits of variable sizes on the anterior and posterior optic surfaces, especially on the anterior surface. The deposits stained positive for calcium. The EDS confirmed the presence of calcium and phosphate within the deposits. **Authors conclusions.** The results obtained suggest the surface deposits to be composed, at least in part of calcium and phosphate. A special polishing technique used in the manufacture of most of these IOLs may have caused changes in lens surface leading to deposit formation.
General Comments	

Evidence Table : Safety
Question : Do Hydrophilic acrylic IOLs or Hydrophobic acrylic IOLs prone to IOL opacification?

Bibliographic Citation	6. Balasubramaniam C, Goodfellow J, Price N *et al.* Opacification of the Hydroview H60M intraocular lens: total patient recall. J Cataract Refract Surg. 2006 Jun;32(6):944-948
Study Type / Methodology	Cross sectional study Aim of the study was to report the prevalence of intraocular lens (IOL) opacification and related clinical features in patients implanted with Hydroview IOL. The study was conducted in Gloucestershire Eye unit, Gloucestershire, United Kingdom. A total of 1330 eyes of 1265 patients who had cataract surgery with Hydroview IOL implantation between September 2000 and April 2001 were reviewed between April and October 2004. Visual acuity, visual symptoms, IOL status, and associated ocular comorbidity were recorded.
LE	II-3
Number of patients and patient characteristics	A total of 1330 eyes of 1265 patients. Mean age 78.9 ± 9.33 (SD); range 35 to 100 years
Intervention	Hydroview IOL
Comparison	
Length of follow up	
Outcome measures / Effect size	193 of 1330 eyes (14.5%) had evidence of IOL opacification. A total of 56 of 193 eyes (4.2%) had visually significant opacification and IOL exchange. The prevalence of IOL opacification ranged from 1.1% in patients who had surgery in September 2000 to 36.3% in December 2000 group. In eyes with IOL opacification, the visual symptoms were decreased vision (57%), glare (32%), and mistiness of vision (27%). 144/193 (75%) with IOL opacification had visual acuity of 6/12 or better. 93 eyes had diabetes, 21.5% of diabetic eyes had IOL opacification compared with 14.3% of non-diabetic eyes (P=0.06); 156 eyes had glaucoma, 20.5% of glaucomatous eyes had IOL opacification compared with 14.0% of non-glaucomatous eyes (P=0.033). **Authors conclusions.** This is the first large sample recall of patients implanted with the Hydroview H60M IOL. The overall prevalence of IOL opacification was 14.5% with peak prevalence in patients who had surgery in December 2000.
General Comments	

Evidence Table : Safety
Question : Do Hydrophilic acrylic IOLs or Hydrophobic acrylic IOLs prone to IOL opacification?

Bibliographic Citation	7. Pandy Sk, Werner L, Apple DJ *et al*.. Hydrophilic acrylic intraocular lens optic and haptics opacification in a diabetic patient: bilateral case report and clinicopathologic correlation. Opthalmology. 2002;109(11):2042-51
Study Type / Methodology	Case report Aim of study was to report clinicopathologic and ultrastructural features of two opacified single-piece hydrophilic acrylic intraocular lenses (IOLs) explanted from a diabetic patient. A 64 year old diabetic white female underwent phacoemulsification and implantation of a single-piece hydrophilic acrylic lens (SC60B-OUV; Medical Developmental Research, Inc, Clear Water, FL) in October 1998 in the left eye and in July 1999 in the right eye. The best corrected visual acuity after surgery was 20/60 in the left eye and 20/50 in the right eye. The patient had marked decrease in visual acuity in June 2000 as a result of a milky, white opalescence of both eyes. Intraocular lens explantation and exchange was performed in both eyes and the explanted IOLs were submitted to Centre for Researchon Ocular Therapeutics and Biodevices, Storm Eye Institute, Medical University of South Carolina, Charleston, South Caroline, USA for detailed pathologic, histochemical, and ultrastructural evaluation. They were stained with alizarin red and the von Kossa method for calcium, and also underwent scanning electron microscopy and energy dispersive radiograph spectroscopy to ascertain the nature of deposits leading to the opacification.
LE	III
Number of patients and patient characteristics	A 64 year old diabetic white female
Intervention	Single-piece hydrophilic acrylic lens (SC60B-OUV; Medical Developmental Research, Inc, Clear Water, FL)
Comparison	
Length of follow up	
Outcome measures / Effect size	Opacification of the IOL was found to be the cause of decreased visual acuity. The opacification involved both the IOL optic and the haptics in the left eye and was confined to the IOL optic in the right eye. Histochemical and ultrastructural analyses revealed that the opacity was caused by deposition of calcium and phosphate within the lens optic and haptics. **Authors conclusions** There are two features that distinguish this case from those reported earlier. This is the first clinicopathologic report of lens opacification that has involved completely the lens optic and the haptics. Second, those two explanted IOLs document the first bilateral case. The process of intraoptic and haptic opacifiaction represents dystrophic calcification of unknown cause. Diabetic patients appear to be more severely and more often affected by lens opacification. Long-term follow-up of diabetic patients implanted with this IOL design should be maintained by surgeons and manufacturers.
General Comments	

