Determining the efficacy of full-time occlusion therapy in severe amblyopia at different ages [version 1; referees: 1 approved with reservations, 1 not approved]

Sameera Irfan, Nausherwan Adil, Haris Iqbal
Mughal Eye Trust Hospital, Lahore, Pakistan

Abstract
Objective: To find out how much visual improvement is possible in severe amblyopia using full-time occlusion therapy and if improvement is influenced by the patient’s age.
Methods: A trial of 115 consecutive cases with unilateral, severe amblyopia was conducted at a tertiary referral center from Jan 2010 to Oct 2012. Patients were divided into three age groups: 3-7 years (n= 38), 8-12 years (n=41), 13-35 years (n=36). After a complete ophthalmological examination by a single ophthalmologist, cases with organic visual loss were excluded; cases with previous part-time occlusion therapy that had failed were included in the study. Patients were given optimal refractive correction for a month, followed by full-time occlusion therapy along with near visual activities for 3-4 hours/day. The therapy was continued until maximum visual recovery was achieved (6/6 Snellen’s). Therapy was gradually reduced and stopped. Patients were followed-up regularly for the next 18 months.
Results: There was 100% success in the 3-7 year group, 92.68% in the 8-12 year group and 97.22% in the 13-35 year group.
Conclusion: Visual improvement is possible in almost all patients with severe amblyopia irrespective of their age with full-time occlusion therapy.

Keywords
Amblyopia, occlusion therapy, age, lazy eye
Introduction

Amblyopia, (‘blunt vision’ in Ancient Greek), also known as lazy eye, is a visual deficiency in an eye that is otherwise physically normal, or that is greater than would be expected from any structural abnormalities of the eye. It is thought that amblyopia results from inadequate stimulation of the fovea or peripheral retina and/or abnormal binocular interaction, resulting in different visual input from the foveae. It has been estimated to affect 2–5% of the population. The global prevalence of amblyopia has not significantly changed over the years.

Amblyopia results in the loss of binocular vision, which is manifested as absent stereoscopic depth perception, poor spatial acuity, low contrast sensitivity and reduced sensitivity to motion. This can be detected clinically by assessing whether the patient has difficulty seeing three-dimensional images on autostereograms.

Amblyopic patients can have poor spatial acuity, low contrast sensitivity, and reduced sensitivity to motion. They may also have poor binocular vision and limited depth perception which can be detected on autostereograms.

The largest study on patient response to amblyopia therapy to date was conducted by the Pediatric Eye Disease Investigator Group (PEDIG) in the USA, which reported that amblyopia due to strabismus and/or anisometropia responds similarly to part-time occlusion therapy in children between the ages of three and seven years. PEDIG also reported that about 75% of children with previously untreated amblyopia respond to treatment with only two or more lines of improvement on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart up to 18 years of age. The upper age limit for optimal therapy was considered to be in the range of nine to ten years. The American Academy of Ophthalmology recommends that all children be considered for treatment of amblyopia, regardless of age.

Recent findings in neuroplasticity have replaced the formerly-held position that the brain is a physiologically static organ and have shown that it changes throughout life. Much evidence of neuroplasticity has been found in adults. According to Levi and Polat, significant improvement of Vernier acuity in adult amblyopes occurred following stereoeacuity by using 3-D video games. Similar findings were announced by researchers at the Goldschleger Eye Research Institute, Tel Aviv University. The mean improvement in distance and near acuity in amblyopic eyes by 12 months was 3.3 and 1.9 lines log MAR (minimum angle of resolution) respectively.

In 2009, a study conducted by MK Mallah and coworkers at Queen’s University, Royal Victoria Hospital, Belfast, Ireland, showed that older people (60–80 years) with a history of amblyopia who develop visual loss in the previously normal eye can experience recovery of visual function in the amblyopic eye over a 12 month period. This recovery in visual function occurred following visual loss in the other, previously normal, eye; distance improved to 3.3 lines and near to 1.9 lines log MAR. This improvement appeared to be sustained.

