

Part-time occlusion therapy for amblyopia in older children

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Aim: To compare the efficacy of part-time versus full-time occlusion for treatment of amblyopia in children aged 7-12 years.

Materials and Methods: Prospective interventional case series. One hundred children between 7-12 years of age with anisometropic (57), strabismic (25) and mixed (18) unilateral amblyopia were randomized (simple randomization) into four groups (25 each) to receive two hours, four hours, six hours or full-time occlusion therapy. Children were regularly followed up at six-weekly intervals for a minimum of three visits.

Statistical Analysis: Intragroup visual improvement was analyzed using paired t-test while intergroup comparisons were done using ANOVA and unpaired t-test.

Results: All four groups showed significant visual improvement after 18 weeks of occlusion therapy ($P < 0.001$). Seventy-three (73%) of the total 100 eyes responded to amblyopia therapy with 11 eyes (44%), 17 eyes (68%), 22 eyes (88%) and 23 eyes (92%) being amblyopia responders in the four groups respectively, with the least number of responders in the two hours group. In mild to moderate amblyopia (vision 20/30 to 20/80), there was no significant difference in visual outcome among the four groups ($P = 0.083$). However, in severe amblyopia (vision 20/100 or worse), six hours ($P = 0.048$) and full-time occlusion ($P = 0.027$) treatment were significantly more effective than two hours occlusion.

Conclusion: All grades of part-time occlusion are comparable to full-time occlusion in effectiveness of treatment for mild to moderate amblyopia in children between 7-12 years of age unlike in severe amblyopia, where six hours and full-time occlusion were more effective than two hours occlusion therapy.

Key words: Amblyopia, full-time occlusion, occlusion therapy, part-time occlusion

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Amblyopia is defined as a decrease of visual acuity caused by pattern vision deprivation or abnormal binocular interaction for which no cause can be detected by the physical examination of the eye and in appropriate cases is reversible by therapeutic measures.¹ It is the most common cause of monocular visual impairment in both children and young adults.² Occlusion therapy with patching of the non-amblyopic eye has long been the mainstay of amblyopia treatment.^{3,4} Initially it was a common belief that occlusion therapy should be prescribed for full time, and that removing the patch even for a short period of time would lead to loss of all the benefit of previous patching.

Recently, various amblyopia treatment groups have started to look into the efficacy of part-time occlusion.⁵⁻⁹ Studies that prescribed occlusion for as less as one to two hours per day to a maximum of 24 h per day have been reported.⁵⁻⁹ While initial studies were retrospective and their results varied,⁵⁻⁶ Pediatric Eye Disease Investigator Group (PEDIG) was set up to

address the need for prospective clinical trials in the treatment of amblyopia.⁷⁻¹¹

The opinion that amblyopia treatment may be ineffective in older children stems from the fact that the age of six to seven years is thought to be the end of the "critical period" for visual development in humans.¹² Various studies have described conflicting results varying from no effect of age to a highly significant effect.¹³⁻²⁷ Recently, Patwardhan¹⁶ has shown that there was no statistically significant change in the success rate of treatment of anisometropic amblyopia, even beyond 12 years of age. PEDIG¹¹ found that for amblyopia treatment in patients aged 7-12 years, augmenting the optical correction with patching therapy of two to six hours daily doubled the treatment responder rate to 53%. Compared to this, Brar *et al.*,²³ in their study in older children (> six years) have reported a substantial improvement in visual outcome in nearly 90% of the children with full-time occlusion.

Hence whether part-time occlusion is equally efficacious as full-time occlusion in older children is still not clear. The aim of the study was to determine the efficacy of part-time occlusion vis-à-vis full time occlusion in children 7-12 years of age with amblyopia.

Materials and Methods

This prospective study was started in January 2004 and enrolled 100 unilateral amblyopic (strabismic, anisometropic

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or combined type) children in the age group of 7-12 years. The study was approved by the ethics committee of the institute. An informed written consent was obtained from the parents of the participating children. The sample size was calculated by assuming an acceptable standard error of 0.05 at 95% confidence level. Baseline testing included measurement of visual acuity, cycloplegic refraction using atropine, and a complete orthoptic and ocular examination of both eyes. The children were corrected for refractive error, if any, for at least six weeks prior to inclusion in the study.

Best corrected visual acuity (BCVA) in the amblyopic eye of 20/30 or less subsequent to the refractive correction for six weeks was used as a diagnostic criterion for amblyopia. Only unilateral cases were selected with BCVA of 20/20 in the normal eye. A difference between the spherical equivalents of the two eyes exceeding 1.00 diopter (D) or astigmatism exceeding 1.5 D was considered anisometropia while amblyopes who had constant esotropia or exotropia were classified as strabismic type. They were randomized into four groups of 25 children each using simple randomization (computer-generated random numbers) to receive two hours, four hours, six hours or full-time occlusion therapy.

