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Cataract phacoemulsification and intraocular pressure in glaucoma patients

Fakoemulsyfikacja zaćmy a ciśnienie wewnątrzgałkowe u chorych z jaskrą

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Summary: Purpose: To evaluate the influence of recently performed cataract phacoemulsification in glaucomatous eyes on postoperative intraocular pressure (IOP).
Material and methods: 100 eyes of 86 glaucoma patients who underwent cataract phacoemulsification with simultaneous intraocular lens implantation, were retrospectively analyzed. The patients were divided into two groups: I – 61 patients (71 eyes) with open angle glaucoma, and II – 25 patients (29 eyes) with angle closure glaucoma. Both groups were subdivided into two subgroups, depending on presence of symptoms of pseudoexfoliation (PEX) syndrome (A = with, and B = without symptoms of PEX syndrome). All patients were examined in the department where the surgeries were performed; before surgery, on the first day after the procedure, and again during the last follow-up examinations, 6 to 30 months after the procedure.
Results: Before surgery, the intraocular pressure (IOP) was at mean value of 19.02 $\pm$ 4.55 mmHg in group I, and 20.01 $\pm$ 6.43 mmHg in group II. On the first day after surgery, the IOP was 17.42 $\pm$ 7.17 and 20.36 $\pm$ 8.98 mmHg, respectively. IOP exceeding 20 mmHg was found in 7 eyes in group I, and in 6 eyes in group II. During the last follow-up examinations the IOP was 14.59 $\pm$ 3.73 and 14.01 $\pm$ 4.50 mmHg, respectively, and was lower than measured before surgery, by an average of 4.43 mmHg in group I ($P < 1 \times 10\text{-}5$), and 6.00 mmHg in group II ($P < 1 \times 10\text{-}4$). In both groups, the reduction of IOP in patients with PEX was even more remarkable. The number of glaucoma medication necessary to control the pressure was reduced on average by 0.28 in group I, and 0.31 in group II.
Conclusions: Phacoemulsification done on glaucomatous eyes results in lowering of IOP, and hence the dosage of glaucoma drugs over the long term can be simplified or even discontinued.

Słowa kluczowe: fakoemulsyfikacja, jaskra otwartego kąta, jaskra zamkniętego kąta, zespół pseudoeksfoliacji, ciśnienie wewnątrzgałkowe.
Key words: phacoemulsification, open angle glaucoma, angle closure glaucoma, pseudoexfoliation syndrome, intraocular pressure.

Patients with both advanced cataract and glaucoma still pose a significant problem for the ophthalmic surgeon. Depending on the severity of each disease, there exist three treatment options for the affected patients. Either both components of the surgical treatment (phacoemulsification of the cataract and trabeculectomy) can be performed simultaneously (phacotrabeculectomy), or these procedures can be done in two consecutive operations. In people with high IOP and early-stage cataract, the anti-glaucoma procedure is performed first, in order to stabilize the pressure, and cataract extraction is done later.

More common, however, is the situation in which cataract significantly impairs visual acuity, while pharmacological therapy keeps the IOP below or only slightly above the target value. In such cases, cataract phacoemulsification is performed first, followed by antiglaucoma surgery if still necessary. The reason for this sequence is that IOP is generally reduced substantially after phacoemulsification or extracapsular cataract extraction (ECCE) (1-7). This phenomenon occurs in most cases – in patients with no glaucoma and patients with ocular hypertension, as well as in glaucoma patients, although the amount of IOP reduction varies in different situations. The greatest reductions of IOP tend to occur in patients suffering from angle closure glaucoma (ACG) (2). However, in patients with open angle glaucoma (OAG), IOP reduction after cataract extraction is also evident (2-4,8).

On the other hand, patients with glaucoma who underwent cataract phacoemulsification first, often had temporarily elevated IOP immediately after cataract extraction, and during the first days afterwards (9). The magnitude and duration of these elevations may result in irreversible glaucomatous effects.