There are unsubstantiated beliefs that it is more difficult to treat amblyopia in older age groups, that children that have already received failed amblyopia therapy do not respond to treatment and that full-time occlusion therapy may result in occlusion (disuse) amblyopia of the good eye. The aim of this study was to assess whether these beliefs are true.

Materials and methods

This was a prospective trial of 115 consecutive cases with unilateral, severe amblyopia conducted at a tertiary referral center in Lahore, Pakistan, from January 2010 to October 2012 after obtaining ethical committee approval by the University of Health Sciences. Eligibility criteria included an age of over three years, visual acuity in the amblyopic eye from 6/60 Snellen’s or even counting fingers only, visual acuity in the sound eye of 6/6, an inter eye acuity difference of three or more lines, and the presence or history of an amblyogenic factor such as refractive, deprivational and strabismic components that met study-specific criteria for strabismus and/or anisometropia. A complete ophthalmic examination was performed by only one ophthalmologist (SI). This included examining the fixation pattern of both eyes, presence or absence of a phoria or a tropia by a cover-uncover test, fundus examination and color vision using Ishihara color plates. Any case with an organic cause for visual loss was excluded from the study after a thorough ophthalmological examination. Assessment of visual acuity of either eye for both near and distance acuity (Snellen’s in literate patients and Kays picture chart for illiterate children (3–5 year olds)), refraction and Best Corrected Visual Acuity (BCVA) was performed by a trained optician who was masked to the study and patient’s demographics.

There were 59 female and 56 male patients and the cases were divided into three age groups:

Group A: age 3–7 years (mean age 5.38±2, median 5 yrs) = 38 cases (37.25% of the total number).

Group B: 8–12 years (mean age 9.73±1.73, median 10 yrs = 41 cases (40.20% of the total number).

Group C: 13–35 years (mean age = 19.26±6, median 17 yrs = 36 cases (22.55% of the total number).

All patients had some degree of anisometropia; two children had stimulus deprivation amblyopia due to traumatic cataract (aged five and seven years) and 82 patients presented with strabismus.
All cases were prescribed an optimal refractive correction for a month after which full-time occlusion therapy was started. After verbal informed consent was obtained from either the parents or the guardians, patients were provided with stick-on commercial eye patches and were instructed to wear the patch over the good eye as soon as possible after waking up in the morning. They were strictly instructed not to take it off during the day, only when they were about to sleep at night. Patients were instructed regarding the near visual activities they should perform for 3–4 hours/day. All patients and both of their parents or care-takers were thoroughly counseled about regular follow up, compliance towards the patching schedule and engaging the children towards near visual activities. The latter included coloring, drawing, reading large prints initially and then as near vision improved, shifting to smaller prints, playing video games on their personal computers and hand held video games inter alia.

Patients were closely followed-up at regular intervals of one day/year age; for instance four year olds were checked every fifth day and six year olds, every seventh day. Children more than 7 years old were followed up every two weeks. Patients were instructed to come into the clinic wearing the occlusive patch. First the vision of the amblyopic eye was checked and then that of the occluded eye; children were instructed to wear the patch immediately thereafter. Any change in fixation pattern of the two eyes was noted after removing the patch.

The criteria for a successful therapeutic outcome in this study was regarded as a maximum visual recovery (achieving 6/6 Snellen’s). Occlusion therapy was continued until this was achieved in all age groups. If after two months of full-time patching no visual improvement was noted, further therapy was stopped. If therapy was successful it was gradually reduced over the next seven weeks and then stopped. The weaning protocol adopted was one day off in the first week, two days off the second week, three days off the third week and so on until the seventh week, when occlusion therapy was discontinued.

Children in the 3–7 year age group were followed-up weekly after therapy discontinuation and any drop in visual acuity during weaning was monitored. Patients over the age of seven were followed-up after every two weeks until occlusion therapy was successfully finished in the seventh week.

