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Review Article

Cataract Surgery in Patients with Age-Related Macular Degeneration

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Abstract

There are many common factors that share cataract and AMD. Both of them increases incidence as people age and factors as tobacco, solar exposition, heritage, free radicals and cardiovascular factors are found in cataract and AMD. Then, it is less likely to detect AMD in patients who have a moderate-severe lens opacity; and finally, cataract surgery in any way could predispose to develop AMD, perhaps through inflammatory mechanisms, or increased light transmittance with formation of free radicals; but, these assumptions have not been correlated in clinical studies, possibly because of the multifactorial conditions that share cataract and AMD. However, cataract surgery has demonstrated to be a safe procedure in the majority of cases (95%), making possible improved vision and quality of life in these patients even in the more advanced stage.

Introduction

Age-related cataracts are a worldwide cause of blindness in 10.8 million of people and 35.1 million were visually impaired in 2010, it means that cataract caused 33.4% of blindness and 18.5% of moderate to severe vision impairment [1]. Cataract prevalence increase as people age, by age 75, half of population have a cataract; by age 80, 70% of whites, 53% of Africans and 61% of Hispanics [1,2]. Cataract surgery is a successful procedure in the majority of cases (about 95%) [2]. Although, it is not free of complications, because of the surgical procedure itself or due to coexisting ocular pathology; for example, the global incidence of post surgical cystoid macular edema is about 1.17%, but it is 4-fold increase in eyes with diabetic retinopathy, 5.6-fold in epiretinal membrane and 30-fold in retinal vein occlusion, nonetheless this data it is still inconclusive in age-related macular degeneration [1-3].

Age related-Macular Degeneration (AMD) is an acquired condition of the retina that causes significant central visual impairment and legal blindness in elderly people [4,5]. In the United States, the prevalence of AMD for people older than 40 years is estimated at 9.2%, then it increases exponentially, reaching 22.8% after 75 years old [6,7]. Recently (2016) an incidence study selected by ethnicity in a population based in the United States was published, finding an overall incidence of 4.1% in Early AMD and 2.3% in late AMD, the white population is the most affected population by 5.3% and 4.1% respectively [3].

Thus, cataract and AMD are both age-related conditions that share similar comorbidities (hereditary, cardiovascular risk, free radicals, tobacco, sun exposition, etc.) [5,8-12]. It is difficult to demonstrate a correlation between cataract surgery and AMD progression or deterioration because of this close relationship. Also, cataract development itself could preclude visualization of posterior pole and prevent a correct diagnosis of AMD [13-16]. Despite this, concern still exists in ophthalmologists about the behavior of the AMD or the choroidal neovascularization in a patient undergoing cataract surgery.

The possible relationship of AMD and cataract surgery was reviewed and discussed. A very extensive searching was made; we analyzed randomized and non-randomized control trials, prospective and clinical trials. We discuss separately each type of AMD following AREDS classification. Likewise, we have intended to extract some recommendations to follow in this complicated scenario according recently clinical evidence.

Early-Intermediate AMD and Cataract Surgery

There are at least four main studies concerning cataract surgery and AMD development, the Beaver Dam Study (BDS), Blue Mountains eye Study (BMS), Rotterdam Eye Study, Los Angeles Latino Eye Study (LALOS). They evaluated the incidence of early manifestations of AMD in patients without signs of AMD at baseline who were submitted to cataract surgery and they did not find a relationship with early AMD.

However, there are numerous publications found a possible relationship and they have suggested mechanisms that could lead to progression in AMD after phacoemulsification: First, it seems that cataract extraction with implantation of an intraocular lens increases the transmission of ultraviolet and blue light, and therefore may accelerate the development of age-related macular degeneration by producing free radicals in the retina [17-19]. Some authors could demonstrate an increase in macular pigment not influenced for the lens opacification or the patient's age [20-22]. Macular pigments, composed by carotenoids lutein, zeaxanthin and meso-Z, has a maximum absorption at 460 nm and protects the retina from (photo)-oxidative injury [21,23]. This assumption is theoretical or based in observation in cell culture or animal experiments and photo-toxicity as a risk factor of AMD could not have been proved in large multicenter and/or epidemiological studies.

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Second theory, the immune system and inflammatory response may induce AMD progression after cataract surgery; the pathophysiology of AMD depends on the imbalance in inflammatory regulation. A study in diabetics and cataract extraction reported an increase of VEGF (64 npm to 746 npm), cytokine levels in aqueous humor the day after surgery [18,19,24].

Despite there is not clear a relationship between cataract surgery and AMD progression, there are studies that suggest the benefits from cataract extraction in patients with AMD in terms of visual function and quality of life, concluding that cataract surgery is cost-effective procedure in all subtypes of AMD [25-29].

Accordingly published data, cataract surgery in early AMD is beneficial in terms of vision recovery and quality of life, despite of the inconsistent data to establish or deny an association of surgery and AMD progression; probably, a previous evaluation of the risk of progression of late AMD (AREDS punctuation) must get before indicate surgery in this scenario.

Advanced AMD and Cataract Surgery

The overall incidence of late AMD is approximately 1.74% (geographic atrophy about 0.81% and neovascular AMD about 1.02%), this entity is the main cause of blindness in older population in developed countries [6].

Geographic AMD

Zhou et al., published a meta-analysis about risk of geographic atrophy and cataract surgery; the main studies analyzed were: BDS (2002), BMS (2006), AREDS (2009) and LALES (2010). A non-association between cataract surgery and geographic atrophy was found (overall OR 3.23 (95% CI 0.63-16.47)) [30].

