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How Efficient Is Pinhole Therapy In Treating Severe Unilateral Amblyopia With Eccentric Fixation?

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ABSTRACT

This prospective, interventional study was conducted to determine whether full visual recovery and/or shift of retinal fixation locus was possible in severe unilateral amblyopia with eccentric fixation.

Methods: 59 consecutive cases between the ages of 7 and 31 (median 19 years) were included. After wearing refractive correction for 12-16 weeks, further visual improvement stopped, and 16 cases dropped out of the study. 43 cases completed the study and were treated with refractive glasses, full-time occlusion of the good eye during all waking hours, and active stimulation of the amblyopic eye by studying books for 6 hours daily. Once further visual improvement stopped, they were made to study through a pinhole in the center of the eyeglass of the amblyopic eye along with patching of the good eye.

Results: Visual acuity improved from 0.05-0.1 in all cases that strictly complied with full-time occlusion alone with an average statistical gain of 0.54 units (paired t-test). For those who complied with patching and pinhole therapy, the average improvement in visual acuity was 0.71 units with a confidence interval of 95%. Patching alone did not change the retinal fixation locus; however, combined patching and pinhole therapy had a statistically significant association (p-value less than 0.05) with retinal fixation with a confidence interval of 95%.

Conclusion: Pinhole therapy of the amblyopic eye combined with full-time occlusion of the good eye is a simple, economical, and efficient method to treat severe amblyopia with eccentric fixation. However, it solely depends upon good patient compliance, irrespective of a patient's age.

Keywords: Amblyopia; Eccentric fixation; Pinhole therapy; Occlusion treatment

INTRODUCTION

For perfect vision, the object of interest must be focussed at the foveal pit (foveola) along an imaginary line called the visual axis. This line connects the object in space with the center of the fovea (the foveal-fixation axis) after passing through the center of the cornea, the pupil, and the two nodal points of the eye (i: the center of the crystalline lens and ii: the central point of the eyeball). [1] The nodal points do not exist anatomically, but they represent mathematical

constructions.[2] The visual axis can be determined clinically by locating the reflected image of the light source from the corneal surface (first Purkinje image).

However, the human eye is not a perfect optical system. It does not always have a central alignment between the fixation object and the foveola. In addition, the centre of every pupil does not fall along the visual axis. Therefore, a slight asymmetry exists between the centre of the cornea and the center of the pupil, which is referred to as the angle Kappa, i.e., the angle formed between the visual and the pupillary axes due to this asymmetry. Each eye has a different angle kappa, which is usually less than 5°. It can be positive when the pupillary axis is temporal relative to the visual axis and gives the appearance of an out-turning of the eye. If the pupillary axis is nasal relative to the visual axis, the angle kappa is negative and gives the appearance of an inward turning of the eye. Its measurement is of paramount significance in refractive and cataract surgery, as an angle more than 0.5 mm will reduce the quality of vision postoperatively.[3]

The term eccentric fixation is used when an eye utilizes a point on the retina other than the normally situated foveola to take up fixation. This is also referred to as the false macula or para-central fixation (instead of the central/foveolar fixation). It may or may not be associated with strabismus but always with amblyopia. There is a gross inequality found in the scientific literature regarding the incidence of eccentric fixation. Cuppers [4] (1958) and Von Noorden (1970) [5] reported that 35% to 44% of amblyopic eyes had eccentric fixation. SRK Malik et.al. [6] reported it as 29.25%. According to Worth (1905) [7], a lack of foveal fixation may occur in longstanding, constant strabismus. In such cases, the macula ceases to be the most sensitive part of the retina; the eye either wanders, without remaining steadily in any definite position (lost fixation), or it may fixate at a paracentral region. Therefore, if the foveolar area is constantly suppressed for a prolonged period, the developing visual cortex adapts to using an eccentric fixation point and creates a new cortical pathway. In these cases, the reduced visual acuity is due to a combination of amblyopia and reduced visual capability of the eccentric point as compared to the foveola.

