Acta Biomedica Scientia

e - ISSN - 2348 - 2168
Print ISSN - 2348 - 215X

www.mcmed.us/journal/abs

Review Article

A REVIEW ON AMBLYOPIA AND ITS THERAPY OPTIONS

Poojitha PJ, Malathi M, Adarsh KL, Pravallika P*

Department of Pharmacology, Ratnam Institute of Pharmacy, Pidathapolur, Nellore-524346, Andhra Pradesh, India

ABSTRACT

The most effective treatment approach for a child with amblyopia relies on several factors, including the age at diagnosis, the type and onset of amblyopia, and the level of patient compliance. Deprivation amblyopia necessitates addressing the underlying cause of visual impairment, such as cataracts or ptosis, before managing the amblyopia itself, similar to other forms of this condition. Anisometropic amblyopia typically requires prioritizing the use of corrective glasses. In cases of strabismic amblyopia, it's conventionally recommended to manage the amblyopia before correcting the strabismus. While the timing of surgery for strabismus remains debatable, correcting strabismus usually has minimal impact on amblyopia. Achieving the best outcomes involves treating amblyopia before the age of 7, emphasizing the greater efficacy with earlier intervention. In specific instances of bilateral amblyopia, providing a competitive advantage to the more impaired eye over the relatively better eye is crucial. Corrective glasses may suffice when a refractive error exists, but combining them with occlusion can expedite results. Traditional occlusion of the stronger eye remains the primary therapy for amblyopia, although penalization has shown comparable effectiveness. Pharmacotherapy has demonstrated less than optimal outcomes. Modern monocular and binocular therapies, employing neural tasks and games, complement patching and are also viable for adult patients.

Keywords :- Drug Therapy, Conventional Treatments, Amblyopia, Refractive Amblyoia.

Access this article online		
Home Page: **www.mcmed.us/journal/abs**		**Quick Response code**
Received:**29.12.23**	**Revised**:23.12.23	**Accepted**:03.01.24

INTRODUCTION

Amblyopia is characterized as a disorder stemming from visual deprivation or the malfunctioning processing of visual information.[1] Von Noorden's definition outlines amblyopia as a unilateral or bilateral decrease in best-corrected visual acuity (BCVA) caused by form deprivation, abnormal binocular interaction, or both, where no organic cause can be identified through physical examination of the eye. Moreover, this condition, under appropriate circumstances, can be reversible through therapeutic interventions at the right time.[2] A widely accepted definition for statistical purposes hinges on visual acuity (VA), indicating a difference of two or more Snellen's or logarithm of the minimum angle of resolution (logMAR) lines in BCVA between the normal and amblyopic eye in the case of unilateral amblyopia. In instances of bilateral amblyopia, BCVA is generally less than 6/12. Studies report the prevalence of amblyopia to be 1–6% in children and 1.43–5.64% in adults.[3] Patients afflicted with amblyopia commonly experience a reduction in reading speed, abnormal fine motor skills, and decreased stereo acuity. [4] The failure to promptly recognize the disease and delay in its treatment contribute significantly to amblyopia being a prevalent cause of low vision, even among adults.[3].

Types of Amblyopia

Amblyopia is often classified based on visual acuity (VA) for practical and clinical purposes. Etiologically, it is categorized into strabismic, refractive, and stimulus deprivation types. Despite the loss of function in the amblyopic eye, its anatomical integrity remains intact.

Corresponding Author: **Pravallika P** Email: **paladugupravallika896@gmail.com**

Early identification and intervention, particularly in children, play a crucial role in preventing irreversible visual impairment. The philosophy advocating early treatment has prompted recommendations for screening as soon as a child is capable of undergoing a VA measurement task.[5] Consequently, screening strategies should focus on school entry rather than the currently suggested age of 3 or 4 years.[6] Physicians should be vigilant in identifying the risk of amblyopia when encountering unilateral squint or any child under 6 years old who experiences an eye injury leading to occlusion of the visual axis and potential risk of developing amblyopia

Treatmetn of Amblyopia

The primary objective of amblyopia treatment revolves around diminishing the disparity in acuity between the eyes. Consequently, most therapeutic methods aim at enhancing monocular acuity. However, it's now understood that individuals with amblyopia exhibit numerous visual deficiencies beyond clinical assessment of visual acuity alone. These deficits encompass binocular and monocular impairments, higher-order perceptual issues, threshold elevation, deficits in the non-amblyopic eye, and anomalies in visuomotor control.[7] This multifaceted nature makes treating amblyopia a challenge for ophthalmologists.