Based on the above-mentioned information, we decided to analyze a group of glaucoma patients who underwent cataract phacoemulsification with intraocu-

lar lens implantation into the capsular bag without any intraoperative anti-glaucoma procedure. The objectives of our study were to evaluate the incidence and magnitude of IOP elevations directly after surgery, and to determine whether cataract phacoemulsification has long-term effects on IOP level that may necessitate changes in glaucoma treatment.

Patients and methods

A retrospective analysis was done on data from treatment of 100 eyes with glaucoma, on which phacoemulsification was performed to remove cataracts that significantly impaired vision. Patients with previous eyeball injuries, any ophthalmic surgeries, laser treatment, or uveitis, as well as patients suffering from congenital, juvenile, and secondary glaucoma, other than pseudoexfoliative syndrome (PEX), were excluded from the study.

The patients were divided into two groups: those with open angle glaucoma (OAG) comprised group I, and those with angle closure glaucoma (ACG) were group II. The diagnosis of OAG was based on gonioscopy, changes in visual field typical of glaucoma, elevated IOP, and/ or characteristic changes in the appearance of the optic nerve disc. The diagnosis of ACG involved the same criteria, and additionally the history of acute angle closure glaucoma.

In total, 86 patients (51 women and 35 men) underwent surgery. The operations were on the right eye in 37 patients, the left eye in 35, and both eyes in 14 patients. Group I included 71 eyes of 61 patients (34 women and 27 men). Pseudoexfoliation syndrome (PEX) was found in 19 eyes in this group. These patients were designated as subgroup I A. The 52 remaining eyes with no PEX became subgroup I B. Surgery was performed on the right eyes of 23 patients, the left eyes of 28 patients, and both eyes of 10 patients in Group I. Group II was comprised of 29 eyes of 25 patients (17 women and 8 men). As with Group I, Group II was divided into subgroups II A (4 eyes) and II B (25 eyes), depending on whether symptoms of PEX were present or absent, respectively. Surgery on group II involved the right eyes of 14 patients, the left eyes of 7, and both eyes in 4 patients.

To prepare each patient for surgery, we performed a full ophthalmologic examination, supplemented by applanation tonometry, gonioscopy, biometry, and intraocular lens (IOL) power calculation. Every patient was checked for symptoms of PEX. IOP was determined once again on the day of the operation. This measurement was used as the baseline IOP in later statistical analyses.

The same surgical protocol was used for all patients. As premedication, 3.75 mg of midazolam (Dormicum, Roche) was orally administered half an hour before the surgery. Surgery was performed under topical anesthesia with proparacaine hydrochloride (Alcaine, Alcon). The procedure consisted of phacoemulsification of the cataract and implantation of the acrylic IOL into the capsular bag through a clear corneal incision. During capsulorhexis and IOL insertion, the anterior chamber and capsular bag were filled with hydroxypropylmethylcellulose 2% (Celoftal, Alcon). At the end of surgery the viscoelastic material was carefully aspirated from anterior and posterior chamber as well as from the space behind the IOL. No peripheral iridectomy was made in any of the procedures.

No complications occurred in 98 of the surgeries. In one patient, rupture of the posterior capsule occurred, with vitreous prolapse. Having performed anterior vitrectomy, a posterior capsulorhexis was made, and a polymethyl-methacrylate (PMMA) lens was inserted into the capsular bag. There were no further postoperative complications in this case. In the other case, in which a clear corneal incision was made, the wound leaked and required one stitch. No other intraoperative complications occurred.

On the day after the surgery, another full ophthalmic examination was conducted, with special attention given to the IOP values. Successive examinations were conducted by the ophthalmologists who were treating the patients before the surgery. For the final follow-up examination, the patients were called after an average observation period of 15.9 months (6-30 months). The observation period averaged 15.3 months (6-30 months) for the patients from group I, and 17.4 months (6-28 months) for the patients in group II.

The pair wise statistical comparisons were made using two-tailed Student's *t* test. Statistical significance was defined as $P \leq 0.05$.

Results

The data regarding age of the patients, duration of glaucoma and the number of glaucoma medications used before the cataract phacoemulsification surgery are presented in Table I.

