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ORIGINAL PAPER

Secondary membrane formation after cataract surgery with primary intraocular lens implantation in children

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Abstract To evaluate the risk factors for secondary membrane (SM) formation after congenital cataract surgery with intraocular lens (IOL) implantation. A retrospective non-interventional comparative study. Thirty-nine patients (63 eyes) aged 1–135 months. The study included patients who underwent cataract extraction and primary IOL implantation between 1994 and 2001 at the University Hospital. The postoperative follow-up was 6–24 months. Thirty-three eyes received a poly(methyl methacrylate) (PMMA) IOL without square edges, 29 eyes received a hydrophobic acrylic IOL with truncated square edges (AcrySof), and there was no data for IOL type in one eye. Thirty-nine eyes had primary posterior capsulotomy (PPC) and anterior vitrectomy (AV) and in 24 eyes the posterior capsule was left intact. Cox proportional hazard regression analysis was performed to identify significant risk factors for SM formation, and Wilcoxon test to evaluate the difference in time from surgery to SM formation. SM developed in 24 eyes (38 %)—58 % of eyes with an intact posterior capsule and 26 % of eyes having PPC and AV, 42 % of eyes with a PMMA IOL, and 34 % of eyes with an AcrySof lens. In multivariate Cox regression analysis intraoperative PPC and AV ($P = 0.02$) and AcrySof lens implantation ($P = 0.097$) were associated with decreased postoperative incidence of SM formation. Median time until SM development was 2.9 months with PMMA IOLs (range 1–17 months) and 6 months with AcrySof lenses (range 1–21.8 months) ($P = 0.037$). Posterior capsule management as well as IOL design and material influence the incidence and the timing of SM formation after primary IOL implantation in children.

Keywords Cataract · Cataract surgery · Intraocular lens · Secondary membrane formation

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Introduction

Posterior chamber intraocular lens (IOL) implantation in children has become a more common and accepted procedure in pediatric patients; however, IOL implantation in children is associated with high postoperative complications compared to adults. Posterior capsule opacification (PCO) or secondary membrane (SM) is the most frequent problem following congenital cataract surgery [1]. The primary purpose of this surgery is to remove lens opacities in order to produce a clear visual pathway, so as to prevent deprivation amblyopia. Therefore, PCO in the pediatric population is a significant complication which may prevent postoperative vision rehabilitation.

Several factors such as patient age [2–5], primary IOL implantation [3], the type of IOL used [6, 7], and patient gender [8] were evaluated for their influence on PCO incidence after cataract surgery.

Moreover, it has been suggested that performing primary posterior capsulotomy (PPC) and anterior vitrectomy (AV) during pediatric cataract surgery may decrease the incidence of postoperative SMs [3, 4, 7]. However, PPC does not guarantee a clear visual pathway as the membranes may grow on the posterior hyaloid face (in the absence of AV), or along the anterior vitreous surface (after limited AV) [3]. Whatever the exact anatomical location of the membranes, they result from same pathological processes—proliferation, metaplasia and migration of lens epithelial cells, causing visual axis obscuration.

To our knowledge, there are few reports in children using multivariate analysis to study the effect of different factors on this pathology [3]. The purpose of this study was to evaluate the influence of different variables on the incidence and the timing of SM formation in children after cataract surgery with IOL implantation.

Methods

The study was approved by the appropriate ethics committee and performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Informed consent was not necessary for this retrospective study.

In the period between 1994 and 2001, 45 children underwent congenital cataract extraction and implantation of a posterior IOL, using one of two different techniques.

