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OCCLUSION THERAPY TREATMENT IN AMBLYOPIC EYE

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ABSTRACT:
Amblyopia is the most common visual disorder of childhood, yet the contributions of the two principal treatments (spectacle wear and occlusion) to outcome are unknown. The MOTAS study investigated the dose-response relationship between occlusion (patching) and improvement in visual acuity. The use of the Occlusion Dose Monitor (ODM) to record the amount of occlusion dose received by the child represents a major innovation and is unique to this study. The most common causes of visual impairment in adults and children, and visual loss may be permanent if not treated in time. Though many studies have been done on occlusion therapy which is the mainstay in the treatment of unilateral amblyopia, discrepancies exist in literature about quantification of treatment and follow up measures. The present study was undertaken to evaluate the factors responsible for the successful outcome of treatment and the optimum time required for the same in children with unilateral amblyopia. Baseline characteristics of 60 verbal patients with unilateral amblyopia (strabismic, anisometropic, mixed) referred to the Strabismus and Amblyopia Clinic at the Dr. NimeshMathur Centre for Ophthalmic Sciences, Navi Mumbai between September 2016 to December 2017 who improved to the desired level of visual acuity after treatment for amblyopia in the mentioned time period, were analyzed to assess for factors that directly or indirectly influenced the optimum visual rehabilitation and the average duration of therapy required for the same. The evaluation included assessment of the baseline best-corrected visual acuity (BCVA) and refractive status in both eyes, the age at presentation, the type of amblyopia present, fixation pattern in the amblyopic eye, intereye visual acuity difference, and evaluation of compliance through a parental diary system.BCVA in the amblyopic eye was similar in all the three groups. Patients with anisometropicamblyopia showed a quicker response to therapy. Compliance to treatment was the major factor affecting the overall time required for a successful outcome in most cases.
Keywords: Amblyopia, Occlusion Therapy, Causal Inference, Bayesian Analysis**.**

1. INTRODUCTION:

Amblyopia, which occurs in two percent of the total population[1] is the visual deterioration of one or both eyes in the absence of organic abnormalities. It is classified into three categories including strabismicamblyopia, anisometropicamblyopia and visual deprivation amblyopia according to the cause.[2,3] While strabismicamblyopia has commonly been reported to be more than anisometropicamblyopia, it was reported that anisometropicamblyopia is more common in the case of amblyopia detected for the first

time after 7 or 8 years of age. Amblyopia is one of the most common causes of visual impairment in both children and adults with a prevalence varying between 0.2 and 5.4 per cent depending on the subsets of the population studied[1-8.] Diagnosis of amblyopia is based on reduced visual acuity, in the absence of any organic lesion accounting for the same in the affected eye. The condition can be bilateral. Other characteristics of amblyopic vision which may affect the quality of vision include reduced spatial sense, decreased contrast, presence of eccentric fixation, etc. Visual loss due to amblyopia can be permanent if corrective measures are not taken in time[1]. Occlusion of the non-amblyopic eye has remained the mainstay of treatment in cases of unilateral amblyopia1,[9-14]. However, considerable inconsistencies have been reported in literature regarding dispensing of occlusion therapy[13], quantification of treatment[13,14]and follow up measures[11,12.] We therefore undertook this study to analyze the factors responsible for optimum visual rehabilitation (attainment of isoacuity in the amblyopic eye with respect to the non-amblyopic eye) in patients with strabismic, anisometropic or mixed amblyopia, which remained stable for at least three months after the desired visual acuity was established, Similarly children above 11yr were excluded, as amblyopia therapy is not considered to be very effective after this age. Patients with bilateral amblyopia including pure ametropicamblyopia, sensory deprivation amblyopia, and those who showed non-compliance with spectacles were excluded from the study. Amblyopia was diagnosed after a 4 wk trial of spectacle wear. It was defined as a difference in the best-corrected visual acuity (BCVA) between the two eyes of two or more lines on the Landolt's C chart or the Illiterate E charts with the non-amblyopic eye having a visual acuity of more than 6/12 on all occasions (the analysis in this study included patients with unilateral amblyopia only)[8,10,15.] Ocular examination included assessment of the uncorrected (UCVA) and the best-corrected spectacle visual acuity (BCVA) with the help of Landolt's C charts or illiterate E charts in both eyes. The difference of visual acuity between the two eyes in terms of Snellen lines was noted and graded as Grade 1:2 line acuity difference between both eyes.