Parameter Parametr	Group I Grupa I	Group II Grupa II
Age (years) Wiek (lata)	71.80 ± 9.12 (45 – 85)	73.56 ± 6.38 (61 – 85)
Duration of glaucoma (years) Czas trwania jaskry (lata)	7.67 ± 5.63 (0,25 – 26)	10.60 ± 11.23 (2 – 40)
Number of glaucoma medications used Liczba stosowanych leków przeciwjaskrowych	1.59 ± 0.62 (1 – 4)	1.52 ± 0.57 (1 – 3)

Tab. I. Age, duration of glaucoma, and number of glaucoma medications used. The mean value, standard deviation and the range of measured parameters (in brackets) are given.

Tab. I. Wiek, czas trwania jaskry oraz liczba stosowanych leków przeciwjaskrowych. W tabeli podano wartość średnią, odchylenie standardowe oraz zakres wartości obserwowanego parametru (w nawiasach).

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Group Grupa	Before surgery Przed zabiegiem	First day Pierwsza doba po zabiegu	Last follow – up Ostatnie badanie	Difference: last follow up – before surgery Różnica: ostatnie badanie - dzień po operacji	P value P
Group I Grupa I	19.02 ± 4,55 (10 – 27)	17.42 ± 7,17 (6 – 50)	14.59 ± 3,73 (6 - 25)	-4.43 ± 3.38 (-11 – +4)	P < 0.00001
I A	20.60 ± 3.32 (13 – 26)	18.60 ± 9,34 (6 – 50)	15.05 ± 2.05 (7 – 20)	-5.55 ± 3.32 (-11 – +2)	P < 0.00001
I B	18.44 ± 4.83 (10 – 27)	16.99 ± 6.24 (8 – 42)	14.43 ± 4.05 (6 – 25)	-4.01 ± 4.01 (-11 – +4)	P < 0.0001
Group II Grupa II	20.01 ± 6.43 (10 – 27)	20.36 ± 8.98 (6 – 43)	14.01 ± 5.06 (8 – 25)	-6.00 ± 5.06 (-16 – +1)	P < 0.0001
II A	22.92 ± 3.78 (20 – 27)	31.62 ± 13.08 (20 – 43)	11.25 ± 4.48 (8 –12)	-11.67 ± 1.57 (-12 – -10)	-
II B	19.54 ± 5.24 (10 – 27)	18.56 ± 6.94 (20 – 42)	14.45 ± 4.44 (8 – 24)	-5.09 ± 4.83 (-16 – +1)	P < 0.001

Tab. II. IOP (mmHg) before surgery, on the first day after surgery, at the last follow-up examination, and the difference between IOP during last follow-up examination and the day of surgery. The means, standard deviations, range of measured parameters (in brackets), and statistical significance are given.
Tab. II. Ciśnienie wewnątrzgałkowe (c.w.) w mmHg przed zabiegiem, w pierwszej dobie po zabiegu, w czasie ostatniego badania kontrolnego oraz różnica w poziomie c.w. pomiędzy dniem ostatniego badania kontrolnego a dniem operacji. W tabeli podano wartość średnią, odchylenie standardowe, zakres wartości obserwowanego parametru (w nawiasach) oraz istotność statystyczną.

Group Grupa	Number of glaucoma medication used (Liczba stosowanych leków przeciwjaskrowych)		Difference Różnica	P value P
	before surgery przed zabiegiem	after surgery po operacji		
Group I	1.59 ± 0.62	1.31 ± 0.64	- 0.28	P < 0.01
I A	1.74 ± 0.73	1.16 ± 0.76	- 0.58	P < 0.05
I B	1.53 ± 0.57	1.36 ± 0.59	- 0.17	P < 0.15
Group II	1.52 ± 0.57	1.21 ± 0.62	- 0.31	P < 0.1
II A	1.50 ± 0.57	1.00 ± 0.00	- 0.50	-
II B	1.52 ± 0.58	1.24 ± 0.66	- 0.28	P < 0.15

Tab. III. Average number of glaucoma medications used before and after surgery.
Tab. III. Średnia liczba leków przeciwjaskrowych stosowanych przed operacją i po niej.

