(31) Glistening phenomenon in acrylic hydrophobic intraocular lenses — how do perioperative factors and concomitant diseases effect it's incidence and severity

Zjawisko "glistening" w sztucznych akrylowych hydrofobowych soczewkach wewnątrzgałkowych – jak na częstość jego występowania i nasilenie wpływają czynniki okołooperacyjne i choroby mu towarzyszące

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Abstract: The aim: To evaluate the effect of selected perioperative factors and concomitant diseases on glistening of acrylic hydrophobic intraocular lens after phacoemulsification in a prospective study.

Material and methods: 252 consecutive patients undergoing phacoemulsification with IOLs AcrySof IQ implantation were enrolled. The relationship between glistening and such factors as time of the surgery, the mean power and time of ultrasound energy, temperature of infusion fluids, type of cartridge, mean power of intraocular lens, trypan blue staining as well as some concomitant systemic and local diseases were analysed. The aforementioned factors were assessed a month 1. and 6. as well as after 1 and 2 years postoperatively.

Results: Glistening incidence and severity increased significantly at each follow up. The use of cartridge D during intraocular lens implantation was related with significantly higher incidence of glistening as compared to using cartridge C. Higher refractive power of intraocular lens was related with increased incidence of glistening. Significantly higher intensity of the glistening was assessed in patients who suffered from diabetes. In turn, patients with uveitis presented with statistically lower severity of glistening. There was no association between other analysed factors and glistening.

Conclusion: Glistening commonly occurs in patients after phacoemulsification and acrylic hydrophobic intraocular lenses (Acry-Sof Alcon Labs) implantation. Some intraoperative factors such as refractive power of the lens and smaller diameter of the cartridge were assessed to be significantly correlated. It might indicate that potential damage to the intraocular lens may play a role in development of glistening. Significantly higher severity of glistening was shown in patients with diabetes, which may imply the role of breakdown of physiological intraocular barriers. It is further supported by the demonstrated lower intensity of glistening in patients uveitis receiving high intensity steroid therapy.

Key words: Abstrakt:

Cel pracy: ocena, jak po zabiegu fakoemulsyfikacji na występowanie zjawiska "glisteningu" w sztucznych akrylowych soczewkach wewnątrzgałkowych AcrySof wpływają niektóre czynniki okołooperacyjne i choroby wspólistniejące.

Materiał i metody: zbadano 252 chorych poddanych fakoemulsyfikacji z wszczepieniem sztucznej akrylowej soczewki wewnątrzgalkowej AcrySof IQ. Stopień zaawansowania zjawiska "glistening" był oceniany wg skali Christiansen w kolejnych badaniach kontrolnych przeprowadzanych po 1 miesiącu, 6 miesiącach, 1 roku i 2 latach od operacji. Określano zależność "glistening" od czynników śródoperacyjnych takich jak czas trwania zabiegu, moc i czas użytych ultradźwięków, temperatura stosowanych plynów infuzyjnych, typ kartridża i barwienie błękitem trypanu oraz od wspólistniejących ze zjawiskiem "glistening" schorzeń ogólnoustrojowych i miejscowych.

Wyniki: w kolejnych okresach pooperacyjnych obserwowano stały znamienny statystycznie wzrost zarówno częstości występowania zjawiska "glistening", jak i stopnia jego nasilenia. Istotnie wyższy stopień zaawansowania zjawiska "glistening" obserwowano u chorych na cukrzycę, istotnie niższy natomiast u pacjentów po przebytym zapaleniu blony naczyniowej. Analiza wpływu czynników śródoperacyjnych wykazała związek między rodzajem użytego kartridża oraz mocą soczewki refrakcyjnej a występowaniem zjawiska "glistening". Analiza pozostałych badanych czynników nie wykazała ich związku z występowaniem tego zjawiska.

Wnioski: zjawisko "glistening" występuje powszechnie u pacjentów poddanych fakoemulsyfikacji z wszczepieniem sztucznej akrylowej hydrofobowej soczewki wewnątrzgałkowej (AcrySof, AlconLabs). Niektóre czynniki śródoperacyjne takie jak siła refrakcyjna soczewki i mniejszy wymiar kartridża istotnie wpływają na powstawanie tego zjawiska. To może wskazywać na uszkodzenie sztucznej soczewki, które może być czynnikiem ryzyka. Istotnie zwiększona intensywność zjawiska "glistening" u chorujących na cukrzycę może sugerować, że na proces jego powstawania na wpływ załamanie bariery naczyniowej. Pośrednio tę tezę potwierdza fakt, że zjawisko "glistening" u pacjentów leczonych lekami przeciwzapalnymi z powodu zapalenia błony naczyniowej jest mniej nasilone.
 Stowa kluczowe: zjawisko "glistening", akrylowe hydrofobowe soczewki wewnątrzgałkowe, fakoemulsyfikacja.

