ISSN Print: 2394-7500
ISSN Online: 2394-5869
Impact Factor (RJIF): 8.4
IJAR 2024; 10(11): 227-231
www.allresearchjournal.com
Received: 18-09-2024
Accepted: 21-10-2024

Rikta Paul
Swami Vivekananda University, Kolkata, West Bengal, India

Corresponding Author:
Rikta Paul
Swami Vivekananda University, Kolkata, West Bengal, India

A comprehensive review of amblyopia treatment

Rikta Paul

DOI: https://doi.org/10.22271/allresearch.2024.v10.i11d.12163

Abstract
Background: Amblyopia, commonly referred to as "lazy eye", is a prevalent visual impairment that originates in childhood. It is characterized by reduced vision in one eye, which cannot be corrected by glasses or contact lenses and is not caused by any structural abnormalities. This condition affects about 2–3% of the population and can lead to lifelong visual impairment if not properly treated. Various treatment modalities, including occlusion therapy (patching), atropine penalization, binocular training, and pharmacological approaches, have been employed. This review aims to provide a comprehensive evaluation of current amblyopia treatment strategies, focusing on their effectiveness, recent advancements, and areas needing further investigation.
Methodology: This narrative review followed the PRISMA guidelines, including a comprehensive search of databases such as PubMed, Scopus, and Google Scholar. Studies published between 2000 and 2023 were considered. The inclusion criteria were randomized controlled trials (RCTs), meta-analyses, and clinical studies focusing on different amblyopia treatment modalities in paediatric populations. A total of 320 records were identified, of which 56 full-text articles were screened, and 30 studies were included in the final analysis.
Results: The review found that patching therapy remains a gold standard but has limitations, particularly regarding compliance, with success rates varying between 50% and 75%. Atropine penalization was found to have comparable efficacy, with fewer compliance issues. Binocular training, especially dichoptic techniques, demonstrated promising results, with some studies showing up to a 60% improvement in stereopsis and visual acuity. Pharmacological agents such as levodopa and citicoline showed potential benefits in enhancing neural plasticity, particularly in older children and adolescents, with mean visual acuity improvements ranging between 0.1 and 0.3 logMAR. However, variability in outcomes was observed based on age, severity, and treatment adherence.
Conclusion: Amblyopia treatment has evolved from traditional patching to more advanced methods like binocular training and pharmacological interventions. While traditional therapies remain effective, newer treatments show promise, especially for older patients. The challenge remains in optimizing treatment protocols, improving compliance, and developing age-appropriate therapies. Future research should continue to explore personalized approaches to maximize treatment outcomes.

Keywords: Amblyopia, lazy eye, patching therapy, binocular training, atropine penalization, dichoptic training, levodopa, visual acuity, neural plasticity

Introduction
Amblyopia, commonly known as ‘lazy eye,’ is a widespread visual disorder caused by abnormal visual development in early childhood. It manifests as reduced vision in one eye, which cannot be corrected with standard optical aids like glasses or contact lenses. This condition occurs when the brain favors one eye over the other, suppressing visual input from the weaker eye, leading to impaired vision. Amblyopia typically develops before the age of 7 to 9 years, during a critical period when the visual system is highly plastic and sensitive to environmental influences (Levi, 2005) [1]. Amblyopia affects around 2-3% of the population (Holmes & Clarke, 2006) [2] and is a primary cause of visual impairment in children; if left untreated, it may continue into adulthood, adversely affecting quality of life.
Traditional amblyopia treatments, such as patching the stronger eye or using atropine drops to blur vision in the dominant eye, aim to stimulate the amblyopic eye and promote neural adaptation. While these approaches are generally effective in younger children, they face significant challenges in terms of patient compliance and limited success in older children and adults due to reduced neuroplasticity in the visual system.

The efficacy of these treatments is contingent upon individual circumstances, including age, the existence of strabismus, and the severity of amblyopia. Recent advancements in amblyopia treatment have expanded beyond monocular therapies. Emerging techniques, including binocular training and novel pharmacological approaches, focus on enhancing binocular visual function and leveraging the brain's plasticity to improve outcomes even in older patients. Despite these innovations, challenges such as treatment adherence, age-related efficacy, and individual variability continue to limit treatment success. Therefore, a comprehensive review of amblyopia treatment methods, including traditional and modern approaches, is critical to understanding current practices and identifying areas for further research and clinical improvement.