Evidence Table : Safety
Question : Do Hydrophilic acrylic IOLs or Hydrophobic acrylic IOLs prone to IOL opacification?

Bibliographic Citation	8. Toboada-Esteve JF, Hurtado-Sarrio M, Duch-Samper AM *et al.* Hydrophilic acrylic intraocular lens clouding: a clinicopathological review. Eur J Opthalmol. 2007;17(4):588-94
Study Type / Methodology	Case series Aim of study was to analyse serious late complication (opacification) of different models of hydrophilic acrylic intraocular lenses (IOLs). Seven lenses were explanted from seven patients:- - 5 SC60B-OUV from MDR - 1 AquaSense from OII - 1 H60M Hydroview lens from Bausch & Lomb. The explanted lenses were subjected to exhaustive study involving photographic analysis, scanning electron microscopy, and energy dispersive X-ray spectroscopy.
LE	III
Number of patients and patient characteristics	Seven patients treated for cataracts with phacoemulsification and implantation of different types of hydrophilic acrylic IOLs who developed important vision impairment in the late post-operative period (1 to 3 years) due to lens opacification.
Intervention	- 5 SC60B-OUV from MDR - 1 AquaSense from OII - 1 H60M Hydroview lens from Bausch & Lomb.
Comparison	
Length of follow up	
Outcome measures / Effect size	Light and scanning electron microscopy revealed diffuse, variable-size granular deposits within the optic of the SC60B-OUV lens, and on the anterior and posterior optic surfaces of the H60M Hydroview lens, though without affecting the haptics in any of the models. Dispersive energy X-ray spectroscopy of the deposits revealed the presence mainly of calcium and phosphorus salts. **Authors conclusions** Hydrophilic acrylic IOL opacification is a serious late complication of unknown aetiology. The condition is more frequent among the diabetic patients, and the only management option is IOL explantation and replacement with the lens of some other material. More frequent and longer follow-up is required in those patients wearing lenses for which opacification have been documented, particularly in the presence of predisposing factors (diabetes, uveitis). Caution is required with new lenses, avoiding their generalised use until they have successfully passed the test of time.
General Comments	

Evidence Table : Safety
Question : Do Hydrophilic acrylic IOLs or Hydrophobic acrylic IOLs prone to IOL opacification?