Difference (Różnica)	Group I/ Grupa I		Group II/ Grupa II	
	Subgroup A Podgrupa A	Subgroup B Podrupa B	Subgroup A Podgrupa A	Subgroup B Podgrupa B
Increase 1 drug Zwiększenie o 1 lek	1	2	-	1
No difference Bez różnicy	10	42	2	18
Decrease 1 drug Zmniejszenie o 1 lek	4	5	2	5
Decrease 2 drugs Zmniejszenie o 2 leki	4	3	–	–
Decrease 3 drugs Zmniejszenie o 3 leki	–	–	–	3

Tab. IV. The difference in number of glaucoma medications used on the day of surgery, and on the last follow-up day.
Tab. IV. Różnica w liczbie leków przeciwjaskrowych stosowanych w dniu operacji oraz w dniu ostatniego badania kontrolnego.

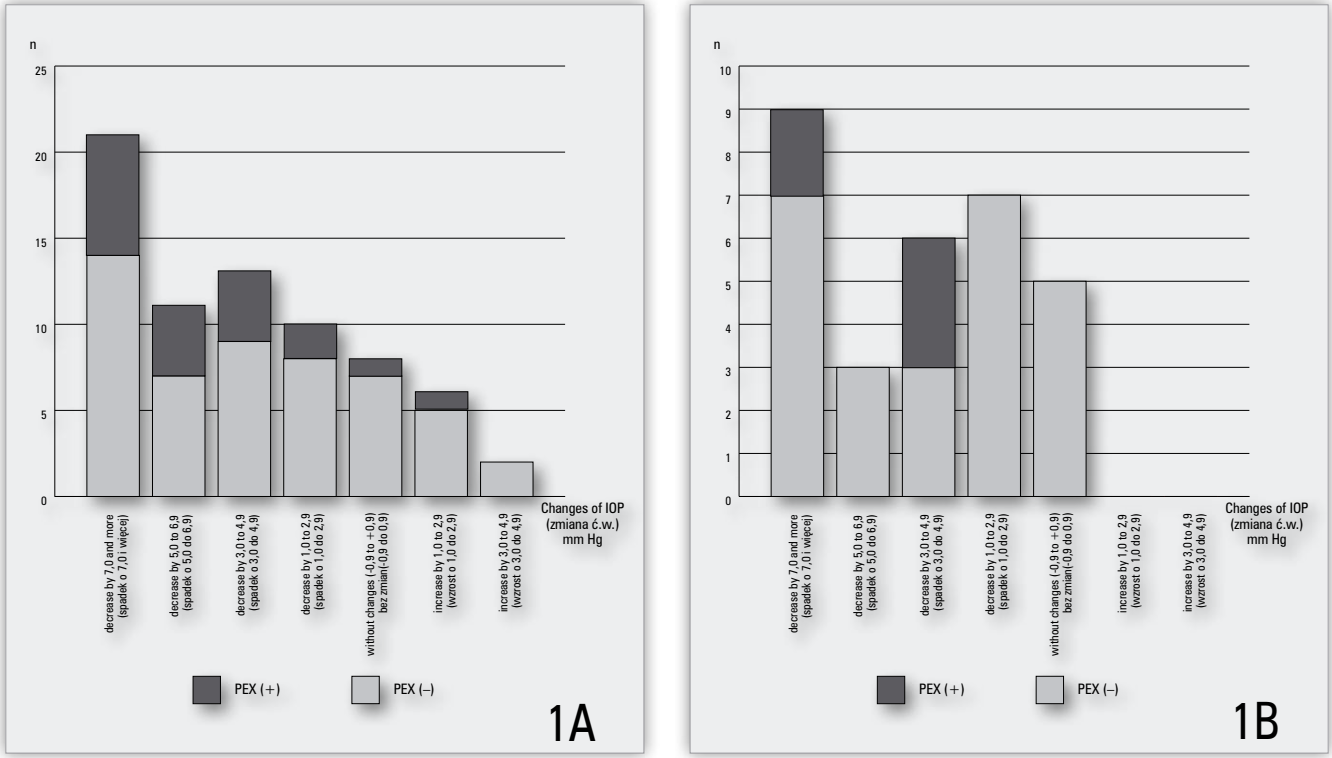

Fig. 1. The difference in intraocular pressure levels on the last follow-up day, versus the day of surgery. (A) – Group I (open angle glaucoma); (B) – Group II (closed angle glaucoma). PEX (+) – patients with pseudoexfoliation syndrome; PEX(-) – patients without pseudoexfoliation syndrome.