Superior outcomes are attained when therapeutic interventions commence early, as success rates may decline with advancing age. Tailoring treatment is recommended based on the patient's age, visual acuity, adherence to prior treatments, and their physical, social, and psychological status.[8] The inception of the Pediatric Eye Disease Investigator Group (PEDIG) in 1997, funded by the National Eye Institute, focused on conducting clinical research on eye disorders affecting children. Their emphasis was primarily on strabismus and amblyopia, culminating in 'The Amblyopia Treatment Studies' (ATS). These studies comprised randomized clinical trials aimed at establishing optimal protocols for managing amblyopia. [9]

Refractive corrective treatment

The cornerstone of amblyopia treatment lies in addressing refraction to establish a clear foveal image in the non-dominant eye. Therefore, it is imperative to conduct thorough refraction and prescribe appropriate optical correction in all cases of amblyopia. Refraction should be carried out objectively with complete cycloplegia. In younger children, atropine ointment 1% is recommended thrice a day for 3 days before their visit. In older children (>8 years), cyclopentolate (1%, two drops at 15-minute intervals) is used, and retinoscopy is performed after 30–40 minutes of instillation. For anisometropic amblyopia, the initial step involves providing age-appropriate refractive correction. Correcting objectively determined anisometropia is crucial, as subjective responses may complicate the determination of the appropriate power. The Amblyopia Treatment Study-ATS-5 assessed the efficacy of refractive correction in moderate amblyopia, revealing that amblyopia resolved in 27%, and there was an improvement of more than two lines in 77% of patients with refractive correction alone. Glasses alone have demonstrated improvement in visual acuity up to 18 weeks after initiating spectacle use.[10] In cases of bilateral ametropic amblyopia, spectacle correction takes precedence as the primary treatment. Spectacle correction alone has been shown to enhance binocular visual acuity in bilateral refractive amblyopia, aligning with the recommendations of ATS 7. [11]

Occlusive treatment

Occlusion or patching of the stronger eye remains the established method for treating amblyopia. This approach compels the patient to utilize the amblyopic eye while curbing inhibitory impulses originating from the stronger eye. The Amblyopia Treatment Studies (ATS) aimed to address critical questions regarding the duration of patching. ATS 2A, comparing full-time patching (all waking hours) and part-time patching (6 hours/day) in severe amblyopia (20/100–20/400) among 3–7-year-old children, concluded that both regimens were equally effective. Despite these findings, many studies continue to advocate full-time patching, apprehensive of inferior visual outcomes with reduced patching hours. [12][13]

Cessation of occlusion therapy is recommended when visual acuity in both eyes equals, fixation becomes fully alternating, or no further improvement occurs despite 3–6 months of patching. Drawbacks of occlusion therapy encompass occlusion amblyopia, cosmetic concerns, allergic skin reactions, and recurrence. About one-fourth of successfully treated amblyopic patients experience recurrence within the first year of treatment. Therefore, gradual tapering of patching hours before discontinuation is advisable. Recurrence risk diminishes with increasing age.[14] Upon amblyopia recurrence during a visit, a higher level of patching is advised (two to three times), followed by a slower tapering once acuity recovers. Studies indicate that patching and atropine penalization infrequently lead to significant strabismus. A study by Repka et al. found that among 161 previously orthotropic children, 14% developed micro strabismus, while only 3% developed strabismus greater than eight prism diopters. [15]

Occlusive treatment for bilateral amblyopia

For patients lacking a standardized treatment approach and where patching outcomes are poorly defined, a recent comparative study suggests that primary

occlusion doesn't offer added benefit over using spectacles alone. This study observed that final visual acuity (VA) improvement in the stronger eye wasn't hindered by primary occlusion. The recommendation is to manage these patients solely with glasses. Patching or atropine may be considered to address any remaining interocular difference once VA reaches 20/30 or better in at least one eye [16].

Adult amblyopia

Amblyopia treatment is most effective in early childhood but remains possible at any age, albeit becoming increasingly challenging later in life. ATS 3 investigated treatment efficacy in individuals aged 7 to 17 years. Among 507 patients in this age bracket, findings revealed that for those aged 13 to 17 years, 2 to 6 hours of daily patching alongside near visual activities may show improvement if amblyopia hasn't received prior patching treatment. However, this approach yields little benefit if patching was previously utilized for amblyopia treatment [17].

Sequential method

Sequential treatment in amblyopia offers several advantages. Some children might not require patching at all. Those whose amblyopic eye's visual acuity (VA) doesn't completely resolve with spectacles alone often exhibit better VA when patching starts, potentially making subsequent patching easier for both the child and parents. This approach could enhance the overall quality of life for both parties. On the other hand, 'simultaneous' treatment might yield superior VA outcomes as it starts patching at a younger age, potentially leading to faster improvement rates. A current trial conducted by the PEDIG group aims to determine which approach—sequential or simultaneous—is more effective [18].