Bibliographic Citation	9. Werner L, Hunter B, Stevens S *et al.* Role of silicon contamination on calcification of Hydrophilic acrylic intraocular lenses. American Journal of Ophthalmolgy. 2006;141(1):35-43
Study Type / Methodology	Case series Aim of study was to verify the presence of the element silicon on hydrophilic acrylic intraocular lenses (IOLs) explanted because of calcification. Twenty explanted IOLs with surface deposits (MemoryLens) and 20 with deposits mostly within their optic substance (SC60B-OUV and Aqua-Sense; 10 each) were used. After gross, microscopic, and histochemical analyses to confirm the presence of deposits, the lenses underwent scanning electron microscopy (SEM) with energy dispersive x-ray spectroscopy (EDS) for elemental composition, on the external surface of MemoryLens IOLs and on the surface and internal substance of SC60B-OUV and Aqua-Sense IOLs. The weight percentage of the element silicon was obtained at the level of deposits, and adjacent deposit-free areas in all lenses.
LE	III
Number of patients and patient characteristics	Forty explanted IOLs with surface deposits. MemoryLens (N=20). Age of patients at implantation 73.13±11.32 years. Time to explantation = 30.00 ± 5.16 months SC60B-OUV (N=10). Age of patients at implantation 72.75±17.75 years. Time to explantation = 20.22 ± 11.02 months Aqua-Sense (N=10) Age of patients at implantation 67.91±17.61 years Time to explantation = 16.27 ± 6.45 months

Intervention	20 explanted IOLs with surface deposits (MemoryLens) 10 explanted IOLs with deposits mostly within their optic substance –central optic area with clear optic edge and clear haptics (SC60B-OUV) 10 explanted IOLs with deposits mostly within their optic substance and haptic components of the lens and on the surface (Aqua-Sense)
Comparison	Lens explanted because of reasons other than optic opacification were also prepared and and analysed for SEM and EDS. Poly (methy methacrylate) (PMMA), N=3, hydrophobic acrylic, N=3, and silicone, N=4.
Length of follow up	
Outcome measures / Effect size	Scanning electron microscopy (SEM) coupled with EDS confirmed that the composition of the deposits was calcium/phosphate in all cases. The element silicon was found in all 40 lenses, on all areas analysed. The silicon weight percentage was higher at the level of the deposits. The presence of aluminum on five MemoryLens IOLs and in most SC60B-OUV and Aqua-Sense lenses might be related to scattering from the aluminum mounting stubs used for surface analyses. SEM coupled with EDS analyses of the control lenses showed the presence of the element silicon on the external surface of only one PMMA lens (weight percentage=0.18). The element silicon was not found on or within the hydrophobic acrylic lenses. The presence of element aluminum was not found in analyses of rigid PMMA lenses. This was associated with foldable lenses, which had been sectioned for analysis of the internal optic surface of cylindrical blocks. Aluminum was found on the external and internal surfaces of three silicone lenses, and on the internal surface of three AcrySof lenses. **Authors conclusions** Silicon compounds have been implicated in the calcification of another hydrophilic acrylic design (Hydroview). They may also have a role in the calcification of other hydrophilic acrylic IOLs. Further investigation on the relationship between the presence of the element silicon and the silicon compounds found on calcified hydrophilic acrylic lenses is necessary.
General Comments	

Evidence Table : Safety
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Bibliographic Citation	10. Neuhan IM, Neuhann TF, Szurman P *et al.* Clinicopathological correlation of 3 patterns of calcification in a hydrophilic acrylic intraocular lens. J Cataract Refract Surg. 2009;35(3):593-7
Study Type / Methodology	Case reports Aim of study was to present 3 cases of opacification in the Biocomfold 92S intraocular lens (IOL) with documented increase in the opacification overtime in 1 case. The explanted lenses were subjected to exhaustive study involving photographic analysis, scanning electron microscopy, and energy dispersive X-ray spectroscopy.
LE	III
Number of patients and patient characteristics	3 cases Case 1. 73 year old woman Cataract surgery Right eye in 2001. Developed IOL opacification and explanted in 2007. Case 2 78 year old woman. Cataract surgery in Right eye in 1999 and left eye in 2001. Developed IOL opacification in left eye and explanted in 2007. Case 3 74 year old woman Cataract surgery in Rt eye in March 2001 and left eye in January 2001. Developed IOL opacification in Right eye and explanted in 2008 Has history of ischaemic heart disease
Intervention	Hydrophilic acrylic (Biocomfold 92S intraocular lens)
Comparison	
Length of follow up	
Outcome measures / Effect size	Histopathological analysis revealed the opacification was caused by calcification in the IOL's optic material. The pattern of calcium deposition, however, was different in each IOL. The causative mechanisms for this complication are unclear. Further research is warranted. Case 1 IOL. Deposits were located in 2 non continuous parallel lines (ie, exhibiting gaps) beneath the anterior and posterior optic surface. The haptics were free of deposits. Case 2 IOL. The granules were located beneath the optic's anterior surfaces in the central optic region; the peripheral option region and the haptics were free of deposits. Case 3 IOL. A fine line of deposits was located just beneath the anterior and posterior surfaces of the entire optic and haptics. **Authors conclusions** We report three particular opacification patterns of the Biocomfold 92S IOL due to calcification. The possible mechanisms leading to this complication are not fully understood at this time and warrant further research.
General Comments	

