Treatment outcomes for amblyopia using PEDIG amblyopia protocols: a retrospective study of 877 cases

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BACKGROUND The landmark Pediatric Eye Disease Investigators Group (PEDIG) Amblyopia Treatment Studies (ATS) 2A and 2B concluded that 6 hours of occlusion were as efficacious as full-time occlusion in treating severe amblyopia and that 2 hours occlusion were as effective as 6 in treating moderate amblyopia. We present the first retrospective study of real-world outcomes of amblyopia treatment using PEDIG amblyopia protocols in 877 patients treated at a single center.

METHODS Electronic patient records were reviewed retrospectively to identify children meeting ATS2A (severe amblyopia) and ATS2B (moderate amblyopia) inclusion criteria who presented at the Gloucestershire Eye Unit from 2013 to 2017. Clinical data for each patient were entered during routine clinical care. Severely amblyopic children were prescribed 6 hours occlusion daily, and moderately amblyopic children 2 hours, after 12 weeks refractive adaptation.

RESULTS A total of 288 children were in the ATS2A group and 589 in the ATS2B group. Of the severely amblyopic eyes, 40% achieved best-corrected visual acuity better than 0.4 logMAR at 32 weeks, increasing to 55% at 48 weeks; of the moderately amblyopic eyes, 71% achieved best-corrected visual acuity better than 0.3 logMAR at 32 weeks. The mean number of lines of visual improvement was 4.2 for severely amblyopic eyes and 2.1 for moderately amblyopic eyes.

CONCLUSIONS This is the largest reported series of amblyopia treated according to PEDIG protocols. The study population achieved outcomes comparable to those demonstrated by the PEDIG studies. This audit represents a "real-world" benchmark for treatment outcomes in clinical practice. (J AAPOS 2019;23:98.e1-4)

The landmark Pediatric Eye Disease Investigator Group (PEDIG) Amblyopia Treatment Studies (ATS) 2A[1] and 2B[2] concluded that 6 hours of occlusion were as efficacious as full-time occlusion in a cohort of 175 children with severe amblyopia (logMAR 0.7-1.3) and that 2 hours of occlusion were as effective as 6 hours in a cohort of 189 children with moderate amblyopia (logMAR 0.3-0.6). This standard of amblyopia management was adopted by the Gloucestershire Eye Unit, United Kingdom, in 2013. Since that time, the unit has used an electronic patient record (EPR; Medisoft, Heidelberg Engineering Ltd, Leeds, UK) to record every clinical interaction in the Paediatric and Orthoptic Services. In this study, we performed a review of clinical outcomes of amblyopia treatment at our institution in order to understand whether our "real-world"[3] outcomes are comparable to those achieved by trial patients who received PEDIG-prescribed treatment doses.

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Subjects and Methods

The study and data collection were deemed institutional review board exempt and conformed to all local laws and were compliant with the principles of the Declaration of Helsinki.

The medical records of patients treated at the Gloucestershire Eye Unit from June 1, 2013, to June 1, 2017, were reviewed retrospectively to identify patients with severe or moderate amblyopia. Severe amblyopia was defined logMAR visual acuity of 0.7-1.3 in the affected eye; moderate amblyopia, as logMAR visual acuity of 0.3-0.6 in the affected eye. The following clinical data were recorded as part of routine care: age at presentation, demographic

information, medical history, presenting acuity, orthoptic examination, cycloplegic refraction, and type of amblyopia.

Data were extracted from the record using the pediatric audit tool on June 1, 2017. Parameters were selected to correspond with the ATS2A (severe) and ATS2B (moderate) inclusion criteria: age <7 years; anisometropic, strabismic, or mixed-type amblyopia; visual acuity in the amblyopic eye corresponding to the moderate or severe amblyopia definition above (groups audited separately). Patients with meridional and deprivation amblyopia were excluded. Patients with visual acuity better than <0.3 or worse than 1.3 in the worse-seeing eye were excluded. Patients treated with atropine were excluded.

After a period of at least 12 weeks refractive adaptation, patients with moderate amblyopia were prescribed 2 hours of daily occlusion therapy. Patients with severe amblyopia were prescribed 6 hours of daily patching. Best-corrected visual acuity in each eye was recorded at each follow-up visit. Patients were prescribed spectacles as per local clinic policy and rechecked after 6 months.

