SCIENTIFIC REPORT

Continued use of dorzolamide for the treatment of cystoid macular oedema in patients with retinitis pigmentosa

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Aim: To determine the value of a topical carbonic anhydrase inhibitor for extended treatment of cystoid macular oedema (CME) in patients with retinitis pigmentosa (RP).

Method: Eight patients with RP and foveal cystic-appearing lesions observed on fundus examination and by optical coherence tomography (OCT) testing were treated with a topical form of carbonic anhydrase inhibitor.

Results: Foveal cystic-like spaces were documented by OCT testing in all eight patients before treatment. All patients had a significant reduction in their foveal thickness (FT) and foveal zone thickness (FZT) in at least one eye after using 2% dorzolamide three times a day for 1 or 2 months. Six patients had an improvement in both eyes. After an additional 6–13 months of the same treatment regimen, out of six patients who had a sustained reduction in FT and FZT in at least one eye, four had this reduction in both eyes. While they were still taking Trusopt, a recurrence (rebound) of CME in both eyes was observed in two patients, whereas one patient had a sustained improvement in one eye and rebound of CME in the other eye. Out of 8 patients, 3 showed an improvement in their visual acuity by $\geq$7 letters, in at least one eye, on Snellen acuity charts, which was determined as clinically significant.

Conclusion: Results from this study suggest that patients with RP could potentially sustain a beneficial effect from continued treatment with a topical form of carbonic anhydrase inhibitor.

Cystoid macular oedema (CME) has been known to be associated with retinitis pigmentosa (RP) in a certain percentage of patients.[1–5] It is responsible for patient complaints of both blurred and reduced visual acuity and subsequent atrophic changes in the fovea. The use of either oral or topical carbonic anhydrase inhibitors has been described as potentially useful for the treatment of CME in such patients.[6–11] However, a recurrence or rebound of macular oedema has been reported in patients with RP, owing to the continued use of both oral acetazolamide[11] and methazolamide.[12]

We observed that a topical form of carbonic anhydrase inhibitor was also effective for treating CME in 15 patients with RP who were treated for an average duration of 4.5 months.[13] To our knowledge, there have been no reports in the literature that document sustained effectiveness of a topical form of carbonic anhydrase inhibitor for CME over a more extended period of time in such patients.

In the present study, we report on eight patients with RP with known CME who were treated with 2% dorzolamide for a period of 7–15 months.

PATIENTS AND METHODS

This prospective study included eight patients with RP with known CME (table 1). All patients were examined by one of the authors (GAF) and diagnosed with RP on the basis of their clinical findings, including poor night vision, restricted peripheral vision and characteristic funduscopic findings. All eight patients had foveal cystic-appearing lesions apparent on fundus examination and confirmed by optical coherence tomography (OCT) testing. One patient (patient 8) had a macular hole of partial thickness in one eye. None of them had other ocular diseases or were taking any treatment that could affect retinal function. These patients were all previously included in an initial study on the short-term use of a topical carbonic anhydrase inhibitor in patients with RP with CME.[13]

A baseline acuity for subsequent best-corrected visual acuities (BCVAs) were obtained on all patients with a Snellen projection chart. On the basis of a previous study,[14] an increase of seven or more letters was considered as a significant change in visual acuity. Slit-lamp biomicroscopy of the anterior segment, intraocular pressure by applanation tonometry, and funduscopic examination by both direct and indirect ophthalmoscopy were also carried out on all patients.

Baseline OCT measurements were obtained for all eight patients with an OCT 3 commercial instrument (Stratus, Carl-Zeiss Meditec, Dublin, California, USA). Six OCT images were acquired by 6 mm radial scans centred on fixation. The central foveal thickness (FT) was calculated as an average of the six measurements obtained at the centre of each scan. We also measured the foveal zone thickness (FZT) from a region within 1000 μ centred at the foveola, where 100 different points are automatically measured by the OCT 3 scanner using retinal mapping software of the OCT. A foveal retinal thickness change >16% (mean (2SD) and FZT change from pretreatment >11% (mean (2SD) were used as a statistically significant intervisit change. These percentages were derived on the basis of the intervisit variability of OCT, FT and FZT in 5 patients with RP (9 eyes) with CME who were untreated.[13] In order to determine the response to continued treatment for each patient, we compared all retinal thickness measurements obtained during the follow-up visits at the baseline.

