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Efficacy of Amblyopic Patching Therapy in Children with Down Syndrome: A Study on Refractive Errors and Visual Acuity Outcomes

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ABSTRACT

Background: Down syndrome (DS), caused by trisomy 21, is associated with developmental delays and a high prevalence of ocular conditions, including refractive errors and amblyopia. To identify the types of refractive errors in children with Down syndrome and to assess the efficacy of amblyopic patching therapy on visual acuity outcomes. **Methods:** This prospective longitudinal study was conducted at the Strabismus Unit of Layton Rahmatulla Benevolent Trust (LRBT), Lahore, from September 2022 to May 2023. Thirty children with Down syndrome aged 8 to 18 years diagnosed with amblyopia were enrolled. The non-amblyopic eye was patched for four hours daily for three months. Visual acuity was assessed using the LogMAR chart, and refractive errors were determined through objective and subjective refraction. Data was analyzed using SPSS version 22.0. Descriptive statistics were used for demographic variables. Repeated Measures ANOVA was applied to compare baseline, one-month, and three-month follow-up measurements. A p-value of < 0.05 was considered statistically significant. **Results:** A total of thirty Down syndrome patients (mean age 14.19 ± 1.04 years; 50% male, 50% female) were enrolled. Hypermetropia was found in 66.7% (n=20) and myopia in 33.3% (n=10) of participants. Visual acuity improved significantly from a baseline mean of 0.55 ± 0.27 to 0.54 ± 0.27 at one month, and 0.41 ± 0.258 at three months ($p = 0.041$). Pairwise comparison showed maximum improvement at the three-month follow-up ($p = 0.001$). Mean glasses prescription improved from 2.13 ± 2.13 at baseline to 2.11 ± 1.40 at one month and 1.71 ± 1.32 in three months ($p = 0.047$), with a significant difference observed at the three-month mark ($p = 0.001$). These findings indicate the effectiveness of patching therapy in improving both visual acuity and refractive correction over time. Compliance was generally good across the cohort. **Conclusion:** Amblyopic patching therapy was effective in improving visual acuity in children with Down syndrome, with the greatest benefit observed after three months of consistent treatment.

Keywords: Amblyopia, Down Syndrome, Hyperopia, Keratoconus, Refractive Errors, Visual Acuity

INTRODUCTION

Down syndrome (trisomy 21) is a genetic disorder caused by the presence of an additional copy of chromosome 21, either complete or partial. This extra genetic material affects growth and development, leading to characteristic physical features, intellectual disability, and increased risk of various health conditions, including ocular abnormalities. Down syndrome is one of the most common chromosomal disorders globally, with an incidence of approximately 1 in every 319–100 live births [1, 2]. Ocular manifestations are observed in nearly 60% of individuals with Down syndrome [3, 4]. These include refractive errors, strabismus, amblyopia, nystagmus, cataracts, keratoconus, lid anomalies, and retinal vascular anomalies. Early identification and management of ocular issues are crucial, as untreated visual problems can significantly impact cognitive and motor development in these children [3, 4]. Amblyopia, commonly known as "lazy eye," is a neurodevelopmental disorder where normal visual development is disrupted, leading to reduced vision in one or both eyes [5]. It is the leading cause of monocular vision impairment in children. Amblyopia typically arises from conditions such as strabismus (misalignment of the eyes), anisometropia (unequal refractive error between the two eyes), significant uncorrected refractive errors (ametropia), or visual deprivation due to opacities like cataracts. Children with Down syndrome are at a higher risk of developing amblyopia compared to the general paediatric population, with reported prevalence rates ranging from 17% to 36% [6-8]. Strabismus, particularly esotropia (inward eye deviation), is highly prevalent in Down syndrome, affecting 18%–57% of individuals [9-11]. Strabismus accounts for more than half of amblyopia cases in this population, while anisometropia and combined mechanisms contribute to the remainder. Notably, unique facial features such as epicanthal folds may obscure or mimic strabismus, leading to underdiagnosis if careful evaluation is not performed [8-12]. Refractive errors, including hyperopia (farsightedness), myopia (near-sightedness), and astigmatism, are also common in Down syndrome which in about 80% of cases [13, 14]. Hyperopia is greater than +5.00 dioptres and is often associated with ametropic amblyopia. Although myopia is less frequently associated with amblyopia, extreme cases can impair near vision as well. Astigmatism, resulting from irregular corneal curvature, can also lead to blurred vision and amblyopia if left uncorrected [8, 15, 16]. Anisometropia, where each eye has a different refractive error, is a particularly significant risk factor for amblyopia if not promptly addressed. Early detection and management of amblyopia are critical. If left untreated, amblyopia can cause lifelong visual impairment, and individuals with Down syndrome may be particularly vulnerable due to difficulties in cooperation during vision screening and assessments. Standard amblyopia therapies include corrective glasses, patching of the stronger eye, or pharmacologic penalization with atropine drops, aiming to encourage use of the weaker eye and stimulate normal visual development [17, 18]. Given the multisystemic involvement and cognitive challenges in children with Down syndrome, understanding the burden of amblyopia and its management is essential. Early intervention can significantly improve visual outcomes, enhance overall development, and reduce the risk of permanent visual disability in this high-risk population. Among these, occlusion therapy, or amblyopic patching, remains a cornerstone of treatment, especially in paediatric populations. However, the efficacy, challenges, and outcomes of patching therapy in children with Down syndrome have not been extensively studied. Given the unique cognitive and behavioural characteristics of this population, adherence to therapy and visual outcomes may differ from the general paediatric population. Therefore, evaluating the impact of amblyopic patching therapy in children with Down syndrome is essential to optimize visual rehabilitation strategies and improve their overall quality of life.

