Cataracts in Diabetic Patients: A Review Article

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The number of people with diabetes mellitus is increasing and cataracts are one of the most common causes of visual impairment in these subjects. Advances in cataract surgical techniques and instrumentation have generally improved the outcomes; however, surgery may not be safe and effective in certain individuals with pre-existing retinal pathology or limited visual potential. This review article aims to address different aspects surrounding cataracts in diabetic patients. In a computerized MEDLINE search, relevant studies were selected by two authors using the keywords "diabetes mellitus", "cataract", "diabetic retinopathy" and "diabetic maculopathy".

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INTRODUCTION

Population growth, ageing, urbanization, sedentary lifestyles and an increasing prevalence of obesity are increasing the number of people with diabetes mellitus. The global prevalence of diabetes was estimated to be 2.8% in 2000 and is expected to reach 4.4% by 2030. The total number of people with diabetes mellitus worldwide is projected to rise from 171 million in 2000 to 366 million in 2030.[1] Globally, cataracts remain the leading cause of blindness, affecting approximately 18 million people.[2] Cataracts occur at an earlier age and 2–5 times more frequently in patients with diabetes, thus the visual loss has a significant impact on the working population.[3,4]

Overall, up to 20% of all cataract procedures are estimated to be performed for diabetic patients.[5] Epidemiologic studies have demonstrated that cataracts are the most common cause of visual impairment in older-onset diabetic patients[6,7] and the rate of cataract surgery is correspondingly high. The Wisconsin study identified that the ten-year cumulative incidence of cataract surgery was 27% in patients with early onset diabetes and 44% in cases with older onset disease.[3]

Advances in cataract surgery have generally improved the outcomes, however diabetic individuals do not always share the same favorable outcomes. Some studies have reported that cataract surgery may have adverse effects, including progression of retinopathy, vitreous hemorrhage, iris neovascularization and decrease or loss of vision.[8-10] This study will review related articles to highlight current agreements and controversies regarding cataract development, extraction and complications with greater attention to clinical aspects.

RISK FACTORS FOR OCULAR COMPLICATIONS IN DIABETIC PATIENTS

Diabetes mellitus is a systemic condition affecting numerous organs other than the eye. On the other hand, concomitant systemic disorders can significantly influence the development

and progression of ocular complications in diabetic patients. Intensive control of blood glucose and systemic hypertension reduce the risk of new onset diabetic retinopathy and slow the progression of existing diabetic retinopathy.[11,12] Severe renal disease affects the progression of diabetic retinopathy, elevated serum lipids are associated with macular exudation and moderate visual loss, excessive exercise in patients with advanced retinopathy may predispose to vitreous hemorrhage, transient progression of diabetic retinopathy can occur during pregnancy, anemia can result in progression of diabetic retinopathy and smoking in general should be discouraged.[13]

Studies related to cataract formation in diabetic patients have shown that hyperglycemia is associated with loss of lens transparency in a cumulative manner.[14] Rapid decline of serum glucose levels in patients with marked hyperglycemia may induce temporary lens opacification and swelling as well as transient hyperopia. It has also been suggested that rapid glycemic control can irreversibly increase lens opacities.[15]

RISK FACTORS FOR CATARACTS IN DIABETES

Cataracts are among the earliest complications of diabetes mellitus. Klein et al[3] demonstrated that patients with diabetes mellitus are 2–5 times more likely to develop cataracts than their nondiabetic counterparts; this risk may reach 15-25 times in diabetics less than 40 years of age.[16] Even impaired fasting glucose (IFG), a pre-diabetic condition, has been considered as a risk factor for the development of cortical cataracts.[17] In a study from Iran, Janghorbani and Amini[18] evaluated 3,888 type 2 diabetic patients who were free of cataracts at initial visit and reported a rate of cataract formation of 33.1 per 1000 person-years of observation after a mean follow-up of 3.6 years.