After baseline BCVA and OCT measurements were obtained, all patients were assigned to use 2% dorzolamide (Trusopt) three times daily in each eye. They then re-visited several times within a period of 7–15 months (average 11.6 months) from baseline (table 1). All patients were asked about the development of any subjective visual improvement or side effects. BCVA, slit-lamp biomicroscopy of the anterior segment, intraocular pressure measurements and funduscopic examination were obtained as performed at baseline. Repeat OCT measures were obtained as well.

This study was approved by an institutional review board at the University of Illinois at Chicago, Chicago, Illinois, USA. Informed consent was obtained from all patients after explaining the nature of the procedures. The study was conducted in accordance with the regulations of the Health Insurance Portability and Accountability Act.

Abbreviations: BCVA, best-corrected visual acuity; CME, cystoid macular oedema; FT, foveal thickness; FZT, foveal zone thickness; OCT, optical coherence tomography; RP, retinitis pigmentosa

Table 1 Best-corrected visual acuity and foveal thickness in patients treated with topical 2% dorzolamide

Patient no	Visit number, months of follow-up	Vision		FT, mean FT difference (%)		FZT,* mean FZT difference (%)	
		OD	OS	OD	OS	OD	OS
1	1	20/50 (−2)	20/30 (−2)	356	491	343	456
	2, 1	20/40 (+2)	20/25 (−1)	**158 (−56)**	419 (−15)	**219 (−36)**	**395 (−13)**
	3, 2	20/25 (−2)	20/25 (−1)	**144 (−60)**	464 (−5)	**208 (−39)**	428 (−6)
	4, 4	20/30 (+2)	20/25 (−2)	**158 (−56)**	482 (−2)	**225 (−34)**	435 (−5)
	5, 10	20/30 (−1)	20/25 (−1)	**255 (−28)**	423 (−14)	**284 (−17)**	404 (−11)
2	1	20/40 (+2)	20/40 (−3)	515	496	514	495
	2, 2	20/40 (−1)	20/40 (−3)	**396 (−23)**	482 (−3)	**412 (−20)**	458 (−7)
	3, 3	20/40 (−2)	20/40 (−2)	**404 (−22)**	441 (−11)	**413 (−20)**	445 (−10)
	4, 5	20/40	20/40 (−2)	**378 (−27)**	**395 (−20)**	**386 (−25)**	**402 (−19)**
	5, 7	20/30 (−2)	20/40 (−2)	**423 (−18)**	444 (−10)	**425 (−17)**	440 (−11)
	6, 9	20/30	20/40 (−1)	**364 (−29)**	**372 (−25)**	**375 (−27)**	**376 (−24)**
	7, 12	20/40 (+2)	20/40 (+2)	461 (−10)	502 (+1)	463 (−10)	493 (−1)
3	1	20/40 (−2)	20/50 (+1)	574	523	530	489
	2, 2	20/30	20/30 (+1)	**174 (−70)**	**201 (−62)**	**235 (−56)**	**254 (−48)**
	3, 3	20/30	20/30 (+2)	**179 (−69)**	**177 (−66)**	**239 (−55)**	**230 (−53)**
	4, 4	20/30	20/30 (+1)	**200 (−65)**	**198 (−62)**	**269 (−49)**	**245 (−50)**
	5, 10	20/30 (+2)	20/30 (+2)	**163 (−72)**	**179 (−66)**	**227 (−57)**	**230 (−53)**
	6, 15	20/30	20/30 (+2)	**234 (−59)**	**221 (−58)**	**288 (−46)**	**260 (−47)**
4	1	20/50 (−3)	20/60 (−1)	315	338	321	333
	2, 1	20/40 (−1)	20/60 (+1)	**250 (−21)**	**280 (−17)**	**264 (−18)**	**284 (−15)**
	3, 3	20/40 (−2)	20/60	**226 (−28)**	**238 (−30)**	**242 (−25)**	**251 (−25)**
	4, 8	20/40	20/60	**213 (−32)**	**242 (−28)**	**239 (−25)**	**261 (−22)**
	5, 13	20/40 (+2)	20/50 (−1)	**213 (−32)**	**281 (−17)**	**243 (−24)**	295 (−11)
5	1	20/30 (+1)	20/40 (+2)	340	311	349	323
	2,1	20/25	20/30 (+2)	**263 (−23)**	**249 (−20)**	**288 (−17)**	**280 (−13)**
	3, 2	20/25	20/25 (−2)	309 (−9)	285 (−8)	318 (−9)	302 (−6)
	4, 3	20/25 (+1)	20/25 (+1)	298 (−12)	**250 (−20)**	309 (−11)	**279 (−14)**
	5, 4	20/25 (−3)	20/30 (+2)	**220 (−35)**	**219 (−30)**	**261 (−25)**	**250 (−23)**
	6, 9	20/25 (−3)	20/30 (−1)	**222 (−35)**	**250 (−20)**	**267 (−23)**	**278 (−14)**
	7, 12	20/25 (−2)	20/30 (−1)	**213 (−37)**	**233 (−25)**	**258 (−26)**	**263 (−19)**
6	1	20/20 (−2)	20/25 (−2)	273	643	303	607
	2, 2	20/20	20/25 (−1)	239 (−12)	**523 (−19)**	273 (−10)	**516 (−15)**
	3, 3	20/20	20/25 (−2)	228 (−16)	**413 (−36)**	**262 (−14)**	**427 (−30)**
	4, 5	20/20	20/20 (−1)	237 (−13)	**512 (−20)**	272 (−10)	**506 (−17)**
	5, 7	20/20	20/20 (−3)	241 (−12)	584 (−9)	280 (−8)	567 (−7)
7	1	20/30 (−3)	20/30 (−1)	310	225	307	256
	2, 1	20/30 (+2)	20/25 (+2)	**228 (−26)**	**162 (−28)**	**251 (−18)**	**217 (−15)**
	3, 3	20/25 (−2)	20/25 (−2)	**169 (−45)**	**150 (−33)**	**215 (−30)**	**207 (−19)**
	4, 5	20/25 (−1)	20/25 (−2)	**217 (−30)**	271 (+20)	**159 (−48)**	**223 (−13)**
	5, 7	20/25 (−1)	20/25 (−2)	**160 (−48)**	**155 (−31)**	**208 (−32)**	**214 (−16)**
	6, 10	20/25 (−2)	20/25 (−1)	**166 (−46)**	**145 (−36)**	**224 (−27)**	**219 (−14)**
	7, 13	20/25 (−2)	20/25 (−2)	**234 (−25)**	**155 (−31)**	**266 (−13)**	**216 (−16)**
8	1	20/60 (+2)	20/30 (+1)	261	326	256	334
	2, 1	20/50 (−3)	20/30 (+2)	**217 (−17)**	**230 (−34)**	**224 (−13)**	**253 (−24)**
	3, 3	20/50 (−2)	20/25 (−2)	NA	**208 (−36)**	NA	**246 (−26)**
	4, 6	20/60 (−2)	20/25 (−2)	**214 (−18)**	**208 (−36)**	237 (+7)	**235 (−30)**
	5, 9	20/70 (+1)	20/30 (−1)	259 (−1)	286 (−12)	260 (+1)	307 (−8)
	6, 11	20/50 (−2)	20/25 (−2)	235 (−10)	**260 (−26)**	270 (+5)	**281 (−16)**