The degree of eccentricity not only affects the visual acuity in that eye but also determines the response to amblyopia therapy; the farther away from the fovea that a patient fixates, the greater the reduction in visual acuity. Also, the fixation becomes increasingly unsteady as the fixation moves farther away from the fovea. [8]

In addition, some amblyopic patients may have a microtropia in which there is no obvious strabismus or anisometropia. There is no movement on a unilateral cover test but eccentric fixation is present in the amblyopic eye. Thus, microtropia occurs when there is a small angle strabismus less than 10 D which is roughly equal to the magnitude of the eccentric fixation i.e in the parafoveolar area. In such cases, there will be a positive 4- prism diopter (PD) test. Therefore, the assessment of fixation pattern is of prime importance before commencing amblyopia therapy. [9]

Eccentric fixation is best diagnosed under monocular viewing conditions. These objective tests provide clinicians with a direct observation of the fixation point on the retina. It requires patients to fixate on the target. It can easily be done in a 4–5-month-old infant with a direct ophthalmoscope with an integrated fixation target or a visuoscope. The traditional visuoscope target has reticule lines placed at 1-PD intervals. In older patients, it can easily be done during a slit-lamp

examination. The patient is asked to cover one eye with his/her hand and to focus at a narrow vertical slit-beam with the amblyopic eye while the retina is being viewed with a 90 D lens (modified Watzke Allen Test). The examiner notices the point of fixation of the slit-beam by the patient, whether it is at the foveola or further away from it [10].

The various treatment options being used by ophthalmologists and optometrists for shifting the fixation from an eccentric point on the retina to the foveola are inverse occlusion (occlusion of the amblyopic eye) [11], pleoptics [12], red filters [13], and Haidinger's brushes. However, all of these are time-consuming, costly, require almost daily visits to the clinic, and a specially trained staff to carry out these therapies. The frequently preferred therapeutic option is refractive correction along with occlusion of the good eye.

In ophthalmology clinics, the pinhole test is used to assess the patient's potential vision without refractive glasses. In this, one eye is tested at a time, using a pinhole occluder to view a distant target amidst bright illumination to predict the visual status. It is based on the principle of a stenopaeic-slit, which allows only central rays to enter the eye whilst eliminating the divergent paracentral and peripheral rays, thus reducing the circle of blur on the foveola. As a result, the depth of focus is increased, and it provides the patient with good distance and near vision. This prospective study was conducted to see if we can use the pinhole therapy to shift the fixation point to the foveola, thus improving the visual acuity of patients with amblyopia due to eccentric fixation.

METHODS

This was a prospective study conducted for 11 years, from January 2014 till December 2024, at two tertiary care centers.

A detailed history was taken regarding the birth (prematurity, birth weight, oxygen therapy, cyanosis, jaundice), neonatal health problems, developmental milestones, duration of strabismus, any visual problems, previous therapy with glasses, atropine penalisation, patching, or strabismus surgery.

Assessment of visual acuity was done by two optometrists randomly. The distance vision was checked first on both the Snellen's & the ETDRS charts projected on a screen by an electronic Visual Acuity Tester (ACP-8 chart projector) at a distance of 6 meters from the patient. It demonstrated the visual acuity as the Snellen's chart (10 lines with an equal number of letters in each line) and its decimal fraction. The patients either wore their previous refractive glasses or unaided in those cases who had not yet been prescribed glasses. It was recorded in the clinical notes in the British system (6/6, 6/9-6/60) and its decimal fraction (6/6=1.0, 6/7.5=0.8). The near vision was assessed by the Reduced Snellen's reading chart held at 14 inches from the patient whilst wearing the refractive correction. Color vision (tested by Ishihara color plates), evaluation of binocularity (by Bagolini's striated glasses and Worth four dot test), amsler grid (to look for central/paracentralscotoma), and stereopsis (Randot stereo test) were also assessed and noted at the initial visit.