Patients were followed-up at two weeks, one month, two months and then every three months for the next 18 months after stopping full-time occlusion.

Results

The clinical demographics of the patients are summarized in Table 1. Success was defined as equalization of visual acuity in both eyes, i.e. 6/6 (Snellen’s).

<table>
<thead>
<tr>
<th>Table 1. Characteristics of patients included in the study.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Person specific characteristics</strong></td>
</tr>
<tr>
<td>Total patient number</td>
</tr>
<tr>
<td>Age: 3–7 years</td>
</tr>
<tr>
<td>Age: 8–12 years</td>
</tr>
<tr>
<td>Age: 13–35 years</td>
</tr>
<tr>
<td>Gender, female (%)</td>
</tr>
<tr>
<td>Gender, male (%)</td>
</tr>
<tr>
<td>Traumatic cataract</td>
</tr>
<tr>
<td>Strabismus</td>
</tr>
</tbody>
</table>

Improvement in visual acuity noted with full-time occlusion therapy was 6/6 Snellen’s in 38/38 (100% success) in group A. In group B, 38 cases out of 41 achieved 6/6 vision (92.68% success). In group C, 35 cases out of 36 achieved 6/6 (97.22%) success (Table 2). The average time duration for successful amblyopia therapy in group A was 8 ± 1 weeks, in group B was 9 ± 2 weeks and in group C was 16 ± 2 weeks (Figure 1).

<table>
<thead>
<tr>
<th>Table 2. Amblyopia therapy success in different age groups.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age group</strong></td>
</tr>
<tr>
<td>3–7 years</td>
</tr>
<tr>
<td>8–12 years</td>
</tr>
<tr>
<td>13–35 years</td>
</tr>
</tbody>
</table>

![Figure 1. Comparison of improvement in visual acuity with the duration of therapy between groups.](image-url)
Visual acuity improved even in the “unsuccessful cases” (not achieving 6/6). The three unsuccessful cases in group B improved from 6/60 to 6/12 and the one unsuccessful case in group C was found to be due to eccentric fixation. Hence an improvement of five lines did occur even with eccentric fixation.

Patient compliance to therapy was found to be an important factor influencing clinical improvement in vision in this study. Groups A and C were noted to be more compliant to therapy than Group B in spite of regular counseling of both the parents and the patients (Figure 2).

All cases showed improvement in near vision prior to distance vision. Color vision in all cases was found to be normal as checked by the Ishihara color plates before and after therapy. We noticed an increase in stereopsis, determined at each follow-up visit after successful amblyopia therapy by the TNO test, but this is beyond the scope of our present study.

A more interesting outcome of the study was that out of the 115 amblyopic cases included in our study, 82 (71.30%) presented with strabismus. Out of these 82 cases, 51 cases (62.19%) became orthophoric once their amblyopia was fully corrected while only 31 cases (37.80%) needed surgery for strabismus correction once their vision was restored in the amblyopic eye (Table 3).

Further analysis of the outcome of amblyopia therapy on strabismus presenting in each group revealed that in group A (38 cases), 33 had strabismus; out of these, 28 cases (84.84%) became orthophoric with amblyopia therapy alone and only 5 (15.15%) needed strabismus surgery. In group B (41 cases), 25 had strabismus; out of these, 16 cases (64%) became orthophoric and 9 (36%) needed surgery for squint correction. In group C (36 cases), 24 had strabismus; out of these, 7 (29.16%) became orthophoric and 17 cases (70.83%) needed strabismus surgery.

Reversal of amblyopia was noted in two cases in group A. One stopped wearing glasses after two months of completing the weaning and visual acuity dropped to two lines when she came for follow-up. She was started again on full-time patching and the visual acuity returned to 6/6. The second case stopped patching abruptly during weaning. On follow-up, the visual acuity had dropped by two lines. It was controlled by resuming full-time patching again. One patient in group C behaved similarly and reversal of amblyopia was controlled by resuming full-time patching and continuous spectacle wear.

