Does cataract surgery really increase the risk for AMD progression?

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in San Francisco

CATARACT surgery may not increase the risk of developing neovascular age-related macular degeneration (AMD) after all, new findings from the Age-Related Eye Disease Study (AREDS) suggest.

The results could stir controversy in the ophthalmic community because they contradict earlier findings by other significant studies, which found a two-to-five-fold increased risk of developing AMD in patients who had undergone cataract surgery, according to Frederick Ferris MD, lead investigator on the new study and director of the division of epidemiology and clinical research at the National Eye Institute in Bethesda, Maryland.

“If we look at all of the evidence, we do not find clear evidence of an association between cataract surgery and neovascular AMD, and most patients can be re-assured,” he said, during his presentation of the study at the annual ASCRS meeting.

In the new study, researchers closely examined 8,200 eyes, taking fundus photos every 12 months over 10 years. Some 1,700 of these eyes underwent cataract surgery and 603 eyes developed neovascular AMD over the course of the study.

The researchers defined AMD based on fundus photographic evidence of lesions associated with advanced neovascular AMD or geographic atrophy, or a clinical history of having had photoagulation for AMD.

In the data analysis, Dr Ferris and his colleagues used four different statistical approaches to test for an association between cataract surgery and AMD and also used the common co-variants for AMD progression such as age, smoking, gender, race and if the patients took any antioxidant supplements.

Disease severity was rated on a nine-point scale that has been associated with disease outcome.

The first analysis used ordinary logistic regression. After adjusting for age, which is crucial because the risk for both cataract and AMD increases with age, the researchers found a risk ratio of 1.0. In other words, there was no increase in risk associated with cataract surgery in this analysis.

In the second analysis, Dr Ferris and colleagues focused on the first five years after cataract surgery, which reduced the total number of eyes that underwent the procedure from 1,700 to 579. Here the findings were inconclusive, but if there was an increased risk, it was small and not statistically significant.

A third analysis evaluated the time until development of neovascularisation using the Cox proportional hazard model. While this analysis found a slight increase in risk, it was not statistically significant.

The fourth analysis involved identifying matched cases and controls, taking the cases that had undergone surgery and if both eyes had cataract surgery, looking at the eye that had cataract surgery first. Then, the researchers compared these eyes to the control eyes that didn’t have cataract surgery while matching for age, AMD severity and AREDS treatment groups. Here the odds ratio was less than 1.0, which indicates a trend in the direction of protection, but again the results were not statistically significant.

“We worked hard to look every way we could because when you don’t have consistent findings, it makes it hard to know what the truth is,” said Dr Ferris.

Contradictions with previous studies

The results are surprising because of the above-mentioned earlier findings and the strong biological plausibility of an association between cataract surgery and AMD progression, he told EuroTimes during a follow-up interview.

The Beaver Dam Eye Study which began in 1987 and was funded by the NEI, enrolled more than 6,000 participants aged between 43 and 84 years of age in Beaver Dam, Wisconsin. The researchers examined the association between cataract surgery and the incidence of age-related maculopathy (ARM) in this population and concluded that signs of geographic atrophy were four times as likely to occur in an eye that had undergone cataract surgery. In addition, signs of exudative macular degeneration were three times as likely to develop after cataract surgery (Klein et al;Arch Ophthalmol; Nov 2002;120:1551-1558).

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Furthermore, data from three large population-based studies concluded that a history of cataract surgery might be associated with a higher prevalence of AMD (Fremman EE et al,Am J Ophthalmol; Nov 2003; 136 (5):961).

These studies made a strong case for an association between cataract extraction and AMD progression largely because they are population based, said Dr Ferris. But, there is also a possible confounding factor involved in the findings.

“Patients come in with decreased vision, drusen near the fovea, but without definite advanced AMD. There is a tendency to say, ‘Let’s take the cataract out and see what happens.’ W hat happens is sometimes advanced AMD develops, not because of the cataract extraction but because early advanced AMD was the cause of the vision loss to start with. It’s easy for us to think the cataract extraction caused the AMD,” when actually the early changes of the advanced AMD caused the cataract extraction,” he said.

Some studies support AREDS findings

But other studies have supported the recent findings by AREDS. The Blue Mountain Eye Study – a large Australian population-based study conducted during the 1990s in more than 3,500 individuals aged 49 years and older – concluded after five- and 10-year follow-ups that there was no evidence of a clear association that could not be explained by the age-related increase in prevalence in both conditions (Wang J; Ophthalmic Epidemiol; 1999 Dec;6(4):317-26).

And a recent review of the current literature concluded that there was no conclusive evidence to support a clear association between cataract extraction and progression of AMD (Smith BT; Curr Opin Ophthalmol. 2005 Jun; 16(3):166-9).

Regarding the biological plausibility, it is expected that cataract surgery would result in the release of cytokines and potentially create an atmosphere where AMD risk increases, Dr Ferris told EuroTimes. Stirring up an inflammatory response in a patient who already has large drusen might tip the balance, he also said.

In part because of the biological plausibility, Dr Ferris is still awaiting the results of further analysis that focuses on patients with geographic atrophy and other subgroups that might face an increased risk.

Preliminary results from this geographic atrophy subgroup indicate this may be so.

“We looked at the most severe eyes, particularly those eyes that already had depigmentation and geographic atrophy away from the centre and in that subgroup there may be an increased risk. However, this is the group that is potentially subject to decreased vision from AMD. Then they have cataract surgery and the AMD does what it would have done anyway; it progresses and it would have done so without the cataract surgery,” he said.

“Whether there is an increased risk through cataract surgery or not, you have to tell patients who have fundus changes putting them at high risk for progression to advanced AMD that they may develop advanced AMD in the next few years, and because of that they should be seen regularly,” he added.

The NEI’s Age-related Eye Disease Study is a multi-centre cohort study designed to assess the clinical progression, prognosis and risk factors of both AMD and cataracts and to evaluate the effects of high antioxidant intake on the progression of both diseases. From 1990 to 1998 more than 4,500 participants were recruited for the study, and findinds continue to be published.

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