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EVALUATION OF MACULAR THICKNESS AND VISUAL ACUITY IN AMBLYOPIC PATIENTS FOLLOWING OCCLUSION THERAPY WITH AND WITHOUT CITICOLINE

Ophthalmology

Dr Trilok Meena Department of Ophthalmology, B.R.D. Medical College, Gorakhpur, U.P.

Dr. Ramyash Singh Yadav M.S., Head of Department of Ophthalmology, B.R.D. Medical College, Gorakhpur, U.P.

Dr Anoop Kumar Singh Department of Ophthalmology, B.R.D. Medical College, Gorakhpur, U.P.

ABSTRACT

The study evaluates the impact of occlusion therapy with and without Citicoline supplementation on macular thickness and visual acuity in pediatric patients with amblyopia. A prospective, observational study was conducted over 12 months with 60 children divided into two groups: occlusion therapy alone and occlusion therapy combined with citicoline. Optical coherence tomography (OCT) was used to measure macular thickness, while visual acuity improvements were assessed through follow-ups. Results indicated that the group receiving citicoline with occlusion therapy showed higher mean improvements in visual acuity and higher total mean change in macular thickness, though the differences were not statistically significant. Additionally, socioeconomic and demographic factors such as age, gender, and socioeconomic status were balanced across groups, though these may influence outcomes. While the addition of citicoline demonstrated consistent yet non-significant improvements, the findings highlight the need for further research with larger sample sizes to validate these trends. The study underscores the potential of citicoline as a complementary treatment for amblyopia, emphasizing the importance of macular thickness as a treatment efficacy metric and advocating for comprehensive follow-up regimens.

KEYWORDS

Amblyopia, Optical coherence tomography, Citicoline

INTRODUCTION

Amblyopia is a neuro- developmental visual disorder, typically causing reduction in visual acuity (VA), as well as other visual deficits such as reduced stereopsis and greater mean accommodative response errors in amblyopic eyes, compared with the fellow eye or non-amblyopic control subjects (Hernández-Andrés et al., 2024). Amblyopia, often called “lazy eye,” is a decrease in visual acuity resulting from abnormal visual development (Doshi and Rodriguez 2007). Amblyopia has a prevalence of about 2–4% in children. However, there is a great deal of evidence showing that amblyopia results in a broad range of neural, perceptual, oculomotor and clinical abnormalities (Levi, 2020). Early recognition of amblyogenic risk factors such as strabismus, refractive errors, and anatomic obstructions can facilitate early treatment and increase the chance for recovery of visual acuity (Doshi and Rodriguez 2007). Amblyopia is considered treatable up to about 8 years of age, and possibly beyond. It is usually treated with occlusion (patching) of the dominant eye, forcing the amblyopic eye to view and reversing the amblyopia because of the plasticity of the visual cortex in children. There is a strong clinical belief that patching is successful, with thousands of children treated every year in the United Kingdom (Dixon-Woods et al., 2006). Occlusion therapy with patching of the sound eye has been the conventional treatment. However, there are many studies stating the effectiveness of some pharmacological agents in the treatment of amblyopia—citicoline is one of them (Campos and Fresina 2006). Citicoline (cytidine-5-diphosphocholine) activates the biosynthesis of structural phospholipids in the neuronal cell membranes, which results in increased levels of neurotransmitters, and thus, has neuroprotective effects (Pawar et al., 2014). Based on principles of geometrical optics, it is expected that visual acuity would be the same at distance and near. However, reports of visual acuity of amblyopic eyes have found that visual acuity at near differs compared to visual acuity at distance.

Despite appropriate treatment for amblyopia, about 50% of children cannot achieve complete vision of 20/20. It is possible that there is subclinical pathology in the retina, especially in the macula of eyes not responding well to conventional amblyopia treatment (Liu et al., 2010). Optical coherence tomography (OCT) provides high resolution images of the retina and its layers. OCT has high repeatability and is not influenced by high refractive errors, age and sex of the subjects. Increased macular thickness and decreased foveal depression have been reported in amblyopic patients using OCT. The reason can be related to lack of ganglion cells apoptosis which normally occurs shortly after birth in healthy infants (Rajavi et al., 2014).

MATERIAL AND METHODS

Study Design: The study was prospective and observational. The study spanned 12 months from June 23 to may 24.

Study Population: A total of 60 children attending the outpatient department of the Department of Ophthalmology, B.R.D. Medical College, were included in the study.

Tests Applied: Unpaired t-test and ANOVA.

Inclusion Criteria

- Subjects were children aged between 5 and 18 years.
- Patients with amblyopia.
- Parents willing to give written and informed consent to participate in the study.
- Patients not allergic to CITICOLINE.

Exclusion Criteria

- Patients aged <5 years and >18 years.
- Parents refusing to sign consent.
- Parents refusing follow-up.
- History of ocular trauma.
- Patients with a history of ocular surgery.
- Patients with any other ocular diseases (e.g., retinopathy of prematurity, retinoblastoma).
- Previous history of amblyopia treatment.
- Patients allergic to CITICOLINE.