On the contrary, in the histopathological study from van der Schaft and Cols a higher prevalence of hard drusen and disciform scars were found in pseudophakic eyes compared to phakic eyes, although there was no statistical difference [14].

The Rotterdam Eye Study published a correlation, particularly between homozygous CFH Y402H genotype carriers and the risk of dry AMD compared to heterozygous and non-carriers after cataract surgery [31].

Moreover, quantification of macular changes has been studied by infrared Autofluorescence (AF) in patients with dry AMD who were submitted to cataract extraction, and the amount of AF was increased by the surgery, but this result could not be discriminated from the change in lens status itself [32]. In addition, news tools as the MD3RI software (a computer-aided image quantification) do not found changes in Cumulated Drusen or Geographic Atrophy area Size (CDGAS) after 12 months of cataract surgery [33]. Conversely, Pipis et al., utilize modern software integrated to optical coherence tomography (advanced software of RPE) and suggest that blue light-filtering intraocular lenses have a significant photoprotective effect on the progression of geographic atrophy after cataract surgery [34].

Again, although there is not a clear association between cataract surgery and progression of geographic atrophy; visual recovery and quality of life is also increased in these patients as AREDS study reported and nowadays, cataract surgery can offer the opportunity of implanting special optics IOLs [35,36], to increase magnification or displace the image to healthy retina; the initials clinical results of a telescopic IOL implanted in patients with dry macular degeneration are safely and acceptable visual quality [35].

Neovascular AMD

It is known that neovascular AMD, can compromise in 90% of cases severely the vision (20/200 or worse) if left untreated [37], but with the advent of anti-vascular Endothelial Growth Factor (anti-VEGF) intravitreal injections as therapy in wet AMD has got stabilize (90%) or even improved vision (30%) in a large number of cases [38-43].

The 10-year follow-up of the BMS, as well many others epidemiological studies, observed the development of neovascular AMD in 3.7% of subjects followed, and an increase in incidence in presence of cataract surgery with an odds ratio of 3.3 (95% CI, 1,1-9.9) [44-48]. However AREDS report 25 [49] study demonstrated no clear effect of cataract surgery on the risk of progression to advanced AMD, likewise the study from Sutter and Cols [41] concluded that pseudophakia did not raise the risk of development of neovascular AMD (odds ratio of 1.035; CI 95% 0.770-1.391).

More recently, studies published have not showed an increase in recurrence, number of injections or worsening of visual acuity when compared with non-operated eyes [15,16,25-27,39-43,50-56]. However, Lee and cols. studied the risk factors associated with recurrence of exudation in a series of 39 post-surgical patients previously treated with anti-VEGF for exudative AMD. They found that shorter delays of cataract surgery after diagnosis of wet AMD and shorter exudation-free periods before cataract surgery were associated with increased risk of recurrence. Thus, they suggested lower risk of recurrence for eyes with stabilized exudation more than 12 months; but, unfortunately this study did not compare with a control group (non-surgical group) [38].

Some other authors have suggested a significant increase in macular thickness at first month after cataract surgery that resolved at the third month, this finding could probably correspond to augmented susceptibility to surgical cystoid macular edema, and not related to recurrence of CNV; however these findings were not properly evaluated with a Fluorescein Angiogram (FAG) [39,52].

Baek et al., proposed the increased frequency of Posterior Vitreous Detachment (PVD) after cataract surgery as a risk factor that could affect the pharmacokinetics or therapeutic effect of anti-VEGF. The study concluded that anti-VEGF agents could penetrate more effectively in operated eyes, but at the same time this may offset by increased clearance promoted in PVD state [40].

A possible relationship between repeated intravitreal injections and increased risk of posterior capsular rupture (2.59 times higher) have been recently published, although this relationship needs to be confirmed with more randomized clinical studies [57].

The studies published about cataract surgery in patients with neovascular AMD are mainly retrospective, FAG was only performed as a diagnostic test and not on the follow-up; some of them without control group and with short periods of follow-up [15,16,25-27,39-43,50-55,58]. In addition, the protocols used in the reported studies, were inhomogeneous (treat and extend, pro-re-nata and monthly injections), but none compared these protocols between them, or even between different anti-VEGF agents (bevacizumab, ranibizumab or aflibercept) [38,39,41-43,52-55]. Then, it is required prospective research of causality and not only epidemiological studies, with long periods of follow-up to clarify studies published until now concerning this issue.

Conclusion

Some pearls can be extracted from these studies: patients with early AMD benefit most from cataract surgery. Also, cataract surgery could be offered to patients with geographic atrophy, in cases with moderate-advanced cataract to improve the visualization of the posterior pole, to improve peripheral vision or in patients with extra-foveal atrophy. In neovascular AMD cases should be stressed the importance of a period time of disease stabilization (6-12 months); the possibility of anti-VEGF intravitreal injection use in peri-operative period (1-2 weeks before cataract surgery, or combined during cataract surgery); a closely monitoring (monthly) in post-surgical patients, especially in those with less than 12 months of stabilization; and, last, if recurrence is suspected, a fluorescein angiogram is recommended in order to establish recurrence related to AMD or to cataract surgery.

qStill, there is insufficient information to support the implantation of light-filtering intraocular lenses for the prevention of the development or progression of AMD, as photo-toxicity could not demonstrate a clear relation with AMD in population studies, so it necessary more clinical studies with sufficient evidence to extrapolate recommendations about this issue.

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