2. EXPERIMENTAL SECTION:

Patients between 5 to 11yr of age with unilateral amblyopia, conforming to the inclusion criteria mentioned below, out of the total number of consecutive new referrals of unilateral amblyopia, presenting to the Strabismus and Amblyopia Clinics at Dr. NimeshMathur Centre for Ophthalmic Sciences, Navi Mumbai between September 2016 to December 2017were included in this analysis. These patients were to demonstrate stable improvement in visual acuity (as assessed for a minimum period of 3 months after achieving isoacuity with the non-amblyopic eye) subsequent to starting occlusion therapy module dependent upon their age at presentation. Slit lamp biomicroscopy with detailed stereoscopic fundus evaluation was performed in every case for any anterior or posterior segment pathology. The fixation pattern was noted in every case with the help of the Linkz (Fixation) Star attachment in the Heine's Direct Ophthalmoscope (Heine Beta 200 Ophthalmoscope Head model, Heine Optical

Instruments, Germany; Heine USA Ltd., USA). Assessment of the binocular status of the eye was performed whenever possible with the help of the Bagolini's striated glasses (Richmond Products, Inc, USA), and the TNO Stereo test.

Thedifferent subtypes of amblyopia were used for diagnosis. A senior consultant faculty made the diagnosis in all cases. The criteria used for the diagnosis are listed below:

1. **Strabismicamblyopia**: This was defined as amblyopia in the presence of a heterotropia at distance or near fixation in the absence of any anisometropia meeting the criteria for a combined mechanism amblyopia.
2. **Anisometropicamblyopia**: This included patients who had amblyopia in the presence of anisometropia that was 1D or greater in spherical equivalent, or a 1.5 D or greater difference in astigmatism between both the eyes that persisted for at least 4 wk after spectacle correction, in the absence of any measurable heterotropia at distance or near.
3. **Mixed amblyopia:** This included patients with either a heterotropia at distance or near along with anisometropia more than 1 D or more in spherical equivalent or a 1.5 D or more difference in astigmatism in any meridian between both the eyes that persisted after at least 4 wk of spectacle correction.

All patients were prescribed full time high percentage occlusion of the non-amblyopic eye for at least 70 per cent of the child's waking hours (approximately 7 h/day) with the help of an opaque adhesive patch (either cut from a 2 inch wide 3 M Micropore adhesive or commercially available as NexcareOpticludeOrthoptic Eye Patch, manufactured by 3 M Nexcare, 3 M Corporate Headquarters 3 M Center, St. Paul, MN 55144-1000, USA) plastered over the non-amblyopic eye as prescribed, which is the routine mode of prescribing occlusion therapy in our institution. The regimen practiced and prescribed in our set up is dependent on the age of the patient and is as follows10,15: 0-2 yr = 2:1 (2 days in the non amblyopic eye and 1 day in the amblyopic eye); >2-3 yr = 3:1 (3 days in the non amblyopic eye and 1 day in the amblyopic eye); >3-4 yr = 4:1 (4 days in the non amblyopic eye and 1 day in the amblyopic eye); >4- 5 yr = 5:1 (5 days in the non amblyopic eye and 1 day in the amblyopic eye); >5-6 yr = 6:1 (6 days in the non amblyopic eye and 1 day in the amblyopic eye); >6 yr or older = occlusion of the non-amblyopic eye for 30 days with repeated monthly evaluations. The younger patients (less than 4 yr) were assessed every 15 days for signs of improvement. The older children were evaluated after 30 days. Since the patients included in this analysis were more than 4 yr of age, their assessment was performed every month. If the patient did not come for assessment within a week of their scheduled assessment, they were to be excluded from the analysis for this study. Compliance was monitored with the help of a parental diary system, which consisted of a small notebook where the prescribed module of treatment for that particular patient was mentioned. An hour to hour description by parents, teacher, siblings or friends regarding how long was the prescribed occlusion actually used by the amblyopic child was noted down. The ratio of the number of hours when occlusion was actually used against the number of hours for which it had been

