Amblyopia - Current Trends in Management

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Introduction

The detection and management of amblyopia lies at the heart of pediatric ophthalmology. As John T Flynn noted in the 17th annual Frank Costenbader lecture “it is to amblyopia to which my heart returns”. Till recently, literature on amblyopia consisted predominantly of retrospective reviews. In 1997, the pediatric eye disease investigator group (PEDIG) was formed to conduct clinical research in eye disorders affecting children. The studies were conducted through simple protocols with limited data collection and implemented by both university and community based pediatric eye care practitioners as part of their routine practice. Amblyopia is the most common cause of monocular visual impairment in children and young and middle aged adults and hence PEDIG has laid emphasis on studies of treatment modalities of amblyopia, the Amblyopia Treatment Studies.

Definition

Amblyopia has been defined as corrected visual acuity of > 20/40 or > 1 line difference in corrected visual acuity between the 2 eyes. This is not a result of any organic problem of the eye or the visual pathway.

Prevalence

The prevalence of amblyopia in the age group 4 years has been reported to be 1.07 % in the population screened at infancy, to 2.57 % in the population that has not been screened at infancy. The optimal timing to screen amblyopia has been a matter of debate. In the Avon longitudinal study of parents and children, an assessment of the effectiveness of early treatment of amblyopia was performed. It was noted that intensive screening protocol at a young age resulted in better amblyopic eye acuity at 7.5 years of age in those who underwent screening. A Cochrane review on the value of programmes for screening showed that the lack of data from randomized trials makes it difficult to analyse the impact of existing screening programmes on the prevalence of amblyopia. This does not imply that vision screening is not beneficial, but that the intervention has not been tested in robust trials.

Neuronal Basis of Amblyopia

The visual processing system is susceptible to the influences of abnormal environmental factors. The seat of amblyopia is not the retina but the striate and the extrastriate cortex. The effects on the lateral geniculate nucleus are minimal. The cells of the layer 1,4,6 from the contralateral and 2,3,5 from the ipsilateral eye can be affected if monocular deprivation occurs early. There were two sets of synaptic inputs and with experience one pathway from the open eye takes over preempting the territory of the closed eye.

In the visual cortex, the principal abnormality is at the level of the primary visual cortex (striate cortex, V1, Brodmann’s area 17). Normally eye inputs to the area IV C are divided equally between the eyes. The deprived eye shows a marked shrinkage of its input stripes (ocular dominance columns) and a corresponding expansion of the nondeprived eye. Radioactive aminoacids and axonal transport from eye to cortex
shows a marked shrinkage of the input stripes (ocular dominance columns) and a corresponding expansion of the non deprived eye. In addition to the differential retraction of terminals, the result is produced by sprouting of axonal terminals. Changes in the area V1 are qualitatively related to the depth of amblyopia. Changes in V1 typically predict smaller deficit than measured behaviourally. Qualitatively abnormalities in the eye dominance columns and the spatial properties of visual cortex neurons were related on a case by case basis to the depth of amblyopia. Quantitative analysis suggests that these abnormalities alone do not explain the full range of visual deficits in amblyopia and there may be unknown abnormalities in the extrastriate cortex. The suggested mechanisms of visual loss in amblyopia include abnormal neural response properties, poor synchronization of neuronal responses, abnormal topographic representation of topographic receptive fields and undersampling of visual space. At the molecular level, synaptogenesis determines the loss of vision and improvement in amblyopia. If performed early in the critical period, patching the good eye can lead to a complete switch in fixation preference. The geniculate innervation of layer IVC reverses and the initially deprived eye can take over much of the lower part of layer IVC, but fails to reverse the domination of the other eye in the upper part of layer IVC. The critical period is different for different cell types. Even after prolonged patching the loss of binocular cells may not reverse and there may be permanent loss of stereopsis. The risk associated with unilateral patching or alternate patching is the loss of stereopsis and not fusion. Levodopa can help in the improvement of visual acuity and pattern VEP amplitudes. Cytidine 5’ diphosphocholine also improves visual acuity, contrast sensitivity and visual evoked potentials of amblyopic subjects. Functional MRI a relatively new modality may reveal changes which can be used to assess the effect of amblyopia treatment in humans.