Ryc. 1. Różnica w poziomie c.w. pomiędzy dniem ostatniego badania kontrolnego a dniem operacji. (A) – grupa I (jaskra otwartego kąta); (B) – grupa II (jaskra zamkniętego kąta). PEX (+) – pacjenci z zespołem pseudoeksfoliacji; PEX (-) – pacjenci bez zespołu pseudoeksfoliacji.

Table IA	PEX (-)	PEX (+)
decrease by 7.0 and more (spadek o 7.0 i więcej)	14	7
decrease by 5.0 to 6.9 (spadek o 5.0 do 6.9)	7	4
decrease by 3.0 to 4.9 (spadek o 3.0 do 4.9)	9	4
decrease by 1.0 to 2.9 (spadek o 1.0 do 2.9)	8	2
without changes (-0.9 to +0.9) bez zmian (-0.9 do 0.9)	7	1
increase by 1.0 to 2.9 (wzrost o 1.0 do 2.9)	5	1
increase by 3.0 to 4.9 (wzrost o 3.0 do 4.9)	2	
Table IB	**PEX (-)**	**PEX (+)**
decrease by 7.0 and more (spadek o 7.0 i więcej)	7	2
decrease by 5.0 to 6.9 (spadek o 5.0 do 6.9)	3	
decrease by 3.0 to 4.9 (spadek o 3.0 do 4.9)	3	2
decrease by 1.0 to 2.9 (spadek o 1.0 do 2.9)	7	
without changes (-0.9 to +0.9) bez zmian (-0.9 do 0.9)	5	
increase by 1.0 to 2.9 (wzrost o 1.0 do 2.9)		
increase by 3.0 to 4.9 (wzrost o 3.0 do 4.9)		

Table II lists the means, standard deviations, and ranges of IOP values measured on the day of surgery, the first day afterwards, and the day of the final follow-up examination.

Table II also summarizes the differences in IOP before and after surgery, and their statistical significance. On the day after surgery, the vast majority of patients had IOP ≤ 20 mmHg, generally lower than immediately before surgery. However, the differences in pre- and post-operative IOP were not statistically significant for these patients.

Unfortunately, there were also patients whose post-operative IOP increased, exceeding 20 mmHg. In Group I (the OAG group), there were seven eyes, with post-operative IOP values of 25, 27, 29, 30, 32, 42 and 50 mmHg. In Group II (the ACG group), post-operative IOP elevations occurred in 6 eyes, to 28, 29, 30, 37, 42 and 43 mmHg, respectively. Thus, post-operative IOP elevations occurred in nearly 10% of the eyes in Group I, and about 20% of the eyes in Group II. After topical administration of 0.5% timolol maleate (Oftensin, Polfarma) and in some cases oral acetazolamide (Diuramid, Polfarma) IOP in all of these eyes quickly returned to normal.

During final follow-up examinations it was evident that most of the eyes showed marked lowering of IOP in comparison to pre-operative values. The post-operative *vs*. preoperative IOP reductions were highly significant ($P < 1 \times 10^{-4}$) in Groups I A and B (OAG

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with and without PEX), and Group II B (ACG without PEX). The change was most pronounced in the A subgroups, although Group II A (ACG with PEX), included only four eyes, and thus could not provide significance statistics. The results are summarized in Figure 1. In the last follow-up, IOP above 20 mmHg were observed in only four patients: two from Group I (22 and 25 mmHg) and two from Group II (both 24 mmHg).

In almost one-fourth of the cases, the post-operative drop in IOP was great enough to permit reduction in the types and dosages of glaucoma medication needed to maintain IOP at a steady, safe level. Four patients, however, required additional drug therapy. These data are shown in tables III and IV.