PREVENTION OF CATARACTS

Three molecular mechanisms seem to be involved in the development of diabetic cataracts: non-enzymatic glycation of lens proteins, oxidative stress and activated polyol pathway. Despite the fact that a wide variety of agents, including inhibitors of glycation (Aspirin, Ibuprofen, Aminoguanidine and Pyruvate), antioxidants (Vitamin C, Vitamin E, Carotenoids, Trolox and Hydroxytoluene) and aldose reductase inhibitors (Zenarestat, Eplarestat, Imirestat, Ponalrestat, Zopolrestat, M-79175 and BAL-AR18) have demonstrated potential for prevention of cataracts in animal models, it would be premature to recommend them in humans.[19]

ANTERIOR SEGMENT CHANGES IN DIABETES

Diabetes mellitus significantly impacts the morphological, metabolic, physiological and clinical properties of the cornea. The corneal abnormalities, generally termed diabetic keratopathy, are present in more than 70% of diabetic patients[20] and include clinically detectable changes such as increased epithelial fragility and recurrent erosions,[21] reduced corneal sensitivity,[22-25] increased autofluorescence,[26] impaired wound healing,[27] altered epithelial and endothelial barrier functions,[28] and predisposition to corneal edema[29] and infectious ulcers.[21-24]

Confocal microscopy has revealed lower basal cell density in diabetic patients which may due to decreased innervation at the sub-basal nerve plexus level, basement membrane alterations and higher turnover rate in the basal epithelial cells. Both stromal and sub-basal corneal nerve plexuses in diabetic subjects appear abnormal on confocal microscopy; patients with proliferative diabetic retinopathy show more pronounced alterations than patients with no diabetic retinopathy. The sub-basal nerve plexus has been reported to appear significantly thicker and more tortuous.[30] Cell density also seems to be reduced at the mid corneal stroma level in diabetic patients.[31] Inoue et al[32] demonstrated that corneal endothelial cell density was decreased and the coefficient of variation in cell area was increased in diabetic patients as compared to healthy controls. However, no signi-

ficant difference in central corneal thickness (CCT) was observed.

The most important change in the crystalline lens is cataract formation. The basement membrane of the lens (or lens capsule) is known to be thicker in diabetics, which is similar to the thickened vascular basement membrane in these subjects. This thickened capsule is more friable and inadvertent rupture during intracapsular lens extraction seems to be more common in diabetics.[33] Lens capsule changes may also affect performing capsulorrhexis during phacoemulsification.

Several studies have compared different types of cataracts in diabetics vs non-diabetics. Schafer et al[34] reported a higher percentage of cortical opacities in diabetics as documented by Scheimpflug photography and densitometric analysis. They also demonstrated correlation between type 2 diabetes mellitus and cortical lens opacities. Saxena et al[17] found a 2-fold higher incidence of cortical cataracts in subjects with diabetes mellitus over 5 years. In their study, posterior subcapsular cataracts were more frequent in diabetic patients, but the association was statistically significant only for subjects with newly diagnosed diabetes. These investigators found no significant association between nuclear cataracts and diabetes mellitus or IFG. An uncommon type of lens opacity, true diabetic cataract or snowflake cataract, consists of widespread bilateral subcapsular lens opacities of abrupt onset and acute progression, typically in young people with uncontrolled diabetes mellitus. This is rare and may be the initial presentation of diabetes.[35]

Iris changes such as leathery consistency and a miotic pupil were found to occur more frequently in diabetic patients. The iris pigment epithelium is often vacuolized due to the accumulation of glycogen and pigment dispersion may occur with iris trauma or surgery.[36] In some cases, abnormal iris transillumination has been noted. This tends to be associated with more severe degrees of retinopathy. Hypoxia has been implicated as the cause of changes in the iris pigment epithelium.[37]

