Visual Acuity and Visual Field Impairment in Usher Syndrome

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**Objective:** To determine the extent of visual acuity and visual field impairment in patients with types 1 and 2 Usher syndrome.

**Methods:** The records of 53 patients with type 1 and 120 patients with type 2 Usher syndrome were reviewed for visual acuity and visual field area at their most recent visit. Visual field areas were determined by perimetry of the II4e and V4e isopters obtained with a Goldmann perimeter. Both ordinary and logistic regression models were used to evaluate differences in visual acuity and visual field impairment between patients with type 1 and type 2 Usher syndrome.

**Results:** The difference in visual acuity of the better eye between patients with type 1 and type 2 varied by patient age \((P=.01, \text{based on a multiple regression model})\). The maximum difference in visual acuity between the 2 groups occurred during the third and fourth decades of life (with the type 1 patients being more impaired), while more similar acuities were seen in both younger and older patients. Fifty-one percent \((n=27)\) of the type 1 patients had a visual acuity of 20/40 or better in at least 1 eye compared with 72% \((n=87)\) of the type 2 patients (age-adjusted odds ratio, 3.9). Visual field area to both the II4e \((P=.001)\) and V4e \((P<.001)\) targets was more impaired in the better eye of type 1 patients than type 2 patients. A concentric central visual field greater than 20° in at least 1 eye was present in 20% \((59\%)\) of the available 34 visual fields of type 1 patients compared with 70% \((67\%)\) of the available 104 visual fields of type 2 patients (age-adjusted odds ratio, 2.9) with the V4e target and in 6% \((21\%)\) of the available 29 visual fields of type 1 patients compared with 36% \((38\%)\) of the available 94 visual fields of type 2 patients (age-adjusted odds ratio, 4.9) with the II4e target. The fraction of patients who had a visual acuity of 20/40 or better and a concentric central visual field greater than 20° to the II4e target in at least 1 eye was 17% \((n=5)\) in the type 1 patients and 35% \((n=33)\) in the type 2 patients (age-adjusted odds ratio, 3.9).

**Conclusions:** Visual acuity and visual field area were more impaired in patients with type 1 than type 2 Usher syndrome. Of note, 27 of 53 type 1 \((51\%)\) and 87 of 120 type 2 \((72\%)\) patients had a visual acuity of 20/40 or better in at least 1 eye. These data are useful for overall counseling of patients with Usher syndrome.


**RESULTS**

Previously reported on heterogeneity of vestibular responses, level of hearing deficit, and, to a lesser extent, visual impairment in patients with type 1 and type 2 Usher syndrome (retinitis pigmentosa and congenital hearing loss). On the basis of their vestibular responses and level of hearing loss, cases were classified into type 1 or type 2 Usher syndrome. Type 1 patients have severe hearing loss (with a pure-tone average of 100 dB or greater), absent vestibular responses on caloric testing, and unintelligible speech, while type 2 patients have vestibular responses to caloric testing and less severely impaired hearing (pure-tone average most often between 40 and 90 dB), with intelligible speech.

Although the phenotypes of patients with type 1 and type 2 Usher syndrome are distinct, based on vestibular and audiometric patterns, the extent of visual impairment both within and between the 2 groups warrants further analysis on a large group of such patients. The purpose of this study was to quantitate the extent of visual acuity and visual field impairment in our population of 53 patients with type 1 and 120 patients with type 2 Usher syndrome. These data are useful for counseling patients as to their potential for loss of visual function.

The median visual acuity of the better eye was 1 line worse in type 1 patients \((20/40)\) than in type 2 patients \((20/30)\). The mean...
PATIENTS AND METHODS

The medical records of all patients in whom type 1 or type 2 Usher syndrome was diagnosed were reviewed retrospectively for accuracy of the original diagnosis and ophthalmic findings. A total of 59 type 1 patients and 123 type 2 patients were identified for possible study. Two patients who were initially diagnosed as having Usher syndrome and later found to have a rare form of metabolic disease were excluded. Briefly, patients with type 1 Usher syndrome demonstrated absent vestibular reflexes to caloric testing, severe hearing impairment, unintelligible speech, and retinitis pigmentosa by electroretinographic and clinical criteria. Patients with type 2 disease had recordable vestibular responses to caloric testing, less severely impaired hearing with intelligible speech, and retinitis pigmentosa.

Patients with other ocular diseases affecting their visual acuity or visual field area were also excluded. Six type 1 patients (1 with bullous keratopathy; 2 children in whom visual acuity could not be determined, 2 without a recorded best-corrected visual acuity, and 1 with uveitis) and 3 patients with type 2 disease (1 with ocular trauma, 1 with retinal detachment, and a patient with an entirely normal speech pattern) were excluded. Thus, 53 type 1 and 120 type 2 patients were included in the study. Patients with cystoid macular edema were included, as were pseudophakic patients.