All patients had full ophthalmic and orthoptic assessment by two ophthalmologists. Fundoscopy and assessment of the fixation site on the retina was performed in children by a direct ophthalmoscope (Welch Allen) in which the patient was

asked to focus at the central circle; in cooperative teenagers and adults, a 90 D lens was used during the slit lamp examination, asking the patient to focus on the narrow vertical streak (1mm width) of the slit-lamp beam. This assessment was performed in a darkened room with low-intensity illumination. The pupils were dilated for an accurate assessment with mydriacyl eyedrops (Mydolate 1%, Ethical Pharma), instilled twice at an interval of 15 minutes. First, the good eye was assessed and then the amblyopic eye. The site of fixation was noted: whether it was foveal or eccentric. If it was eccentric, then whether it was nasal/temporal or superior/inferior to the foveola and how far away from it, whether it was perifoveal (< 2.5° or 1.25 mm from the foveal pit), macular (≥ 2.5°to ≤ 5°), or peripheral. It was repeated 3-4 times to note whether the fixation was stable or unstable. A horizontal streak of the slit-lamp beam was used to measure the distance of the fixation point from the fovea or the markings on the visuoscope target of the ophthalmoscope.

Cycloplegic refraction was carried out only in children between the ages of 7 to 13 years as they were unable to maintain constant fixation at a distant target. In patients with exotropia or exophoria, 1% cyclopentolate eye drops were instilled 3 times at 15 min intervals in the clinic to confirm the refractive error. Atropine 1% eyedrops were prescribed 3 times/day for 3 days (along with punctal occlusion by the parent) to cases with esophoria or esotropia. Once the effect of the cycloplegic drug had worn off, i.e., after one week, subjective refraction was performed by the optometrists. Patients were prescribed the maximum refractive correction that gave the Best Corrected Visual Acuity for both near and distant vision. They were called for follow-up after 2-3 months of constant spectacle wear (the period of refractive adaptation), and an improvement of the BCVA was noted.

Inclusion Criteria:

- We included only the literate, cooperative patients (in whom the BCVA and fundus assessment could be accurately performed), from the age of 7 years and above, with unilateral amblyopia and strabismus with an eccentric fixation.
- Patients were considered amblyopic if they had a visual acuity difference of at least two lines persisting between the two eyes after the period of refractive adaptation (12-16 weeks of constant spectacle wear).
- Amblyopia was classified according to its etiology as anisometropic, strabismic amblyopia, mixed variety, or microtropia, and according to the severity of visual loss as mild, moderate, or severe.
- Patients with previous strabismus surgery or failed attempts at amblyopia therapy were also included in the study.

Exclusion criteria:

- Sensory deprivation amblyopia (complete ptosis, congenital cataract, retinal pathology) or an organic cause for poor vision were also excluded (central corneal scarring, optic atrophy, optic disc coloboma or hypoplasia, maculopathy, and nystagmus (it gets worse by occlusion).
- Bilateral ammetropic amblyopia.

- Patients in whom a spontaneous improvement in the visual acuity occurred after the period of Refractive/optical Adaptation.

- Amblyopia with foveal fixation and microtropia.

Definite amblyopia therapy: Amblyopia therapy was started in patients in whom no further improvement in the BCVA was noted after 12-16 weeks of constant spectacle wear. For this, informed verbal consent was obtained from the patients and their parents. The study was conducted according to the Declaration of Helsinki of the World Medical Association. It was approved by the Ethics Committee of the centres.

All our cases had severe amblyopia. They could not continue with their normal daily activities after occluding the good eye. Therefore, they were issued a medical leave certificate for 4-6 weeks as they had severe amblyopia and were not able to follow the usual routine once the good eye was occluded full-time. They were instructed to stay at home and follow the treatment protocol. The amblyopia therapy comprised of two steps:

(i) At first, all cases were advised full-time occlusion of the good eye by wearing a commercially available adhesive eye patch over the closed eyelids during all waking hours (to be taken off only during sleep). They were instructed to wear their refractive glasses over the eyepatch and actively use the amblyopic eye for studying their books (from their school, university syllabus) and then write whatever they had studied for a minimum period of 5-7 hours daily. They were instructed to start reading an enlarged font that was visible to them with their glasses on (a newspaper, magazine, school book, or print-outs of their study syllabus taken from a computer). Then, they should gradually reduce the font size every second day.