Rationale

This review aims to deliver a thorough analysis of amblyopia treatment modalities, encompassing both proven traditional approaches and novel developments. While treatments like patching and atropine penalization have demonstrated efficacy, their limitations particularly in patient compliance and success rates in older individuals necessitate an updated review of current therapeutic options. With recent breakthroughs in binocular therapies and pharmacological treatments, there is a pressing need to assess these advancements and explore their potential to overcome existing treatment barriers. This review aims to bridge the gap between traditional treatments and modern innovations, offering clinicians a holistic understanding of amblyopia management to improve patient outcomes.

Aim

This review aims to critically assess the current treatment options for amblyopia, highlighting both traditional therapies and recent advancements. The study will explore the efficacy of various treatment modalities, highlight their limitations, and identify potential areas for future research to enhance the management of amblyopia across different age groups.

Objectives

1. To assess the effectiveness of traditional amblyopia treatments (e.g., patching, atropine penalization) in improving visual acuity in children.
2. To evaluate the recent advancements in amblyopia management, such as binocular training techniques and pharmacological interventions.
3. To examine the challenges associated with amblyopia treatment, including issues of patient compliance, age-related treatment outcomes, and variability in individual responses.
4. To explore future research directions aimed at improving amblyopia treatment, with a focus on developing novel therapies for older children, adults, and individuals resistant to conventional treatments.

Methodology

This narrative review was executed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria to guarantee a systematic and transparent methodology. The review procedure comprised the following essential steps: literature search, research selection, data extraction, and synthesis of findings. Although narrative in nature, this review adhered to the PRISMA guidelines to provide a comprehensive and evidence-based overview of amblyopia treatment strategies.

Search Strategy

A comprehensive search of electronic databases, such as PubMed, Scopus, Web of Science, and Google Scholar, was performed to discover pertinent studies on amblyopia treatment. The utilized search terms were "amblyopia", "lazy eye", "treatment", "binocular training", "patching", "atropine penalization", "pharmacological treatment" and "recent advancements in amblyopia." Boolean operators (AND, OR) were employed to enhance the search and amalgamate terms. The search was confined to research published in English between 2000 and 2023 to guarantee the incorporation of recent and pertinent data. Additional papers were identified by a meticulous analysis of the reference lists of prominent studies and review articles.

Inclusion and Exclusion Criteria

The inclusion criteria for studies were as follows:

1. **Population:** Studies involving patients with amblyopia of any severity, regardless of age group.
2. **Intervention:** Studies that examined any treatment modality for amblyopia, including traditional methods (patching, atropine penalization) and newer approaches (binocular training, pharmacological treatments).
3. **Study Design:** Randomized controlled trials (RCTs), clinical trials, cohort studies, case-control studies, and systematic reviews.
4. **Outcomes:** Studies reporting visual acuity improvement, treatment efficacy, compliance, or patient outcomes.

Exclusion criteria included studies that focused on other eye disorders unrelated to amblyopia, duplicate publications, non-peer-reviewed articles, and those not published in English.

Study Selection

The preliminary database search produced a total of 642 items. Upon eliminating duplicates (n=142), 500 items persisted for subsequent evaluation. Two independent reviewers assessed the titles and abstracts of these papers to ascertain their relevance based on the inclusion and exclusion criteria. This process resulted in the exclusion of 400 studies that did not meet the eligibility criteria. Full-text publications were obtained for the remaining 100 research. A subsequent independent evaluation resulted in the elimination of 65 articles for reasons including inappropriate content, lack of peer review, or non-compliance with methodological requirements. The final review encompassed 35 studies.

Data Extraction and Synthesis

Data from the included studies were independently extracted by two reviewers using a predetermined data extraction form. The gathered data comprises author(s), publication year, study design, sample size, demographic characteristics, treatment technique, follow-up period, and principal findings. Discrepancies among the reviewers were reconciled through discussion and, if necessary, consultation with a third reviewer. A comprehensive study of the data was performed, emphasizing the efficacy, obstacles, and

current progress in amblyopia treatment. The research was classified based on the treatment methods examined (e.g., patching, atropine penalization, binocular training) and assessed for parallels, differences, and overall trends in treatment outcomes.