Patients were excluded if they had anterior segment pathology besides cataract, if they had systemic abnormalities or in cases where 6-month follow-up was not available. Therefore, two patients with trisomy 21 were excluded from the study, as well as four other patients whose postoperative data was missing—one passed away soon after surgery and three failed to attend 6-month postoperative clinical appointments. Consequently, 63 eyes of 39 children were included in the study. All patients underwent extracapsular cataract extraction and IOL implantation. Two types of surgical incisions were used. Common to all techniques was the following procedure—two paracentesis ports were opened at the limbus at 2 and 10 o'clock. An anterior chamber maintainer (Visitec, Warwickshire, UK) was used and capsulorhexis was performed with a bent 25-gauge needle. Lens material was aspirated with an Anis aspirating cannula (Storz, St. Louis, MO, USA). The corneal incision was closed with interrupted 10/0 Mersilene sutures (Ethicon, Edinburgh, UK).

In 33 eyes, undergoing surgery between 1994 and 1998, the following modifications were performed—a scleral groove was created 2 mm from the limbus with a no. 64 Beaver blade, a scleral pocket was constructed with a crescent knife (Alcon, Forth Worth, TX, USA), and dissection was extended for 1 mm into the clear cornea. Using a 3.6-mm keratome (Visitec), the anterior chamber was entered through the scleral tunnel, and a 6.0-mm optic, single-piece poly(methyl methacrylate) (PMMA) IOL without square edges (Hanita Lenses, Kibbutz Hanita, Israel) was implanted. In 29 eyes, undergoing surgery between 1998 and 2001, the cornea was entered at the 12 o'clock meridian just anterior to the terminal ends of the conjunctival blood vessels as they cross the limbus, and a 6.0-mm optic three-piece foldable hydrophobic acrylic IOL with truncated square edges (AcrySof; Alcon) was implanted. The data regarding IOL type was missing in one eye.

primary posterior capsulotomy and AV were performed in 39 eyes with an occutome (CooperVision, Irvine, CA, USA) and in 24 eyes the posterior capsule was left intact.

All operations were performed by the same surgeon (AS), using the same surgical technique, modified as described for each group. All patients were treated postoperatively with dexamethasone and neomycin eye drops, applied six times a day for 1 week and then four times a day for two additional weeks plus 0.5 % tropicamide twice a day for 2 weeks.

Postoperatively, the clearance of the visual axis of the operated eye was evaluated (as part of a complete eye examination). The time of onset of SM formation was recorded as well as the age of the patient at which the ophthalmologist first recognized the opacity.

Statistical analyses were performed using SAS (Statistical Analysis Software) version 9.1. A backward-stepwise Cox proportional hazard regression analysis was used to evaluate factors related to SM formation. Parameters studied were sex, age at surgery (months), laterality (right versus left), type of cataract (complete versus incomplete), whether the cataract was familial, associated persistent hyperplastic primary vitreous (PHPV), management of the posterior capsule (intact capsule vs PPC with AV) and IOL type. Before running the multivariate analysis, the association between each independent variable and the clinical outcome (presence or absence of secondary membrane) was estimated by means of univariate Cox proportional hazard regression analysis. Variables associated with the clinical outcome at a maximum of 20 % significance in the unilateral analysis as well as those believed from previous studies to affect the rate of SM formation were included in the backward-stepwise Cox proportional hazard regression analysis.

The Wilcoxon test was used to compare the difference in time from surgery to SM formation between different groups.

P-values < 0.05 were considered significant.

Results

Sixty-three cases were included in this study. The median age at cataract surgery was 42 months (range 1–135 months), and the median follow-up was 15 months (range 6–24 months).

Secondary membrane developed in 24 eyes (38 %) between 1 week and 21.8 months postoperatively (median 4.5 months). It occurred in 14 eyes (58 %) with an intact posterior capsule and in 10 eyes (26 %) having PPC and AV. It was diagnosed a median of 6 months (range 0.5 week–21.8 months) after surgery in eyes with intact capsule, and 2.9 months (range 1 week–10 months) in eyes that had PPC and AV ($P = 0.14$). The complication was observed in 14 eyes (42 %) with a PMMA IOL and in 10 eyes (34 %) with an AcrySof lens. It was diagnosed a median of 2.9 months (range 1 week–17 months) after surgery in eyes with a PMMA IOL and 6 months (range 1–21.8 months) in eyes with an AcrySof lens ($P = 0.037$).