Inclusion criteria for the study included unilateral amblyopia associated with strabismus, anisometropia, or both in children ranging from 7-12 years of age, having ability to record visual acuity accurately on Carl Zeiss chart projector (SZP 350). The above model of Carl Zeiss chart projector projects a single letter for 20/400 line, two letters each for the 20/200 and 20/160 lines, three letters for the 20/125 line and four letters for each subsequent line. Children were deemed to have read the line if they read all letters of 20/400, 20/200, 20/160 and 20/125 lines and at least three out of four letters for all subsequent lines.²³ The chart has a regular doubling of the visual angle between different lines, so a logMAR conversion was done to facilitate calculation of mean visual acuity and its comparison between different groups.

Exclusion criteria included presence of a known cause of reduced visual acuity, myopia more than a spherical equivalent of -6.00 D, history of previous amblyopia treatment within one year of enrolment, prior intraocular surgery and known skin reaction to patch or bandage adhesive. Dropouts and non-compliant patients were excluded from final analysis.

Patients were prescribed patching as per the following regimes:

Non-amblyopic eye was patched for limited number of hours each day; two hours in Group 1, four hours in Group 2 and six hours in Group 3. Patch was applied continuously during waking hours. In addition to occlusion, the parents were instructed to have the child spend at least one of the hours of patching time each day performing near visual activities. The near visual activity advised was performing their routine homework. Non-amblyopic eye was patched for all waking hours or all but one hour in group 4 children for all seven days a week. Patch could be removed during the night but it was to be applied first thing in the morning.

Six-weekly follow-up was done for a minimum period of 18 weeks. During each follow-up visit, visual acuity was recorded on the same visual acuity chart projector (Carl Zeiss SZP 350) by an independent observer who did not have

access to the patient's treatment protocol. Parents were told to maintain a diary in which the treatment (hours of occlusion and performance of near activities) received each day was noted. The diary was reviewed at each follow-up visit.

The primary outcome was the BCVA in the amblyopic eye at 18 weeks. Amblyopia responders, defined as those who gained at least two lines of vision between the first and the final visit, were calculated for each of the four groups. The children were further subdivided into two subsets of mild-moderate and severe amblyopia to study the independent effect of occlusion therapy in each subset. Mild-moderate amblyopia was defined as a BCVA between 20/30 to 20/80 in the amblyopic eye while severe amblyopia was defined as BCVA of 20/100 or less in the amblyopic eye.

Statistical analysis between pre-treatment and post-treatment change in acuity was done by paired t-test. The difference between the two groups in the variance of the change in amblyopic eye visual acuity produced was analyzed using Analysis of Variance (ANOVA) test and unpaired t-test.

Results

Out of 100 cases, there were 57 cases of anisometropic amblyopia, 25 cases of strabismic amblyopia and 18 cases of mixed amblyopia. The group-wise distribution of the three types of amblyopes is provided in Table 1. The mean age was 8.9 ± 1.7 years in Group 1, 9.5 ± 2.1 years in Group 2, 10.0 ± 1.8 years in Group 3 and 9.3 ± 2.1 years in Group 4. The baseline BCVA was 0.67 logMAR units (range 20/40 - 20/400) in Group 1, 0.80 logMAR units (range 20/40 - 20/400) in Group 2, 0.68 logMAR units (range 20/30 - 20/400) in Group 3 and 0.76 logMAR units (range 20/30 - 20/400) in Group 4. The four groups were matched for age ($P=0.355$), distribution of the three types of amblyopes ($P=0.3$) and pre-treatment BCVA ($P=0.183$). Post-treatment visual acuity was measured at completion of 18 weeks and was compared with pre-treatment visual acuity using paired t-test [Table 1]. The results showed significant visual improvement in all four groups at the end of the study period ($P<0.001$).

Seventy-three (73%) of the total 100 eyes responded to amblyopia therapy with 11 eyes (44%), 17 eyes (68%), 22 eyes (88%) and 23 eyes (92%) being amblyopia responders in each group respectively, with least number of responders in the two hours group. ANOVA test revealed a statistically significant difference ($P=0.002$) in visual improvement among the four groups. On further analysis with unpaired t-test, a significantly better outcome was seen when visual improvement in Group 2 (four hours occlusion) was compared with Group 1 (two hours occlusion) ($P=0.026$). Similarly Group 3 (six hours occlusion) had a better visual outcome compared to Group 1 (two hours occlusion) ($P=0.002$). Full-time occlusion Group 4 also fared significantly better compared to the two hours occlusion Group 1 ($P=0.001$). However, the difference was non-significant when visual outcome in six hours occlusion Group 3 ($P=0.486$) and full-time occlusion Group 4 ($P=0.103$) was compared with four hours occlusion Group 2 or when six hours occlusion Group 3 was compared with full-time occlusion Group 4 ($P=0.274$).