Follow-ups: All cases were instructed to comply strictly with two weekly follow-ups. This was essential to monitor the improvement in the amblyopic eye and to note occlusion-amblyopia in the good patched eye. At each visit, assessment of the BCVA for near and distance (first with the amblyopic eye and then the good eye after removing the eye patch), binocular vision, stereopsis, measurement of the angle of strabismus, and assessment of the fixation locus on the retina was performed. Diplopia or eye patch-associated skin problems were also noted.

(ii) Pinhole therapy: Once a patient stopped showing further visual improvement on 2 consecutive follow-ups, the pinhole therapy was added to the full-time patching. In this, the patients were instructed to continue wearing the eye patch over the good eye, and they must read, write, and perform all daily activities with the amblyopic eye seeing through a pinhole made over the spectacle glasses. In this, the centre of the pupil was marked over the eyeglass as the patient focussed straight ahead at a pen torch with the amblyopic eye whilst the good eye was patched. A pinhole was cut in the center of dark tape applied over the eyeglass for the amblyopic eye at the marked point. The follow-ups were continued twice weekly, as explained above.

End-point of Therapy: The whole therapeutic regimen was continued till an improvement in the BCVA equal to that in the good eye and/or the fixation point shifted to the foveola. It was stopped when no further improvement in the BCVA was noted on two consecutive follow-ups.

Therapy was considered successful if there was a minimum improvement of 4-5 lines in the BCVA of the amblyopic eye and/or the fixation shifted to the foveola or closer to it from the extra-foveal site.
Resolution of amblyopia was defined as an improvement in the BCVA of the amblyopic eye to within 1 line of the fellow eye, i.e., 0.8-1.0 (6/9-6/6).

The weaning protocol for occlusion therapy was commenced once the BCVA equalised in both eyes or when no further improvement was noted in the amblyopic eye on 2-3 consecutive follow-up visits. Patients were instructed not to patch the good eye for one day in the first week and then two days in the second week, while they would continue the patching full-time during the remaining days of the week. BCVA was checked after two weeks, and if it remained stable, then further weaning was continued with the patch off for 3 days in the third week, 4 days off in the 4th week, till patching was off after 7 weeks. If any regression of amblyopia was detected during the weaning period, full-time patching was resumed again for a further 2 weeks, and weaning re-started once full visual recovery was noted. Patients were regularly followed up at monthly intervals for the next 12-24 months. At each visit, the visual acuity for both distance and near vision, the angle of strabismus, and stereopsis were measured.

Compliance with therapy was assessed by:

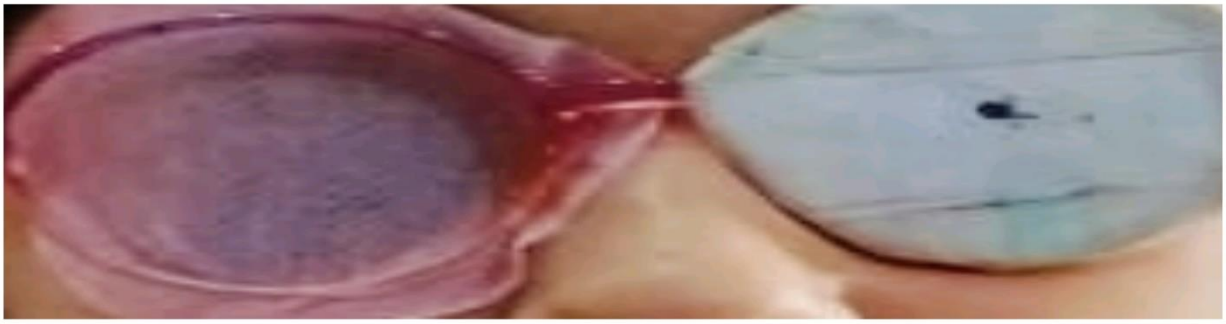
(i) How regularly the patients came for the follow-up visits.

(ii) Noting eye patch-related skin discoloration, redness, or rash (few macules/papules) after removing the eye patch.