Data Collection

Parents of patients meeting the inclusion criteria were required to provide written and informed consent to participate in the study. After obtaining consent, data regarding the patient's profile, detailed history, and examination were collected. Patients with amblyopia were randomly divided into two groups: one treated with occlusion therapy and the other treated with both occlusion therapy and citicoline. Patients were followed up monthly for three months. Macular thickness by optical coherence tomography and visual acuity were recorded in a pre-designed proforma.

Optical Coherence Tomography (OCT)

The principle of "Michelson interferometry" or low -coherence interferometry is used in OCT.

Statistical Analysis

Collected data were analyzed using SPSS version 22 software. Appropriate statistical tests (unpaired t-test and ANOVA) were applied to evaluate the data.

Ethical Clearance

Ethical clearance was obtained from the institutional ethical committee.

Treatment Compliance

The degree to which a patient correctly follows the prescribed treatment protocol, including occlusion therapy hours and citicoline supplementation dosage. Compliance will be monitored through regular follow-up visits and patient or caregiver self-reports.

RESULTS

In this study, we assessed the comparative efficacy of two distinct therapeutic interventions within a clinical setting. The baseline characteristics compare two treatment groups. Younger children and females were more frequent in the group receiving occlusion therapy with citicoline, while older children and males were more in the occlusion-only group. Both urban and rural participants were equally distributed across groups. High socioeconomic status was more common in the occlusion-only group, while low and middle socioeconomic statuses were more in the occlusion + citicoline group. This data ensures balanced representation and highlights potential demographic differences between the groups.

Table 1: Distribution Of Amblyopia Severity Among Study Population.

Amblyopia	Severity Level	Number of Participants	Proportion
	Mild	15	25%
	Moderate	28	46.66%
	Severe	17	28.33%

The table 1 indicates the distribution of amblyopia severity among 60 participants: 25% with mild, 46.66% with moderate, and 28.33% with severe amblyopia. This outlines a descending trend in severity from mild to severe within the group.

Table 2: Comparison Of Mean Of Macular Thickness And Volume Between Treatment Groups

Thickness (µm)	Group A (Occlusion therapy)	Group B (occlusion + citicoline)	Difference	Significance
Foveal minimum	219.72	219.34	- 0.38	
Average foveal (1.5 mm)	267.32	274.58	+ 7.26	*
Parafoveal macula - Nasal	260.87	261.00	+ 0.13	
Parafoveal macula- Superior	259.08	260.62	+ 1.54	
Parafoveal macula- Temporal	261.25	261.21	- 0.04	
Parafoveal macula - Inferior	257.87	254.18	- 3.69	
Perifoveal macula - Nasal	249.49	255.60	+ 6.11	*
Perifoveal acula - Superior	250.35	249.28	- 1.07	
Perifoveal macula- Temporal	250.09	254.79	+ 4.70	
Perifoveal macula - Inferior	245.91	255.67	+ 9.76	*
Volume (mm^3)	7.08	7.01	- 0.07	

The table 2 compares mean retinal layer thickness and volume measurements between Group A and Group B across various macular regions. Foveal minimum thickness shows minimal difference, but Group a has lower average macular thickness. Parafoveal macula measurements have minor variations without significant differences, except for the inferior quadrant. Perifoveal macula thickness reveals significant differences in the nasal and inferior quadrants, with Group B having greater thickness, except in the superior quadrant, where Group A is thicker. Volume measurements between the groups are similar, with a slight increase in Group A. Significant findings are marked with a symbol.

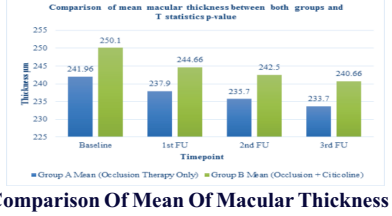

Figure 1: Comparison Of Mean Of Macular Thickness Over Time Between Occlusion Therapy And Combination Of Occlusion Therapy With Citicoline

The figure 1 compares mean macular thickness over time between Group A (occlusion therapy only) and Group B (occlusion therapy + citicoline). Group B consistently shows higher mean thickness than Group A at all time points, but none of the differences reach statistical significance (P-values > 0.1). This indicates that although Group B generally has a thicker macula, the differences are not statistically significant, and thus, no definitive conclusion can be made about the superiority of one treatment over the other based solely on macular thickness.