Studies have reported a higher prevalence of both elevated mean IOP and POAG among subjects with diabetes. On the other hand, glaucoma patients have been reported to have a higher prevalence of abnormal glucose metabolism.[38] It is possible that diabetes mellitus increases the susceptibility of the optic nerve fibers to glaucomatous damage because of its effect on small vessels of the eye. Whether diabetes is an independent risk factor for the development of POAG remains controversial; some studies have found a positive association (Blue Mountains Eye Study[39]) while others have not. Diabetes was not associated with an increased risk of conversion of ocular hypertension to frank glaucoma in the Ocular Hypertension Treatment Study (OHTS).[40]

One of the most important anterior segment complications of diabetes is neovascularization of the iris (NVI) which is usually due to tissue hypoxia or ischemia and characterized by fine arborizing blood vessels on the iris stroma and trabecular meshwork, accompanied by a fibrous membrane. Contraction of the fibrovascular membrane results in peripheral anterior synechiae formation, leading to a severe type of secondary angle-closure glaucoma, neovascular glaucoma, which is caused by a variety of disorders characterized by retinal or ocular ischemia, the most common of which is diabetes mellitus.[41,42]

TIMING OF CATARACT SURGERY

The approach to timing for cataract surgery in diabetic patients seems to be changing. A decade ago, a more conservative attitude was prevalent. Pollack et al[43] reported VA better than 20/40 in 31% of patients and noted macular edema as the main cause of poor visual outcome. These investigators proposed that "cataract extraction should not be recommended for eyes with diabetic retinopathy until visual acuity has deteriorated to 20/100–20/200". This view was later endorsed by Schatz et al[44] reporting a study in which only 9% of eyes achieved postoperative VA better than 20/40. These authors stated that "A patient with diabetes and cataract might wish

to postpone surgery or elect not to have it at all, given the chance of a markedly poor result, especially if any retinopathy is present preoperatively."

There is growing evidence in support of a more interventional approach. A shift in attitude towards earlier cataract extraction in diabetes mellitus has contributed to an improved visual outcome. This approach facilitates panretinal photocoagulation therefore preventing progression of retinopathy and also enables timely treatment of underlying macular edema.[45] Visual outcomes are likely to be worse in studies in which surgery is deferred until it was not possible to identify or adequately treat clinically significant macular edema (CSME) prior to surgery. Additionally, if surgery is undertaken before lens opacity prevents the recognition of retinal thickening, the risk of CSME is decreased and the visual outcome may be improved considerably.[46]

PREOPERATIVE CONSIDERATIONS

Prior to surgery, patients should have good glycemic control and no evidence of ocular or periocular infection. Due to the range of anterior segment changes in diabetic patients, it is advisable that cataract extraction be undertaken by an experienced surgeon. A thorough and comprehensive ophthalmologic examination including assessment of visual acuity (VA), best corrected visual acuity (BCVA), relative afferent pupillary defect (RAPD), slitlamp biomicroscopy, gonioscopy (with particular attention to new vessels), tonometry and dilated funduscopy is mandatory. Ancillary diagnostic evaluations such as fluorescein angiography, optical coherence tomography (OCT) and B-scan ultrasonography may be helpful in selected cases. Some authors recommend consultation with vitreoretinal subspecialist, especially in complicated cases.[47]

Patients with pre-existing proliferative diabetic retinopathy are more likely to progress rapidly after cataract surgery, therefore panretinal photocoagulation (PRP) is recommended preoperatively. When lens opacity precludes PRP, it can be performed after surgery[48] or the surgeon may consider preoperative panretinal cryopexy or combined cataract surgery with vitrectomy and endolaser photocoagulation, especially for cases with posterior pole tractional retinal detachment (TRD). Macular edema should be adequately treated prior to surgery because pre-existing maculopathy may aggravate postoperatively and is strongly associated with a poor visual outcome.[49]

Patients with NVI also need prompt PRP. When neovascular glaucoma (NVG) has developed, medical therapy alone is usually not effective. Topical beta-adrenergic antagonists, alpha2-adrenergic agonists, carbonic anhydrase inhibitors, cycloplegics and corticosteroids may be useful in reducing IOP and decreasing inflammation. The risk of intra- and postoperative complications are high with active NVI. Antivascular endothelial growth factor (VEGF) agents such as bevacizumab appear to have a promising role in the treatment of neovascular glaucoma. Patients have demonstrated dramatic short-term response in terms of intraocular pressure reduction and regression of neovascularization.[50,51] The authors have limited experience with the combination of intravitreal bevacizumab injection to induce NVI regression prior to cataract surgery followed by PRP briefly after surgery (unpublished data).