FT, foveal thickness; FZT, foveal zone thickness; OD, oculus dexter; OS, oculus sinister.
*FZT (defined as the central 1000 μ centred on the fovea).
†Bold numbers represent a significant difference of FT and FZT between visits for each patient. Determination of significant difference was based on intervisit variation (upper range and mean (2SD)) of FT and FZT changes in a control group (n = 5) with retinitis pigmentosa patients with continuing medical education (CME) (FT>16%, FZT>11%).
Positive and negative values for differences represent a direction of change: a ''+'' value indicates an increase in the FT or FZT, whereas a ''−'' value indicates a decrease in the FT or FZT. NA indicates that data could not be obtained.

RESULTS

After 1 or 2 months of treatment, 7 of the 8 patients experienced a small degree of subjective improvement in their visual acuity. Three of them showed an improvement of their visual acuity by 7 letters on Snellen acuity charts. All three maintained this improvement on follow-up examinations during 7–15 months from their baselines (table 1).

Out of eight patients, four showed a reduction in FT and FZT in both eyes (patients 3–5 and 7), and an additional four patients in one eye (patients 1, 2, 6 and 8) after the usage of dorzolamide for a period of 1 or 2 months. With further treatment for an additional period of 6–13 months, six of the eight patients maintained their initial OCT response (patients 1, 3–5, 7 and 8) in at least one eye (table 1, fig 1). Four of these six patients maintained their initial response in both eyes (patients 3–5 and 7).