MATERIALS AND METHODS

A prospective longitudinal study was conducted at the strabismus unit of the Ophthalmology Department, Layton Rahmatullah Benevolent Trust (LRBT) Hospital, Lahore, from September 2022 to May 2023. Thirty participants with Down syndrome, aged 8 to 18 years and of both genders, were enrolled using a convenient random sampling technique. Exclusion criteria encompassed motor disability, neurodevelopmental disorders, systemic diseases, congenital glaucoma, retinitis pigmentosa, prior surgeries, or adverse skin reactions to patch adhesives. Ethical approval was obtained before the study, and informed consent was secured from all participants or their guardians, adhering strictly to the principles of the Declaration of Helsinki. Updated spectacles were prescribed based on cycloplegic refraction findings, with participants instructed to wear them full-time. Following Paediatric Eye Disease Investigator Group (PEDIG) protocols, six weeks of full-time optical correction (refractive adaptation) were implemented to allow for potential visual improvement with spectacles alone before initiating patching therapy. Amblyopia was defined as a

three-to-five-line difference in LogMAR acuity between eyes. Patching therapy was prescribed for the non-amblyopic eye at a regimen of four hours daily, which included two hours dedicated to near-vision activities (e.g., crafts, colouring, tracing, reading).

DATA COLLECTION PROCEDURE

Data collection began with obtaining a detailed patient history for each participant. Initial assessments included visual acuity measurement using the LogMAR chart (recorded for baseline comparison at follow-ups) and fundus examination performed with a direct ophthalmoscope. Cycloplegic refraction was then conducted to eliminate accommodation and determine accurate refractive error: cycloplegia was induced using 1% cyclopentolate drops instilled twice, ten minutes apart, followed by objective refraction performed 30 minutes later using an autorefractometer. Subjective refraction and a post-mydriatic test were subsequently performed to determine the best-corrected visual acuity (BCVA). After the six-week refractive adaptation period of full-time spectacle wear, patching therapy (4 hours daily, including 2 hours of near activities) was initiated for eligible participants. Patients were followed for a total of 12 weeks after starting patching therapy. At each follow-up visit, visual acuity was reassessed using the LogMAR chart, compliance with the patching regimen was recorded, and any improvements in visual function were documented.

STATISTICAL ANALYSIS

All statistical analyses were performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics, including frequencies, percentages, mean values, and standard deviations, were calculated for demographic and baseline clinical variables. Visual acuity outcomes were analysed at baseline and follow-up intervals to evaluate the effect of patching therapy. To compare changes in best-corrected visual acuity (BCVA) over time within the same individuals, the Repeated Measures Analysis of Variance (RMANOVA) test was used. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 30 participants with Down syndrome, aged between 8 to 18 years, were included in the study. The mean age of the participants was 14.19 ± 1.04 years. The participants were equally divided between male and female (50% each) (Table 1). In terms of refractive errors, 66.7% of participants (n=20) were hypermetropic, while the remaining 33.3% (n=10) were myopic (Table 1).

Table 1: Distribution of Demographic Data & Refractive Errors

Demographic Data (n=30)	
Age (years)	4.19 ± 1.04 †
Gender (M: F) ‡	(15: 15)
Refractive Errors (n (%)**)**	
Hypermetropia	20 (66.7)
Myopia	10 (33.3)
Total	**30 (100)**

† Data are presented as mean ± standard deviation for age.

‡ M:F represents the male-to-female ratio

The repeated measures ANOVA test was applied to analyze visual acuity at baseline, one month, and three months following amblyopic patching therapy. The mean baseline visual acuity was 0.55 ± 0.27, which improved to 0.54 ± 0.27 in one month and 0.41 ± 0.258 in three months, showing statistically significant improvement (p = 0.041) (Table 2). The repeated measures ANOVA test was also used to assess baseline and follow-up glasses prescriptions after one month and three months of amblyopic patching therapy. Significant improvement was observed in glasses prescriptions, with the mean baseline prescription of 2.13 ± 2.13 improving to 2.11 ± 1.40 at one month and 1.71 ± 1.32 at three months (p = 0.047) (Table 2).