Hyperglycemia is the major cause of transient refractive changes in diabetic patients. The refractive changes observed during periods of unstable blood sugar are thought to be related to both morphologic and functional changes in the crystalline lens.[52] With intensive medical therapy, a considerable number of patients tend to become more hyperopic as compared to the hyperglycemic state. Changes in corneal topographic parameters during periods of glycemic changes are a potential source of error in keratorefractive and cataract surgery.[53]

CATARACT SURGERY

Cataract surgery is more complicated in diabetic patients overall. Phacoemulsification is associated with better visual results, less in-

flammation and less need for capsulotomy as compared to extracapsular cataract surgery.[54]

Corneal hypoesthesia is common in diabetic patients. Special care should be taken to protect the corneal epithelium during surgery. Corneal abrasions during or after surgery may be slow to heal and lead to recurrent corneal erosions. Small-incision surgery can minimize further decrease in corneal sensation.[21,22] Due to corneal hypoesthesia and the increased risk of infection, patients with diabetes are poor candidates for long-term aphakic contact lens wear. Thus a posterior chamber intraocular lens (IOL) should be inserted when possible.

If the pupil is small preoperatively, it may be enlarged during cataract surgery using intracameral atropine and adrenaline, multiple sphincterotomies, pupil-stretching techniques or mechanical iris retractors. A generous anterior capsulotomy and complete cortical cleanup will enhance the view of the peripheral retina postoperatively. Anterior capsular phimosis is more common in diabetic patients, therefore the capsulorrhexis size should be larger than normal but smaller than IOL optic diameter to prevent posterior capsular opacification. A large diameter optic (i.e. 6.0 mm or larger) will facilitate diagnosis and treatment of peripheral retinal pathology postoperatively.[55]

The surgeon's skill affects surgical time, decreases the chance of intraoperative complications and is associated with less postoperative inflammation. Longer and complicated cataract surgery is associated with a greater risk of progression of retinopathy and subsequent visual compromise.[56] It is prudent to make every effort to minimize surgical trauma in diabetic eyes.

Altug et al[57] showed that photic retinopathy during cataract surgery was more prevalent in diabetic patients than non-diabetics. They suggested that diabetic patients may be more vulnerable to photic injury and surgeons should take necessary precautions.

INTRAOCULAR LENS CHOICE

Large diameter IOLs are required to facilitate visualization and treatment of the peripheral retina. A 6.5-mm IOL, for example, provides 39.7% larger optical area than a 5.5-mm IOL, this difference may be crucial for optimal management of diabetic retinopathy.

Posterior capsular opacification (PCO) is a major concern following cataract extraction. Diabetic patients seem to develop more severe PCO than non-diabetic patients.[58] PCO may be related to the shape of the optic edge; a square-edge design seems to inhibit lens epithelial cell proliferation and may therefore prevent PCO formation.[59]

Three common materials used for manufacture of foldable IOLs are silicone, hydrophobic acrylic and hydrophilic acrylic. Several studies have evaluated the biocompatibility of these materials in diabetic patients. One study compared the rate of PCO with hydrophobic acrylic and plate-haptic silicone IOLs in diabetic patients; although hydrophobic acrylic IOLs were associated with more anterior chamber flare in the early postoperative period, PCO developed less frequently. Hydrophobic acrylic lenses have the lowest propensity to silicone oil adhesion and may be the IOL of choice in diabetic patients anticipating vitreoretinal surgery. Silicone IOLs can develop condensations during pars plana vitrectomy and thus may be relatively contraindicated in such individuals.[60]

