

Clinical Evaluation of Management of Amblyopia in Adolescent Age Group (10-19 Years) with Addition of Citicoline to the Conventional Occlusion Therapy

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Abstract

Clinical evaluation of management of amblyopia in adolescent age group (10-19 years) with addition of citicoline to the conventional occlusion therapy. **Abstract Aim** - To evaluate efficacy of citicoline as an adjuvant to occlusion and near activity exercise in management of amblyopia in adolescent age group. **Material and Methods**- We included 79 eligible patients of age group 10-19 years for study. Consent was taken from each of patients. All patients undergone full ophthalmological examination to establish diagnosis of amblyopia and were prescribed their best corrected spectacles. They were divided in three groups using randomization chart, Group A-received full time occlusion, Group B - received full time occlusion and near activity exercises and Group C - received full time occlusion and oral citicoline 500 mg BD for three months. They were followed up four weekly up to 24 weeks. **Result**- During follow up 9 patients lost to follow up. Out of 70 patients who completed study, 36 (51.43%) showed improvement in their vision for distance. We recorded this improvement in lines on snellen's chart. No improvement was present in 14 patients (58%) in group A, 15 patients (60%) in group B and 5 patients (23.81%) in group C. Among groups, responders were 41.67%, 40% and 76.2% in group A, B and C respectively. The difference among three groups was statistically significant (p value-0.024 chi-square test). **Conclusion**- Oral citicoline added to occlusion therapy is a new, safe and effective modality for amblyopia management and chances of improvement in visual acuity is better than other treatment options.

Keywords: Strabismus; Amblyopia; Occlusion; Citicoline.

Introduction

Amblyopia is defined as a unilateral or bilateral decrease of visual acuity for which no organic cause can be detected by the physical examination of the eye and in appropriate cases is reversible by therapeutic measures. It is the most common cause of monocular visual impairment in both children and young adults. It affects 3-4% of adult population. There is consensus that amblyopia can be effectively treated in young children up to age of 10 years as in early age visual system shows lability and ability of reversal of the effect of deprivation. But it has been proved that age is no bar for the success of treatment of anisometropic amblyopia. However there are many studies in older children and adults with amblyopia,

showed response to treatment. Various treatment options have been tried for the management of amblyopia but occlusion remains the gold standard.

There is evidence that plasticity of visual system during the sensitive period is dependent on input from noradrenergic neurons and is subject to pharmacological manipulations. More recently there is effort to treat amblyopia with catecholamine which appear to either deactivator or extend the visual system sensitive period of neural plasticity.

Occlusion therapy with patching of sound eye has

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been the conventional treatment in older children along with addition of drug like citicoline is also effective. Hence this study was done to evaluate the various treatment modalities to treat adolescent amblyopia.

Now a day, various studies revealed that there is no demonstrable distinct advantage to prescribing greater number of hours of patching in either the rate or magnitude of improvement after fixed months of therapy. Thus it is most logical to appreciate that pharmacological enhancement to occlusion therapy may overcome certain shortcomings as compliance, cosmetic blemish of the established occlusion therapy. However, role of occlusion in older children and teenagers is still debatable. Thus, addition of some pharmacological agent potentiates the effect of occlusion in older children and fear of compliance and cosmetic blemish is avoided in young children.

Citicoline (cystidine-5-diphosphocholine) is an intermediate in the making of phosphatidylcholine which is phospholipids in neuronal cell membrane. When the demand of acetylcholine increases, phospholipids in neuronal cell membrane catabolized to supply the needed choline. Thus citicoline stabilized the neuronal cell membrane as well as affect the level of different neurotransmitter and neuromodulators. It has been shown that it increases acetylcholine; nor epinephrine and dopamine level in central nervous system. Recent animal study showing citicholine raised the retinal dopamine concentration thus helps in retinal ganglionic cell regeneration. Choline 1000mg per day was found to be significantly improves visual acuity in patients with amblyopia.

Aims & Objective

To discuss the different treatment modalities of amblyopia in adolescent age group (10-19 years)

To study the effect of addition of citicoline to the conventional occlusion therapy.

Material and Methods

This prospective comparative study was conducted in patients with amblyopia in age group 10-19 years, presenting in OPD of ophthalmology department of MLN Medical College, Allahabad, after taking permission from ethical committee of institute.

Total 79 eligible amblyopic of age group 10-19 years were included in study. Consent were taken from each candidate's parents. Inclusion criteria were,

Patients between age of 10-19 years with amblyopia, Inter eye acuity difference of 2 or more lines, history of or presence of amblyogenic factors strabismus, anisometropia or both. Refractive correction prescribed and worn for at least four weeks prior to enrollment in study Patients with any history of previous treatment, Stimulus deprivation amblyopia, Amblyopia with eccentric fixation and presence of nystagmus were excluded.