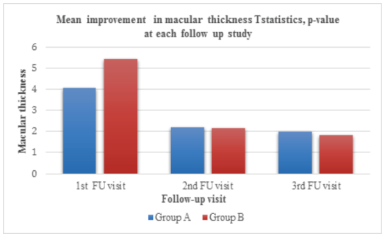

Figure 2: Comparison Of Mean Change In Macular Thickness Between Occlusion Therapy Alone (group A) And Occlusion Therapy Combined With Citicoline (group B) Across Three Follow Up Visits

The figure 2 compares the mean improvement in a specific metric at follow-up visits after initial treatment between Group A (occlusion therapy only) and Group B (occlusion therapy + citicoline). At the 1st follow-up, Group B showed greater mean improvement (5.44) compared to Group A (4.06), but the difference was not statistically significant (p=0.163). In the 2nd and 3rd follow-ups, Group A had higher mean improvements (2.2 and 2) than Group B (2.16 and 1.84), but again, these differences were not statistically significant (p=0.504 and 0.68). Overall, Group B showed a higher total mean improvement (9.44) across all follow-ups compared to Group A (8.26), but none of the differences between groups reached statistical significance.

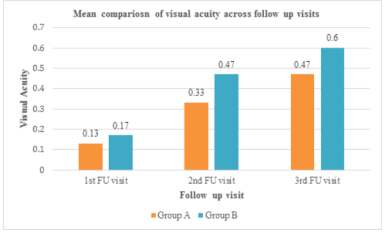

Figure 3: Comparison Of Mean Improvement In Visual Acuity (improvement In Lines Of Snellen Chart) Between Occlusion Therapy Alone (group A) And Occlusion Therapy + Citicoline (group B) Across Three Follow Up Visits

The figure 3 compares mean improvement in visual acuity between Group A (occlusion therapy only) and Group B (occlusion therapy + citicoline) across follow-up visits. At the 1st follow-up, Group B showed higher mean improvement (0.17 vs. 0.13) with a T-statistic of 0.355 and p-value of 0.723. This trend continued at the 2nd (0.47 vs. 0.33, T-statistic 1.046, p=0.299) and 3rd follow-ups (0.60 vs. 0.47, T-statistic 1.026, p=0.308). Overall, Group B consistently demonstrated higher mean improvement in visual acuity, but the differences were not statistically significant.

DISCUSSION

Our study aimed to investigate the effects of occlusion therapy alone versus occlusion therapy combined with citicoline supplementation on a cohort of patients with a certain condition. The baseline characteristics highlight the demographic distribution in the treatment groups. The Occlusion + Citicoline group has more females (59%) while the Occlusion Therapy Only group has more males (66.7%) than females (41%). Age distribution is even across both groups. Socioeconomic status (SES) analysis shows the Occlusion Therapy Only group has more high SES participants. This demographic and SES variation could influence treatment outcomes and should be considered in the study's interpretation. Additionally, the severity of amblyopia is categorized as 25% mild, 46.66% moderate, and 28.23% severe within the study group. Similar study by Kavitha V et al., aimed to compare the characteristics of children with non-occlusion and

occlusion therapy at baseline. Our study aimed to compare retinal thickness and volume measurements between Group A and Group B across various macular regions. The results in Table 1 show minimal difference in foveal minimum thickness between Groups A and B, but a notable decrease in average foveal thickness in Group A. Minor variations were found in the parafoveal region, with no significant differences. Significant differences were observed in the perifoveal region, with Group B showing greater thickness in the nasal and inferior quadrants. Volume measurements showed a slight increase in Group A compared to Group B. similar study by Chan A et al., utilized OCT3 to measure the macular thickness in 37 healthy eyes. The study compared occlusion therapy alone (Group A) with occlusion therapy plus citicoline (Group B) for amblyopia treatment. Group B consistently showed higher mean change in visual acuity and macular thickness, but the differences were not statistically significant, with p-values above 0.1. While the total mean change was higher in Group B, further research with larger sample sizes is needed to confirm these trends and determine the clinical significance.

CONCLUSION

The study concluded that Baseline characteristics indicate a higher proportion of females in the Occlusion + Citicoline group and more patients from high socioeconomic status in the Occlusion Therapy Only group. Follow-up visits show consistently higher mean macular thickness values for Group B across all visits, though these differences were not statistically significant. Macular thickness measurements reveal Group B has a thicker macula than Group A throughout the study, without statistically significant differences. The combined treatment of Occlusion and Citicoline results in a higher mean change in visual acuity and total macular thickness change (sum of mean change in all follow up visits) compared to Occlusion Therapy Only, though the differences are not statistically significant.

Recommendation

1. Consider implementing occlusion therapy combined with citicoline as a treatment method for amblyopia in children, as it may improve visual acuity and macular thickness.
2. Analyze the role of macular thickness as a viable metric for assessing treatment efficacy in amblyopic patients, utilizing optical coherence tomography for precise measurements.
3. Utilize a comprehensive follow-up regimen to monitor improvements in visual acuity and macular health over time, ensuring detailed assessments at each visit.
4. Consider further studies to explore the long-term effects and potential side effects of citicoline in pediatric patients, enhancing the safety profile of amblyopia treatments.
5. Encourage collaboration between research institutions to validate findings and refine treatment protocols for amblyopia, aiming for standardized care procedures.
6. Care must be taken regarding the adverse drug reactions and allergic reactions to any of citicoline component.

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