In patients who cannot afford the cost of chronic medical therapy or in whom compliance is a problem, trabeculectomy is a viable alternative as initial treatment. However, they should be warned of the higher rate of developing cataracts, which may negate the cost-effectiveness of surgical therapy.

The quality of life of patients with glaucoma appears to be negatively affected with increasing severity of the disease. It is essential that ophthalmologists educate these patients regarding the nature of their disease and provide them optimal treatment to lessen the impact on the quality of life.

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Advanced Glaucoma Intervention Study (AGIS)[1]

Reviewed by Jesus Altuna, MD

STUDY SUMMARY

The Advanced Glaucoma Intervention Study is a multicenter, prospective, randomized study on advanced primary open-angle glaucoma patients (POAG) that have failed initial medical treatment. The study assessed the outcomes of sequences of interventions involving trabeculectomy and argon laser trabeculoplasty. Specifically, the association between control of intraocular pressure (IOP) in the two treatment sequences and visual field preservation was determined.

Patients with advanced open-angle glaucoma aged 35 to 80 years old were enrolled into the study. Eligible eyes had to be phakic, on maximum tolerated medical therapy, with best corrected Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity score of at least 56 letters (Snellen equivalent approximately 20/80 or 6/24, consistently elevated intraocular pressures of 18 mm Hg or greater, glaucoma visual-field defect score ranging from 1 to 16, and optic disk rim narrowing. Visual-field defect scores derived from Humphrey 24-2 threshold fields were developed for this study and range from 0 (no defect) to 20 (end-stage glaucoma).

Eyes were randomly assigned to one of two sequences of glaucoma interventions: initial argon laser trabeculoplasty followed by trabeculectomy and trabeculectomy (ATT), and initial trabeculectomy followed by argon laser trabeculoplasty and trabeculectomy (TAT).

The outcome measure is a change from baseline in follow-up of visual-field defect score. The relationship between intraocular pressure (IOP) and progression of visual-field damage over 6 or more years of follow-up was determined.

The AGIS 7 report can be viewed as a dose-response analysis. Two analyses were used by the investigators. In the predictive analysis, the "dose" was the average IOP from the first three 6-month visits. In the associative analysis, the "dose" was the percent of visits over 6 years at which the treated eye achieved target IOP (<18 mm Hg). The response for both analyses was visual-field progression. The predictive analysis was designed to assess whether IOP during early follow-up is predictive of subsequent change from baseline in visual-field defect score. Seven hundred thirty eight eyes were categorized into three groups in accordance with the average IOP over the 6th, 12th, 18th month visits: Group A (<14 mm Hg), Group B (14-17.5 mm Hg) and Group C (>17.5 mm Hg). The associative analysis is a measure of consistency of IOP control. Five hundred eighty six eyes were further categorized into four groups based on the percent of 6-month visits over the first 6 follow-up years in which eyes presented with IOP less than 18 mm Hg: Group A (100%), Group B (>75% - <100%), Group C (50% - 75%) and Group D (0% - <50%).

In the predictive analysis, eyes with average IOP greater than 17.5mm Hg had an estimated worsening during subsequent follow-up that was 1 unit of visual-field defect score greater than eyes with average IOP less than 14 mm Hg ($p = 0.002$). This amount of worsening was greater at 7 years (1.89 units; $p < 0.001$) than at 2 years (0.64 units; $p = 0.071$). In the associative analysis, eyes with 100% of visits with IOP less than 18 mm Hg over 6 years had mean changes from baseline in visual-field defect score close to zero during follow-up, whereas eyes with less than 50% of visits with IOP less than 18 mm Hg had an estimated worsening over follow-up of 0.63 units of visual-field defect score ($p = 0.083$). This degree of worsening was greater at 7 years (1.93 units; $p < 0.001$) than at 2 years (0.25 units; $p = 0.572$).

COMMENTS

This study has a long follow-up period of up to 7 years with a large sample size of 591 patients s(789 eyes). Standardized protocol was followed in all the different centers participating in the study. Eligibility measurements were separated from baseline measurements obtained for all patients once they were randomized to the two treatment sequences.

Study limitations

Predictive and associative analyses were not part of the original protocol but added afterwards. Bias may therefore be introduced into the analyses. Moreover, only one visual field was obtained to document baseline glaucomatous defects prior to treatment. Several studies[2,3] have shown the neccesity of obtaining several visual fields as baseline, due to the short-term fluctuation present in threshold sensitivities.

In the analyses, the cases were not stratified according to the degree of glaucoma damage. In spite of the title "Advanced Glaucoma," advanced cases with visual-field defect score greater than 16 were excluded. Early cases of glaucoma were also included because the inclusion criteria of the visual-field defect score ranged from 1 to 16.

Responses to the two treatment sequences described were among the white and black patients. This may not apply to patients from other ethnic groups.

IMPLICATIONS ON CLINICAL PRACTICE

The AGIS showed that early response to treatment predicts a more favorable outcome. The predictive analysis suggests that patients who achieved the target IOP following initial intervention have better preservation of the visual field. Conversely, those who have not achieved target IOP after 6 months did worse. It is worthy to note that when IOP is more resistant to surgical or medical intervention, the outcome is generally worse. Low IOP is desirable as long as complications are avoided or kept to a minimum. The risk-to-benefit ratio of any treatment should always be weighed by both physician and patient. The treatment objective should always be individualized.

An important issue for any study to address is clinical applicability. The AGIS study does not apply to all glaucoma patients, but is limited to advanced POAG. Glaucoma patients from other ethnic groups may also have different responses to the surgical treatment programs used in AGIS.

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