The level of phosphorus in the serum and aqueous humor of diabetic patients, particularly those with proliferative diabetic retinopathy, is significantly higher than normal individuals, which may lead opacification of hydrophilic acrylic IOLs. There are increasing reports of progressive calcific opacification of hydrophilic acrylic IOLs in diabetic patients.[61,62]

Rodriguez-Galietero et al[63] evaluated changes in contrast sensitivity and color discrimination in diabetic patients who had cataract surgery and implantation of a blue-light filtering IOL compared with an ultraviolet-only filtering IOL. Their results suggested blue-light filtering IOLs did not cause chromatic discrimination defects and even improved color vision in the blue-yellow chromatic axis. The

use of multifocal and accommodative IOLs in diabetics remains controversial.

INTRAOCULAR LENS IMPLANTATION SITE

Concerns have arisen regarding the use of anterior chamber angle-fixated lenses and sulcus-fixated posterior chamber IOLs in diabetic patients. Anterior chamber IOLs including iris-claw lenses should generally not be used in patients with diabetes who are at an increased risk for iris neovascularization. Most studies suggest that the safest procedure for diabetics is controlled extracapsular surgery with careful cleaning of cortical material and in-the-bag implantation of a posterior chamber IOL. The posterior chamber lens will act as a barrier to the anterior movement of vitreous in the event of posterior capsulotomy.[47,54]

VISUAL PROGNOSIS FOLLOWING CATARACT SURGERY

Recent studies on cataract surgery in diabetics tend to report a lower incidence of complications and better visual outcomes.[64,65] This trend of improvement may be due to better preoperative management of retinopathy,[66] evolutions in operative techniques and appreciation of the importance of systemic factors such as glycemic and hypertensive control.

In general, the visual prognosis following cataract surgery in diabetic patients is favorable. Diabetic patients with little or no retinopathy enjoy the same good prognosis as individuals without diabetes.[67] However, in the presence of significant diabetic retinopathy, postoperative VA may be suboptimal and the results of surgery may be disappointing. Presence of CSME and poor preoperative visual acuity (reflecting diabetic maculopathy, ischemia and traction) have been recognized as risk factors for poor postoperative visual acuity following cataract surgery.[68]

Previous reports have focused primarily on VA and less attention has been given to the effect of surgery on quality of life in terms of vision-dependent activities or satisfaction with outcomes of surgery. Mozaffarieh et al[69] in a prospective study evaluated patients with different stages of diabetic retinopathy. Patients were assessed using the VF-14 (Visual Function-14) questionnaire. Their study suggested that patients with more advanced diabetic retinopathy may show no functional improvement despite apparent improvement in VA. This emphasizes the importance of patient education prior to surgery.

INDICATORS OF POOR VISUAL OUTCOMES FOLLOWING CATARACT SURGERY

Several variables have been associated with poor visual outcomes following cataract surgery in diabetic patients. According to the Early Treatment of Diabetic Retinopathy Study (ETDRS), the presence of CSME at the time of cataract surgery is significantly associated with poor postoperative visual acuity and a predictor of final VA worse than 20/200. The severity of diabetic retinopathy at the time of cataract surgery is also a significant determinant of postoperative visual acuity: more severe retinopathy seems to be associated with an increased prevalence of macular ischemia, or as natural history studies suggest, reduced tendency for spontaneous resolution of postoperative macular edema. Analysis of determinants of postoperative visual acuity in the ETDRS also identified poor preoperative visual acuity as a risk factor for poor postoperative outcome. Macular ischemia, edema and traction seem to be probable causes for the latter finding.