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Question : Do Hydrophilic acrylic IOLs or Hydrophobic acrylic IOLs prone to IOL opacification?

Bibliographic Citation	11. Kim CJ, Choi SK. Analysis of aqueous humour calcium and phosphate from cataract eyes with and without Diabetes Mellitus. Korean Journal of Ophthalmology. 2007;21(2):90-94
Study Type / Methodology	Cross sectional study Aim of the study was to compare levels of calcium and phosphorus in the aqueous humour and serum of non-diabetics and diabetics to investigate the basis for the increased incidence of late opacification of hydrophilic acrylic intraocular lenses in diabetic patients. Patients who had undergone phacoemulsification with IOL implantation between Oct 23, 2003 and Feb 23, 2005 at Seoul Veterans Hospital. Only senile cataract patients without prior intraocular surgery or history of complications like glaucoma or uveitis were enrolled. They divided the patients into two groups:- -76 non-diabetic cataract patients -52 diabetic cataract patients Diabetic group was divided into 3 subgroups:- - 26 patients with no diabetic retinopathy - 13 patients with non-proliferative diabetic retinopathy - 13 patients with proliferative diabetic retinopathy The authors compared the levels of calcium and phosphorus in the serum and aqueous humour of cataract patients.
LE	II-3
Number of patients and patient characteristics	128 patients Average age was 68 years old (51-84 years old). 106 males 22 females
Intervention	Hydrophilic acrylic
Comparison	
Length of follow up	
Outcome measures / Effect size	In serum, neither calcium nor phosphorus differed significantly between diabetics and non-diabetics (serum calcium, P=0.253, serum phosphorus, P=0.34) In aqueous humour, the mean value of phosphorus was significantly higher in diabetics than in non-diabetics (2.19±0.47 mg/dl, P=0.002). No significant difference between calcium levels in diabetics and non-diabetics, P=0.19. When non-diabetics were compared to the three diabetic subgroups, calcium levels did not differ in serum or aqueous humour, but the phosphorus levels in diabetics with proliferative diabetic retinopathy were significantly higher than those in non-diabetics, diabetics without diabetic retinopathy, and diabetics with non-proliferative diabetic retinopathy. **Author conclusions** The level of phosphorus in the aqueous humour and serum of diabetics was significantly increased, especially in diabetics with proliferative diabetic retinopathy. This result may be related to hydrophilic acrylic IOL opacification. Future studies regarding the pathogenic role of a high concentration of aqueous humour and serum phosphorus are required.
General Comments	

Evidence Table : Safety
Question : Do Hydrophilic acrylic IOLs or Hydrophobic acrylic IOLs prone to IOL opacification?