prescribed over a period of 1 month (the time for the next follow-up visit) was recorded as a percentage and graded as Grade 1 compliance of 90 per cent or more with the prescribed regimen; Grade 2 compliance between 70 to 90 per cent; and Grade 3 compliance of 70 per cent or less with the prescribed regimen. This system has the intrinsic bias of the observers not noting down the actual occlusion time properly. However, it does offer some objectivity and those patients that are observed to be irregular can automatically be put into the Grade 3 category. The end-point of therapy (successful outcome) was taken to be stable isoacuity between both the eyes maintained for a period of at least three months (the amblyopia therapy was to continue during this period). The total duration of therapy as evaluated for each patient included these three months of maintenance therapy. In patients with strabismic and mixed amblyopia this indicated a change of the occlusion regime to 1:1 (1 day over the previously amblyopic eye and one day over the non-amblyopic eye) with the appropriate refractive correction worn. In patients with anisometropicamblyopia, partial (Menon*et.al*2006) occlusion with nail varnish painted over the back of the spectacles or graded layers of cello-tape plastered over the back of the spectacles in the non-amblyopic eye was prescribed. In case of any regression in the BCVA in this period of more than 2 lines, the patients were excluded for the purpose of this analysis. If the patients met the success criteria, they were subsequently taken up for strabismus surgery, contact lens fitting or both as the case may be. This subsequent management was however not a part of this analysis. The age of presentation, gender, the depth of amblyopia (as assessed by the BCVA at presentation), the inter-eye BCVA difference, the refractive errors and the fixation pattern seen in the amblyopic eye, the compliance monitoring and the time taken for the patient to achieve stable isoacuity in the amblyopic eye equal to that in the non-amblyopic eye were factors taken up for statistical analysis, in those patients who had a successful outcome. The BCVA in Snellen notations were converted to Snellen fractions and the logarithm of the minimum angle of resolution (logMAR values) and both were used for statistical analysis.

3. RESULT & DISCUSSION:

The all patients were prescribed full time high percentage occlusion of the non-amblyopic eye for at least 75 per cent of the child's waking hours (approximately 7 h/day) with the help of an opaque adhesive patch (either cut from a 2 inch wide 3 M Micropore adhesive or commercially available as NexcareOpticludeOrthoptic Eye Patch, manufactured by 3 M Nexcare, 3 M Corporate Headquarters 3 M Center, St. Paul, MN 55144-1000, USA) plastered over the non-amblyopic eye as prescribed, which is the routine mode of prescribing occlusion therapy in our institution. The regimen practiced and prescribed in our set up is dependent on the age of the patient and is as follows10,15: 0-2 yr = 2:1 (2 days in the non amblyopic eye and 1 day in the amblyopic eye); >2-3 yr = 3:1 (3 days in the non amblyopic eye and 1 day in the amblyopic eye); >3-4 yr = 4:1 (4 days in the non amblyopic eye and 1 day in the amblyopic eye); >4- 5 yr = 5:1 (5 days in the non amblyopic eye and 1 day in the amblyopic eye); >5-6 yr = 6:1 (6 days in the non

amblyopic eye and 1 day in the amblyopic eye); >6 yr or older = occlusion of the non-amblyopic eye for 30 days with repeated monthly evaluations. The younger patients (less than 4 yr) were assessed every 15 days for signs of improvement. The older children were evaluated after 30 days. Since the patients included in this analysis were more than 4 yr of age, their assessment was performed every month. If the patient did not come for assessment within a week of their scheduled assessment, they were to be excluded from the analysis for this study. Compliance was monitored with the help of a parental diary system, which consisted of a small notebook where the prescribed module of treatment for that particular patient was mentioned. An hour to hour description by parents, teacher, siblings or friends regarding how long was the prescribed occlusion actually used by the amblyopic child was noted down. The ratio of the number of hours when occlusion was actually used against the number of hours for which it had been prescribed over a period of 1 month (the time for the next follow-up visit) was recorded as a percentage and graded as Grade 1 compliance of 90 per cent or more with the prescribed regimen; Grade 2 compliance between 70 to 90 per cent; and Grade 3 compliance of 70 per cent or less with the prescribed regimen. This system has the intrinsic bias of the observers not noting down the actual occlusion time properly. However, it does offer some objectivity and those patients that are observed to be irregular can automatically be put into the Grade 3 category. The end-point of therapy (successful outcome) was taken to be stable isoacuity between both the eyes maintained for a period of at least three months (the amblyopia therapy was to continue during this period). The total duration of therapy as evaluated for each patient included these three months of maintenance therapy. In patients with strabismic and mixed amblyopia this indicated a change of the occlusion regime to 1:1 (1 day over the previously amblyopic eye and one day over the non-amblyopic eye) with the appropriate refractive correction worn. In patients with anisometropicamblyopia, partial occlusion with nail varnish painted over the back of the spectacles or graded layers of cello-tape plastered over the back of the spectacles in the non-amblyopic eye was prescribed. In case of any regression in the BCVA in this period of more than 2 lines, the patients were excluded for the purpose of this analysis. If the patients met the success criteria, they were subsequently taken up for strabismus surgery, contact lens fitting or both as the case may be. This subsequent management was however not a part of this analysis. The age of presentation, gender, the depth of amblyopia (as assessed by the BCVA at presentation), the inter-eye BCVA difference, the refractive errors and the fixation pattern seen in the amblyopic eye, the compliance monitoring and the time taken for the patient to achieve stable isoacuity in the amblyopic eye equal to that in the non-amblyopic eye were factors taken up for statistical analysis, in those patients who had a successful outcome. The BCVA in Snellen notations were converted to Snellen fractions and the logarithm of the minimum angle of resolution (logMAR values) and both were used for statistical analysis. The results were analyzed using the relevant statistical methods

