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Review Article

Current concepts in management of amblyopia- A major review

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ABSTRACT

Amblyopia is the leading cause of preventable blindness in children and young. The prevalence of amblyopia in childhood varies between 1-5%, although these values may differ. Most of the visual impairment in amblyopia is reversible if treated early at appropriate time. Various treatment modalities in children include: refractive correction, patching, atropine penalization, binocular therapy, liquid crystal display eyeglasses and transcranial magnetic stimulation. Motive of this article is to give an emphasis on newer management strategy and newer trends in amblyopia therapy. A thorough search of literature was done in PubMed, Scopus, Embase and reference list of articles until December 15, 2020 containing "amblyopia treatment or therapy" was retrieved.

1. Introduction

Amblyopia (means Lazy eye) is defined as uniocular or binocular reduction of best corrected visual acuity caused by form vision deprivation and /or abnormal binocular interaction.[1] It is the main cause of preventable blindness in young with prevalence of approximately 1-5%.[2] The common amblyogenic risk factors include preterm babies, small for gestational age,[3–7] delay in achieving milestone,[7] history of amblyopia in first degree member,[8,9] maternal smoking, drugs and alcohol use during pregnancy. Visual loss in amblyopia is reversible if detected early and treated in time.[10] In amblyopia, there is decrease in best corrected visual acuity, contrast, vernier acuity and contour detection.

The causes of amblyopia include- Strabismus (most common), anisometropia, ametropia, sensory deprivation and organic causes.

Amblyopia is mainly categorized as follows:

1. Strabismic amblyopia- Due to poor alignment of the visual axis, eyes do not receive equal stimulation.[11]
2. Anisometropic amblyopia- Occurs due to difference in refractive error of two eyes. In hypermetropia (> 1 dioptre) and in myopia (> 2.5 dioptres).
3. Deprivation amblyopia- It occurs in condition in which light does not reach upto the retina like in ptosis, media opacities and nystagmus.
4. Mixed amblyopia- It is considered mixed when two factors causing amblyopia is present simultaneously like in microtropia and monofixation syndrome.[11,12]

Bilateral amblyopia is usually defined as when best corrected visual acuity is less than 20/50 in children of age less than 4 years, less than 20/40 in children of age 4-5 years, or less than 20/30 in children of age more than 5 years. Unilateral amblyopia is defined as a difference in best corrected visual acuity of 2 or more lines between eyes.[13]

1. Mild amblyopia is classified as best corrected visual acuity of 6/9 to 6/12.
2. Moderate amblyopia is best corrected visual acuity of 6/12 to 6/36.

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3. Severe amblyopia is best corrected visual acuity less than 6/36.

2. Recent trends in Amblyopia Treatment

The cornerstone of treatment is based on increasing stimulation of eye having less visual acuity by temporarily patching the good eye, either by using patch or atropine. It requires special effort by the child and family members. The treatment method should be tailored according to the age, degree of amblyopia and socioeconomic status of patient. The response to therapy depends upon factors such as age at which therapy was started, visual acuity at presentation, method of therapy, duration of therapy, compliance and cause of amblyopia. The critical period beyond which efficacy of amblyopia therapy reduces was considered to be seven years of age.[14]

2.1. Optical correction

Refractive error correction by spectacles prescription is the basic and foremost step in management of amblyopia no matter what the intrinsic cause. A guideline is given by the American Academy of Ophthalmology in 2018 for refractive prescription.[15] By advising the best refractive correction , a sharp image is provided to fovea which leads to gain in visual acuity. The favourable outcome of optical correction on amblyopia has been confirmed by studies. Moseley et al conducted a study in amblyopic children and found that there is significant gain in visual acuity (VA) occurs after a time of 4-24 weeks alone in response to refractive error correction.[16] Stewart et al found that optical correction alone in new cases of amblyopia resulted in gain in visual acuity after 18 weeks of treatment.[17]

The suggested time duration to achieve paramount response of optical correction is 18-22 weeks. [18] Hence, it is recommended that optical correction of refractive error in amblyopic patient should be the first and foremost line of management.

2.2. Occlusion therapy

If there is no gain in visual acuity occurs in amblyopic eye by using glasses alone, and there is a difference of 0.2 log MAR or more between each eye, patching should be started. Patching involves covering of better eye to stimulate the amblyopic eye using opaque adhesive patch which should be applied directly onto the eye under spectacles. There are different methods of patching by means of gauze piece, transpore tape, rubber patch, opaque patch under or on the glasses.

Paediatric Eye Disease Investigator Group (PEDIG) has done several multicentric studies to assess different patching methods for distinct degree of amblyopia (mild, moderate and severe) as Amblyopia Treatment Study (ATS). The effect of full time patching vs.6 hours of patching in 3-7 years of children (VA in amblyopic eye 20/100-20/400) was compared and result (VA improvement) was similar in both groups [ATS 1].[19] The effect of 6 hours patching vs. 2 hours patching in 3-7 years of children (VA in amblyopic eye 20/40 to 20/80) was compared and showed that two hours of daily patching was as effective as six hours of patching per day[ATS2a].[20] In older children (13-17 years) trial of patching should always be given, even if they have not been treated earlier.[21–23] During patching time, parents are instructed to involve child in near work or activities that requires coordination between hand and eye like sketching, playing video games, picture outlining or puzzle solving.[24]

2.3. Atropine penalization

Atropine ointment 1% produces cycloplegia in the dominant eye. It is used as an auxiliary choice to patching, particularly in case of poor compliance. Atropine ointment 1% leads to loss of accommodation by paralyzing the ciliary muscle which defocuses the non- amblyopic eye.