Of the 24 eyes with a SM, 22 were treated with neodymium:YAG (Nd:YAG) laser capsulotomy, and one eye had secondary membranectomy with anterior vitrectomy. A recurrence of the membrane that required additional treatment with laser was observed in eight eyes.

Using univariate Cox regression analysis the method using posterior capsule management was found to significantly affect the probability of SM formation ($P = 0.04$). In contrast, other variables including sex, age at surgery and IOL type did not influence the probability of this complication ($P > 0.05$). Table 1 shows the characteristics of patients with and without SM formation and the results of the univariate analysis. Figure 1 presents a Kaplan–Meier survival plot by posterior capsule management, showing a significant difference in the probability of survival (not developing SM) between eyes with an intact posterior capsule and those with PPC and AV. Figure 2 shows a Kaplan–Meier survival curve by IOL type, demonstrating an insignificant difference in survival probability between eyes with an AcrySof IOL and those with a PMMA lens.

A backward-stepwise multivariate Cox proportional hazard regression analysis was used to evaluate the independent effect of different risk factors on the probability of SM formation (Table 2). The following factors were examined—sex, age at surgery, method of posterior capsule management and IOL type. The method of posterior capsule management was found to be a statistically significant independent risk factor ($P = 0.02$). When relative risks were analyzed according to the group having PPC and AV, the presence of an intact capsule increased the probability of the complication by 2.73-fold. Moreover, a trend was found for the effect of IOL type ($P = 0.097$), and when relative risks were examined according to the group with AcrySof IOLs, having a PMMA IOL increased the risk of membrane formation by 2.07-fold. On the other hand, sex and age at surgery were not found to influence the probability of SM formation ($P > 0.2$).

Discussion

While primary implantation of an IOL has become an increasingly common and accepted procedure in pediatric cataract surgery, it is associated with SM formation [3] that may result in deprivation amblyopia and consequently jeopardize visual rehabilitation after surgery. Despite being influenced by several factors, to our knowledge, there are few reports [3] analyzing the independent effect of the different factors on the probability of this complication in children by multivariate analysis. Using such a method, our study shows

Table 1 Univariate Cox regression analysis of the risk factors for SM formation after primary IOL implantation in children

Factor		Eyes with SM ($n = 24$, 38 %)	Eyes without SM ($n = 39$, 62 %)	HR (95 % CI)	*P* value
Sex, *n* (%)	Male	13 (42 %)	18 (58 %)	0.84 (0.37–1.90)	0.67
	Female	11 (34 %)	21 (66 %)		
Age at surgery, mean ± S.D (months)		51.8 ± 43.8	39.9 ± 32.2	1.01 (0.99–1.02)	0.20
Laterality, *n* (%)	Right	10 (32 %)	21 (68 %)	0.61 (0.27–1.42)	0.25
	Left	14 (44 %)	18 (56 %)		
Familial cataract, *n* (%)	Yes	9 (35 %)	17 (65 %)	0.82 (0.35–1.88)	0.63
	No	15 (41 %)	22 (59 %)		
PHPV, *n* (%)	Yes	1 (20 %)	4 (80 %)	0.47 (0.06–3.47)	0.46
	No	23 (40 %)	35 (60 %)		
PC Management, *n* (%)	Intact PC	14 (58 %)	10 (42 %)	2.36 (1.03–5.40)	0.04
	PPC + AV	10 (26 %)	29 (74 %)		
IOL type, *n* (%)[a]	PMMA	14 (42 %)	19 (58 %)	1.64 (0.71–3.79)	0.25
	AcrySof	10 (34 %)	19 (66 %)		

SM secondary membrane, *HR* hazard ratio, *CI* confidence interval, *PHPV* persistent hyperplastic primary vitreous, *PC* posterior capsule, *PPC* primary posterior capsulotomy, *AV* anterior vitrectomy, *PMMA* poly(methyl methacrylate)