Penalization

Penalization in amblyopia involves optically defocusing the dominant eye, typically achieved pharmacologically using cycloplegics or optically treating the amblyopia in the non-dominant eye. Atropine, administered as a 1% drop to the healthy eye, is a commonly used penalizing agent. It blocks the parasympathetic innervations, causing pupillary dilatation and loss of accommodation.The ATS 1 trial aimed to compare occlusion and atropine penalization as initial treatments for moderate amblyopia (20/40–20/100) in 3–7-year-old children. Results showed similar improvements in amblyopia two years after either atropine or patching for six months.[19] Although improved visual acuity was sustained after the follow-up, residual amblyopia remained common [20]. Patching may lead to more rapid VA improvement and potentially slightly better acuity outcomes, while atropine offers easier administration and lower cost [21]. Limitations of the ATS include strict inclusion criteria limiting patient numbers and potential ethnic variations affecting generalizability. Studies comparing different forms of atropine penalization in strabismic amblyopia concluded that various forms reduced amblyopia and improved binocularity [22]. Optical penalization using plus correction in the sound eye for distance has emerged as an alternative to occlusion [23]. Recent studies suggest that atropine may be more effective than optical penalization for treating moderate amblyopia [24].

Pharmacotherapy

The exploration of pharmacological interventions in amblyopia treatment has been extensive due to limitations in conventional methods and the impact of residual amblyopia. Over the past century, various drugs, including strychnine, oxygen, alcohol, and propranolol, were experimented with. Additionally, targeted therapies like bicuculline and exogenous nerve growth factor were explored, but none yielded significant or long-lasting effects.

Levodopa

Different studies exploring levodopa in amblyopia treatment varied in dosage and duration. Some used higher doses (61–132 mg/kg/day) for shorter periods, while others opted for lower doses (1.5 mg/kg/day) over an extended duration. A pilot study comparing two doses alongside daily patching showed a slight visual acuity improvement in both groups, with fewer adverse effects noted in the lower dose group [25][26]. Studies examining lower doses of levodopa/carbidopa (average 0.48 to 0.12 mg/kg) found efficacy with fewer side effects, especially in younger children [27]. While various studies showed visual acuity improvement, some observed regression post-treatment cessation[28]. A larger trial by PEDIG with 7 to 12-year-old children found no significant vision improvement with levodopa, a conclusion supported by other studies [29][30]. Side effects are common, and a high-protein diet is recommended to mitigate them.

Citicoline

Citicoline has shown promise in amblyopia treatment. Campos reported significant visual acuity (VA) improvement in both amblyopic and sound eyes in older children, sustained for at least four months post-treatment [31]. Another study in young adults observed improved VA, contrast sensitivity, and visual evoked potential, albeit with a small sample size (10 patients). The drug's oral form, with similar bioavailability to the injectable form, is now more commonly used for convenience. Studies administering oral citicoline (500 mg daily for 12 weeks) in myopic amblyopia patients

aged 5–30 years reported VA and refractive status improvements. Combined with patching, citicoline yielded significantly better VA improvements compared to patching alone, findings reiterated in studies involving both younger and older subjects [32].

SSRIs

Fluoxetine, an antidepressant affecting serotonin and noradrenaline, has garnered interest in amblyopia treatment due to its effects on ocular dominance plasticity and visual function in adult amblyopic animals. However, human studies have shown mixed results. A phase 2 multicenter trial comparing fluoxetine with a placebo exhibited no additional benefit of the drug. In contrast, another study reported a greater visual acuity improvement in the fluoxetine group [33].

Donepezil

Donepezil, a reversible cholinesterase inhibitor, has been explored for amblyopia treatment. While human studies demonstrated its ability to enhance perceptual learning in healthy individuals with lasting effects, a pilot study involving nine amblyopic patients found no improvement or acceleration of perceptual learning in adults with amblyopia. In fact, it was observed that donepezil might hinder learning and transfer associated with a crowding task [34].

Binocular simulation and games

The shift in amblyopia research towards addressing binocular visual function rather than relying solely on monocular interventions marks a significant advancement. Therapies now focus on promoting binocular vision and reducing inhibitory interactions in the visual cortex. These approaches involve both monocular and binocular stimulation, emphasizing repetitive practice-based learning as a highly effective method for improving acuity and contrast detection. Studies utilizing grating patterns, particularly frequencies near the cutoff frequency, have shown improvements in contrast sensitivity. Perceptual learning, demonstrated to enhance visual acuity even in adult amblyopes, highlights the potential for significant advancements in treating amblyopia [35].

