# Role of Citicoline for Management of Myopic Amblyopia Patients in Teriary Care Hospital of India

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#### **ABSTRACT**

**Introduction:** Myopia is a very common condition affecting people worldwide. Current research aimed to study the effects of oral citicoline as treatment option in myopic amblyopia.

**Material and Methods:** Patients of myopic amblyopia of age group 5-30 years were evaluated between June2018 to March2019. Detailed eye examinations including visual acuity, refraction, and dilated fundoscopy were done. Patients were randomly divided into 2 groups. 1 group of patients were given oral citicoline(500mg) daily for 12 weeks. Other group of patients was given placebo daily for 12 weeks. All patients were followed up to at monthly interval for 6 months; visual acuity and refraction were done in each follow up visit.

**Results:** Total 378 patients with myopic amblyopia were identified. Visual acuity improved or became stable over time following citicoline therapy, as compared to placebo. Maximum improvement in visual acuity was from 6/60 to 6/9(p).

**Conclusion:** Citicoline therapy resulted in significant improvement or stability of visual acuity in myopic amblyopic patients.

**Keywords:** Myopic amblyopia, Citicoline, Visual acuity, Refraction

#### INTRODUCTION

Myopia is a very common condition affecting people of all age group, now a days, the increasing trend seen in people of young and middle age group. It is characterized by an increased axial length, increased corneal curvature and many more changes in the retina that includes progressive retinal pigment epithelium (RPE) thinning, irregularly distributed RPE atrophy, grossly attenuated fundus, peri-papillary atrophy, tilted optic disc, myopic temporal crescent, Lacquer cracks in the posterior pole, posterior staphyloma and many more.

# Mechanism of action of citicoline

Citicoline (Cytidine 5-diphosphocholine) stimulates dopaminergic system in the brain and retina, thus increases retinal neurotransmitter (dopamine) levels. Chronic citicoline treatment leads to increase in dopamine receptor densities and promotes partial recovery of dopamine receptor functions (which normally decreases with aging).<sup>2,3</sup> Citicoline activates the biosynthesis of structural phospholipids (phosphatidylcholine) in neuronal cell membranes, thus an increased neurotransmitter levels and enhanced neuroprotection.<sup>3,4</sup> It stimulates glutathione synthesis and facilitates preservation of sphingomyelin, thus promoting signal transduction in nerve cells of retina.<sup>5</sup> It reduces retinal

nerve fibre layer (RNFL) damage by reducing Nitric Oxide synthase levels and attenuates Nitric Oxide function in the neurons of retina and spinal cord.<sup>2</sup> In the current study, we aimed to study the effects of oral citicoline as a treatment option in myopic amblyopia by looking at the progression, arrest or regression of myopia.

#### MATERIAL AND METHODS

This observational hospital based study was performed in a tertiary care centre of India between June 2018 to March 2019. Patients of myopic amblyopia of age group 5-30 years were included in the study.

#### Inclusion criteria were-

- Visual acuity < 6/60 or poor
- Myopia > -6.00D or more

## Exclusion criteria for both groups were-

- Media opacities
- Squint
- History of previous ocular surgery
- Ocular trauma

All participants provided informed consent before being included in this study. Detailed eye examinations including visual acuity, refraction, and dilated fundoscopy by indirect ophthalmoscope were done. The whole study population (378 patients) was randomly divided into 2 groups- Group A had 203 patients and were given oral citicoline (Tab Citimet 500mg) daily for 12 weeks and Group B had 175 patients and were given placebo (anti-oxidant) daily for 12 weeks. All patients were called for follow-up after 1month, 3months and 6months. Visual acuity and refraction were done in each follow up visit. Data was analysed using SPSS software. All differences associated with chance probability of ≤0.05 were considered statistically significant.

#### **RESULTS**

A total of 378 patients (age 5-30 years) were enrolled in our study out of which 225 patients were male (59.52%) and 153 patients were females (40.47%) with M: F ratio was 1.47:1.