Patch related mild contact dermatitis was noted in 60% patients, which was managed by steroid skin cream at night while the patch was off. No other patch related complication was noted.

### Table 3. Impact of amblyopia therapy on strabismus.

<table>
<thead>
<tr>
<th>Group</th>
<th>Amblyopia cases presenting with strabismus</th>
<th>Strabismus correction with amblyopia therapy</th>
<th>Cases requiring surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (n=38)</td>
<td>33</td>
<td>28 (84.84%)</td>
<td>5 (15.15%)</td>
</tr>
<tr>
<td>B (n=41)</td>
<td>25</td>
<td>16 (64%)</td>
<td>9 (36%)</td>
</tr>
<tr>
<td>C (n=36)</td>
<td>24</td>
<td>7 (29.16%)</td>
<td>17 (70.83%)</td>
</tr>
<tr>
<td>Total (n=115)</td>
<td>82 (71.30%)</td>
<td>61 (74.39%)</td>
<td>21 (25.60%)</td>
</tr>
</tbody>
</table>

**Discussion**

Amblyopia is the most common cause of monocular visual impairment among children, young, and middle-aged adults. Occlusion of the good eye by a stick-on eye-patch is the main therapy, which may be applied full-time or part-time. The standard teaching has been that children being treated with full-time occlusion therapy need to be observed at intervals of one day per year of age so as to avoid occlusion amblyopia of the good eye. The Amblyopia Treatment Studies (ATS) have helped to provide new information on the effects that result from patching of various durations (2–6 hours per day). Studies have shown that patching or occlusion therapy compliance is a major factor that influences the outcome of treatment. Most of the visual improvement in this study was obtained in the first four hundred hours of occlusion therapy.
Full-time patching is quite difficult, particularly when a teenager or an adult is asked to manage with a poorly sighted amblyopic eye; it needs a major life style modification for at least 2–3 weeks after which the near vision is improved to such an extent that the patient can manage on his own. Hence a positive approach by the patient, the family and the treating ophthalmologist is very important for a successful outcome following full-time patching.

In our study, a 100% positive outcome was seen in children between age three to seven years. This seems to be correlated with excellent compliance due to education and regular counseling of both parents to fully comply with the therapy and to return for regular follow-ups. All of these cases had severe amblyopia with vision of counting fingers at 6/60. They achieved 6/6 Snellen's visual acuity after six weeks of constant full-time patching in all three literate cases, (100%) in this age group. In the remaining eight children, visual acuity was checked by Kay's picture test and a 100% improvement was noted. Results from a study done by MX Repka and coworkers showed that improvement of visual acuity in children between three and seven years of age with moderate amblyopia was a mean of 3.7 lines in the part-time patching group and 3.6 lines in the atropine group, from baseline. A study conducted by Schie- man and coworkers, in 2004 on 404 patients aged 7–17 years found 49% of treatments were successful in 7–12 year olds and 23% were successful in 13–17 year olds. They observed that near vision activities had a beneficial impact on visual acuity in the 13–17 year age group even when amblyopia was not being treated; this was more pronounced if amblyopia was treated by 2–6 hours patching/day. Their study confirms that near visual activities have a positive visual outcome. However, the difference in their results in terms of success differs from our study because of the different patching technique; 2–6 hour patching in their study had no significant impact and only resulted in 2–4 lines improvement in visual acuity. Our study implemented full time patching, which was shown to be promising results even in severe amblyopia in children between 3–4 weeks of therapy. We did not hospitalize our patients but focused on motivating them at each follow-up visit.

The fact highlighted by this study is that amblyopia can also be successfully treated in adults and that there is no clear upper age limit for recovery of vision though older patients may require two to three months of full-time patching compared to younger age groups who achieved 100% improvement within two months of therapy.