Table 2: Assessment of Visual Acuity and Prescription of Glasses Across Follow-ups

Visual Acuity	Mean ± SD	p-value
Baseline Visual Acuity	0.55 ± 0.27	0.041
First follow-up after 1 month	0.54 ± 0.273	
Second follow-up after 3 months	0.41 ± 0.258	
Prescription of Glasses		
Baseline Prescription	2.1333 ± 2.1333	0.047
First follow-up Prescription	2.1167 ± 1.40463	
Second follow-up Prescription	1.7167 ± 1.32407	

Post-hoc pairwise comparison of visual acuity between baseline and follow-up visits indicated significant improvement at the three-month follow-up (p = 0.001), with maximum improvement observed at the three-month mark (Table 3).

Table 3: Post-Hoc Pairwise Comparison of Visual Acuity on Repeated Follow-Ups

Time Comparison	Mean Difference	Std. Error	95% Confidence Interval for Difference	Post-hoc p-value	Greenhouse-Geisser adjusted p-value
Baseline vs 1 Month	.010	.006	-.004 to .024	.249	0.001
Baseline vs 3 Months	.142	.036	.049 to .234	.002	
1 Month vs Baseline	-.010	.006	-.024 to .004	.249	
1 Month vs 3 Months	.132	.034	.044 to .219	.002	
3 Months vs Baseline	-.142	.036	-.234 to -.049	.002	
3 Months vs 1 Month	-.132	.034	-.219 to -.044	.002	

Pairwise comparison between baseline and follow-ups demonstrated statistically significant improvements in glasses prescriptions at the three-month follow-up (p = 0.001), indicating a significant effect of patching therapy with maximum improvement recorded at the three-month mark (Table 4).

Table 4: Pairwise Comparison of Glasses Prescription

Time	Follow-up	Mean Difference	Std. Error	95% Confidence Interval for Difference	Post-hoc p-value	Greenhouse-Geisser adjusted p-value
1	2	.017	.012	-.013 to .046	.482	0.001
	3	.417	.042	.310 to .524	.000	
2	1	-.017	.012	-.046 to .013	.482	
	3	.400	.039	.301 to .499	.000	
3	1	-.417	.042	-.524 to -.310	.000	
	2	-.400	.039	-.499 to -.301	.000	

The current study demonstrated that amblyopic patching therapy significantly improved visual acuity and glasses prescription, with maximum improvement observed at the three-month follow-up.

DISCUSSION

This study assessed the effect of amblyopic patching therapy on visual acuity and glasses prescription in children with Down syndrome, demonstrating significant improvements over three months. The findings reveal that amblyopic patching not only enhances visual acuity but also reduces the strength of glasses prescription, with maximum improvements observed at the three-month follow-up. One possible mechanism behind the observed improvements is neuroplasticity in children, particularly those who undergo consistent visual therapy at a younger age. Neuroplasticity could enhance cortical responsiveness to visual input, even when intellectual disabilities are present, thereby enabling gradual correction through interventions like patching. While studies on amblyopic therapy's effectiveness in children with Down syndrome are limited, our findings support the growing body of evidence suggesting that targeted visual therapies can lead to clinically meaningful improvements.

Our findings show both similarities and contrasts with previous research examining refractive errors and strabismus in children with Down syndrome. In a longitudinal study of 55 children with Down syndrome, refractive errors were noted, though many children initially emmetropic experienced refractive errors developing over time, while those with early refractive errors often did not achieve emmetropization. This study identified a high strabismus prevalence of 29%, independent of hypermetropia or anisometropia, suggesting that Down syndrome itself may predispose these children to strabismus regardless of refractive status.[22] In our study, we found similar trends in the persistence of refractive errors and prevalence of amblyopia, highlighting the importance of early detection and intervention to manage these conditions. However, our data shows a significant improvement in visual acuity following amblyopic patching therapy over a shorter period, suggesting that even brief, targeted treatments can yield positive outcomes. These comparative findings reinforce the need for consistent vision screening in children with Down syndrome and may guide tailored treatment approaches to address the unique visual development challenges faced by this population.