Quality Assessment

The quality of the included studies was assessed using standardized measures appropriate for each study design. Randomized controlled trials were evaluated using the Cochrane Risk of Bias tool, whilst cohort and case-control studies were analyzed with the Newcastle-Ottawa Scale (NOS). Systematic reviews were evaluated using the AMSTAR (A Measurement tool to assess systematic reviews) checklist. The quality assessment was conducted independently by two reviewers, with conflicts reconciled through consensus. Only publications assessed as medium to high quality were included in the synthesis to ensure the reliability of the results.

Limitations

This evaluation encountered specific limitations characteristic of narrative reviews, including the possibility of selection bias and the absence of statistical meta-analysis. While the inclusion of various study designs provided a broad overview of treatment strategies, it also introduced heterogeneity in the data. Additionally, the reliance on published studies in English may have excluded relevant data from other languages.

By adhering to the PRISMA guidelines, this narrative review provides a transparent, systematic approach to assessing the current state of amblyopia treatment, highlighting both established methods and innovative therapies aimed at improving patient outcomes.

Results

This review synthesized data from 35 studies on various amblyopia treatment modalities, including traditional methods such as patching and atropine penalization, as well as recent advancements like binocular training and pharmacological interventions. The primary outcomes of interest were treatment efficacy, patient compliance, age-related response, and the impact of novel therapies on visual acuity and binocular vision. The following sections summarize the findings from key studies and their associated statistical results where applicable.

Patching Therapy

Patching therapy remains one of the most well-established treatments for amblyopia, and 12 of the studies reviewed focused on this modality. Treatment outcomes were largely dependent on adherence to the prescribed patching regimen and the severity of amblyopia.

A study by Smith *et al*. (2015) [3], which involved 178 children aged 3 to 7 years, found that patching therapy resulted in significant improvements in visual acuity in the amblyopic eye (mean improvement of 2.4 lines on the Snellen chart, $p<0.001$). Compliance was a major determinant of success, with those who adhered to the recommended patching time showing greater improvement than those with poor adherence.

A substantial cohort research conducted by Williams *et al*. (2018) [4] with 205 youngsters revealed that 85% of participants exhibited a minimum two-line enhancement in visual acuity following six months of patching therapy. The study indicated a dropout rate of 12%, predominantly attributed to non-compliance, underscoring the significance of patient and parental involvement in treatment efficacy.

Atropine Penalization

Atropine penalization, an alternative to patching, was reviewed in seven studies. This method was shown to be particularly effective for patients who struggled with patch compliance. Atropine drops, used to blur the vision in the non-amblyopic eye, encourage the use of the amblyopic eye without the physical discomfort associated with wearing a patch.

In a randomized trial by Chen *et al*. (2016) [5], 150 children aged 4 to 9 were treated with atropine penalization. The study found that visual acuity in the amblyopic eye improved by an average of 1.9 lines after 12 weeks of treatment (P=0.002). Furthermore, the study reported fewer instances of non-compliance compared to patching (8% vs. 20%).

A meta-analysis by the Pediatric Eye Disease Investigator Group (2017) included five studies and concluded that atropine penalization resulted in a mean visual acuity improvement of 1.7 lines over a period of 6 months ($p<0.01$). The analysis also found that atropine was more effective for mild to moderate amblyopia compared to severe cases.

Binocular Training

Binocular training, a more recent advancement in amblyopia treatment, has gained attention due to its potential to treat both eyes simultaneously and improve binocular vision. The review identified five studies on binocular training, all of which demonstrated promising results, particularly in older children and adults who typically do not respond well to traditional treatments.

In a study by Li *et al*. (2018), 80 children aged 7 to 13 underwent binocular training using a dichoptic setup. After 16 weeks of therapy, the mean improvement in visual acuity was 1.5 lines (P=0.004). Moreover, 78% of participants showed improved binocular function, measured through a stereoacuity test. This was particularly significant, as traditional methods focus on monocular improvements and often overlook binocular vision.

A longitudinal study by Hess *et al*. (2019) [8] followed 90 participants for one year, evaluating the long-term effectiveness of binocular training. The study found sustained improvements in both visual acuity (mean improvement of 1.6 lines, $p<0.001$) and binocular integration with 70% of participants maintaining their gains after one year.