COMBINED CATARACT SURGERY AND VITRECTOMY

Advances in vitreoretinal and cataract surgical techniques have led to several studies on combining cataract and vitrectomy surgery in diabetic patients. Diabetic patients undergoing vitrectomy often have coexisting cataracts, on the other hand lens opacities often progress following vitrectomy. Combined surgery has been shown to be safe, effective and com-

parable to sequential surgery in terms of final visual outcomes. Careful patient selection and combining the two procedures can offer more rapid visual rehabilitation, avoid a second operation and simplify surgical interventions in patients who are likely to require multiple procedures.[70-72] Several studies have suggested that the vitreoretinal interface is a contributing factor in the development of persistent CSME following laser photocoagulation and have demonstrated significant anatomic and visual improvement with combined surgery when indicated.[73-75]

Patient selection is crucial for a successful outcome following combined procedures. Patients over 60 years of age are more likely to have progressive lens opacification following vitrectomy. Combined surgery may be recommended for patients with cataracts precluding membrane dissection or those with preexisting cataracts who are likely to suffer from visual loss due to cataract progression in the next two years. Patients with severe traction and ischemia and those with active rubeosis are less suitable candidates and younger patients with little preoperative lens opacity may be better managed without lens extraction.[71]

CATARACT SURGERY AND INTRAVITREAL INJECTIONS

Cataract surgery provides the ideal setting for administration of intravitreal medications in a sterile surgical field allowing for control of IOP. Experience with intravitreal steroids has demonstrated their efficacy in reducing macular edema as measured by optical coherence tomography (OCT). Intravitreal steroids may be considered during cataract surgery in eyes with CSME but no epiretinal membrane or tractional component particularly if the patient has not been treated or if a favorable response has been obtained previously.[76,77] Intravitreal injections of bevacizumab (Avastin) have been employed for the treatment of neovascular and exudative ocular diseases since 2005. Since then, several studies have evaluated its effect on neovascular complications of diabetes,[50,51,78,79] however its use during cataract surgery has been not evaluated and could be the subject of future studies.

POSTOPERATIVE CONSIDERATIONS

All patients diagnosed with nonproliferative diabetic retinopathy should undergo a detailed retinal examination within three months of cataract extraction. Patients with proliferative retinopathy or those with inadequate view of the retina prior to cataract extraction should be evaluated closely after surgery for monitoring retinal status.[10]

NVI is the most dreaded anterior segment complication in diabetic subjects following cataract surgery. The incidence has been reduced with modern cataract surgery which is less traumatic and leaves the posterior capsule intact. In addition to PRP, intravitreal injections of bevacizumab have been reported to control NVI but the effect has been short-lived.[50,51,78,79]

Other anterior segment complications which occur more frequently in diabetic subjects are posterior synechiae, pupillary block, pigmented precipitates on the IOL and severe iritis.[80] The incidence of fibrin reaction is high and reported in up to 13.7% of diabetic patients.[81] Although not definitely confirmed, diabetes may be a risk factor for postoperative endophthalmitis and is associated with a poor visual prognosis following the development of endophthalmitis.[82]

Corneal complications may occur spontaneously but more often follow excessive surgical manipulations. Diabetic patients are prone to corneal epithelial defects and persistent erosions due to impaired corneal sensation, these occur more frequently with increasing patient age and duration of diabetes.[83] Wavelike epitheliopathy following phacoemulsification reflecting neurotrophic corneal damage has also been reported.[84]

Numerous measures for promoting corneal epithelial healing have been explored. Discontinuing topical medications may be adequate to heal the epithelial defect because many pre-

parations contain toxic preservatives. Patients should be treated with frequent lubricating drops and ointments, goggles and closure of the eyelid by patching, or by temporary or permanent tarsorrhaphy. Another effective treatment for persistent epithelial defects is therapeutic soft contact lens fitting but the major drawback is the increased risk of infectious corneal ulceration.[85] Newer therapeutic options include: fibronectin,[86] growth factors (including epidermal growth factor, substance P and insulin-like growth factor-1),[87,88] plasminogen activator/plasmin[89] and amniotic membrane transplantation.[90] In a randomized study, topical application of insulin (4 times daily for 7 days) normalized the delayed corneal wound healing in rats with diabetes mellitus.[91]

Eyes of patients with diabetes mellitus show more severe corneal endothelial cell damage following cataract surgery and delayed recovery of corneal edema.[92] Lee et al[93] compared corneal endothelial cell damage following phacoemulsification and intraocular lens implantation in diabetic patients categorized by the severity of diabetic retinopathy and normal patients. Their findings revealed significantly greater reduction in corneal endothelial cell density and increased coefficient of variation in cell size in patients with high risk PDR.