Results

We identified a cohort of 288 children who met the ATS2A (severe) inclusion criteria and 589 children who met the ATS2B (moderate) inclusion criteria. The baseline characteristics of the two groups were similar to the PEDIG patient cohorts in terms of mean pretreatment visual acuity in the amblyopic eye, mean age at presentation, and type of amblyopia (Table 1). Outcomes were assigned in 4-week time-windows around each time interval. In the ATS2B group, 79 children were lost to follow-up by 32 weeks; in the ATS2A group, 47 were lost to follow-up by 48 weeks.

Results are presented as a cumulative frequency distribution for the moderate and severe amblyopia cohorts, respectively, in Figures 1 and 2, showing the distribution of visual acuity at baseline, 16, 32, and 48 weeks. PEDIG outcomes are included for reference.

Of the severely amblyopic eyes, 110 (40%) achieved best-corrected visual acuity better than 0.4 logMAR at 32 weeks, increasing to 147 (55%) at 48 weeks. There was no further improvement in visual acuity with continued treatment after this point. Of the moderately amblyopic eyes, 386 (71%) achieved best-corrected visual acuity better than 0.3 logMAR at 32 weeks; there was no further improvement at 48 weeks (74% best-corrected visual acuity better than 0.3 logMAR). The mean number of lines of visual improvement was 4.2 for severely amblyopic eyes, and 2.1 for moderately amblyopic eyes.

For reference, in ATS2A and ATS2B, after 12-14 weeks' refractive adaptation and 17 weeks' patching, 67% of severely amblyopic eyes achieved best-corrected visual acuity better than 0.4, with a mean of 4.8 lines visual acuity improvement, and 81% of moderately amblyopic eyes achieved best-corrected visual acuity better than 0.3, with mean 2.4 lines visual acuity improvement (Table 2).

Table 1. Comparison of baseline characteristics according to treatment group: Gloucestershire Eye Unit (GEU) versus PEDIG

	Moderate amblyopia		Severe amblyopia	
	GEU	ATS2B	GEU	ATS2A
No. participants	589	189	288	175
Mean presenting VA amblyopic eye, logMAR	0.43	0.48	0.90	0.90
Mean age, years	4.3	5.2	4.3	4.8
Type of amblyopia, percent				
Strabismic	42	40	33	27
Anisometropic	30	33	30	34
Mixed	28	27	37	38

VA, visual acuity.

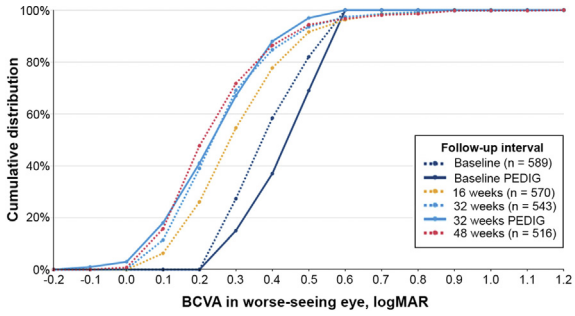

FIG 1. Visual acuity cumulative frequency distribution (comparison with PEDIG study): moderate amblyopia.

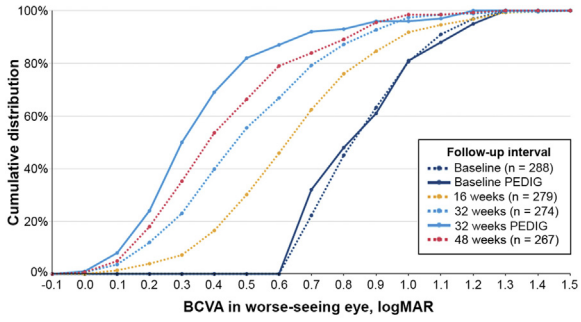

FIG 2. Visual acuity cumulative frequency distribution (comparison with PEDIG study): severe amblyopia.

Discussion

Our population achieved outcomes comparable to the PEDIG studies, albeit after a longer duration of treatment. It is encouraging that evidence from trials can be replicated in clinical practice, despite the well-established differences between clinical trial participants and patient groups not enrolled in clinical trials,[4] including differences in motivation for compliance with treatment, and attending follow-up appointments.

The "plateau" in visual acuity improvement noted after 32 weeks' treatment in moderately amblyopic eyes and after 48 weeks of treatment in severely amblyopic eyes, may guide clinicians in terms of planning duration of treatment.

Table 2. Comparison of outcomes according to treatment group

	Moderate amblyopia		Severe amblyopia	
Outcome	GEU	ATS2B	GEU	ATS2A
BCVA ≥0.4 logMAR, percent				
32 weeks			40	67
48 weeks			55	
BCVA >0.3 logMAR				
32 weeks	71	81		
48 weeks	74			
Mean no. lines improvement in VA	2.1	2.4	4.2	4.8

BCVA, best-corrected visual acuity; *VA*, visual acuity.