The mean (±SEM) ages of all 53 type 1 and 120 type 2 patients were 31.8±2.2 years and 35.7±1.1 years, respectively (P=.08; 2-sample t test). The median ages were 30.0 years for type 1 patients and 36.0 years for type 2 patients. The sex ratios were similar, with 21 type 1 patients (40%) and 63 type 2 patients (32%) being male (P=.12; χ² test).

Since there were relatively few instances of multiple subjects from a single family (14 patients from 6 type 1 families and 23 patients from 11 type 2 families), no adjustments were made for intrafamilial correlation, and all subjects were included in the analysis.

Snellen visual acuity at the most recent patient visit was converted to logarithm of the minimum angle of resolution (logMAR) acuity by taking the log₁₀ of the inverse of the Snellen ratio. Patients with a visual acuity in the better eye of counting fingers (type 2, 2 patients), hand motions (type 1, 2 patients; type 2, 2 patients), and light perception (type 2, 1 patient) were assigned Snellen (logMAR) acuities of 20/2400 (2.1), 20/4800 (2.4), and 20/9600 (2.7), respectively. These estimated Snellen acuities were arrived at by approximate extrapolation from a Feinbloom low-vision chart used in our clinic, which was used to record a visual acuity as low as 3/600 (20/2400). Because our analyses were on visual impairment in the better eye, visual acuity in only 2 type 1 and 5 type 2 patients was recorded as counting fingers, hand motions, or light perception in the data. None of the patients included in this study had lost all vision in both eyes.

Kinetic visual field isopters to the V4e and I4e targets were plotted from nonseeing to seeing regions by means of a standard calibrated Goldmann perimeter. Visual field areas on the most recent visit were available for 29 type 1 patients (55%) and 94 type 2 patients (78%) with the I4e target, and 34 type 1 patients (64%) and 104 type 2 patients (87%) with the V4e target. Visual fields recorded as unobtainable in both eyes were excluded (I4e, no type 1 and 3 type 2 patients; V4e, no type 1 or type 2 patients). The visual field areas were determined by planimetry with the use of a digitizing tablet and computer software and expressed in square inches. The total area of remaining visual field was computed, subtracting any scotomatous regions that may have been present within an isopter. Patients with an intact concentric central region of greater than 20° of visual field (ie, the 10° isopter) on the most recent visit were identified by inspection.

Reviewing visual acuity and visual field data over time from individual patients with type 1 Usher syndrome and profound deafness convinced us that reliable information from subjective tests of visual function could be obtained from such patients with the use of an interpreter.

A linear regression model was used for the statistical evaluation of the effects of age and type of Usher syndrome on the continuous variables of logMAR visual acuity and visual field area. In an attempt to reflect the changing relationship of the response variables with age, quadratic curves were used to fit the data. With the use of a multivariable model with effects for age, type of Usher syndrome, and their interactions, a single coefficient of multiple determination (R²) for the whole model is reported. We analyzed visual acuity and visual field data from the better eye of each patient.

Logistic regression models were used to evaluate the influence of age and type of Usher syndrome on the following dichotomous variables: visual acuity of 20/40 or better, concentric central visual field greater than 20°, and both visual acuity of 20/40 or better and concentric central visual field greater than 20° in at least 1 eye. A probability value of greater than .05 was considered nonsignificant. As in the linear regression model, we analyzed visual acuity and visual field data from the better eye of each patient.
(±SEM) ages of these patients were 45.8±5.5 years for type 1 and 52.4±2.9 years for type 2 (P=.26). The mean ages of these patients were 21.2 and 19.2 years greater, respectively, than those of the patients with visual acuities of 20/40 or better in at least 1 eye.

Because the main dichotomous response variable was chosen to be a visual acuity of 20/40 or better in at least 1 eye, statistical analysis was not performed on the subgroups of patients with visual acuities of 20/50 to 20/100 and 20/200 or worse to avoid repeated statistical testing of the data.

Visual field area to the II4e target was markedly depressed in both type 1 and type 2 patients (Figure 2, top). The mean (±SEM) visual field area of the eye with the larger field area (ie, the better eye) to the II4e target was 1.14±0.61 sq in for 29 type 1 patients and 2.81±0.49 sq in for 94 type 2 patients. The median visual field area to the II4e target was 0.23 sq in for the type 1 patients and 0.66 sq in for the type 2 patients. Among patients with measured visual fields to the II4e target, the mean (±SEM) age of the type 1 patients (29.0±2.2 years) was marginally significantly (P=.06) younger than that of the type 2 patients (33.6±1.2 years). No significant difference was detected between the shapes of the II4e target visual field area–age curves (Figure 2, top) for the type 1 and type 2 patients (P=.61; df=2). A statistically significant difference was also not apparent if comparisons were made between the log of remaining visual field areas (P=.26). However, with the assumption of similar shapes in the curves for the 2 groups, there was significant separation between the curves (P=.001), with the type 1 patients being more impaired (2.73 sq in smaller average field area). The correlation coefficient, R², was 0.29 (Figure 2, top).