Statistical Analysis: Two variables were tested: visual acuity and retinal fixation locus. Relations between these variables were examined by a paired t-test. Firstly, the effect of full-time patching on visual acuity was compared with measurements taken before and after the patching by the paired t-test. Secondly, paired t-test was performed for patients who received both patching and the pinhole therapy and the difference in the above mentioned two variables were tested.

Fisher's Exact test was applied to find the change in retinal fixation with patching alone and then after adding the pinhole therapy.

Fig. 1: Left Esotropia with Amblyopia and eccentric fixation.



Full-time patching Right eye and studying from the left amblyopic eye through pinhole.

RESULTS

Initially, 59 consecutive cases were included in the study. Out of these, 16 participants refused to start the full-time patching once the period of refractive adaptation was over and dropped out of the study. Therefore, the results were compiled for 43 cases that completed the study. The demographics of these 43 cases are demonstrated in **(Table 1)**.

Table 1: Demographics of 43 cases who complied with the therapy

Parameter		Percentage
Age	7 - 31 years (Median 19 yrs)	
Gender	Males: 21 Females: 22	
Type of Amblyopia	Strabismic=12 cases Mixed = 31 cases	27.9% 42.09%

Parameter		Percentage
Fixation Pattern (Initial)	Perifoveolar=23 cases Macular. = 5 cases Peripheral. =15 cases Stable fixation = 30 cases Unstable. = 13 cases	53.48% 11.6% 34.8% 69.8% 30.2%

They were between the ages of 7 to 31 years (median age of 19 years), with 22 females and 21 males. All cases had severe amblyopia with the initial BCVA of 0.05-0.1 (6/60). They all had moderate to large angle strabismus.

Regarding the cause of amblyopia: pure strabismic amblyopia (without anisometropia) was noted in 12 cases (27.9%), while anisometropia and strabismus (mixed variety) were present in 31 cases (42.09%). All grades of eccentric fixation were found: perifoveolar (n=23=53.48%), macular (n=5=11.6%), and peripheral fixation (n=15 =34.8%). The fixation was stable in 30 cases (69.8%) and unstable in 13 cases (30.2%).

The visual acuity gradually improved in all cases that strictly complied with the treatment protocol, as demonstrated in **(Table 2)**. The improvement in visual acuity to 0.8-1.0 (6/6) occurred earlier in patients with perifoveal fixation, i.e., within 18-24 weeks (median 22 weeks). Their fixation locus also shifted from the perifoveal (23 cases) to the foveola in 21 cases (91.3%). Two cases could not comply with the pinhole therapy; their fixation remained perifoveal, and their final BCVA was 0.6-0.8 (6/9) from the initial 0.1 (6/60) at the start of therapy.

Table 2: Results of Therapy with regards to Visual Improvement & Shift of Fixation Point:

Retinal Fixation Point	Initial BCVA	Final BCVA	Shift of Fixation	Compliance with PINHOLE Therapy	Duration of Rx in weeks
PERIFOVEAL 23 Cases	0.1-0.2	0.8-1.0 in 23 cases	Foveal: 21 cases (91.3%) Perifoveal: 2 cases	Yes=21 cases No=2 cases	18-24 wks Median 22
MACULAR 5 cases	0.05-0.1	0.7-0.8 in 2 cases 0.5-0.6 in 3 cases	Fixation shift to Perifoveal= 2cases Fixation remained Macular= 3 cases	Yes=2 cases No=2 cases	22-26 weeks
PERIPHERAL 15 Cases	0.05-0.1	0.7 in 3 cases 0.2-0.3 in 12 cases	Fixation shifted to Macula in 2 cases. It remained Peripheral in 13 cases	Yes= 2 cases, fixation shifted to Macula No= 13 cases	26-30 wks

Retinal Fixation Point	Initial BCVA	Final BCVA	Shift of Fixation	Compliance with PINHOLE Therapy	Duration of Rx in weeks
Compliance with Pinhole Therapy				Yes: 21 + 2 + 2= 25 cases No: 2 + 2 + 13= 17 cases	

The BCVA of 5 cases with initial stable fixation at the macular area improved from 0.05 to 0.2-0.25 with patching alone. Only 2 cases complied to the pinhole therapy and their BCVA improved further to 0.6 (6/9) in 22-24 weeks. Their retinal fixation also shifted to the perifoveolar area. The remaining 3 cases could not comply with the pinhole therapy; their final BCVA remained at 0.2-0.25 after which they were gradually weaned to part-time patching for 6 hours daily for another 10-12 weeks.