Bibliographic Citation	12. Nakome S, Watanabe H, Tanaka K *et al.* Calcification of Hydroview H60M intraocular lenses: Aqueous humor analysis and comparisons with other intraocular lens materials. J Cataract Refract Surg. 2008;34:80-86
Study Type / Methodology	Experimental (Laboratory study) Aim of study was to compare the level of calcification on Hydroview H60M hydrophilic acrylic intraocular lenses (IOLs)(Bausch & Lomb) and other IOL materials. The study was conducted in Omori Medical Centre, Department of Ophthalmology, Toho University, Tokyo, Japan. The levels of calcification on Hydroview H60M hydrophilic acrylic IOLs, AcrySof SA60AT hydrophobic acrylic IOLs (Alcon Surgical, Inc), Sensar AR 40e hydrophobic acrylic IOLs (Advanced Medical Optics), Clariflex (Advanced Medical Optics) silicone IOLs, and MeniFlex ENV13 (Menicon) poly(methyl methacrylate) IOLs were compared in calcium phosphate solution containing albumin. In a concentration-change experiment, the calcium and phosphate concentration levels were changed and the results observed by scanning electron microscopy.
LE	III
Number of patients and patient characteristics	
Intervention	Hydroview H60M hydrophilic acrylic IOLs
Comparison	AcrySof SA60AT hydrophobic acrylic IOLs (Alcon Surgical, Inc), Sensar AR 40e hydrophobic acrylic IOLs (Advanced Medical Optics), Clariflex (Advanced Medical Optics) silicone IOLs, and MeniFlex ENV13 (Menicon) poly(methyl methacrylate) IOLs
Length of follow up	
Outcome measures / Effect size	The Hydroview H60M IOL had the largest amount of deposits. Small amount of deposits were found on the other IOLs in the following decreasing order: AcrySof SA60AT, Sensar AR40e, ClariFlex, and MeniFlex ENV13. The amount of deposits on the Hydroview H60M IOLs was statistically significantly greater than the amount on the other IOLs ($p<0.01$). **Authors conclusions** The hydrophilic acrylic IOLs (Hydroview H60M) had significantly higher amounts of calcified deposits than IOLs of other materials, indicating that hydrophilic acrylic IOLs easily accumulate calcified deposits in the body when the concentrations of calcium, phosphate, and albumin in the aqueous humour fluctuate as a result of a blood-aqueous barrier breakdown.
General Comments	

Evidence Table : Safety
Question : Do Hydrophilic acrylic IOLs or Hydrophobic acrylic IOLs prone to IOL opacification?

Bibliographic Citation	13. Mattova J, Bhacova E, Murgasova Z *et al.* Opacification of hydrophilic MemoryLens U940A intraocular lenses: analysis of 2 explanted lenses. J Cataract Refractive Surg. 2004;30(9):1934-9.
Study Type / Methodology	Cross sectional study Aim of study was to determine the rate of opacification of hydrophilic MemoryLens U940A intraolcular lenses (Mentor Opthalmics, Inc) in the given cohort and perform a histopathological and spectrophotometer analysis of 2 explanted opacified IOLs. The study was conducted at the Ophthalmology department, Faculty Hospital, Nitra, Slovakia. The 182 patients (205 eyes) were examined using a slitlamp to detect the presence of IOL opacification. In 4 cases the lens were explanted because of significant opacification and patient-related problems; 2 lenses were provided for further analysis. All IOLs were stained with the von Kossa to determine the presence of calcium in the opacification. To confirm the components presence of an ultraviolet (UV) absorber, the IOLs were examined with Avatar 330 Fourier transfer infrared spectroscope and a UV visible spectrophotometer. The IOLs and the IOL packaging were examined to determine the presence of silicone.
LE	II-3
Number of patients and patient characteristics	182 patients (205 eyes) who had implantation of a MemoryLens U940A IOL from June 1997 to June 2000.
Intervention	Hydrophilic acrlylic -MemoryLens U940A intraolcular lenses (Mentor Opthalmics, Inc) 2 explanted lenses were further analysed
Comparison	One unused MemoryLens (reference IOL)
Length of follow up	
Outcome measures / Effect size	Various amounts of opacification were found in MemoryLens U940A IOL in 30 eyes (14.63%). Two explanted IOLs were positive for calcium deposits; the reference lens staining was negative. Spectrophotometry showed that the reference IOL and the opacified IOLs were of the same polymer. The presence of the UV absorber on the benzophenone base was seen in the reference lens but not on the opacified IOLs. In contrast, increased concentration of low-molecular-weight components generated during degradation of the polymer was present in the opacified IOLs. The white cover of the IOL is of polydimethyl siloxane, a silicone rubber. However, no silicone rubber was present in any examined lens. **Author conclusions** The results indicate opacification of the hydrophilic MemoryLens U940A was caused by premature consumption of the UV absorber in the polymer component of the IOLs optic, with a subsequent degradation of the polymer. Whether silicone from the white cover led to the IOL opacification, as reported with the other types of hydrophilic acrylic IOLs, could not be confirmed.
General Comments	