Conclusion

This study shows that any severity of amblyopia can be reversed at any age with full-time occlusion therapy. A 100% improvement in visual acuity is possible within a period of 2–3 months. In comparison only a 3–4 line improvement (30–50%) in visual acuity occurs after a period of six months to one year with part time patching. The only factor that determines a successful outcome following full-time occlusion therapy is patient’s total compliance to therapy.

Other recent technological approaches such as the perceptual learning technique, Pac-man technique, racing games and other computer soft-ware tools are not only complicated but a financial burden on the economy of under-developed countries. In comparison, occlusion therapy by a patch is very an economical, affordable and the only feasible option in countries such as Pakistan. The extent of visual improvement
achieved by full time occlusion therapy is more effective than other techniques.

Author contributions
Sameera Irfan formulated the study, ophthalmological examination of patients, parent’s and patient’s counselling, wrote the final study. Nowsherwan Adil made the data spread sheet, did the statistical analysis, plotted the graphs. Haris Iqbal: helped with the clinical study, did literature search, kept patient’s records throughout their follow-up. All authors actively revised the manuscript.

Competing interests
No competing interests were disclosed.

Grant information
The author(s) declared that no grants were involved in supporting this work.

References
Open Peer Review

James Loughman
Department of Optometry, College of Sciences and Health, Dublin Institute of Technology, Dublin, Ireland

Irfan et al. have reported on the efficacy of occlusion therapy in severe amblyopia among subjects aged 3 to 35. The authors present a series of interesting, but somewhat surprising results. Most notably the authors conclude that (a) any degree of amblyopia can be resolved with full time occlusion therapy, with almost 100% success even in those aged 13 to 35, in reaching and maintaining 6/6 acuity, and (b) that amblyopia correction is an effective treatment for strabismus, creating orthophoria in almost two-thirds of cases.

These findings are potentially groundbreaking, but are so contrary to conventional clinical experience (including experience in the days when full time occlusion was routine), and to the extensive body of prior research evidence (some of which, including the PEDIG study are cited by the authors), that a serious and in-depth evaluation of the scientific robustness of the study methods and interpretation of reported findings is needed.

Although it is beyond the scope of a short review such as this to explore the flaws in substantial detail, I will outline in brief, a number of significant flaws in the study methods and interpretation of findings as presented in this manuscript.

The study sample is very poorly described. For example, we are not given any idea as to the degree of anisometropia, the type (e.g. accommodative) and magnitude of strabismus, or participants’ past ocular history. Patient history is a very important potential confounder that is not at all addressed in this study. The reader is left clueless as to key factors such as why the participants have been referred to the clinic, whether they have undergone any previous ocular treatment (possibly including occlusion therapy) or whether they have previously worn spectacles among many other unknown factors. The inclusion criteria allow for participation of subjects having “failed” previous occlusion therapy, yet there is no information at all as to how many of such participants were included, or how the investigators deemed that past therapy had indeed “failed”. Without such information, the reader simply cannot be certain as to whether the study participants have true amblyopia, or simply took some time to adapt to new spectacles.

The study methodology is certainly unclear, and most likely flawed. For example, the authors state that the optician was masked as to the subjects' demographics. Quite how an investigator can be masked to patient demographics is beyond me (e.g. a child age 3 versus an adult age 31).

Another important aspect is the acuity chart used. Firstly, the Snellen and Kay’s picture charts are inappropriate for amblyopia assessment, but that remains a minor point. The major concern is whether
the same chart and series of letters was used throughout the study. The methods describe that subjects were assessed at a minimum of every 2 weeks (and much more frequently for those under 7, such as every 5 days for 4 year olds). VA in the amblyopic eye was assessed first, then in the normal eye. Surely, the failure to randomise charts and letters is potentially a major flaw in the study (the reader must assume that letter or chart randomisation did not occur as it is not stated as a prescribed method). The effect of learning could be truly substantial, with subjects becoming increasingly familiar with the charts and letters at every visit. Despite even the best of participant intentions, such a learning effect would be impossible to avoid and could entirely explain the results observed in older observers. Although the authors dismiss it as not within the scope of their paper, I am unclear as to the reasons why the reported improvements in stereopsis are not explored in detail in the manuscript. Surely, a paper concerned with neural plasticity in older age groups should report on stereopsis when the test has been included in the study protocol.