[a] Missing data of IOL type (one case)

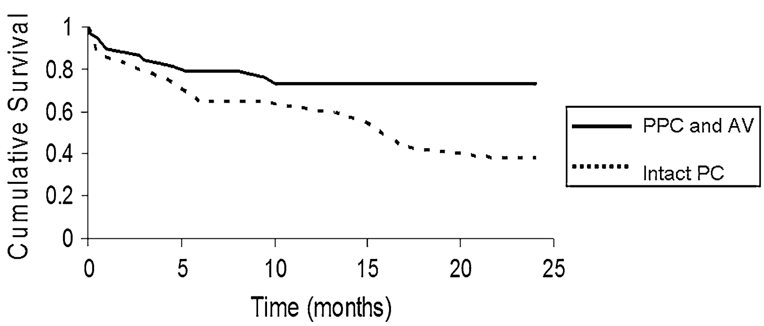

Fig. 1 Kaplan–Meier survival plot by posterior capsule management. There was a significant difference in the probability of survival (not developing SM) between the intact posterior capsule (Intact PC) group and the primary posterior capsulotomy and anterior vitrectomy (PPC and AV) group ($P = 0.04$, univariate Cox regression analysis)

that both posterior capsule management and the type of the IOL implanted during pediatric cataract surgery may influence the risk of postoperative SM formation. Furthermore, these factors may affect the postoperative timing of the development of this complication.

In our case series, posterior capsule management was the most significant predictor of SM formation; the complication was observed in 58 % of eyes with an intact posterior capsule, as opposed to 26 % of the eyes having PPC with AV (Table 1, Fig. 1). Moreover, using multivariate analysis, posterior capsule management was found to have a significant independent effect on the probability of SM formation ($P = 0.02$; Table 2).

A similar effect was demonstrated by Hosal et al. [3] in a case series mostly composed of aphakic eyes; SMs were found in 22.5 % of eyes with combined PPC and AV, and in 78.6 % with an intact capsule. Ram et al. [7] further established this finding in pseudophakic eyes; 16 % of eyes with PPC and AV developed SMs, as opposed to 78 % with an intact capsule. An even more significant effect was found by Vasavada et al. [9] in a prospective study of pseudophakic children >2 years; the complication was found in 6.7 % of eyes with PPC and AV, as opposed to 83.8 % with an intact capsule. The same authors [3, 9] also compared SM rates following PPC performed with and without AV, and found a decreased incidence

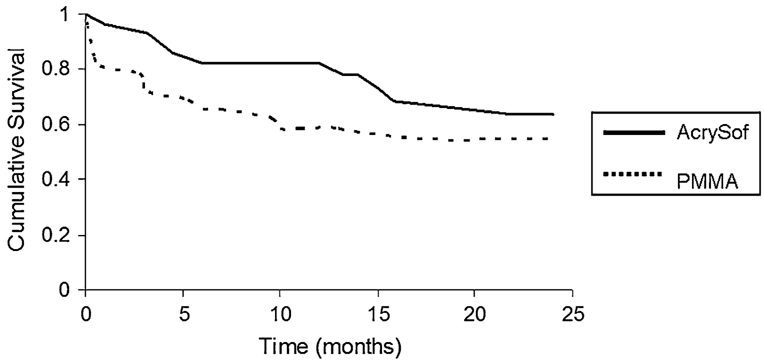

Fig. 2 Kaplan–Meier survival plot by IOL type. There was no significant difference in the probability of survival (not developing SM) between the poly(methyl methacrylate) IOL without square edges (PMMA) group and the group with an hydrophobic acrylic IOL with truncated square edges (AcrySof) ($P = 0.25$, univariate Cox regression analysis)

Table 2 Multivariate Cox regression analysis of the risk factors for SM formation after primary IOL implantation in children