The mean (±SEM) visual field area in the better eye to the V4e target was 5.72±1.24 sq in for 34 type 1 patients and 9.45±0.94 sq in for 104 type 2 patients. The median visual field areas to the V4e target were 1.99 sq in for the type 1 group and 5.47 sq in for the type 2 group.

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Among patients with measured visual fields to the V4e target, the mean (±SEM) age of the type 1 patients (29.5±2.1 years) was significantly (P=.01) less than that of the type 2 patients (35.3±1.1 years). Again, the shapes of the V4e visual field area–age curves (Figure 2, bottom) were not significantly different for the type 1 and type 2 patients (P=.36; df=2). Assuming similar shapes for the 2 curves, type 1 patients exhibited significantly worse (6.22 sq in smaller average field area) V4e visual field areas than did type 2 patients (P<.001). Comparing the log of remaining visual field areas still showed no significant difference between type 1 and type 2 patients (P=.54) in the shapes of their area-age curves. The correlation coefficient, R², was 0.31 (Figure 2, bottom).

Visual field isopters to the II4e and V4e targets were inspected to identify those patients who had a concentric central region of greater than 20° in at least 1 eye (Table). Among patients with measured visual fields to target II4e, the mean (±SEM) age of the type 1 group (19.6±3.0 years) was 8.1 years less (P=.06) than that of the type 2 group (27.7±1.7 years). For target V4e, the mean (±SEM) age of the type 1 patients (24.8±1.8 years) was 7.2 years less (P=.005) than that of the type 2 patients (32.0±1.2 years). After adjusting for changes with age in a logistic regression model, the type 2 patients were more likely to have a concentric central visual field of greater than 20° to both the II4e (P=.006) and V4e (P=.03) targets than were the type 1 patients (odds ratio, 4.9 and 2.9, respectively) by the logistic regression model.

As shown in the Table, the type 2 patients were also more likely to have, in at least 1 eye, both a visual acuity of 20/40 or better and a concentric central visual field area greater than 20° in the same eye to both the II4e (P=.02) and V4e (P=.002) targets than were the type 1 patients (odds ratio, 3.9 and 4.3, respectively). These results were again adjusted for the effects of age by means of a logistic regression model.

Visual acuity and visual field area in the type 1 patients were more severely impaired than those in the type 2 group. The type 1 patients were less likely than the type 2 patients to have a visual acuity of 20/40 or better and/or a concentric central visual field region greater than 20°. However, a majority of both type 1 and type 2 patients showed a visual acuity of 20/40 or better into the middle portion of their fifth decade of life, after which the visual acuity tended to become substantially more impaired. Of note, only 7 (4%) of our entire population of 173 patients with Usher syndrome showed a visual acuity of counting fingers or worse in their better eye, and none had no light perception in both eyes.

Visual acuity was more impaired in the type 1 than the type 2 patients with Usher syndrome by about 2 lines of Snellen acuity until the fifth decade of life (about age 45 years). There was a trend for severity in these 2 groups of patients to become more similar as both groups developed greater impairment of visual acuity. However, it is difficult to confirm this trend statistically because of the different shapes (P=.01) of the visual acuity–age curves in the 2 groups and the small number of patients older than 50 years.

It has previously been shown that patients with Usher syndrome are susceptible to visual loss from posterior subcapsular cataracts, atrophic-appearing or cystoid macular lesions, and epiretinal membranes, which can be seen in patients with retinitis pigmentosa. Type 1 patients are more likely than type 2 patients to have an atrophic macular lesion, and this may, in part, contribute to the decreased visual acuity observed in this group. Cataracts were unlikely to have a major influence on our findings because patients with visually significant cataracts had been referred for lens extraction. Furthermore, the severity of posterior subcapsular cataract, which is recorded systematically in our patients, was similar in patients with types 1 and 2 disease. For example, 22 of 53 patients (42%) of the type 1 group and 43 of 120 patients (36%) of the type 2 group had no cataract, and 7 of 53 patients (13%) and 12 of 120 patients (10%) had undergone lens extraction (data not shown).

Although a prospective study on a large number of patients with Usher syndrome during a long period might be difficult to complete successfully, such an investigation would potentially better define the natural course of visual loss in these patients. Furthermore, in future prospective studies, it would be interesting to correlate visual measures and phenotypes of such patients with specific genetic mutations, such as in the myosin VIIA gene identified in some patients with type 1b Usher syndrome.

Our data support the hypothesis that patients with type 1 disease are more visually impaired than patients with type 2 disease. It is of interest that, in this substantial patient population, 51% of patients with type 1 and 72% of patients with type 2 Usher syndrome had a visual acuity of 20/40 or better in at least 1 eye, and none of them lost all vision in either eye. These findings will be useful for the overall counseling of patients with Usher syndrome.

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