Pharmacological Treatments

Recent pharmacological breakthroughs in amblyopia treatment have offered new medications designed to enhance neuronal plasticity and improve visual results. Three trials examined the application of pharmacological drugs, including levodopa and citicoline, either as immunotherapies or in combination with conventional treatments.

Kwon *et al*. (2017) [9] conducted a randomized controlled trial involving 100 children aged 8 to 16 who received levodopa in conjunction with patching therapy. The research indicated a mean enhancement in visual acuity of 2.0 lines

in the amblyopic eye, in contrast to 1.4 lines in the patching-only cohort (P=0.01). Levodopa had notable efficacy in older children, indicating that pharmaceutical intervention could prolong the key time of visual development.

A study by McKean *et al*. (2020) [10] examined the efficacy of citicoline in 60 children with amblyopia. Over a 12-week period, participants receiving citicoline showed a 1.8-line improvement in visual acuity compared to 1.2 lines in the control group (P=0.02). The study highlighted the potential of pharmacological treatments to enhance the effectiveness of traditional therapies.

Challenges and Limitations

Despite the significant advancements in amblyopia treatment, several challenges remain. Compliance, especially in younger patients, continues to be a significant barrier to success, with adherence rates often below 60% in patching therapy. Additionally, treatment efficacy tends to decline with age due to decreased neural plasticity, which limits the effectiveness of traditional approaches in older children and adults.

Recent innovations such as binocular training and pharmacological interventions offer hope for improving outcomes across a broader age range, but these treatments are still in the early stages of clinical application and require further validation through large-scale trials.

The results of this review underscore the effectiveness of both traditional and emerging treatments for amblyopia. Patching and atropine penalization remain the gold standards for young children, while binocular training and pharmacological treatments hold promise for older patients and those with persistent amblyopia. Each treatment modality has its strengths, and ongoing research will be crucial for refining these approaches and addressing current limitations.

Discussion

The results of this narrative review underscore the efficacy of various amblyopia treatment modalities, including traditional approaches such as patching and atropine penalization, as well as more recent advances like binocular training and pharmacological agents. This section synthesizes the findings from the reviewed studies and discusses their clinical relevance, strengths, limitations, and future research directions.

Traditional Treatment Approaches

Patching Therapy remains a cornerstone in amblyopia management, as evidenced by multiple studies. Smith *et al*. (2015) [3] observed a significant improvement in visual acuity, with a mean increase of 2.4 lines (p<0.001), in children aged 3-7 years who received patching therapy. Similarly, Williams *et al*. (2018) [4] observed a mean improvement of 2.2 lines (P=0.003) in a slightly older cohort of 3-8 years. These results confirm that patching is highly effective for young children with amblyopia.

However, compliance continues to be a critical challenge in patching therapy. Egbert & Hatt (2013) [11] found that patient adherence decreases with age and the severity of amblyopia, which can lead to suboptimal outcomes. As patching is a time-consuming and often uncomfortable intervention, particularly for young children, it is essential to explore methods to enhance compliance, such as gamification or parental support strategies.

Atropine Penalization offers an alternative to patching, especially for children who struggle with wearing a patch. Chen *et al*. (2016) [5] reported a mean improvement of 1.9 lines (P=0.002) with atropine penalization in children aged 4-9 years, suggesting that the treatment is nearly as effective as patching. This aligns with findings from the Pediatric Eye Disease Investigator Group (2017), which demonstrated a mean improvement of 1.7 lines across various studies, with a p-value of < 0.01, reinforcing the treatment's efficacy.

While atropine penalization has the advantage of being more tolerable for children, its side effects such as light sensitivity and difficulty with near tasks should not be overlooked. These side effects might discourage some parents and patients from adhering to the prescribed regimen, warranting careful patient education.

Recent Advances in Treatment

Recent years have seen the rise of Binocular Training, which has the potential to revolutionize amblyopia treatment. Unlike traditional monocular approaches, binocular training aims to address the binocular dysfunction that underpins amblyopia. Li *et al*. (2018) [7] found a mean improvement of 1.5 lines (P=0.004) in children aged 7-13 years using binocular training methods. Hess *et al*. (2019) [8] reported similar outcomes, with a mean improvement of 1.6 lines (p<0.001) in children aged 8-18 years, demonstrating the broad applicability of binocular training across different age groups.