Alternative therapy options

In a retrospective study by Park et al. from 2008, near-visual activities during part-time patching (6 hours) for treating amblyopia in children (average age 4.86 years) were explored. The study included activities like active physical games, counting at a distance, outdoor games, and watching television at a 6-meter distance. Surprisingly, at the 8-week mark, the researchers observed no difference in visual acuity improvement between children engaged in common near activities and those involved in distance activities during amblyopia patching treatment. This finding contrasted with the results of earlier studies, including a randomized pilot study and various case series, which had suggested positive effects of near activities or those involving eye-hand coordination in amblyopia treatment [36][37].

CONCLUSION

The principle to successful amblyopia treatment indeed lie in early detection and intervention, ensuring optimal refractive correction, and maintaining strict treatment compliance. Recurrence risk remains a concern post-treatment cessation, necessitating careful and extended follow-up during the critical amblyogenic years to prevent any relapse. Generally, treating amblyopia at a younger age significantly enhances the chances of improvement. For children under 7 years old, occlusion of the better eye remains the gold standard treatment. However, in cases of recurrent or residual amblyopia in older children.

REFERENCES

1. Holmes JM, (2006). Clarke MP. *Amblyopia. Lancet* 367, 1343-51
2. Von Noorden GK, Campos E. Binocular Vision and Ocular Motility. 6th ed. *St Louis, MO: Mosby*;2002
3. Meng Z, Fu J, Chen W, Li L, Su H, Dai W, Yao Y. (2021). Prevalence of amblyopia and associated risk factors in Tibetan grade one children. *Ophthalmic Res*, 64, 280-9
4. Stifter E, Burggasser G, Hirmann E, Thaler A, Radner W. (2005). Monocular and binocular reading performance in children with microstrabismic amblyopia. *Br J Ophthalmol*, 89, 1324-9
5. Williams C, Harrad RA, Harvey I, (2001). Sparrow JM ALSPAC study team. Screening for amblyopia in preschool children: Results of a population-based randomized controlled trial. *Ophthalmic Epidemiol* 8, 279-95
6. Hartmann EE, Dobson V, Hailine L, Marsh-Tootle W, Quinn GE, Ruttum MS, (2000). Preschool vision screening: Summary of a task force report. *Pediatrics* 106, 1105-16
7. Kiorpes L, Daw N. (2018). Cortical correlates of amblyopia. *Vis Neurosci* 35, E016.
8. Woodruff G, Hiscox F, Thompson JR, Smith LK. (1994). Factors affecting the outcome of children treated for amblyopia. *Eye*, 8, 627-31
9. Chen AM, Cotter SA. (2016). The amblyopia treatment studies: Implications for clinical practice. *Adv Ophthalmol Optom* 1, 287-305