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Sl.	Age group	Total	Groups		Improvement in V		Stability in V <sub>A</sub> and re-		Statistical		
No.	(years)	patients (n=378)	Group A	Group B placebo	and refractive status (%)		fractive status (%)		significance		
		(11–376)	(n=203)	(n=175)	Group	Group	Group	Group			
					A	В	A	В			
01	5-10 years	100	57	43	39	1	18	42	p ≤0.05		
		(26.45%)			(68.42%)	(2.32%)	(31.58%)	(97.68%)	_		
02	10-15 years	124	65	59	41	6	24	53	p ≤0.05		
		(32.80%)			(63.07%)	(10.17%)	(36.93%)	(89.83%)	_		
03	15-20 years	101	59	42	33	3	26	39	p ≤0.05		
		(26.71%)			(55.93%)	(7.14%)	(44.07%)	(92.86%)			
04	20-25 years	31	17	14	6	2	11	12	Not significant		
		(8.20%)			(35.29%)	(14.29%)	(64.71%)	(85.71%)			
05	25-30 years	22	5	17	1	0	4	17	Not significant		
		(5.80%)			(20.00%)	(0.00%)	(80.00%)	(100.0%)			
	Table-1:										

Sl. No.	Group	No. of patients	Improvement	Stability	Statistical significance				
01	Group A (n=203)								
	Males	128	56.25%	43.75%	p ≤0.05				
	Females	75	64.00%	36.00%					
02	Group B (n=175)								
	Males	97	7.22%	92.78%	Not significant				
	Females	78	7.69%	92.31%					
	Table-2:								

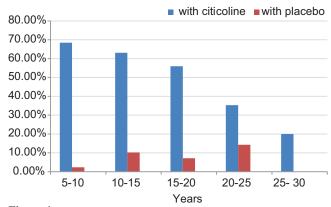
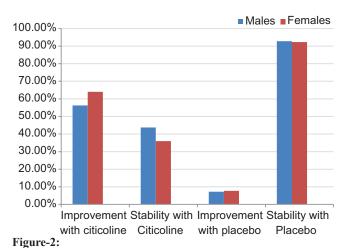


Figure-1:



Mean age of included patients was 14.20±6.02. Patients were divided into 2 groups- Group A consisting of 203 patients and Group B consisting of 175 patients. To study

the effect of age on outcome patients were categorised on the basis of age [Table1]. After 6 month follow up maximum improvement in visual acuity and refractive status 68.42% was seen in 5-10 years age group, followed by 63.07% in 10-15 years, 55.93% in 15-20 years, 35.39% in 20-25 years and minimum improvement 20.20% in 25-30 years age group[Table1][Figure1]. In sex wise category female showed better improvement in visual acuity and refractive status (64.00%) as comparison to male (56.25%)[Table2] [Figure2].

Data regarding age wise distribution of patients and effects of citicoline is given in table 1.

Data regarding sex-prevalence of patients and effects of citicoline is given in table 2.

Figure 1 shows age wise distribution of patients and improvement of refractive status of eye with citicoline and placebo.

Figure 2 shows sex distribution of patients and improvement in refractive status of eye with citicoline.

## **DISCUSSION**

This study showed that there is some improvement in visual acuity and refractive status of eyes of patients with citicoline. The improvement was markedly noted in patients of age group 5-15 years- highest improvement was seen in age group of 5-10 years (68.42%). After 15 years of age, refractive status became stable with use of glasses. Among males and females, females showed comparatively better results in improvement in refractive status and visual acuity with the use of citicoline (64%).

Currently, no study is available regarding role of citicoline in progression, arrest or regression of myopic amblyopia in patients. However, study published by *Junfeng Mao et al* showed that intraperitoneal injection of citicoline retarded the myopic shift induced by form deprivation in guinea pigs.<sup>2</sup> Another study published by *Prachee Vasant Pawar et al* showed that improvement in visual acuity with citicoline along with patching was significantly more than that with patching alone, in one year of treatment of amblyopia.<sup>6</sup>

Many studies have shown neuro-protective effects of citicoline in glaucoma, amblyopia, non arteritic ischemic optic neuropathy, cerebral stroke, dementia, Parkinson's disease and many other diseases due to increase in dopamine levels in brain and protective effects of phosphatidylcholine in retinal as well as nerve ganglion cells. Improvement in visual acuity and refractive status of patients of myopia with citicoline therapy was perhaps due to increase in retinal dopamine levels which retards myopia progression and neuroprotective effects of phosphatidylcholine and sphingomyelin.

This study had several limitations. The sample size was small. Due to high cost of citicoline tablet, the compliance of the patients were about 80% due to which some patients didn't turn up for follow-up. We didn't calculate axial length of the eyes of patients prior to and after the treatment. The present study shows some improvement in visual acuity and refractive status of patients of myopic amblyopia with citicoline therapy, specially in children (below 20 years of age) and females.

## **CONCLUSION**

Citicoline has got some role in improvement of visual acuity and refractive status of eyes of patients of high myopia, resulting in myopic amblyopia till 20 years of age and females. It may prove to be a promising therapy in retardation of myopia progression and myopic amblyopia in future.

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