Recent Concepts in Management

Atropine versus patching

This was studied in the first PEDIG trial (amblyopia treatment study 1). The objective was to compare patching of the sound eye with atropine instillation. In this prospective randomized multicenter clinical trial, moderate amblyopes (20/40 to 20/100) in the age group 3 to 7 years were included. 419 patients with an average age of 5.3 years were enrolled. 96% completed examination at 6 months. The atropine group received 1 drop of 1% atropine in the sound eye daily. If by 4 months, acuity had not reached 20/30 or improved by 3 lines from baseline, distance correction was removed to augment atropine effect. Patching group was prescribed minimum 6 hours patching daily, if by 4 months they had not reached 20/30 or improved by 3 lines from baseline, full time patching was prescribed. The mean visual acuity in the amblyopic eye at enrolment was 20/63 with a mean difference of 4.4 lines between eyes. Visual acuity improved 3.16 lines in the patching group and 2.84 lines in the atropine group. Improvement initially was faster in the patching group, but at 6 months difference in acuity between the 2 groups was clinically insignificant. At 6 months, 79% in patching group and 74% in the atropine group had acuity 20/30 or better and/or improvement from baseline by 3 lines. The conclusions were both treatments were well tolerated, though atropine had more tolerability and patching works faster than atropine. A 2 year follow up of the same study group to look at the long term follow up revealed that the improvement was 3.6 lines in the atropine group and 3.7 lines in the patching group. In moderate amblyopia, atropine and patching both showed moderate improvement. The amblyopic eye acuity was also noted to be 2 lines less than the worse eye. This study gave concrete evidence about the well known aspects of atropine and patching.

Part time occlusion

Patching regimens used to be divided into full time patch for days depending on the age. Compliance and the risk of occlusion amblyopia was an issue with these regimens. The ATS 2A (amblyopia treatment study 2A) compared 6 hours versus full time patching for severe amblyopia (20/100 to 20/400) in children 3 to 7 years old. In this prospective study 175 patients were enrolled with an average age of 4.8 years. The severe amblyopic patients were randomized to 6 hours or full time (all but 1 waking hour daily patching). The mean acuity at enrolment was 20/160, with a mean difference in acuity between the eyes of 7.8 lines. The 4 months follow up
was completed by 90 % patients. Mean improvement in the visual acuity was 4.8 lines in the 6 hour group and 4.7 lines in the full time group. At 4 months there was no difference in acuity between the groups. 86 % of the patients in the 6 hour group and 82 % in the full time group had improvement in acuity of more than 3 lines from baseline. This study formed the basis for a paradigm shift from full time daily patching routines to part time occlusion.13

The amblyopia treatment study (ATS 2B), compared 2 hours versus 6 hours of daily patching for moderate amblyopia in children aged 3 to 7 years old. In this prospective study 189 patients were enrolled with a mean visual acuity of 20/63 and randomized to 2 or 6 hours of patching. Visual acuity improved in both groups and at 4 months there was no difference between the 2 groups. 62 % of patients in each group had a visual acuity 20/30 or better and or improvement of 3 lines. It was noted that prescribing greater hours of patching did not seem to have a significant beneficial effect in the first 4 months of treatment. It was also noted that the hours of patching did not affect the rate of improvement 14-17.

Recurrence of amblyopia after discontinuation of treatment

The amblyopia treatment study 2C was undertaken to study the recurrence of amblyopia after discontinuation of treatment. In this prospective trial, 156 children less than 8 years of age, who received continuous treatment for amblyopia for the previous 3 months ( prescribed at least 2 hours of daily patching or at least 1 drop of atropine per week) and who had improved at least 3 log MAR levels of treatment. Follow up was performed at 52 weeks to assess the recurrence of amblyopia defined as 2 or more log MAR line reduction of visual acuity from enrolment, confirmed by a second examination or restarting of treatment due to a 2 or more log MAR level reduction of visual acuity. Approximately one fourth of the children were noted to have a recurrence of amblyopia in the first year post treatment. This is similar in the patching and atropine group. In patients with intense patching (6-8 hours per day), recurrence was more common when the treatment was not reduced prior to cessation, than when treatment was reduced to 2 hours per day prior to cessation 18.

Older children

The amblyopia treatment study 3, ATS 3, evaluated the effectiveness of treatment in children aged 7 to 17 years. In this prospective randomized clinical trial, 507 patients were studied with a visual acuity ranging from 20/40 to 20/400. The optimal optical correction was given followed by randomization to treatment group (2-6 hours per day of prescribed patching combined with near visual activities for all patients plus atropine sulphate for children aged 7 to 12 years) or optical correction alone. With treatment 53 % responded and with optical correction 25 % responded. For patients aged 7 to 12 years, 2 to 6 hours of patching with near visual activities and atropine improves the visual acuity even if the amblyopia has been previously treated. For patients aged 13 to 17 years, 2 to 6 hours of patching per day with near visual activities may improve when amblyopia has not been previously treated, but is of little benefit if amblyopia was previously treated with patching 19.