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Introduction

Cataract is currently one of the most common causes of vision decrease in subjects aged over 60 worldwide. Phacoemulsification with intraocular lens (IOL) implantation is a standard surgical approach in uncomplicated cases. Technically advanced equipment and surgeon experience have improved the rates of intraoperative and postoperative complications nowadays. Despite the use of advanced polymeric hydrophobic or hydrophilic acryl materials and cutting edge IOL technology, some late complications connected with physical and/ or chemical changes within IOL such as glistening are observed. Glistening was first described by Ballin in 1984 and defined as a presence of small crystals within the intraocular lens. Some clinical observations eventually confirmed the presence of small cystic spaces contained with fluid (microvacuoles) in the polymeric structure of IOL (Fig. 1).



Fig. 1. Glistening seen with a slit lamp in an artificial intraocular lens.Ryc. 1. Zjawisko "glistening" w sztucznych soczewkach wewnątrzgałkowych.

Although glistening is commonly observed in hydrophobic acrylic IOLs, it can be observed in all IOL materials. The number of glistening microvacuoles tends to increase in some types of IOL (1–4). Divergent data about the effect of glistening on vision in pseudophakic patients explains the need to more accurately identify factors, which influence its formation either in experimental models or in clinical setting.

Numerous studies, for istance by Miyata et al. (5), Yoshida et al. (6), Allers et al. (7) or Waile et al. (8) proved that glistening had no effect on visual acuity or contrast sensitivity. These contradict with other studies such as the one by Chritiansen et al. (9), who proved reduced visual acuity in group of patients with glistening above level 2+. Furthermore, Dhaliwali et al. (10) or Gunenc et al. (11) noticed significant influence of glistening on reduced contrast sensitivity.

Considering very high patient expectations regarding postoperative vision quality and divergent data about glistening formation (3, 8, 9, 12–19), it seems reasonable to define and evaluate factors which can help identify patients at potentially higher risk of such IOL changes. In a prospective study we assessed the effect of some perioperative factors on glistening in acrylic hydrophobic IOL.

Material and methods

294 patients were chosen randomly from among 987 patients scheduled to undergo phacoemulsification with acrylic hydrophobic IOL implantation. All patients consented to participate in the study. Cataract surgery was performed between February 2012 to December 2012. 252 patients (252 eyes), aged from 38 to 98 years (the mean age 74.5 \pm 10.62), completed the entire follow-up protocol. During the preoperative assessment, information about concomitant ocular and systemic diseases (Tab. I) and previously used medications was collected. Additionally, distant best corrected visual acuity (BCVA; Snellen) was assessed. Contrast sensitivity was evaluated using Pelli Robson charts, at the uniform illumination (from 6 to 12 cd/m²) and a distance of 1 meter from the chart and expressed as a decimal logarithm. The type and density of cataract according to the LOCS III scale was assessed after maximum mydriasis using 1% of Tropicamidum and 10% of Phenylephrine (Neosynephrin – POS). Finally, stereoscopic fundus examination was carried out with indirect ophthalmoscopy VOLK 78D. Alternatively, ultrasound scan was performed in patients with significant

	Conditions concomitant with gliste- ning/ Choroba współistniejąca ze zjawiskiem "glistening"	Patients (%)/ Pacjenci (%)
Concomitant ocular diseases/ Wspófistniejące choroby miejscowe	Glaucoma/ Jaskra	25.6
	Pseudoexfoliative syndrome/ Zespół pseudoekfoliacji	14.4
	Uveitis/ Zapalenie błony naczyniowej	9.6
	Corneal dystrophy/ Dystrofia rogówki	10.4
	Central macular degeneration/ Central- ne zwyrodnienie siatkówki	31.2
Concomitant systemic diseases/ Wspólistniejące choroby ogółnoustrojowe	Diabetes treated with oral drugs/ Cukrzyca leczona lekami doustnymi	15.6
	Diabetes treated with insulin/ Cukrzy- ca leczona insuliną	7.4
	Arterial hypertension/ Nadciśnienie tętnicze	71.5
	Coronary artery disease/ Choroba wieńcowa	45.6
	Asthma/ Astma oskrzelowa	7.2
	Malignancies/ Nowotwory	6.4
	Renal failure/ Zaburzenia nerek	6.4
	Implanted pacemaker/ Rozrusznik serca	5.6
	Myocardial infarction / Zawał serca	8.8
	Atrial fibrillation/ Migotanie przed- sionków	7.2
	Thyroid disease/ Choroba tarczycy	8.0

 Tab. I.
 Distribution of concomitant ocular and systemic diseases in study cohort.