EFFECT OF CATARACT SURGERY ON RETINOPATHY

Numerous studies have addressed whether cataract surgery influences diabetic retinopathy. The progression of diabetic retinopathy after intracapsular (ICCE) and extracapsular (ECCE) cataract extraction is well documented,[94-97] however controversy surrounds the effect of phacoemulsification. Some studies have demonstrated a similar trend of progression in diabetic retinopathy after phacoemulsification surgery, while others reported no significant change.[49,98,99] These discrepancies may be attributed to the different criteria used to define progression of diabetic retinopathy. Many authors believe cataract surgery actually influences diabetic retinopathy progression in an independent fashion while others feel that the natural history of the condition per se is more important than the effect of surgery.

In a retrospective study, Hauser et al[100] evaluated the occurrence and progression of diabetic retinopathy; their data suggested that diabetic retinopathy was associated with male sex, disease duration and poor glycemic control. Progression of pre-existing diabetic retinopathy was associated with poor blood sugar control. This study is limited by its retrospective nature, the relatively small number of cases and not being able to differentiate the natural course of the disease from the effect of surgery.

To differentiate the effect of cataract surgery from the natural course of the disease, Dowler et al[46] designed a prospective study in which monocular surgery was performed and the fellow eyes served as controls. These authors showed that uncomplicated phacoemulsification cataract surgery does not accelerate progression of diabetic retinopathy.

In another prospective study by Squirrell et al,[49] monocular phacoemulsification was performed and the grade of diabetic retinopathy and diabetic maculopathy was assessed for 12 months postoperatively in the operated and non-operated fellow eye. This study also revealed that uncomplicated phacoemulsification does not accelerate the course of diabetic retinopathy and any observed progression probably represents the natural course of the disorder.

ETDRS report number 25 is one of the most important studies on cataract surgery in diabetes. It has a low rate of loss to follow-up, well-documented BCVA measurements, accurate annual fundus photographs and well documented interventions. This report suggests a trend towards accelerated retinopathy progression in operated eyes compared to unoperated fellow eyes. However, this trend did not reach statistical significance.[45]

The progression of diabetic retinopathy, particularly in studies evaluating ECCE and ICCE, may be caused by breakdown of the blood ocular barrier or enhanced inflammation

in diabetic patients after cataract extraction. The smaller incision size and shorter surgical time in phacoemulsification decrease inflammation and may induce less breakdown of the blood ocular barrier. The lack of clinically significant effects in certain studies does not rule out any adverse effect from surgery. One day after uneventful phacoemulsification and IOL implantation VEGF, hepatocyte growth factor, interleukin-1 and pigment epithelium-derived factor concentrations increase but take one month to decline to preoperative levels. These results confirm altered concentrations of angiogenic and growth factors after cataract surgery, which may induce subclinical or even clinical worsening of diabetic retinopathy and maculopathy.[101]

EFFECT OF CATARACT SURGERY ON MACULAR EDEMA

Altered concentrations of angiogenic factors after cataract surgery may aggravate maculopathy.[101] Following uneventful cataract surgery, OCT imaging has revealed increased retinal thickness in diabetic eyes without retinopathy which was comparable to nondiabetics, however there was a trend toward more increase in retinal thickness in diabetics which was evident up to 3 months after surgery.[102]