There were 15 cases with unstable paramacular or peripheral fixation. BCVA improved from 0.05 to 0.1 (a visual acuity gain of 2-3 lines) with full-time patching alone. Only 2 cases complied with pinhole therapy and showed further improvement to 0.2 (2-3 lines, 6/30). Their point of fixation shifted to the macular area after 26-30 weeks of therapy. When further improvement in the BCVA was not noted on two consecutive follow-ups, full-time patching and pinhole therapy were stopped. They were advised to patch the good eye part-time (6-8 hours) for another 10-12 weeks to stabilize the improved visual acuity. The remaining 13 cases that had unstable peripheral fixation could not study through a pinhole with the densely amblyopic eye. Their BCVA remained at 0.1 (6/60). Since they did not notice any significant improvement in their vision, they stopped doing further patching, and the BCVA regressed to 0.05 after 6-8 weeks.

The adverse effects of therapy: Patients and their parents were warned about the adverse effects of therapy like the possible development of diplopia, occlusion amblyopia, and eye-patch associated problems as demonstrated in **(Table 3)**. However, diplopia did not occur in any of our cases.

Table 3: Complications of Full time Occlusion Therapy:

Parameter	No of cases	Percentage
Occlusion amblyopia	4	9.3%
Regression of amblyopia	9	20.93%
Eyepatch related problems	Allergic rash: 1 Macule papule: 13 Lacrimation : 5	2.3% 30.23% 11.62%

Parameter	No of cases	Percentage
Diplopia	Nil	

- Occlusion amblyopia of 1-2 lines reduction in the BCVA occurred in only 4 cases (9.3%) as they missed 2-3 consecutive follow-ups and continued, unsupervised occlusion therapy for 6-7 weeks. It was particularly noted in relatively younger patients, 9-12 year old. However, it reversed readily within 1-2 days by taking the patch off the good eye.

- Regression of amblyopia by 1-2 lines following a successful therapy was noted in 9 cases (20.93%) as they had stopped wearing their refractive correction for 2-4 months after a successful therapy. It was managed by resuming the full-time patching and pinhole therapy for 2-4 weeks followed by its gradual weaning.

- Allergic rash to the eye-patch (contact dermatitis) occurred only in one case (2.3%); he was advised to wear the eye patch over the eye glasses. Patch-associated few macules and papules were noted in 13 cases (30.23%). This was treated with a mild steroid skin cream applied at night when the eye patch was taken off, and placing the eye patch over the spectacle-glass for a few days till the rash had cleared up.

- Ocular irritation and watery eye occurred in 5 cases (11.62%). This was due to in-turned eyelashes. The parents were advised to place a folded tissue paper over the closed eyelids and then apply the eye patch over it. This prevented the eyelid from opening under the patch and in-turning of eyelashes. No other patch- related complication was noted during therapy.

- **Cases requiring strabismus surgery** following resolution of amblyopia: In 5 cases (9.4%), no strabismus surgery was needed as the angle of deviation reduced from moderate (10-15*) exotropia to small angle (5*) exotropia after the resolution of amblyopia. 26 cases underwent bilateral strabismus surgery for large angle strabismus once the vision was equalized in both eyes by amblyopia therapy. 12 cases that did not comply with the pinhole therapy underwent cosmetic strabismus surgery.

Statistical Analysis

- Firstly, the effect of full-time patching on visual acuity was compared with measurements taken before and after the patching. The mean difference (the average change in visual acuity from before to after patching) was 0.545 units. The t-statistic was (t)= 13.186. The degree of freedom was 42 since there were 43 paired samples. The p-value was < 2.2e-16 with a confidence interval of 95%.