Tab. I. Procentowy rozkład chorób współistniejących ze zjawiskiem "glistening" w badanej grupie. lens opacification. The severity of concomitant eye diseases was not taken into account for statistical analyses. In patients with history of uveitis, non-preserved 1% Dexamethason was administered once a day from one week before surgery until 1 year afterwards.

All patients underwent a planned phacoemulsification with implantation of acrylic, hydrophobic IOL SN60WF or SN6AD (Alcon Labs). The refractive power of the IOL ranged from +10.0 D to 28.5 D and were implanted using cartridge type D or C, diameter 2.2 or 2.4 mm, respectively. Infusion fluids used during operation had been stored in room temperature (22°C) or cooled to 4°C to improve stabilization of blood-aqueous barrier.

The assessed intraoperative factors included time of surgery, ultrasound power and total time, type of cartridge (D or C) and the temperature of BSS infusion 4°C vs. 22°C.

The follow up examination was performed on day 30 ± 7 , 180 ± 28 , 360 ± 32 and 720 ± 68 postoperatively.

The presence and intensity of glistening was assessed biomicroscopically with the 2 mm wide and 10 mm high slit at 25 x image magnification. Additionally, the photographic documentation of IOL was taken using Topcon Camera DC 1 and IMAGEnet i-base software version 3.12.0 Topcon. Glistening was graded using Christiansen scale (levels 0 to 4), where the presence of fewer than 10 microvacuoles was considered level 0, 20 microvacuoles level 1+, up to 30 - level 2+, and up to 40 - level 3+. Over 40 microvacuoles visible within the IOL were considered level 4 (9).

The study was approved by the Bioethical Committee at Medical University of Lodz (approval no. RNN/27/10/KB).

Statistical methods

The Shapiro-Wilk test was used to determine the normality of distribution of quantitative variables. Since distribution normality was not confirmed, the Mann-Whitney U-test was used to evaluate significance of differences between means of variables. The chi-square test or the chi-square test with Yates' correction were used to determine statistical significance of intergroup differences in qualitative variables. To evaluate correlations between quantitative variables, Spearman correlation coefficient was calculated with α = .05 and p \leq .05 considered statistically significant.

Results

At the consecutive follow up examinations we observed statistically significant steady increase of incidence and intensity of glistening. One month postoperatively, glistening was detected in 115 patients (52.3%) and its mean intensity on Christiansen scale was 1.5.

Two years postoperatively, glistening was observed in 210 patients (83.2%) and its mean intensity was 2.9 (Fig. 2).

There was no significant correlation between glistening and such intraoperative factors as surgery time ($\chi^2 = .016$), ultrasound mean power ($\chi^2 = .016$) and total time ($\chi^2 = .004$), the temperature of BSS solution ($\chi^2 = .019$) or use of trypan blue dye ($\chi^2 = .084$) (p > .05) (Fig. 3).

Increasing incidence of glistening strongly correlated with the use of D cartridge for IOL implantation (p < .05,

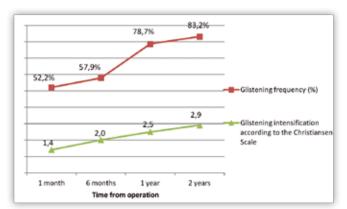


Fig. 2. Incidence of glistening (%) and its severity based on Christiansen scale in the follow up.

Ryc. 2. Częstość występowania zjawiska "glistening" (%) i jego nasilenie wg skali Christiansena w badaniach kontrolnych.

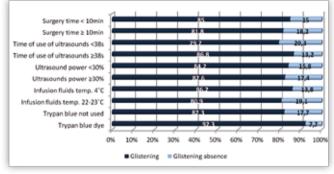


Fig. 3. Glistening incidence depending on selected intraoperative factors.

Ryc. 3. Częstość występowania zjawiska "glistening" w zależności od czynników śródoperacyjnych.

 $\chi^2 = 3.929$ Chi-square test of independence). Two years postoperatively, glistening was observed in 93% of patients after IOL implantation using D cartridge as compared to 77% of patients in whom C cartridge was used.