A detailed history was taken from each patient at the time of presentation including family history. A complete ocular examination were done, which included baseline visual acuity at 6 meters with snellen chart, refraction under cycloplegia, best corrected visual acuity, ocular motility and alignment evaluation, anterior segment examination by slit lamp, fundus examination and assessment of fixation pattern, binocular function by Worth Four Dot Test, Stereopsis by TNO test, synaptophore examination as required Refractive correction prescribed and worn for at least four weeks prior to enrollment in study. Then they were randomly divided in to three groups Patients were given spectacle correction for one month and then randomly divided into three groups.

Group A (28) received only occlusion therapy along with full refractive correction.

Group B (28) received occlusion, near activity exercises along with full refractive correction.

Group C (23) received oral citicoline 500mg BD for three months, occlusion along with full refractive correction.

Follow up was done at one week, two weeks, one month, two months and three months. The frequency and composition of successive follow up evaluation was depend upon age of the patient and severity of amblyopia. At every follow up, each patient was assessed for visual acuity, line of improvement, fixation pattern, stereo acuity, side effects of occlusion including occlusion amblyopia, and level of compliance. Side effect of drug, speed of recovery.

Finally a meticulous counseling was performed for regular maintenance of a diary by patients/ parents and its regular check-up. All efforts were done to build up confidence towards occlusion method of therapy thus making good compliance and acceptance to achieve a much higher level of success.

Results

Total 70 patients were enrolled in the study. Out of which 9 patients were excluded from the study

due to irregular follow up or poor compliance to patching and prescribed treatment. We assessed them and made our observation on the following parameters: Age, Sex, Laterality of eye, Presenting complaint, Type of amblyopia, Depth of amblyopia, Refractive error, Visual acuity improvement in each group, responders/nonrespondes, side effects The mean age of our study group was 14.67 years (SD - 2.90). Our study population consisted of 60% male and 40% female patients. Most common presenting complaint in our patients was diminution of vision (75.71%), followed by deviation of eye (24.28%). Anisometropia was the most common cause of

amblyopia in our study population affecting 74% of population, followed by combined anisometropia and strabismus affecting 17.14% patients, 4.48% isometropia and 4.48% strabismus. Most common type of refractive error found in our study population was hypermetropia (70% of patients) followed by myopia (17.14% of patients) and astigmatism (12.86%).

Baseline visual acuity was FC-6/60 in 57.12% of total patients, 6/60-6/36 in 25.71%, 6/36-6/24 in 11.42% and 6/24-6/18 in 5.7% of patients in study population.

Table 1: Baseline visual acuity in study groups

Visual acuity	Group A	Group B	Group C
FC - 6/60	13	15	12
6/60 - 6/36	6	7	5
6/36 - 6/24	3	3	2
6/24 - 6/18	2	0	2

Table 2: Depth of amblyopia in different groups

Depth of Amblyopia	Group A (n=24)	Group B(n=25)	Group C(n=21)
Mild ($\leq 6/18$)	2	0	2
Moderate ($> 6/18$ to $\leq 6/36$)	9	10	7
Severe ($\geq 6/60$)	13	15	12

Table 3: Visual improvement in each groups

Line of improvement	Group A	Group B	Group C
0	14	15	5
1	4	4	6
2	5	4	5
3	1	2	2
>3	0	0	3

Table 4: Responders / Non responders

Groups	Responders	Non - Responder
Group A	10	14
Group B	10	15
Group C	16	5

In group A 8.33% patients were of mild amblyopia 37.5 % patients were of moderate amblyopia and 54.17% patients were of severe amblyopia. In group B patients of moderate and severe amblyopia were 40% and 60%. In group C patients of mild moderate and severe amblyopia were 9.52%, 33.33% and 57.14%

Out of total 70 patients who completed the study, 36 patients (51.43%) showed improvement in their vision for distance; remaining 34 patients (48.57%) were non responders.

Among groups, responders were 41.67%, 40% and 76.2% in group A, B and C respectively. The difference among three groups was statistically significant (p value-0.024 chi-square test). Among groups,

nonresponder were 20%, 21.4% and 7.14% in group A,B and C respectively

Side Effects

4 patients (5.71%) complaint of rash due to occlusion given to them. One patient in group C complaint of mild headache which got relieved by medication after two days. Remaining 65 patients developed no complication.

Discussion

Treatment of amblyopia remains a therapeutic

challenge to the ophthalmologists. It has perplexed clinicians over the centuries, both as regards to its diagnosis and treatment. This is further highlighted by the vastness and variety of treatment modalities tried and the research done in this field.