Subset A (mild-moderate amblyopia) included 47 children while Subset B (severe amblyopia) included 53 children. The two subsets were matched for age ($P=0.7$).

Comparison of various treatment protocols in mild-

Table 1: Visual outcome in the 4 groups at 18 weeks with varying hours of patching therapy

Groups	No. of patients	No. of Aniso/ Strabismic/ Mixed amblyopes	Mean age (yrs)	Pre-treatment mean BCVA	Post-treatment mean BCVA	Mean change in BCVA	P value (paired t test)
Group 1	25	14/ 5/ 6	8.9	0.65 ± 0.29	0.48 ± 0.27	0.17 ± 0.11	< 0.001
Group 2	25	15/ 6/ 4	9.5	0.80 ± 0.28	0.54 ± 0.30	0.26 ± 0.17	< 0.001
Group 3	25	15/ 7/ 3	10.0	0.68 ± 0.27	0.38 ± 0.22	0.30 ± 0.16	< 0.001
Group 4	25	13/ 7/ 5	9.3	0.76 ± 0.33	0.41 ± 0.28	0.36 ± 0.22	< 0.001

$P=0.002$ on ANOVA test for inter-group comparison, No. - Number; Aniso - Anisometropia; yrs - Years; BCVA - Best corrected visual acuity

moderate amblyopia: Out of the 47 patients in subset A, 15 patients were included in Group 1, 10 patients in Group 2, 12 patients in Group 3 while 10 patients were in Group 4. The four groups were matched for age ($P=0.3$) and the pretreatment visual acuity ($P=0.5$). ANOVA test revealed no statistically significant difference ($P=0.083$) in visual improvement among the four groups [Table 2].

Comparison of various treatment protocols in severe amblyopia: Out of the 53 patients in subset B, 10 patients were included in Group 1, 15 patients in Group 2, 13 patients in Group 3 and 15 patients in Group 4. The four groups were matched for age ($P=0.41$) and the pretreatment visual acuity ($P=0.57$). ANOVA test revealed a statistically significant difference ($P=0.036$) in visual improvement among the four groups [Table 3].

On further analysis with unpaired t-test, a significantly better visual outcome was seen in six hours group ($P=0.031$) and full-time group ($P=0.015$) when compared with the two hours group while comparative improvement in the four hours group ($P=0.33$) was not significantly different from the two hours group. Also, there was no significant difference in visual improvement among the four hours group and the six hours group ($P=0.284$), four hours group and the full-time group ($P=0.068$), and among the six hours group and the full-time group ($P=0.341$).

Discussion

Initial reports on occlusion therapy in older children found that the age of the patient at which the treatment was initiated had a direct bearing on the visual outcome.¹³⁻¹⁵ Epelbaum *et al.*,¹⁴ reported in strabismic amblyopia that the recovery of acuity of the amblyopic eye was maximum when the occlusion was initiated before three years of age, the improvement further decreased as a function of age and was about null by the time the patient was 12 years of age. Similarly Rutstein *et al.*,¹⁵ reported that the visual acuity improvement is somewhat lesser in patients older than seven years than in younger patients.

However, in recent years a large number of studies have shown a comparable beneficial effect of occlusion therapy in older children too.^{11,16-23} Brar *et al.*,²³ have reported a substantial improvement in visual acuity with full-time occlusion in nearly 90% of the children. They showed that visual acuity could be improved uniformly for strabismic, anisometropic or a combination of strabismic and anisometropic amblyopia in older children. The authors observed improvement in visual acuity in 98.7% of children younger than 12 years and in 46.2% children older than 12 years at the time of initiation of occlusion therapy. Patwardhan¹⁶ has recently shown that there is no statistically significant change in the success rate of treatment of anisometropic amblyopia, even beyond 12 years of age. The present study also included patients

Table 2: Visual outcome in the 4 groups in patients with mild/ moderate amblyopia

Groups	No. of patients	Mean age (yrs)	Pre-treatment mean BCVA	Post-treatment mean BCVA	Mean change in BCVA	P value (paired t test)
Group 1	15	9.3	0.45 ± 0.15	0.31 ± 0.14	0.14 ± 0.11	< 0.001
Group 2	10	8.6	0.50 ± 0.12	0.27 ± 0.11	0.23 ± 0.12	< 0.001
Group 3	12	9.8	0.43 ± 0.12	0.21 ± 0.11	0.23 ± 0.11	< 0.001
Group 4	10	8.9	0.41 ± 0.14	0.18 ± 0.14	0.23 ± 0.08	< 0.001