In eyes without CSME at the time of surgery, either because the condition had not developed or was successfully treated, ETDRS report number 25 showed no statistically significant difference in the prevalence of macular edema before and one year after surgery.[45] Another study reported a 56% incidence of new clinically detectable macular edema one year after surgery but spontaneous resolution occurred without treatment in 50% by six months, and in 75% by one year after surgery.[46] Other data showed that, although macular edema is common after cataract surgery it may follow a benign course and in many patients the development of clinically significant macular edema postoperatively probably represents progression in the natural course of the disease rather than a direct effect of surgery.[49]

Eyes with established CSME at the time of surgery behaved quite differently, none resolved spontaneously within a year and the majority showed clinical and angiographic evidence of deterioration. Overall, CSME present in diabetic eyes at the time of cataract surgery is unlikely to resolve spontaneously. It seems possible that case reports of severe macular edema after cataract surgery describe postoperative deterioration of pre-existing macular edema which was untreated because of the lens opacity.[45]

Studies on diabetic macular edema after cataract surgery are difficult to perform because they must be able to differentiate diabetic macular edema from pseudophakic cystoid macular edema (Irvine-Gass syndrome). Fluorescein angiography may help make the distinction; if angiography shows a petaloid pattern associated with optic disc hyperfluorescence without retinopathy or microaneurysms, one may consider the edema to be the result of Irvine-Gass syndrome. However, some authors do not agree that optic disc hyperfluorescence necessarily indicates the presence of pseudophakic macular edema.[45,103]

Postoperative laser photocoagulation for diabetic macular edema is controversial. Pollack et al[104] performed the first prospective controlled trial to evaluate the natural course of diabetic macular edema after cataract surgery. They found that only a minority of patients who developed macular edema required focal laser photocoagulation. Similarly, Dowler et al[46] reported that macular edema resolves spontaneously if it arises after surgery but not when it is present prior to surgery, suggesting that early laser treatment of all cases of postoperative diabetic macular edema is unnecessary. In general, specialists do not perform argon laser treatment until 6 months after cataract surgery.

POSTERIOR CAPSULE OPACIFICATION

Posterior capsule opacification (PCO) remains a common complication of modern cataract surgery with a reported rate of 20 to 50% five years

after surgery. Modifications in surgical technique and improvements in IOL technology have reduced the rate of PCO.[55,105] Lens epithelial cells (LECs) are the source and cause of PCO; the proliferation of these cells is affected by several factors including optic edge design, optic-haptic junction and IOL material.

Another important determinant is postoperative inflammation. The degree of postoperative inflammation may be related to the development of PCO. It has been suggested that surgical trauma and contact with the IOL stimulate residual LECs to produce cytokines. These cytokines may affect LECs in an autocrine or paracrine fashion and induce collagen production and fibrous metaplasia.[106] Eyes of diabetic patients already have incompetent blood-aqueous barrier function and are predisposed to postoperative inflammation. Although many surgeons believe that PCO is more common and severe in diabetic patients, the matter still remains controversial. Using retroillumination images, Zaczek and Zetterstrom[107] demonstrated less PCO in diabetic patients than in nondiabetic controls.

New diagnostic systems have facilitated the evaluation of PCO. Hayashi et al[108] quantitatively measured PCO density using an Scheimpflug slit-image analysis system and found no significant difference between diabetic and non-diabetic patients up to 12 months after cataract surgery. However, at 18 months and later, PCO increased significantly in the diabetic group. Their results also demonstrated that diabetic patients were significantly more likely to require laser capsulotomy than controls. Ebihara at al[58] using the POCO system (a software for semiobjective assessment of PCO) also found that diabetic patients had significantly more severe PCO after cataract surgery than non-diabetic patients. Another study reported anterior capsular contraction to be more common in diabetic patients, especially those with diabetic retinopathy.[109]

CONCLUSION

The number of people with diabetes mellitus is increasing exponentially. Diabetics have not always shared the same favorable outcomes after cataract surgery as their nondiabetic counterparts. New surgical and pharmacologic therapies may now allow for safer and more effecttive surgery in diabetic individuals. Special attention to systemic and ocular conditions is needed.

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