Foley-Nolan et al conducted a study in which he found that atropine penalization for amblyopia due to improper alignment / difference in refractive error has been as good as patching.[25]

PEDIG trials have compared the effect of patching for 6 hours per day vs. atropine drops 1% every morning in children aged 3-7 years with moderate amblyopia.[26–29] VA improvement occurs more in the patching group as compared to the atropine group after 6 months of therapy.[28] Repka MX et al conducted 2 prospective study in children with severe amblyopia. In trial 1**–**, 60 children of age 3-6 years were enrolled and in trial 2**–,** 40 children of age 7-12 years were enrolled. They found that weekend use of atropine (1%) also improve the visual acuity in children.[30]

Also daily use of atropine when compared with weekend use of atropine showed equivocal results [ATS4].

2.4. Optical penalization

It refers to the blurry of sound eye by using translucent filters, overplus glasses, tape on glasses. It is mainly given in child who has been previously managed with atropine ointment 1%, but failed to gain normal visual acuity. It has been presumed that optical penalization and atropine might have synergistic effect as a combined therapy.[31,32]

3. Medical Therapy

3.1. Levodopa

Dopamine is a chemical which is present in retina and cortex and is involved in visual system plasticity in cortex. PEDIG investigators conducted a randomized trial for treatment of amblyopia in children aged 7-12 years. They prescribed daily levodopa-carbidopa in addition to 2 hours patching per day and found that there is no improvement occurs in

best corrected visual acuity.Sofia et al reported that there is significant gain in visual acuity occurs at 1 year of follow-up; however, the dose of levodopa was thrice as compared to PEDIG study.[33]

3.2. Citicoline

It is also known as cytidine diphosphatecholine. Citicoline have a neuroprotective effect by maintaining cell membrane integrity.[34] A RCT was conducted in children between age 4-13 years and was found that the gain in visual acuity with citicoline and patching was significantly higher as compared to patching alone after one year of treatment.[35]

4. Need for Newer Treatment Modalities

Conventional treatment modalities have dominated in the field of strabismus for many years but due to many side effects of occlusion therapy and atropine, patient compliance is poor. Side effects of patching is occlusion amblyopia, cosmetic problem, psychological problems, suppression, difficulty in depth perception and ocular deviation due to fusion disruption. Atropine penalization also have side effects due to systemic absorption of drug, allergic reaction.

5. Newer Treatment for Amblyopia

Newer modalities for amblyopia management has been a topic of interest among clinicians and ophthalmologist.

Intermittent occlusion glasses liquid crystal eyeglasses has been introduced as an alternative modality for amblyopia treatment. It provides an electronic, controlled occlusion of the sound eye.[36,37]

The lenses used in glasses can be programmed to turn opaque, which work as a patch that flickers on and off in front of non-amblyopic eye. The flickering interval depends upon patient's age, level of amblyopia and duration of treatment. There have been one study which compare the effect of liquid crystal eyeglasses and patching in which they found that in children of age 3-8 years with moderate unilateral amblyopia, 4 hours per day intermittent occlusion with LCG was as effective to 2 hours patching daily after 12 weeks of treatment.[38]

6. Perceptual Learning

Perceptual learning is defined as any consistent change in the perception of a sensory task following repeated practice.[39,40] It involves administrating a single visual stimulus to each eye simultaneously. Visual task include vernier acuity, positional discrimination, contrast detection, letter identification in noise.[41]

When it is given with patching for short time result is better as compared to patching for long time with passive stimulation for improving uniocular visual acuity.[42]

7. Binocular Therapy/ Dichoptic Therapy

In binocular therapy, images are projected to each eye separately and image having reduced contrast are given to sound eye to negate suppression and allow binocular vision.[43] A PEDIG trial was conducted in 385 children having amblyopia of age between 5 to 12 years to compare the efficacy of using iPad game for a hour daily versus patching for 2 hours daily on visual acuity. At 16 weeks of treatment, visual acuity improvement occurs slightly more in patching group.[44]

8. Surgery for Refractive Errors

It is mainly performed in children having large difference in refractive errors and isometropia amblyopia.

Alio et al conducted a meta-analysis of visual outcome in anisometropic amblyopia after refractive surgery and found that a remarkable gain in best corrected visual acuity occurs in all patients and gain in acuity was better for patients undergoing surface ablation as compared to LASIK.[45]

9. Conclusion

Amblyopia is a neurodevelopmental disorder of the visual system due to abnormal visual stimulus. Screening and treatment of amblyopia should begin as early as possible. Visual loss in amblyopia may be reversed with appropriate visual stimulation. Studies have shown that older amblyopic children also respond well to treatment. Thus, trial of amblyopia therapy should always be given to older children on diagnosis. The current treatment modalities include refractive correction, patching, followed by atropine penalization. However, the amblyopia treatment still remains burdensome due to poor compliance. Recently newer treatment modalities have developed in order to improve compliance and binocular function and more and more emphasis is being given on binocular visual stimulation. It is based on visual stimulation which leads to improvement in visual acuity. Binocular amblyopia treatments, which include playing videogame and watching movie might be fascinating to children and improve their compliance to treatment.[46]

10. List of abbreviations

Best corrected visual acuity (BCVA), Visual acuity (VA), Randomized controlled trials (RCTs), Logarithm of the Minimum Angle of Resolution (log MAR), Pediatric Eye Disease Investigator Group (PEDIG), Liquid crystal glasses (LCG), Perceptual learning (PL).

11. Conflict of Interest

The authors declare that they have no conflict of interest.

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