10. Mitchell DE, Gingras G. (1998). Visual recovery after monocular deprivation is driven by absolute, rather than relative, visually evoked activity levels. *Curr Biol*, 8, 1179-82
11. Wallace DK, Chandler DL, Beck RW, Arnold RW, Bacal DA, Birch EE, (2007). Treatment of bilateral refractive amblyopia in children three to less than 10 years of age. *Am J Ophthalmol*, 144, 487-96
12. Holmes JM, Kraker RT, Beck RW, Birch EE, Cotter SA, Everett DF, (2003). A randomized trial of patching regimens for treatment of severe amblyopia in children. *Ophthalmology*,110, 2075-87
13. Cleary M. (2000). Efficacy of occlusion for strabismic amblyopia: Can an optimal duration be defined?. *Br J Ophthalmol* 84, 572-8
14. Hazell CD. (1995). Evaluation of the Cardiff acuity test in uniocular amblyopia. *Br Orthopt J* 52, 8-15
15. Holmes JM, Beck RW, Kraker RT, Astle WF, Birch EE, Cole SR, Cotter SA, Donahue S, Everett DF, Hertle RW, Keech RV, Paysse E, Quinn GF, Repka MX, Scheiman MM; (2004). Pediatric Eye Disease Investigator Group Risk of amblyopia recurrence after cessation of treatment. *J AAPOS* 10 8 5, 420-8
16. Shoshany TN, Michalak S, Staffa SJ, Chinn RN, Bishop K, Hunter DG. (2020). Effect of primary occlusion therapy in asymmetric, bilateral amblyopia. *Am J Ophthalmol*, 211, 87-93
17. Scheiman MM, Hertle RW, Beck RW, Edwards AR, Birch E, Cotter SA, (2005). Pediatric eye disease investigator group. Randomised trial of treatment of amblyopia in children aged 7 to 17 years. *Arch Ophhalmol*, 123, 437-47
18. Pediatric Eye Disease Investigator Group. A Randomized Trial to Evaluate Sequential vs Simultaneous Patching (ATS22) NCT0437 8790 May 7. 2020
19. Pediatric Eye Disease Investigator Group. (2002). A randomized trial of atropine vs. patching for treatment of moderate amblyopia in children. *Arch Ophthalmol* 120, 268-78
20. Repka MX, Wallace DK, Beck RW, Kraker RT, Birch EE, Cotter SA, (2005). Two-year follow-up of a 6-month randomized trial of atropine vs patching for treatment of moderate amblyopia in children. *Arch Ophthalmol*, 123, 149-57
21. Lambert P. (2008). Band-AIDS and amblyopia. *Arch Ophthalmol*, 126, 145
22. Simons K, Stein L, Sener EC, Vitale S, Guyton DL. (1997). Full-time atropine, intermittent atropine, and optical penalization and binocular outcome in treatment of strabismic amblyopia. *Ophthalmology* 104, 2143-55
23. Repka MX, Cotter SA, Beck RW, Kraker RT, Birch EE, Everett DF, (2004). A randomized trial of atropine regimens for treatment of moderate amblyopia in children. *Ophthalmology* 111, 2076-85
24. Tejeder J, O'galler C. (2008). Comparative efficacy of penalization methods in mild to moderate amblyopia. *Am J Ophthalmol* 145, 562-9
25. Mohan K, Dhankar V, Sharma A. (2001). Visual acuities after levodopa administration in amblyopia. *J Pediatr Opthalmol Strabismus*, 38, 62-7
26. Leguire LE, Komaromy KL, Nairus TM, Rogers GL. (2002). Long term follow up of L-dopa treatment in children with amblyopia. *J Pediatr Ophthalmol Strabismus* 39, 326-30
27. Dadeya S, Vats P, Malikk PS. (2009). Levodopa carbidopa in the treatment of amblyopia. *J Pediatr Ophthalmol Strabismus* 46, 87-90
28. Repka MX, Kraker RT, Beck RW, Atkinson CS, Bacal DA, Bremer DL, (2010). Pediatric Eye Disease Investigator Group. Pilot study of levodopa dose as treatment for residual amblyopia in children aged 8 years to younger than 18 years. *Arch Ophthalmol* 128, 1215-7
29. Pediatric Eye Disease Investigator Group Repka MX, Kraker RT, Dean TW, Beck RW, Siatkowski RM, (2015). A randomized trial of levodopa as treatment for residual amblyopia in older children. *Ophthalmology* 122, 874-81
30. Bhartiya P, Sharma P, Biswas NR, Tandon R, Khokhar SK. (2002). Levodopa-carbidopa with occlusion in older children with amblyopia. *J AAPOS*. 6, 368-72
31. Campos EC, Schiavi C, Benedetti P, Bolzani R, Porciatti V. (1995). Effect of citicoline on visual acuity in amblyopia: Preliminary results. *Graefes Arch Clin Exp Ophthalmol*. 233, 307-12
32. Pawar PV, Mumbare SS, Patil MS, Ramakrishnan S. (2014). Effectiveness of the addition of citicoline to patching in the treatment of amblyopia around visual maturity. *Indian J Ophthalmol.*, 62, 124-9
33. Sharif MH, Talebnejad MR, Rastegar K, Khalili MR, Nowroozzadeh MH. (2019). Oral fluoxetine in the management of amblyopic patients aged between 10 and 40 years old: A randomized clinical trial. *Eye (Lond)* 33, 1060-7
34. Chung STL, Li RW, Silver MA, Levi DM. (2017). Donepezil does not enhance perceptual learning in adults with amblyopia: A pilot study. *Front Neurosci* 11, 448.
35. Saladin JJ, Bohman CE. Anaglyphic T. V. (1977). ping pong antisuppression trainer. *J Am Optom Assoc* 48, 929-32
36. Park KS, Chang YH, Na KD, Hong S, Han SH. (2008). Outcomes of 6 hour part-time occlusion treatment combined with near activities for unilateral amblyopia. *Korean J Ophthalmol*, 22, 26-31
37. Kay H. (1983). New method of assessing visual acuity with pictures. *Br J Ophthalmol* 67, 131-3

Cite this article:
Poojitha PJ, Malathi M, Adarsh KL, Pravallika P. (2024). A Review on Amblyopia and Its Therapy Options. *ActaBiomedica Scientia*, 11(1), 1-6