I am further concerned by the authors’ interpretation of the effect of occlusion therapy on strabismus, stating that "Out of these 82 cases, 51 cases (62.19%) became orthophoric once their amblyopia was fully corrected while only 31 cases (37.80%) needed surgery for strabismus correction once their vision was restored in the amblyopic eye". The effect of refractive correction on the reported strabismus is not explored in the paper. Inspection of the amblyopia data provided reveals, as would be expected, a strong relationship between refractive error type and strabismus type (i.e. esotropia mostly associated with hyperopia, and exotropia with myopia). It would seem entirely more likely that the actual reason that strabismus is rendered orthophoric, simply relates to the provision of appropriate spectacles, and not to occlusion therapy success as described. Accommodative esotropia, for example, remains the most common cause of childhood esotropia, and is readily treated with spectacle provision, not requiring surgery.

This study simply does not stand up to proper scientific scrutiny. The methods are flawed, the interpretation is inaccurate, and the results are most likely explained away by factors not explored in the paper. I am concerned that this article could potentially create confusion among the general public and possibly even among clinicians inexperienced in the art of evaluating scientific publications.

**Competing Interests:** No competing interests were disclosed.

I have read this submission. I believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Referee Report 31 July 2013
https://doi.org/10.5256/f1000research.1649.r1187

Robert Taylor
Ophthalmology, York University Hospital, York, UK

This publication is a prospective case series of patients who are reported to have amblyopia, who underwent full time occlusion following one month of refractive adaption. The authors have divided the patients in to three age groups. They claim 100% success in achieving 6/6 Snellen in the younger group, with high percentages claimed in the other two age groups exceeding 90%. The authors also claim that the full time occlusion treated heterotropia in 85% of the younger age group who had a strabismus, 64% of the middle age group (age 8-12) and 29% of the older age group. The latter claim is not discussed further. Very few visually related problems are aired, with two children, and one patient in the older age category relapsing, with vision being restored with further occlusion. The authors have reported a high
incidence of contact dermatitis - treated with topical steroid.

On the face of it the authors seem to have solved the problem of amblyopia management, declaring results far in excess of other published studies. They have also managed in some way to treat strabismus, even though occlusion is not normally thought to be a treatment for strabismus.

There are a number of observations that might explain the discrepancy between this publication’s results and those of others.

The first is the case selection. Paragraph 1 of the methods is confusing. If the better eye has to be 6/6 for inclusion, it would be much more simple to state that all amblyopic eyes were equal to or less than 6/12 (assuming a three line difference of 6/7.5, 6/9 and 6/12). If all amblyopic eyes were 6/60 or less (as is suggested later in the discussion) than this is not a difference of three lines. We are not told how many lines there are on their charts, which can be highly variable. We are also told that there are “study specified criteria for strabismus and/or anisometropia”, but are not told what these are. We are told that those with organic visual loss are excluded, although cases of stimulus deprivation are included. One has to assume therefore that in these cases the cause of the stimulus deprivation has been removed. The cases have been referred to a tertiary centre, so it is not clear how much treatment might have been instituted in the past, and again an assumption that many of these cases have been treated by other methods could be made, possibly with an initial good outcome at some point in the past. Although the cases selected are probably all amblyopic, it is possible that some may not be, if they have not been refracted for many years. Lastly by selecting patients with 6/6 in the better eye, cases of bilateral ammetropic amblyopia have been excluded.