- Secondly, the result of paired t-test to determine the effect of combined patching and pinhole therapy: The degrees of freedom (df) was 25 indicating the number of cases who complied to both therapies. The t-statistic was 32.524. The p-value was <2.2e-16, indicating a statistically significant difference, with a confidence interval of 95%. The true mean difference in visual acuity between before and after treatment was 0.67 and 0.76, indicating that on average, a patient's visual acuity improved by 0.71 units after receiving both therapies.

- Thirdly, Fisher's Exact Test indicated that the combined effect of patching and pinhole therapy was more effective in shifting the fixation locus to the fovea.

DISCUSSION

Amblyopia with eccentric fixation is a therapeutic challenge as the visual outcome is known to be poorer than in amblyopia with foveal/central fixation. In this study, we studied the effect of our therapy in such patients on two clinical parameters: an improvement in the BCVA and the shift of fixation point from the eccentric position to the foveola or closer to it. Our therapy comprised of two parts: initially, full-time patching of the good eye was commenced in all cases. Once further improvement in the BCVA was not noted on two consecutive follow-up visits, pinhole therapy for the amblyopic eye was added.

The age of a patient at the start of therapy has been considered as the most significant predictor for visual improvement in all types of amblyopia, especially with eccentric fixation[14]. The PEDIG-ATS include 23 studies that are followed by ophthalmologists worldwide. The meta-analysis of 4 PEDIG RCTs showed that children between 13-17 years of age had a visual improvement of 2-3 lines in only 14% of their cases. They concluded that amblyopia was more responsive to treatment in children younger than 7 years of age compared with children 7 to 12 years of age [15,16]. This trend of treating younger patients was observed in other studies too [17,18]. As a result, older children and young adults are refused amblyopia therapy worldwide. However, in our previous study of 1701 consecutive cases [19], only 28% were children between 4-7 years, 36% were between 8-12 years, while 36% were between 13-56 years of age. In all of these age groups, the visual improvement to 0.8-1.0 occurred in 96% of cases, even in patients with severe amblyopia (54% of cases), despite their age at presentation. The visual improvement notably occurred much earlier (8-12 weeks) in younger children less than 7 years of age than older patients (in 18-24 weeks).

In our present study, we selected older patients (> 8-9 years of age) who could easily understand the rationale and follow the mode of therapy which becomes difficult in younger patients. Another benefit of selecting literate, older patients was that we could easily and accurately assess both study parameters mentioned above.

The overall improvement in the BCVA: BCVA improved to some extent in all 43 cases who complied to full time patching. As demonstrated in Table 2, the extent of visual acuity gain depended on the initial fixation point on the retina and whether it shifted to the foveola or closer to it. The cases with a perifoveolar fixation gained 6-8 lines by patching alone as their BCVA improved from the initial 0.05-0.2 to 0.7-0.8. Cases with initial macular fixation gained 3-4 lines while those with peripheral fixation gained only 1-2 lines. No shift in fixation was noted with patching of the good eye

alone. However, after adding the pinhole therapy at that point, the cases that fully complied to it demonstrated not only further improvement in the BCVA but also a shift of fixation point to/closer to the foveola.

The shift in fixation point to the foveola was noted only in the cases that had a perifoveal fixation initially and complied with the pinhole therapy (in 21 cases (91%) out of 23). Two cases that did not comply with the pinhole therapy, their fixation remained perifoveal. The fixation point shifted from macular to perifoveal region in 2 cases (out of 5) and from peripheral to macular fixation in the 2 cases who fully complied with the pinhole therapy. Therefore, all the cases that strictly complied to both parts of the therapy, demonstrated not only an improvement in the BCVA to 0.8-1.0, but also a shift in retinal fixation point. This is because the pinhole therapy strongly and efficiently stimulates the foveola resulting in the shift of retinal fixation in a relatively short period. Although it appears difficult to study through the pinhole and manage daily activities, but patients who are able to understand the rationale, strictly comply with the therapy; as they notice an improvement in the visual acuity, they are motivated further to continue.