Discussion

Small-incision phacoemulsification, followed by implantation of a foldable intraocular lens, is currently a standard approach in cataract treatment. The high effectiveness and low risk suggest that there may be wider applications for this procedure. In recent years it has been observed that the procedure also results in a statistically and therapeutically significant drop in IOP, in many patients without glaucoma (1,2,4,6,7), as well as in patients with glaucoma (1-6,8). Thus, phacoemulsification of cataract in an eye with glaucoma may be the method of choice because, in addition to restoring visual acuity, it is likely to have a beneficial effect on treatment of the glaucoma (2,4-6,8).

On the other hand, there is a well-documented risk that phacoemulsification will cause transient IOP elevations immediately after the cataract surgery (9-11). This risk applies to all patients, regardless of the condition of their eyes before the procedure. There are several possible causes of the sudden IOP increases. Some published studies indicated that the main cause is that the viscoelastic substance introduced during surgery, is not completely removed from the anterior chamber. Other potential causes of IOP spikes include inflammation caused by the cortex remnants, blood cells, pigment particles, and free radicals released during phacoemulsification (6,12,13). In glaucomatous eyes, the additional factor contributing to IOP spikes is obstruction of the routes for outflow of the aqueous humor from the eyeball (6). Thus, such sudden IOP spikes may be more frequent, and of larger amplitude in patients suffering from glaucoma. This, in turn, may lead to irreversible visual field changes.

In most of our patients, IOP measured in the first 24 hours after surgery was lower than before the surgery. Unfortunately, IOP spikes on the first day after surgery occurred in about 10% of the group I patients and 20% of the group II patients. Such IOP spikes directly after the procedure have been well-documented (6,10). Shingelton, et al. (6) observed, as we did, IOP spikes to levels as high as 44 mmHg in glaucoma patients during the first 24 hours after phacoemulsification. Despite the fact that IOP elevations of this type tend to normalize when treated properly, they may still lead to permanent changes. Therefore it is necessary to pay special attention to intrasurgical preventive measures. These mainly consist of very thorough removal of cortical masses and viscoelastic agent from the eye (particularly when sodium hyaluronate is used), and minimal contact of the surgical instruments with the iris during phacoemulsification.

We were particularly interested in why the post-surgical IOP drop was so stable and long-lasting. The IOP decrease as result of ECCE and cataract phacoemulsification has been the subject of many studies (1-7). However, it is hard to directly compare data in the literature, because different authors investigated many different groups of patients (for example, otherwise healthy, suspected glaucoma, patients with OAG, ACG or secondary glaucoma due to PEX syndrome), and observations were made over different time intervals. Among OAG patients, IOP fell immediately after surgery, and remained at near-normal levels from 12 months to 4 years following the surgery. According to different sources, the drop in IOP was 1.4-1.9 mmHg (3), 1.55 mmHg (4), 1.88 mmHg (13), 2.9 mmHg (6), 3.1 mmHg (14), and 4.9-5.3 mmHg (2). Thus, the values recorded in our study are within the upper limit of those in the literature. The average IOP reduction amounted to 4.43 mmHg in our OAG patients, and up to 6.00 mm Hg in our ACG patients. Hayashi reported IOP reductions of 6.9 mmHg 12 months after the procedure, and 7.2 mmHg at the two-year follow-up (2).

Merkur and his colleagues also presented interesting findings (14). In their glaucoma patients with PEX, the average IOP reductions after phacoemulsification were even greater (2.31 mmHg) than in OAG patients (1.88 mmHg). We also observed this in our study: the reductions averaged 5.55- and 4.01 mmHg in our OAG patients with, and without PEX, respectively, and 11.67- and 5.09 mmHg in our ACG patients with, and without PEX, respectively.

For many of our patients, the IOP reductions allowed a decrease in the number and/or dosage of antiglaucoma drugs (Table IV). Similar findings were reported in studies already cited (3,5,6,8). Hayashi, et al., observed IOP reductions large enough that they were able to discontinue anti-glaucoma medication in 19.1% of their OAG patients, and 40.5% of their ACG patients (2). Link, et al., were able to do the same for six of their 16 patients (4). Our outcome was similar. After surgery, six OAG eyes and 3 ACG eyes in our cohort achieved target pressure without glaucoma medication.