The second concern is the method of assessing visual acuity. All studies of amblyopia currently use crowded logMAR testing on all patients, even those with the inability to read letters. The use of Snellen does not lend itself to statistical analysis (as the authors have done to plot their graphs) as it is a non linear scale. Furthermore the authors have stated that Kay’s pictures are used for those who are unable to read letters. It is assumed that these are single optotypes and not crowded. This method of assessment is highly correlated to over-estimations of visual acuity, and may go some way to explain the apparent good results. We are not told of the proportion of those who have been tested using this method.

The third concern is the length of time allowed for refractive adaption. Most authors would agree that a month is not long enough, with much variation in the literature, but up to 18 weeks being common. It is possible that some of the reported improvement in acuity is as a result of the refractive adaption rather than occlusion.

The authors might have given more information on how compliance was assessed. Many studies report poor compliance. Having said this the apparent high association of contact dermatitis suggests good compliance.

There are a number of omissions that are of concern. In such a group of children with strabismus and amblyopia, I would have expected some children to have small angle, constant esotropia with no binocular vision (and suppression). The paragraph on page 4 (last paragraph in right hand column) seems to divide patients into those with orthophoria and those that had surgery. It seems odd that there are no patients in the group that have small angle manifest strabismus, but did not need surgery. Are we to assume the patients with orthophoria have binocular vision? It is unlikely in patients who started the study with dense amblyopia.

Another omission is any information on binocular vision. In the UK, the practice of occlusion therapy is associated with assessments of the depth of suppression, albeit without much data to support it. The concern is the complication of diplopia, by removing suppression with occlusion. Any publication expounding the virtues of full time occlusion needs to be careful not to create an environment where diplopia is created to the detriment of the patients overall vision.

A further concern is occlusion amblyopia. It would appear from the graphs that occlusion was applied for a mean of 14 weeks. Full time occlusion in patients as young as 4 might be associated with this complication, which it would appear did not occur.
Lastly it would be of interest if there were any patients who were lost to follow up. These patients are important as often associated with treatment failure. Again it would appear not to have occurred.

In the discussion, much of the first paragraph could be edited. On page 5, the first complete paragraph, it is confusing as the authors describe group A, as being 3 patients (“three literate cases”) and “the remaining eight children” - which makes 11 cases, however there were 38 in this group. Language and Typographical errors: Page 4, first paragraph on the right, talks about reversal of amblyopia. I think the authors are talking about the amblyopic eye visual acuity decreasing. I think “regression” might be a better term as reverse amblyopia is a term used to describe the reduction of vision in the previously better eye, described above as occlusion amblyopia.

Page 5 first paragraph - “can manage on his own” would be better “can manage independently”.

Page 5 right hand column talks about “100% improvement”. I do not understand this. 100% of what?

Page 5, second to last full paragraph on left, word “improvent” should be improvement, and first full paragraph on the right, strabismica - should be strabismic. Third to last line on page 5 - “is very an economical” - delete “an”.

Page 6, column on the right, first line, “performed the literature search, kept the patients’ records...” would read better.

Overall the authors have produced a piece of work that is thought provoking. Although the overall results are challenged, they are still impressive. Consideration of full time occlusion, with care to avoid occlusion amblyopia and diplopia, may be an accepted form of treatment in selected cases.

Declaration: Sameera Irfan (first author) is a former trainee of the reviewer (1995 - 1996).

Competing Interests: No competing interests were disclosed.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Discuss this Article

Version 1

Author Response 15 Mar 2014

sameera irfan, Mughal Eye Trust hospital, Pakistan

In response to both referee reports we are now working on a revised and updated version of this article. However in the mean time I would like to add the following comments to my original study:

1) All cases included in the study had dense amblyopia with a visual acuity of 6/60 or 6/36 Snellen's, the other eye being 6/6.