Factor		HR (95 % CI)	*P*-value
PC management	Intact PC	2.73 (1.17–6.37)	0.020
	PPC + AV	1.0 (reference)	
IOL type[a]	PMMA	2.07 (0.88–4.90)	0.097
	AcySof	1.0 (reference)	

HR hazard ratio, *CI* confidence interval, *PC* posterior capsule, *PPC* primary posterior capsulotomy, *AV* anterior vitrectomy, *PMMA* poly(methyl methacrylate)

[a] Missing data of IOL type (one case)

of the complication when AV was added. Evaluation of the effect of PPC without AV was not possible in our study, since we had no patients receiving only PPC.

Earlier reports [1, 9] showed that SMs developed in all eyes of young children when PPC and AV were not performed during cataract surgery. Therefore, in our study PPC and AV were included in all surgeries of young patients. This high correlation existing between posterior capsule management and patient age may explain the insignificant association between patient age at surgery and SM formation in this study unlike former studies, showing that the younger the child, the higher the incidence of this complication [2–5].

In our study, posterior capsule management also influenced the timing of SM formation after surgery. Eyes with an intact capsule developed SM throughout the 24-month follow-up period. In contrast, eyes having PPC with AV acquired it only during the first 10 months after surgery. Therefore, patients in the PPC with AV group who have clear visual axis for 10 months after surgery can be reassured regarding their low probability of developing the complication in the future.

We could not find a statistically significant difference in the effect of IOL type on the risk of SM formation. However, our results suggest that compared to the PMMA lens without square edges, AcrySof IOLs may have a protective effect of reducing the incidence of SM formation (Table 1; Fig. 2). This non-statistically significant trend was confirmed using multivariate analysis ($P = 0.097$; Table 2). A former study in adults [6] showed reduced risk of postoperative PCO in eyes receiving an AcrySof IOL compared to a PMMA lens, which may result from the difference in the IOL material type and optic design. On the other hand, Ram et al. [7] could not find a similar effect of IOL type in children. Therefore, further research is required to clarify the relationship between IOL type and SM formation.

In addition, we found that the postoperative development of SM was delayed with an AcrySof IOL compared with a PMMA lens without square edges ($P = 0.037$; Fig. 2). A similar effect was found by Ram et al. [7]. This finding is important especially in children for two reasons. Firstly, in adults, a few months of delay in development of the SM does not affect the final visual acuity, whereas in children the younger the child when the complication develops, the higher the risk of deprivation amblyopia. Secondly, when the complication is diagnosed and requires intervention, the younger the child, the lower the possibility for his cooperation with laser capsulotomy, obviating the need for general anesthesia during surgery, which may expose him to severe adverse effects.

Using multivariate analysis, Hosal et al. [3] also evaluated the risk factors for SM formation after cataract surgery in children. In their study the complication was associated with an intact posterior capsule, the presence of a primary IOL and young age. However, only 19 eyes out of the 190 included in that study had a primary IOL, and consequently, risk factors for SM formation in pseudophakic eyes could not be separately analyzed owing to the small case number in this subgroup. Moreover, of the 19 eyes with primary IOL implantation, 18 received the same PMMA IOL, and therefore the effect of different IOL type was not evaluated.

In conclusion, our results suggest that intraoperative management of the posterior capsule influences the incidence of SM development after pediatric cataract surgery with IOL implantation. In addition, development of SM was delayed with an AcrySof IOL compared to a PMMA lens. Furthermore, while in eyes with an intact capsule, the complication developed throughout the 24-month postoperative period, in those having PPC and AV it was acquired only during the first 10 postoperative months. However, since none of these factors could completely eliminate SM formation in pseudophakic children, repeated postoperative evaluations are required in order to diagnose and treat this complication as soon as possible to prevent deprivation amblyopia.

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Conflict of interest The authors don't have any commercial concern in this study that can cause a conflict of interest, and don't have any financial relationship with the organization that sponsored the research.

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