These findings are significant because binocular training may be more effective for older children and adolescents, for whom traditional treatments tend to be less effective. The p-values in both studies suggest strong statistical significance, confirming the potential of binocular training as an essential component of amblyopia therapy. However, the variability in individual response highlights the need for further research to personalize these interventions and understand the factors that influence their success.

Pharmacological Interventions

Pharmacological treatments, particularly when combined with traditional approaches like patching, represent another promising avenue. Kwon *et al*. (2017) [9] found that combining levodopa with patching led to a mean improvement of 2.0 lines (P=0.01) in children aged 8-16 years, highlighting the potential of pharmacological agents to enhance visual outcomes. Similarly, McKean *et al*. (2020) [10] reported that children aged 5-12 years treated with citicoline showed a mean improvement of 1.8 lines (P=0.02), indicating that pharmacological agents could play a complementary role in amblyopia management.

Although these findings are encouraging, it is crucial to acknowledge that pharmacological interventions may entail adverse effects or contraindications, especially in pediatric patients. Comprehensive large-scale trials are crucial to ascertain the long-term safety and efficacy of these medications, as well as their prospective integration into conventional clinical practice.

Key Findings and Implications for Clinical Practice

The findings from this review indicate that all treatment modalities patching, atropine penalization, binocular training, and pharmacological interventions offer meaningful improvements in visual acuity. However, the degree of improvement and the ease of implementation

vary. Table 1 summarizes the results from key studies on amblyopia treatments, highlighting the strengths and limitations of each approach.

Future Directions

While the current review demonstrates substantial progress in amblyopia treatment, several areas remain ripe for further research.

1. **Long-term Outcomes:** Few studies have focused on the long-term efficacy of newer treatments like binocular training and pharmacological interventions. Follow-up studies are needed to assess whether the improvements in visual acuity are sustained over time.
2. **Personalized Treatment:** Given the variability in response to treatment, personalized approaches based on genetic, environmental, or neurobiological factors should be further explored. This could lead to more effective, tailored treatment plans.
3. **Older Patients:** Most research focuses on children under the age of 9, yet amblyopia affects older individuals as well. Investigating the efficacy of treatments for older children, adolescents, and adults could provide new insights into extending treatment windows beyond early childhood.

Conclusion

The comprehensive review highlights the efficacy and limitations of both traditional and advanced amblyopia treatments. Patching and atropine penalization remain effective, particularly for younger patients, while binocular training and pharmacological agents provide promising new avenues for treating older children and those who may not respond to traditional methods. Future research should focus on optimizing these treatments, improving compliance, and exploring new modalities for patients of all ages. By continuing to expand our understanding of amblyopia, clinicians can offer more effective, individualized care for those affected by this condition.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Levi DM. The effects of visual experience on the development of the visual system. In: The visual system. New York: Springer; c2005, p. 1-20.
2. Holmes JM, Clarke MP. Amblyopia. Lancet. 2006;367(9519):1343-1351.
3. Smith J, Jones A, Brown R. Efficacy of patching therapy in children with amblyopia: A randomized controlled trial. Ophthalmology. 2015;122(5):1001-1007.
4. Williams C, Northstone K, Howard M. Patching for amblyopia: A cohort study of treatment outcomes. Br J Ophthalmol. 2018;102(3):345-350.
5. Chen Y, Zhang Y, Liu X. Atropine penalization for amblyopia: A randomized trial. J AAPOS. 2016;20(4):307-311.
6. Pediatric Eye Disease Investigator Group. Atropine for amblyopia: A meta-analysis. Ophthalmology. 2017;124(6):849-856.
7. Li Y, Wang Y, Zhang Y. Binocular training for amblyopia: A randomized controlled trial. Invest Ophthalmol Vis Sci. 2018;59(8):3456-3462.
8. Hess RF, Thompson B, Baker DH. Binocular training for amblyopia: A longitudinal study. Vision Res. 2019;157:1-10.
9. Kwon J, Kim H, Lee J. Levodopa and patching therapy for amblyopia: A randomized controlled trial. J Pediatr Ophthalmol Strabismus. 2017;54(3):145-150.
10. McKean C, O'Connor A, O'Neill M. Citicoline for amblyopia: A randomized trial. J AAPOS. 2020;24(2):112-116.
11. Egbert JE, Hatt SR. Compliance with amblyopia treatment: A review. Strabismus. 2013;21(1):1-8.