The statistically significant correlation was also confirmed between the incidence and severity of glistening and refractive power of the IOL (p = .00864, χ^2 = 6.896 in the chi-square test of independence). Higher refractive power of IOL was related to higher incidence and level of glistening. The mean refractive power of IOL, that is, +22.50 D, was taken as a cut-off value for later consideration. Significantly higher incidence of the glistening was observed in patients who were implanted IOLs of refractive power \geq +22.5 D (94.3%), as compared to the pseudophakic patients with IOL refractive power < 22.5 D (66.7%), p = .00118 (Z = 3.244 Mann-Whitney U-test).

Epidemiological data pointed to hypertension, coronary heart disease and type II diabetes as the most common concomitant systemic conditions (71.5%, 45.6% and 15.6%, respectively), whereas primary open angle glaucoma, secondary open angle glaucoma with pseudoexfoliation syndrome (PEX) and dry age-related macular degeneration (AMD) were the most common concomitant ocular diseases in our cohort (25.6%, 14.4% and 9.6%, respectively) (Tab. I).

Statistically significant higher intensity of glistening was observed in patients who suffered from diabetes treated with insulin as compared to group of patients treated with oral drugs, 3.86 and 2.83 degree respectively (p = .01, Z = -2.569, Mann--Whitney U-test).

Interestingly, it was found that uveitis patients had lower glistening intensity level 1.5 degree as compared to the group of patients without this concomitant disease (p=0.020165, Z=2.323 Mann-Whitney's test).

The mean preoperative BCVA and contrast sensitivity (CS) was 0.29 (\pm 0.204) and 0.567 (\pm 0.402), respectively. Post-operatively BCVA was 0.68 (\pm 0.286), 0.706 (\pm 0.272), 0.639 (\pm 0.309), 1 month, 6, 12, 24 months respectively. Two years postop. BCVA was lower 0.61 (\pm 0.289), but the its decrease was not statistically significant (Fig. 4).

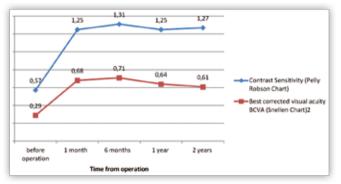


Fig. 4. Best corrected visual acuity and contrast sensitivity in the follow up.

Ryc. 4. Najlepsza skorygowana ostrość wzroku i poczucie kontrastu w badaniach kontrolnych.

The follow up CS improved significantly to 1.248 (± 0.336), 1.310 (± 0.267) 1.247 (± 0.371) and 1.267 (± 0.369), 1 month, 6, 12, 24 months respectively (Fig. 2= 4). There was no correlation between frequency as well as intensity of glistening in postoperative follow up with respect to mean value of BCVA (p > .05) and to value of the contrast sensitivity (p > .05).

Discussion

Nowadays, the majority of implanted IOLs are made of hydrophobic or hydrophilic acrylic polymer. Since its approval for clinical use by the Food and Drug Administration in 1994, the acrylic hydrophobic lens has become one of the most frequently implanted IOL worldwide. Relatively good compatibility of acrylic material, lower incidence of postoperative complications and decreased rates of posterior capsule opacification are the basic reasons behind its popularity (20-24). First data about physicochemical changes within the material of implanted acrylic IOL was reported soon after market launch (25). However, glistening in artificial IOL initially described as the presence of crystal particles in optical part of IOL was eventually identified as fluid-filled microvacuoles (10). Despite successful attempts to create an experimental model of glistening based on rapid temperature changes of the fluid surrounding IOL, the etiological factors which affect its development in a clinical setting have not been identified yet. Likewise, the effect of the glistening on pseudophakic eve function still remains unclear.

The reported prevalence of glistening in pseudophakic patients ranges from 45% to 75%. Davison at al. pointed out to the differences in the incidence of glistening occurring with postoperative time. They observed glistening in 11% of pa-

tients as early as 2 to 5 weeks after phacoemulsification (26). Moreno-Monteres reported similar results (3). Our research conducted in a significantly larger cohort confirmed the presence of glistening in 47.7% of patients at one month postoperatively, which gradually increased with time to reach 83.2% at two years postoperatively. Christiansen et al. who implanted hydrophobic IOL model MA30BA or MA60BM, observed some degree of glistening in all study subjects (n=42) at 2 years postoperatively (10). Similarly, Waite et al. found glistening in all patients (n=53) 3 years after the implantation of a single-piece AcrySof IOL (SA60, SN60) (8). In 2010, as a part of ASCRS study, Fry et al. found glistening in 94% of eyes implanted with a single-piece AcrySof hydrophobic lense (Alcon Labs) 3 years postoperatively (27).