This is a third world country with a patient pool which is totally neglected. There is hardly any visual screening in schools hence the anisometropic amblyopia worsens with age. When we started the study, we planned to include all amblyopic cases with at least a 3 lines difference of visual acuity between the two eyes. However, upon conclusion of the study, we were surprised to find that all consecutive cases had at least 6-7 lines difference between the two eyes.
2) In the Snellen's chart there are 7 lines, with 1 letter in the first line, 2 in the second, 3 in the third, 4 letters in the 4th line, 5 in the 5th line, 6 in the 6th line and 7 in the 7th line.

3) All cases of organic amblyopia were excluded from the study. That included cases with dense corneal opacities in children, macular scarring or optic atrophy.

4) Cases with sensory deprivation were included: 2 cases had unilateral traumatic cataract at the age of 4 years. They had cataract surgery with intraocular lens implant at the age of 5 and 7 years and were referred for the management of amblyopia post-operatively.

5) Out of the total of 105 cases included in the study, 39 (37.14%) had a past history of being treated with part-time occlusion therapy for 2-6 hours for a period of 3-5 months - 22 out of 41 cases in Group B, (8 - 12 years old); and 17 out of 36 cases in Group C. Since it only improved their vision to 2-3 lines, the parents and the patients ceased treatment which resulted in regression of amblyopia.

6) All cases had minimal refractive error in the good eye with an uncorrected vision of 6/6. The 37.14% cases of Group B and C wore corrective glasses only for a 6 month period while part-time occlusion therapy was done. Since it did not significantly improve their vision, the patients stopped wearing glasses. The remaining 62.86% were never prescribed glasses.

7) The degree of anisometropia: anisomyopia of -5.5D to -12 with a mean of -6.5D, anisohypermetropia of +3.5 - +6.00 with a mean of +4.00 D was present.

8) An important objection raised by the referees is that the same charts were used at each follow-up visit and the probability of learning or memorizing the letters in each line can therefore not be ruled out. We submitted this paper for publication in July 2013 and after receiving these objections, we are now assessing the visual acuity on both the Snellen's and the ETDRS charts in all follow-up cases since the last seven months and have found similar results. An amblyopic eye that cannot appreciate two letters on the second line of Snellen's chart is densely amblyopic and at the end of therapy, if it can read all 7 letters clearly on either a Snellen's or the last line (tenth line) ETDRS then surely that is a huge success. The ETDRS charts include pictures and E letters which we are now using for illiterate children.

9) We did not mention the improvement in stereopsis in detail in the paper as we wanted to write another detailed paper on this later. Since our follow-up on all the treated cases has continued, the stereopsis as tested by the Titmus Stereo test at 40cm with patients wearing polarised spectacles over their refractive glasses, has gradually improved from 800" to 100" and from 60 to 40 seconds of arc in all cases who have achieved 6/6 Snellen's or 1.0 on the ETDRS charts.

10) In response to the referee's objection that the actual reason the strabismus has been rendered orthophoric is due to the provision of appropriate spectacles and not due to occlusion therapy success. I would like to respond that it is important to realize that a densely amblyopic, esotropic eye will not become orthophoric with full hypermetropic correction worn for 3-6 months or even longer unless its vision has improved to 6/6 Snellen's or 1.0 ETDRS and that is a fact. In dense amblyopes/amblyopia, the brain needs to be retrained to start seeing clearly with both eyes and that can only be achieved by occluding the good eye full-time to avoid brain-confusion.

11) The time allowed for refractive adaptation: we allowed only 4-6 weeks for refractive adaptation though the referees have recommended a minimum of 18 weeks.
After 4-6 weeks of continuous spectacle wear, we found only 1-2 line improvement in vision so instead of waiting further, occlusion therapy was started. I agree with the referees that if we had allowed more time, some more improvement in vision might have occurred but still they cannot deny the role of occlusion therapy in achieving a 100% improvement in vision which cannot be achieved with refractive correction alone no matter how long it is worn.

12) A 100% improvement in visual acuity means as compared to the other normal eye which was 6/6 Snellen's or 1.0 ETDRS.

Competing Interests: There are no competing interests.