Update on Diagnosis and Management of Amblyopia

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Abstract
Amblyopia is common in the paediatric age group, however it is not well understood. This article highlights the need for diagnosis and management of amblyopia. The current treatment options are also mentioned in detail.

Introduction
Amblyopia is a reduction in visual acuity that cannot be attributed to the structural abnormality of the eye. The prevalence of amblyopia varies in different parts of the world. In India, it has been documented to be between 1% and 6% in different studies. Any child with a visual acuity in either eye of 6/12 or worse at age three to five years or 6/9 or worse at age six years or older, or a two-line difference in acuity between eyes, is diagnosed to have amblyopia. In addition to reduction in visual acuity, there is a decrease in contrast sensitivity, vernier acuity, spatial distortion, and contour detection. Crowding (a reduction of visual acuity when optotypes are presented in a line or surrounded by bars) is a feature of the developing visual system, which is seen in children with amblyopia and cerebral visual impairment. Visual acuity tests with single uncrowded letters seem to be insensitive to amblyopia. Thus, most tests for amblyopia use isolated letters surrounded by crowding bars or letters which are presented in a line of 4 or 5 letters. Amblyopia is more than four times as common in infants who are premature, small for gestational age or who have a first-degree relative with amblyopia. Eyes with dense amblyopia, meridional amblyopia, and age over 6 years at presentation are risk factors for treatment failure.

Etiology
The causes of amblyopia can be divided as follows:

- Strabismus (50%)
- Anisometropia (17%)
- Combined Strabismus & Anisometropia (30%)
- Ametryopia (<3%)
- Visual/Sensory deprivation (<3%)
- Organic causes-retinal or the optic nerve pathology (<3%)

Anisometropia of more than 1 dioptre in hypermetropes and 2.5 dioptres in myopes can cause amblyopia and decreased binocularity. Meridional amblyopia occurs if the astigmatism is more than 1.5 dioptres. Ametropic amblyopia occurs in children with hyperopia greater than 4.50 diopters and myopia more than 6 dioptres. The degree of cylindrical ametropia necessary to produce meridional amblyopia is not known, but most ophthalmologists recommend correction of greater than 2.0 D of cylinder.

Pathophysiology
Physiological basis of amblyopia is located in the visual cortex and lateral geniculate nucleus. The visual cortex shows reduced gray matter volume on voxel-based morphometry. V1 is the anatomic site in the visual pathway to be affected first as seen on functional magnetic resonance imaging. Gamma-Aminobutyric acid (GABA) is thought to play a key role in suppression of inputs from the amblyopic eye within the visual cortex. Amblyopia causes re-allocation of ocular dominance from the amblyopic eye to the good eye resulting in under representation of the amblyopic eye in the cortex. Plasticity of the visual system is greatest in infancy and it decreases with age. The critical period beyond which amblyopia treatment reduces efficacy was thought to be 7 years of age. However, anisometropia and sensory deprivation leads to formation of a defocused image, while in strabismus, the images are misaligned. Both these conditions lead to sensory deficits, however their magnitude of deficit does not correspond to the physiological changes in V1. Therefore, in addition to disturbances in V1, amblyopia also alters processing in extrastriate areas of the brain.

Diagnosis
In children younger than 3 years, it is difficult to make an accurate diagnosis of amblyopia. Visual acuity in young children and disabled adults can be tested by preferential looking techniques (Teller acuity cards; Cardiff acuity test), fixation preference tests or picture charts (Kay charts and Lea symbols). These tests usually underestimate amblyopia, especially strabismic amblyopia. A small overestimation in visual acuity is seen with Snellen E test and Landolt C. Lea symbols on the other hand give a better estimation of the visual acuity as compared to the other charts. Use of a non-logMAR scale (Snellen chart) introduces errors due to the nonequal increments from one line to the next. Examples of logMAR-based tests are HOTV optotypes used in the Amblyopia Treatment Study, the Glasgow cards and Early Treatment Diabetic Retinopathy Study test. LogMAR tests conform to a regular geometric progression, have equal number of letters in each line and use letters of near equal legibility and therefore permit interpolated scores.