Some reports highlight that glistening tends to stabilise after an initial rapid onset (2–4, 6). Our results support this suggestion showing that progression of glistening had decreased between 1 and 2 years after IOL implantation.

Same experimental studies proved that storing IOL in the container at higher temperature ranging from 37 degrees up to 60 followed by chilling the fluid to 23–34°C can induce glistening (5, 17, 28–31). However, using the chilled BSS during surgery did not affect glistening in our patients. While we commonly use chilled infusion fluid in our practice to improve stabilization of blood-aqueous barrier, especially in patients with higher risk of postoperative complications, including diabetes or uveitis, this information seems to be very important and practical. Considering our results, it seems reasonable to continue research whether elimination of temperature differences between infusion fluid and aqueous or even temperature of IOL before implantation decreases the incidence of glistening.

Moreno-Montenes reported the correlation between refractive power of the IOL and the incidence of glistening (3). On the contrary, Colin et al. did not confirm this association (32). We showed higher incidence of glistening in patients implanted with IOLs of refractive power higher than 22.5 D as compared to the lower refractive power. This finding can be explained by the fact that higher refractive power requires thicker optical part of IOL which potentially promotes higher compressive forces affecting IOL. The potential damage of IOL surface could have taken place during its folding or pushing by plunger and passage through the cartridge. This hypothesis is supported by the study by Tognetto et al., who highlighted a potential role of mechanical damage to the polymeric acryl fibre structure of IOL (1). Moreover, it might be supported by our own observations of more severe glistening in the central, thicker part of the IOL optic, which is more likely to be damaged during implantation.

In 1999, Mitook et al. showed a strong correlation between concomitant diabetes and incidence and severity of glistening (18). Our correlation analysis for glistening and concomitant ocular and systemic diseases gave interesting results. We proved that diabetic patients treated with insulin presented with significantly more severe glistening. Therefore, it can be assumed as suggested by some investigators that blood aqueous barrier breakdown commonly observed in diabetic patients can impact glistening formation. Collin et al. found that higher incidence and severity of glistening is associated with concomitant glaucoma (32). They observed glistening in 80.7% of treated patients with 49.1% presenting with level 3 glistening. In our research, glistening was observed more frequently in glaucoma patients as compared to subjects without glaucoma (90.8% vs. 80.7%, respectively). The difference, however, was not statistically significant.

The analysis of patients with history of uveitis provided particularly interesting findings. We found that severity and incidence of glistening in this group was lower as compared to patients without uveitis and the difference was statistically significant. Obtained results seem to be very intriguing, considering that the breakdown of blood aqueous barrier (BAB) commonly seen in active uveitis and even during remission of the disease should worsen glistening. Our results deny this hypothesis. However, patients with higher risk of complications (e.g. uveitis) are intensively treated with anti-inflammatory drugs, mostly steroids, which are known to stabilize the BAB, so this finding should not surprise.

One of the most important glistening-related problems is its effect on functional parameters of pseudophakic eye. Our data shows that although postoperative glistening increases in intensity with time, it does not significantly influence either BCVA or contrast sensitivity. Similar conclusions can be found in literature published in the last few years (5–7, 11). These contradict the results by other authors, who observed significant decrease of contrast sensitivity or visual acuity in patients with glistening (9, 10). It is impossible, though, to compare our results cannot to above studies, as patients with concomitant ocular diseases affecting visual acuity and contrast sensitivity were not excluded from statistical analysis.

The disturbed contrast sensitivity increased by glistening is particularly significant in patients with multifocal intraocular lenses, where the presence of microvacuoles may amplify light diffraction.

Conclusions

Glistening commonly occurs in patients after phacoemulsification and acrylic hydrophobic intraocular lenses (AcrySof Alcon Labs) implantation. After initial increase in severity, it stabilizes between one and two years postoperatively. A strong correlation between glistening and refractive power of implanted IOL as well as a smaller diameter of cartridge strongly support the use of bigger diameter cartridges when implanting IOLs of refractive power above 22.5 D. The lack of changes in incidence and severity of glistening after using chilled infusion solution, which is a common practice aimed at stabilising the BAB, is an important finding.

A negative correlation between the severity of glistening and uveitis treated intensively with anti-inflammatory drugs might imply the role of blood aqueous barrier breakdown in its pathogenesis. This, in turn, encourages a discussion whether patients with higher risk of blood aqueous breakdown, e.g. diabetes or uveitis, should be implanted acrylic hydrophobic IOLs in the first place.

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