The cases with perifoveal fixation demonstrated good compliance with pinhole therapy as their visual acuity had already improved to 0.6-0.7 with patching alone. It improved further to 0.8-1.0 within 3-4 weeks with pinhole therapy. In comparison, the cases with a peripheral fixation gained only 2-3 lines by patching alone and required much longer duration of pinhole therapy to improve their BCVA further. Therefore, they stopped it after 1-2 weeks. Compliance with therapy is the main factor that decides visual improvement in this condition and highlights the significance of good counseling.

The results of our study were almost similar to the study by Von Noorden [20] who examined the therapy success for different fixation loci. Their 82% cases with initial parafoveolar fixation achieved central fixation and only 27% of the patients with peripheral fixation achieved central fixation. Mehmed et. al. [21] reported 80% of their patients less than 6 years of age achieve foveolar fixation during the first 4 months of therapy regardless of the initial locus of eccentric fixation. These studies highlight the fact that the shift of fixation to the foveola is easier in younger children as the depth of foveolar suppression is not deep. It becomes difficult to retrain the fovea to resume its normal functioning in older patients as demonstrated in our study. With increasing age, the angle of strabismus increases as the amblyopia deepens, and the retinal fixation point moves further away from the fovea.

There is always a chance for regression of visual acuity following therapy if the patients stop wearing their refractive correction for a few weeks. This occurred in our 9 cases (20.93%). However the visual loss was readily recovered by resuming the full-time patching. Therefore, strong counseling of the patients and parents is essential. They must understand the necessity of wearing refractive glasses daily and come for regular follow ups, at least 6 monthly.

In our statistical analysis, the t-statistic for the 43 cases that complied to patching initially (t= 13.186) was large and positive, indicating a substantial difference between the before and after patching measurements (the after patching measurements are significantly higher than the before measurements). The extremely small p-value of < 2.2e-16 indicated a statistically significant difference; the observed change in visual acuity was not due to random chance but with a confidence interval of 95%. The mean difference of 0.545 suggests that, on average, patients experienced a 0.545 unit improvement in visual acuity after patching.

In the Paired t-test for 25 cases who complied with both treatments (patching & pinhole therapy), the very large t-statistic (32.524) indicated a strong difference between visual acuity before and after treatment. The extremely small p-value of less than 0.05 led us to conclude that both patching and pinhole therapy combined significantly improved visual acuity with the mean difference of 0.71 units, indicating much higher value than those who complied with patching alone. The overlap between the two confidence intervals is minimal which also suggests that the combined treatment (patching + pinhole) led to a larger improvement in visual acuity compared to patching alone, and that the difference between these two treatments is meaningful. The Fisher's Exact Test, used to assess the impact of therapy on the change in retinal fixation locus, confirmed that patching plus pinhole therapy had a significant impact on fixation than patching alone.

The strengths of this study are:

- Its prospective nature.
- Inclusion of literate, cooperative, relatively older children/young adults in whom the assessment of visual acuity and the site of eccentric fixation was accurately carried out.
- The BCVA was assessed at each follow-up visit by two optometrists randomly. They had no access to the clinical records of patients and were unaware of their previous BCVA.
- This is the first study in which 80% of the cases were young adults (median age of 21 years) with severe, unilateral amblyopia in whom the BCVA improved to 0.8-1.0 and a shift of eccentric fixation was noted in all 25 cases (out of the total 43 cases) that complied to the pinhole therapy.

The relative bias or weakness of the study:

- The assessment of the site of eccentric fixation was carried out by a single ophthalmologist at each visit.
- The number of cases included in the study was small as we had enrolled older patients.

CONCLUSION

Pinhole therapy proved to be an efficient method to treat severe unilateral amblyopia with eccentric fixation. It is a simple and economical technique that does not require frequent clinical visits. When combined with full-time patching of the good eye, the visual loss was fully treatable, and fixation could be shifted to the foveola irrespective of the age of the patients. It solely depends on good compliance to therapy.

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