Treatment
The Pediatric Eye Disease Investigator Group (PEDIG) has conducted a series of randomized clinical trials of amblyopic
treatment for children aged 3–17 years. Similar studies have been conducted by the Monitored Occlusion Treatment of Amblyopia Study (MOTAS) Cooperative Group and the Randomized Occlusion Treatment of Amblyopia (ROTAS) Cooperative Group. This trial was conducted to evaluate the effectiveness of amblyopia treatment and to define optimal treatment protocols. Occlusion of the good eye using eye patches, atropine or filters has been used to treat amblyopia for many years. It has been suggested that spectacle correction alone if used for 4-5 months leads to an improvement of more than 2 lines in children with anisometropic, strabismic and combined amblyopia. Thus, refractive correction should be the sole initial treatment for amblyopia. Patching should be started once stable visual acuity has been achieved. In patients with moderate amblyopia, patching 2 hours/day versus 6 hours/day yields similar results. In severe amblyopia, 6 hours/day and 12 hours/day of patching have been found to be equally effective. If amblyopia persists after a period of two-hourly patching, then a dose increase to 6 hours can improve visual acuity further. Atropine and patching are equally effective in treating amblyopia when used as initial treatment.

A secondary form of treatment is started if the visual acuity in the amblyopic eye reaches a plateau and fails to improve further, with a persistent difference of 0.20 logMAR or more compared with the better-seeing eye or the level of visual acuity normal for the child’s age. Children are monitored at eight- to twelve-weekly intervals until the visual acuity in the amblyopic eye normalizes, or until no further improvement is noted (Table 1). It was thought that patching beyond 7 years of age would not be effective due to loss of plasticity of the visual system, however it has been proven that patching can help improve vision beyond 7 years, although the rate of response to treatment may be slower, may require a higher dose of patching, and the extent of recovery may be less complete. The American Academy of Ophthalmology proposes the following for refractive error correction for prevention of amblyopia as shown in Table 2.

### Table 2

|                    | Age 0-1 yr | Age 1-2 yrs | Age 2-3 yrs | PEDIG |
|--------------------|-----------|------------|------------|-------|
| Isometropia        |           |            |            |       |
| Hyperopia          | ≥-6.00    | ≥-5.00     | ≥-4.50     | ≥-3.00|
| Hyperopia with esotropia | ≥-2.00    | ≥-2.00     | ≥-1.50     |       |
| Astigmatism        | ≥±3.00    | ≥±2.50     | ≥±2.00     |       |
| Anisometropia      |           |            |            |       |
| Myopia             | ≥-2.50    | ≥-2.50     | ≥-2.00     | ≥-1.00|
| Hyperopia          | ≥-2.50    | ≥-2.00     | ≥-1.50     | ≥-1.00|
| Astigmatism        | ≥±2.50    | ≥±2.00     | ≥±2.00     | ≥±1.00|

Recent studies have tested the use of binocular I-pad games in the treatment of amblyopia. The principle of binocular therapies was that high contrast images were presented to the amblyopic eye and low contrast images to the fellow eye to achieve binocularity. It was found that with the use of red-green glasses, when children played the ‘falling blocks’ game, improvement in visual acuity was not as good as 2 hours of patching. Also, no improvement was seen in visual acuity or stereopsis with Dig Rush iPad game at the end of 8 weeks.

Citicoline acts as a neuroprotectant in degenerative diseases as it prevents nerve cell damage and impacts the brain-remodeling activity. It also increases the level of neurotransmitters such as dopamine. For the same reason, its role has been studied in amblyopia. Some studies show improvement in visual acuity while others have found patching to be more effective. More studies need to be conducted to understand the role of citicoline in amblyopia.

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