There is a plausible explanation for the large and long-lasting IOP reduction in patients with ACG. ACG patients usually develop enlargement and thickening of the lens. This leads to partial pupillary block, narrowing of the iridocorneal angle, shallowing of the anterior chamber, and eventually, to permanent impairment of aqueous humor outflow through the angle. Extraction

of the altered lens restores the normal anatomic relations within the anterior segment of the eye, deepening the anterior chamber, widening the filtration angle, and allowing proper drainage of the aqueous humor through the trabecular meshwork. This hypothesis, supported by the results, suggests that early cataract extraction would especially benefit patients with angle closure glaucoma.

It is more difficult to postulate a mechanism for the post-surgical IOP reductions in eyes with OAG. Three possible mechanisms have been suggested in the literature: (a) a decrease of aqueous humor production, (b) improved aqueous humor outflow through the trabecular meshwork and Schlemm's canal, and (c) improved uveoscleral drainage. Hypothesis (a) seems unlikely, because decreased aqueous humor production, even if it occurs directly after the surgery, is only temporary. Mechanisms (b) and (c) are more plausible ways of reducing the IOP. They are consistent with results reported by Meyer, et al., who showed that performing phacoemulsification on patients with suspected glaucoma, increased the outflow rate of aqueous humor (12). The most probable mechanism might be the increased prostaglandin release. PGE_1 increases the outflow through the conventional, while $PGF_{2\alpha}$ – through the alternative way. Improving of meshwork drainage ability and conventional drainage way in primary glaucoma eyes is less probable in an eye with primary glaucoma due to permanent dysfunction of the outflow through this pathway in an eye with simple glaucoma. Based on our measurements and observations, in comparison with those of Altan, et al. (1), we believe the most probable mechanism is (c); the improvement of the drainage through the alternative (uveoscleral) pathway. We are, however, still far from fully understanding long-term IOP reduction in OAG.

It is somewhat easier to hypothesize how greater IOP reductions occur in eyes with PEX syndrome. Others previously reported this (14,15,16), and our observations confirm their findings. Possibly the simplest hypothesis is that pseudoexfoliative material is, at least in part, washed out from the anterior chamber, particularly from the filtration angle, during phacoemulsification. This would be expected to result in increased outflow of aqueous humor through the trabecular meshwork. Another contributing factor may be that the zonular apparatus of the crystalline lens is very weak in some patients with PEX syndrome. This could enable the whole lens to move anteriorly, resulting in anterior chamber shallowing, and ACG. In these patients, replacement of the crystalline lens with a much thinner IOL implant should result in deepening of the anterior chamber, alleviating symptoms of ACG. The combination of washing out the pseudoexfoliative debris and deepening the anterior chamber may act synergistically to lower the IOP. For eyes with both cataract and glaucoma, our findings, and similar data from other ophthalmology centers, show that cataract extraction by phacoemulsification not only improves visual acuity; it can also produce marked, long-term lowering of IOP. In most of our patients, IOP remained unchanged, or fell gradually, for several months after cataract extraction. This simplified, and in some cases eliminated, glaucoma medication. However, when glaucoma is difficult to control, and maintenance of lower IOP is the first priority, cataract phacoemulsification with intraocular lens implantation is not the only option. In such cases trabeculectomy should be performed first, and cataract extraction later, or alternatively the two surgeries should be performed simultaneously. The benefit must be weighed against the risk of transient IOP spikes immediately after the phacoemulsification and IOL implantation. This risk can be minimized by appropriate material and instrument handling, and proper technique by a deft surgeon.

Conclusions

1. Performing phacoemulsification with intraocular lens implantation on glaucomatous eyes, in most cases reduces IOP by a few mmHg immediately after surgery. This reduction gradually continues, or remains stable over periods of time extending to years. In these instances, glaucoma therapy may be simplified, or even discontinued.
2. IOP decreases are more evident in cases of angle closure glaucoma and pseudoexfoliative glaucoma, than in cases of open angle glaucoma.
3. The first day after the surgery, sudden IOP spikes can be expected in some cases, and their occurrence will require a conservative therapy.

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