The Medisoft EPR is a powerful tool for collating and interrogating clinical data and is currently the sole EPR available to clinicians capable of performing built-in audit in this manner. Data were entered into the EPR in lieu of paper notes at the same time as the clinical encounter, without the need for additional orthoptist time. This approach affords a high degree of data completeness; in our series, there were no missing data points for visual acuity and refraction at each clinic visit. The audit itself is performed within minutes, and parameters can be selected such that audit standards match the ATS2A and 2B inclusion criteria, thereby generating graphics that compare local data with the PEDIG trial results.

For this study, we selected audit parameters that corresponded with the PEDIG inclusion criteria. However, other parameters can be selected, depending on the audit outcome measure of interest. We have found a useful function of the audit tool is to produce probability tables based on selecting patient age and presenting acuity in the amblyopic eye. This allows a personalized prediction to be made for each child, based on the previous outcomes at our center. For example, Table 3 represents a probability table has been generated by the EPR based on outcomes for children presenting at age 5, with baseline visual acuity of 0.9–1.0 logMAR. We are able to inform parents or caregivers that in our center, 48% of such children achieve visual acuity of 0.4 logMAR after 48 weeks of treatment, and 27% achieve visual acuity 0.3 logMAR. Presenting the information in this way allows parents and caregivers to apply the information directly to their child and can aid motivation for compliance with treatment.

The figures generated by the EPR are interactive, allowing the clinician to "drill down" into the individual patient records that comprise the datapoints. For example, the bubble plot of Figure 3 illustrates 4 patients with severe amblyopia in whom visual acuity did not improve from worse than 1.0 logMAR after 48 weeks treatment, and 2 in whom visual acuity worsened from 0.61-0.80 to 0.81-1.0 after the same period (denoted by asterisks). By selecting the bubble, the individual patient records can be reviewed. In this example,

Table 3. Personalized probability for children aged 5 years, presenting acuity VA of 0.9-1.0

	Best measure VA in Worse-seeing eye, logMAR												
Follow-up interval	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0	1.1	1.2	1.3	1.4
Baseline, % (n = 38)	0	0	0	0	0	0	0	0	45	100	100	100	100	100
32 weeks, % (n = 35)	0	3	11	34	49	60	71	89	94	94	97	97	97	97
48 weeks, % (n = 33)	0	6	27	48	70	82	88	91	100	100	100	100	100	100

VA, visual acuity.

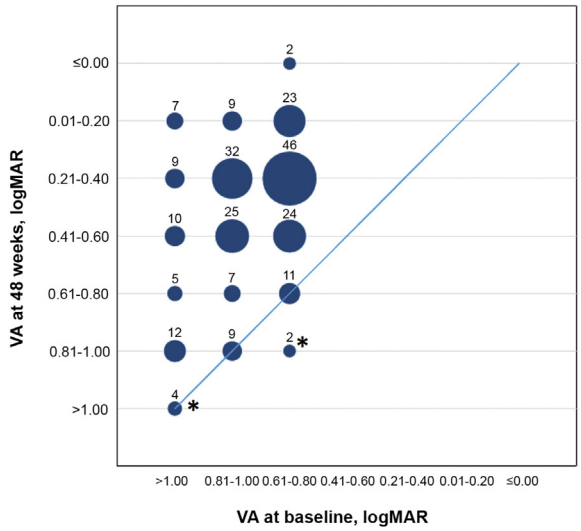

FIG 3. Bubble plot visual acuity outcomes at 48 weeks: severe amblyopia.

of the 6 outliers with poor outcomes, 2 patients had a high degree of anisometropia (>4 D) and 4 were noted to have low compliance with treatment and missed follow-up appointments. Data regarding compliance with patching were not recorded but will be captured in the updated version of the EPR software.

The EPR audit provides continually updated metrics for the patient group of interest, including the number of patients with the condition, demographics, number of follow-up visits, and treatment outcomes. This information is useful on a service level, for example to managers and commissioners.

This study is limited by outcomes being both from a single center and retrospectively derived. The authors hope similar outcome data from other centers will be published. With increasing uptake of the EPR as part of routine practice, there may be opportunity to collate a national amblyopia database of treatment outcomes. Such outcomes could provide a useful benchmark applicable to the general patient population.

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