Our findings aligned with previous research indicate a higher prevalence of refractive errors in patients with Down syndrome (DS). In comparison, a study showed significantly greater mean spherical equivalent (SE) values in both myopic and hyperopic DS patients relative to controls, along with a higher prevalence of oblique astigmatism in DS (20.4% vs. 6.1% in controls). This aligns with our findings, reinforcing evidence that emmetropization in DS is impaired or delayed, leading to sustained refractive errors throughout development [19, 20]. Our study's findings regarding refractive errors in Down syndrome (DS) are consistent with those reported in previous studies. For instance, a Hong Kong-based study of Chinese children with DS revealed a high prevalence of refractive errors, with 58% of participants affected, and this prevalence increased with age, particularly as children reached school age. This pattern aligns with our observation of prevalent and persistent refractive errors in DS patients, further supporting the need for regular visual assessments in this population to monitor and manage refractive issues effectively over time [20]

In examining the impact of amblyopia therapy, both our study and the study conducted on the health-related quality of life during occlusion therapy highlight critical aspects of treatment outcomes. While our study found a statistically significant improvement in visual acuity over three months of patching therapy (mean visual acuity improvement from 0.55 ± 0.27 at baseline to 0.41 ± 0.258, $p = 0.041$), the other study provides insights into the perceived quality of life during similar treatment. Notably, their findings suggest that children experience less distress than anticipated by their parents, especially concerning activities like games and watching TV, with quality-of-life scores correlating negatively with the angle of strabismus in children over five years old. This aligns with our results, as visual acuity improvements likely contributed positively to children's engagement and comfort during daily activities, supporting the benefits of occlusion therapy in both functional and psychological dimensions. Furthermore, while our study focused on quantitative measures of visual improvement, their qualitative insights emphasize that children with milder visual impairment (visual acuity ≥ 0.6 logMAR) reported minimal difficulties, aligning with our findings of progressive improvement in visual function over the treatment period [16, 21].

In comparison to other studies, our findings are consistent with previous research highlighting the effectiveness of occlusion therapy in improving visual acuity in amblyopia. For instance, Singh et al. observed a 96% improvement rate in children with

amblyopia after six months of part-time occlusion therapy, with strabismic amblyopia showing a better response. Similarly, our study demonstrated significant improvement in visual acuity at the three-month follow-up ($p < 0.001$), with the maximum improvement occurring at this time point. Both studies underscore the importance of early and consistent therapy, although our shorter follow-up period (three months) also yielded comparable improvements, aligning with the positive outcomes reported in longer studies [22, 23].

A study was conducted in 2002 on the usage of patching therapy to treat amblyopia. The Amblyopia Treatment Study 1 group included 419 children with mild amblyopia, aged six to seven, with mixed amblyopia, or strabismic, anisometropic, and visual acuity in the amblyopic eye ranging from 6/12 to 6/30. The mean age was 5.3 years. In 38%, 37%, and 24% of cases, anisometropia, strabismus, or both were to blame [24]. Amblyopic eyes had a mean acuity of 0.53 logMAR. Initially, 43% of patients randomly assigned to patching had 6 hours of occlusion each day, whereas 17% received full-time occlusion. The degree of blindness remained constant, independent of the origin of the amblyopia. People with strabismus had considerably lower visual acuity in their healthy eyes than individuals with anisometropia (P=0.001). The patching therapy techniques used were extremely diverse [25].

LIMITATIONS AND RECOMMENDATIONS

This study's limitations include its modest sample size (n=30) and use of convenient random sampling at a single canter, restricting generalizability. The 12-week follow-up period post-patching may be insufficient to evaluate long-term efficacy and regression risks. Exclusion of common Down syndrome comorbidities (e.g., neurodevelopmental disorders) limits applicability to real-world populations. Future research should prioritize multi-canter trials with larger, more diverse cohorts and longitudinal designs (≥6 months) to assess the sustainability of visual gains. Incorporating objective compliance monitoring (e.g., electronic timers) and comparing alternative patching regimens (e.g., varying durations, binocular therapies) would strengthen evidence. Expanding age ranges to include younger children and exploring genetic subtypes of Down syndrome could provide deeper insights into treatment response variability.

CONCLUSION

In conclusion, our study demonstrates that amblyopic patching therapy leads to a significant improvement in visual acuity, with the maximum improvement observed at the three-month follow-up ($p < 0.001$). The pairwise comparison of visual acuity between baseline and follow-up visits further supports the effectiveness of occlusion therapy, particularly at the three-month mark. These results align with other studies that have shown the positive impact of occlusion therapy on amblyopia, with notable improvement observed in both strabismic and anisometropic amblyopia. The findings suggest that part-time occlusion therapy is an effective modality for managing amblyopia, and a continued focus on timely intervention and consistent follow-up is critical for optimal visual outcomes. Further long-term studies are recommended to evaluate the sustained effects of therapy beyond the three months.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHORS' CONTRIBUTION

FG contributed to conceptualization, methodology, and writing (original draft); AA supervised data collection and formal analysis; AU managed resources and investigation; SU performed statistical analysis; IM curated data and visualization; SSQ assisted in validation and project administration; AY provided critical review/editing and oversight. All authors approved the final manuscript.

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