$P=0.083$ on ANOVA test for inter-group comparison, No. - Number; yrs - Years; BCVA - Best corrected visual acuity

Table 3: Visual outcome in the 4 groups in patients with severe amblyopia

Groups	No. of patients	Mean age (yrs)	Pre-treatment mean BCVA	Post-treatment mean BCVA	Mean change in BCVA	P value (paired t test)
Group 1	10	8.6	0.95 ± 0.17	0.73 ± 0.23	0.22 ± 0.11	< 0.001
Group 2	15	10.1	1.00 ± 0.15	0.71 ± 0.25	0.29 ± 0.19	< 0.001
Group 3	13	10.2	0.90 ± 0.15	0.54 ± 0.17	0.36 ± 0.17	< 0.001
Group 4	15	9.6	1.00 ± 0.15	0.56 ± 0.24	0.44 ± 0.25	< 0.001

$P=0.036$ on ANOVA test for inter-group comparison, No. - Number; yrs - Years; BCVA - Best corrected visual acuity

of strabismic and mixed amblyopia in addition to children with anisometropic amblyopia, who after randomization, were uniformly distributed in the four groups [Table 1]. The distribution of amblyopes is important as it can have a bearing on the final outcome. Most studies report best-to-worst ranking of anisometropic, strabismic, and combined amblyopia for visual acuity at initial visit and outcome at the end of treatment.^{5,24,25}

A very important factor determining the outcome of occlusion therapy in these older children could be the patching compliance. It is obvious that lesser the hours of patching in a day better the compliance with the treatment.²⁶ Hence the concept of part-time occlusion holds stronger ground in the case of older children. Two studies have recently looked into the role of part-time occlusion in older children. One of these is a multicentric study by PEDIG.¹¹ The study found that augmenting the optical correction with part-time patching therapy and atropine penalization doubled the responder rate (53% vs. 25%) and the response to treatment was seen regardless of the severity of amblyopia. Hence this study established the role of part-time occlusion in older children. A significant difference from our study is that none of the children in the present study were prescribed atropine in the dominant eye in addition to the occlusion therapy. The PEDIG study¹¹ did not compare the effectiveness of varying hours of part-time occlusion among themselves.

Recently Lee *et al.*,²⁷ have also studied the effect of part-time occlusion in older children (29 eyes) aged 8-12 years. They reported a beneficial effect of part-time occlusion therapy in nearly 96% of the eyes. Visual improvement and occlusion time showed a significantly positive correlation. However, only two children received less than three hours of daily occlusion therapy for a limited period of one month. Hence this study was also limited by the lack of a proper comparative analysis between full-time occlusion and varying hours of part-time occlusion in addition to involving a very limited number of patients.

We planned and conducted this prospective randomized study comparing the effect of varying hours (two hours, four hours and six hours) of part-time occlusion therapy with full-time occlusion therapy in children aged 7-12 years. We observed that both full-time patching and part-time patching, even as little as two hours a day, led to significant improvement in visual outcome at 18 weeks of treatment. We observed a much higher responder rate (73%) compared to the PEDIG study (54%); this could be because in their study a large majority of patients received either two hours patching (50%) or four hours patching (41%) while very few (9%) received six hours patching and none received full-time patching. However, we distributed the patients equally in four groups of 25 each. Among children who received two or four hours of patching, 28 of the 50 children (56%) responded to the treatment, a figure comparative to the PEDIG study. However, in children who received six hours or full-time occlusion, 45 of the 50 children were treatment responders (90%). The difference was predominantly due to the fact that, in children with severe amblyopia, full-time patching and six hours/day patching was found to have a significantly better outcome when compared to two hours of patching therapy. While in patients with mild to moderate amblyopia all treatment protocols produced

comparatively similar outcome. This is similar to observations of PEDIG in younger children.⁷⁻¹⁰

The limitations of the study include its smaller sample size and shorter follow-up. Moreover, it does not address the issue of maintenance therapy and the recurrence of treated amblyopia in this age group. Still, the present study suggests a beneficial effect of part-time occlusion therapy in older children. Larger studies with longer follow-up are needed to address issues of recidivism and extent of improvement with part-time occlusion in older children.

Hence it can be concluded that for treatment of mild to moderate amblyopia, as little as two hours/day of patching may be adequate in the 7-12 years age group while in severe amblyopia, six hours and full-time occlusion are more effective than two hours occlusion therapy in this age group.

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