Occlusion remains the gold standard treatment modality of amblyopia. By means of removing the suppression effect of brain cells driven by the sound eye over the brain cells which are involved in processing vision in the amblyopic eye, patching helps in improving the vision. Major failure of occlusion therapy is because of poor compliance due to cosmetic blemish. The other drawbacks like occlusion amblyopia, problems of fusion disruption and increase in angle of deviation, disturbing child's family.

Anisometropia was the most common cause of amblyopia in our study population. It was found to be the cause in 74% followed by combined 17.14%, 4.48% isometropia and strabismus (4.48%). As found by *Attebo et al* and *Pediatric Eye Disease Investigator Group* 54.17% patients of severe amblyopia, 37.14% patients of moderate amblyopia and 5.71% patients of mild amblyopia. Patients of severe amblyopia are more In our study population may be because severe amblyopia comes in notice earlier than mild and moderate amblyopia. The treatment outcomes are influenced by the severity of the amblyopia as stated by *Stewart, Fielder et al.*

Most common type of refractive error found in our study population was hypermetropia (70% of patients) followed by myopia (17.14% of patients) and astigmatism (12.86%). These findings are consistent with finding of *McMullen* who stated that Amblyopia is more common and of a higher degree in patients with anisohypermetropia than in those with anisomyopia. Because when myopia is unequal, the more myopic eye can be used for near work and the less myopic eye for distance. Therefore, unless the myopia is of a high degree, both receive adequate stimulation and amblyopia does not develop.

In our study visual improvement after occlusion therapy (41.67%) was better than spectacle correction alone (18%) This outcome of study is comparable with the *Cleary (2000)* study who concluded that occlusion is more effective in treatment of amblyopia than spectacle alone.

In our study 40% children (10-19 years) showed improvement in their visual acuity with patching and near vision exercises which is comparable to the study of *Ghosh S et al.*

In our study 51.43% amblyopic patients of 10-19 years showed improvement in their visual acuity

which is comparable to the study of *Neela A Patwardhan et al.*

In our study we found that on addition of oral citicoline 500mg b.d. to conventional occlusion therapy with near vision exercises in the treatment of amblyopia improves the visual acuity in 77% of patients which is comparable to study of *Campos et al [5]* who recorded that citicoline was effective in the treatment of amblyopia and statistically significant improvement in visual acuity was found both for the amblyopic and sound eye in 46 of the 50 patients (92%). The improvement remained stable for at least four months.

Similarly *Porciatti et al [6]* was conducted the study in adult with a mean age of 24.8 years recorded that visual acuity improved 1.4-1.5 lines in the amblyopic eyes and 0.4 in the normal eyes with citicoline.

Ghosh S and Ghosh R [7] conducted study on amblyopic patients, in age group of 10-18 years, reported that 71% of the patients had shown visual improvement with adding drug i.e. citicoline to occlusion and near activities. Our study is comparable to this study in terms of improvement as we also found 76% patients improved by adding citicoline, which was significantly better than remaining two groups ($p < 0.02$).

Prachee Vasant Pawar et al [8], also studied effectiveness of addition of citicoline to patching in the treatment of amblyopia in the age group of 4-13 years. At the end of five months, in phase 2 showing significantly better improvement in younger and older patients with citicoline along with patching ($p < 0.05$).

In our opinion he should have continued drug for some more period as most of the studies had used the drug for longer time, as it may take time for full effect of drug to come.

In our study, we found 41.67% patients improved in group A, 40% in group B and 76.2% in group C. Difference among groups was statistically significant ($p < 0.02$). Total 51.41% patients of 10-19 years of age group improved with treatment. This is encouraging that those patients who were older enough should also be given a chance to improve. We cannot comment on stability of vision improvement as this requires a longer follow up which we are doing at our institute

Compliance remains the major challenge with occlusion therapy and near exercises and results with these modalities will depend upon compliance of patients. So compliance was given extra importance and carefully monitored

- Regular counselling of patients and parents
- Regular maintenance of a diary by patients/parents and its regular check up.
- All efforts were done to build up confidence towards otherwise simple looking occlusion method of therapy, thus making compliance and acceptance to achieve a much higher level.

Contrary to this, compliance was much better with the drug therapy. Patient/parents think they will be benefited by medication. Along with this, the side effects associated with the drug are less, as seen in various studies. Therefore this drug is safe to use.

There are few studies using citicholine for amblyopia treatment. Our study is showing promising results with citicoline, which had been shown by most of the previous studies. So it can be concluded that use of citicoline can give better results in amblyopic patients, even in adolescent age group.

Limitations of our study were lesser number of patients and a need of longer follow up period to see whether the gain in vision remains stable or deteriorates in longer follow up period.

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