Evidence Table : Safety
Question : Do Hydrophilic acrylic IOLs or Hydrophobic acrylic IOLs prone to IOL opacification?

Bibliographic Citation	14. Waite A, Faulkner N, Olson RJ. Glistenings in the single-piece, Hydrophobic, acrylic intraocular lenses. American Journal of Ophthalmology.2007; 144(1):143-144
Study Type / Methodology	Cross sectional study Aim of study was to study glistening in single-piece AcrySof (models SA60 and SN60; Alcon, Fort Worth, Texas, USA) IOLs. Patients with single-piece IOLs (models SA60 and SN60; Alcon) implanted 12, 24, or 36 months earlier were studied. Ten patients were enrolled for each group. Exclusion criteria; Capsular opacification, glaucoma, or macular pathologic features. Best-corrected logarithm of the minimum angle of resolution visual acuity, glare testing, contrast sensitivity, and wavefront analysis were performed. All IOLs were photographed, and glistening were analysed for size, and density by a computer programme.
LE	II-3
Number of patients and patient characteristics	53 IOLs in 32 patients. -18 males and 14 females
Intervention	Hydrophobic acrylic single-piece AcrySof (models SA60 and SN60)
Comparison	
Length of follow up	
Outcome measures / Effect size	All IOLs had glistenings, and neither size, density, nor severity index (size and density) correlated with visual acuity, glare testing or wavefront analysis results. High spatial resolution contrast acuity had a borderline correlation with severity index (P=0.06), as did progress over time (P=0.04). **Author conclusions** All IOLs studied had glistening. High spatial resolution contrast sensitivity impact and severity progression over time deserve further study.
General Comments	

Evidence Table : Safety
Question : Do Hydrophilic acrylic IOLs or Hydrophobic acrylic IOLs prone to IOL opacification?

Bibliographic Citation	15. Iwase T, Sugiyama K. Early opacification of a single-piece hydrophobic acrylic intraocular lens after triple procedure. J Cataract Refract Surg. 2007 Feb; 33(2):329-332
Study Type / Methodology	Case report Patient had triple procedure of vitrectomy, phacoemulsification, and IOL implantation for cataract and a dense vitreous haemorrhage in the left eye.
LE	III
Number of patients and patient characteristics	1 patient, 64 years old man
Intervention	Hydrophobic acrylic single-piece AcrySof (models SA60T, Alcon)
Comparison	
Length of follow up	
Outcome measures / Effect size	The IOL was clear on the day after surgery, but by the third day, a dusty haze was observed on the surface due to the presence of numerous, small brown corpuscles. Analysis of the explanted IOL indicated the presence of proteinaceous material but there was no calcium on the surface of the lens. **Author conclusions** Early post-operative opacification of the single-piece hydrophobic acrylic SA60AT IOL might occur in combined cataract and vitreous surgery, even in eyes in which the posterior capsule is intact and there is no operative complication.
General Comments	

APPENDIX 4

LIST OF EXCLUDED STUDIES

1. Kim SM, Choi S. Clinical efficacy and complications of intraolcular lens exchange for opacified intraocular lenses. *Korean Journal of Ophthalmology.*2008; 22:228-235

2. Lee SJ, Sun HJ, Choi KS *et al*. Intraocular lens exchange with the removal of the optic only. *J Cataract Refract Surg*. 2009;35:514-518