Optical correction

A study was conducted to evaluate the results of 2 hours of daily patching for amblyopia in children aged 3 to 7 years old. There were 2 phases (1) spectacle phase in which maximum improvement with spectacles was noted and the (2) randomized trial comparing a group using patching treatment and spectacles with a control group using spectacle correction alone. In the spectacle phase 84 children with anisometropia were enrolled and in the randomized trial there were 180 children. In the randomized trial group, children were assigned to either 2 hours of daily patching with 1 hour of near visual activities or spectacles alone. 96 % patients were seen after 5 weeks. With optical correction alone amblyopia improved in 77 % of the patients and resolved in 27 %. In the randomized group, visual acuity improvement from baseline to best measured visual acuity at any visit averaged 2.2 lines in the patching group and 1.3 lines in the control group. Following treatment with spectacles, 2 hours of daily patching combined with 1 hour of near visual activities modestly improves moderate to severe amblyopia in children 3 to 7 years old 20-21.

In another study on the treatment of bilateral refractive amblyopia in children 3 to less than 10 years of age,
113 children with previously untreated bilateral refractive amblyopia were treated with optimal spectacle correction. Bilateral refractive amblyopia was defined as 20/40 to 20/400 best corrected binocular visual acuity in the presence of 4 diopters or more hypermetropia by spherical equivalent, 2 diopters or more of astigmatism or both in each eye. There was improvement in visual acuity by 3.4 lines in the group with visual acuity 20/40 to 20/80 and 6.3 lines in the group 20/100 to 20/320. The probability of a binocular visual acuity of 20/25 or better was 74 % at 52 weeks. The conclusion of this study was treatment of bilateral refractive amblyopia with spectacle correction improves binocular visual acuity in children 3 to less than 10 years of age 22.

Role of near activities

A study was designed to determine whether children randomized to near or non-near activities would perform prescribed activities and to obtain a preliminary estimate of the effect of near versus non near activities on amblyopic eye visual acuity when combined with 2 hours of daily patching. In this study 64 children in the age group of 3 to < 7 years were randomly assigned to receive either 2 hours of daily patching with near activities or 2 hours of daily patching without near activities. Parents completed daily calendars for 4 weeks. After 4 weeks, there was greater improvement in the amblyopic eye visual acuity in those assigned to near visual activities. Children patched and instructed to perform near activities for amblyopia spent more time performing those near activities compared to children not instructed. Performing near activities while patching may be beneficial in treating amblyopia 23.

Dose response relationship

In this study the dose-response relationship for amblyopia therapy was studied. There were 3 distinct phases – baseline: to measure visual status, refractive adaptation: an 18 week period of spectacle wear with 6 weekly measurements of logMAR visual acuity, occlusion: participants prescribed 6 hours of patching per day. Patching was monitored using a dose response monitor attached to the patch. The average concordance with patching was 48 %. Increasing the dose rate beyond 2 hours per day hastened the response but did not improve outcome. More than 80 % of the improvement occurred within 6 weeks. Treatment outcome was significantly better for children < 4 years of age than those older than 6 years 24.

The PEDIG studies suggested radical changes in the management protocols for amblyopia. It is interesting that another study was conducted to see the effect of the randomized trial of patching regimens for treatment of moderate amblyopia on pediatric ophthalmologists. Two questionnaires were mailed one in 2003 and one in 2006 to 560 members of the American Association for Pediatric Ophthalmology and Strabismus. Of the 107 responses (20 %) received, it was noted that 55 % of the respondents had decreased their prescribed patching regimens as compared to 28 % in 2003. There was no significant increase in the prescription of near visual activities or only a 2 hour patching regimen 25.

Conclusions

These studies conducted by PEDIG put forth new ideas and concepts in the management of amblyopia based on prospective trials. The conclusions of the various studies have been summarized below.

- Patching works faster than atropine, however at 6 months the improvement is the same with patching and atropine in moderate amblyopes.
- Improvement with full time and 6 hours patching similar in severe amblyopes.
- In moderate amblyopes 2 hours patching gives similar results to 6 hours of patching.
- About 25 % of the children have a recurrence of amblyopia in the first year post treatment.
- Recurrence is less common when patching was tapered to 2 hours per day before stopping.
- In patients 7 to 12 years of age, visual acuity improves with treatment even if amblyopia has been previously treated; in the 13 to 17 year age group, there may be little benefit if the amblyopia has been previously treated.
- Refractive correction improves visual acuity in untreated anisometropic amblyopia
- Most cases of moderate amblyopia (20/40 to 20/100) resolve.
- Performing near activities while patching may be beneficial in treating amblyopia.
Bilateral refractive amblyopia can be treated with spectacle correction with remarkable improvement of visual acuity.

Maximum improvement with therapy occurs in the first 6 weeks.

Younger the child better the outcome.

References