By comparison, our initial study[13] on 15 patients with RP with cystoid macular oedema who were treated with dorzolamide followed patients for 2–9 months (average 4.5 months). Of the 15 patients, 10 patients were followed for only

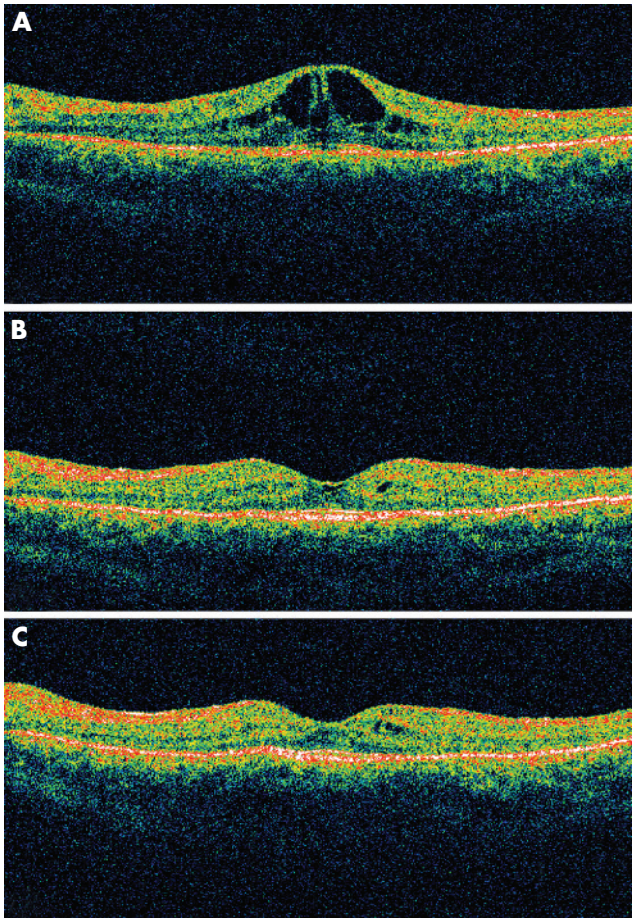

Figure 1 Patient 3. (A) Baseline optical coherence tomography (OCT; 60°) of the left eye before treatment with 2% dorzolamide shows foveal cystic-appearing spaces. (B) OCT of the same patient after 1 month of treatment. (C) OCT of the same eye after an additional 15 months of treatment.

⩽4 months, and only one was followed for >7 months. The eight patients in the current study were followed for 7–15 months, with an average of 11.6 months. Seven of the eight patients were followed for 10–15 months.

DISCUSSION

Cystoid macular oedema (CME) can compromise central visual function in patients with RP.[1–4] Previous studies have reported on the results of treatment of such patients with oral and topical forms of carbonic anhydrase inhibitors.[7–13] This treatment has been documented to show an initial improvement in CME by both fluorescein angiography and OCT imaging.[7–13] However, with the extended use of methazolamide or acetazolamide, some patients with RP showed a recurrence of macular oedema.[12–14]

In our current series of eight patients treated with 2% dorzolamide, two patients also showed a rebound in cystoid macular oedema in both eyes (table 1). However, six patients showed a sustained improvement of CME in at least one eye compared with those at baseline for a period of 7–15 months. This compares with a recently conducted study[15] that showed a recurrence of macular oedema in three of six patients with RP treated with acetazolamide within only 2–3 months of the treatment. It is reasonable to speculate that a recurrence of CME in patients with RP while taking a topical form of carbonic anhydrase inhibitor might be either delayed or even possibly occur less frequently compared with the use of an oral form in the treatment of such patients. Although only three of the eight patients in the current study showed an improvement of their visual acuity by ⩾7 letters, there is still likely to be merit in treating macular oedema in patients with RP for the possible prevention of further reduction of visual acuity in such patients.

Although the number of patients in our study is not substantial enough to make a broad generalisation, our prospective evaluation suggests that any improvement in CME with the use of a carbonic anhydrase inhibitor in patients with RP may be sustained for a longer duration with topical application than with oral administration, as monitored by OCT imaging.

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Competing interests: None.

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