('t' test, correlations, regression analysis, single factor ANOVA and the Pearson's χ2 test)

3.1 Refractive errors in the amblyopic eye:

Twenty nine patients had hypermetropic refractive error in the amblyopic eye as compared to 17 patients with myopia and 17 with emmetropia (only in cases of SA). The average magnitude of the refractive errors in patients with SA was 2.32 ± 0.17D, 2.88 ± 0.19D in patients with AA and 2.6 ± 0.18D in patients with MA. The difference in the magnitude of the refractive error was significant when one compared patients with SA and AA (P< 0.05, df = 60) indicating that lesser the dioptric power of the eye.

3.2 Compliance:

Compliance to therapy was monitored by a parental diary system; 58 patients (92.04%) showed a compliance of more than 70 per cent of the prescribed schedule (Table). On performing a regression analysis taking compliance as the dependent variable, we found that only the age at presentation had a significant relation (P< 0.05) with the compliance seen. The older the child, more was the compliance to therapy. Poor visual acuity in the amblyopic eye, eccentric fixation or higher refractive errors did not significantly affect compliance to therapy, thus indicating that once the child had understood the need for undergoing treatment, there was greater compliance even if the BCVA in the amblyopic eye was poor. Duration of therapy: The average duration taken by all the patients to achieve a stable isoacuity (which did not change over a period of 3 months after isoacuity was achieved) was 7.2 ± 6.4 months. The average occlusion undertaken was 6.72 ± 0.155 h/day. This corresponded to about 39.24 ± 0.97 h/wk and an overall average of 1089.32 ±48.61 h/ patient.

Table 3.1 Characteristics of patients with unilateral amblyopia

Characteristics	Total (n=62)	SA (n= 32)	AA (n=16)	MA (n=16)
Ageat presentation (yr)	7.3 ± 5.6	7.3 ± 5.9	8.2 ± 5.7	6.3 ± 3.7
BCVA (amblyopic eye): Snellen fraction	0.212 ± 0.09	0.219 ± 0.09	0.231 ± 0.085	0.178 ± 0.091
BCVA (non-amblyopic eye) Snellen Fraction	0.812 ± 0.192	0.699 ± 0.142	0.971 ± 0.126	0.865 ± 0.202
Refractive errors: Hypermetropia	29	9	10	10
Myopia	17	5	7	5
Emmetropia	17	17	0	0
Total occlusion (h)	1089.82 ± 48.61	1189.89 ± 80.02	966.91 ± 69.3	1020.21 ± 79.57

***Values are mean ± SD (mean, range) BCVA, best corrected visual acuity; SA, Strabismicamblyopia; AA, anisometropicamblyopia; MA, mixed amblyopia; logMAR, logarithm of the minimum angel of resolution.**

4. CONCLUSION:

Opinions vary on the hours of occlusion that should be prescribed for optimal results. To maximize the visual acuity outcomes, most ophthalmologists recommend a minimum of 3 trials of high percentage (> 75% of all waking hours) occlusion without any measurable improvement in visual acuity before classifying the case as one of occlusion failure. Insufficient occlusion trial may result in sub-optimal restoration of visual acuity. Lack of compliance is often blamed as a major reason for the failure of occlusion therapy9-20. As the burden of administrating occlusion therapy often falls on the parents, explaining the procedure increases the acceptability and compliance in both the patients and the parents. Parental diary keeping is the conventional mode of monitoring compliance clinically, which has compared favourably with objective evaluation of compliance through devices like the Occlusion Dose Monitor which may not be financially viable in a developing country like ours for mass scale use[21-23].We observed that the average duration of therapy (including 3 months where the visual acuity was maintained at the same level) was about 1100 h of full time occlusion with an average of about 7-8 h of occlusion per day depending on the age of the patient. Subtracting the 3 months maintenance therapy, this approximated about 600 h/patient, similar to the value of 400 h mentioned in a previous study. However, determining an optimum period for which occlusion therapy should be given before labeling the patient as a case of occlusion failure,requires a long-term continued analysis of patients undergoing treatment."

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