Original Article

Effectiveness of the addition of citicoline to patching in the treatment of amblyopia around visual maturity: A randomized controlled trial

Prachee Vasant Pawar, Sachin S Mumbare[1], Mrunal Suresh Patil, Seema Ramakrishnan[2]

Aim: To study the effectiveness of the addition of citicoline to patching in the treatment of amblyopia in the age group of 4-13 years. **Materials and Methods:** A randomized controlled trial, which included patients who were randomly divided into two groups. Both the groups received patching therapy till plateau was achieved in phase 1 of the study. Then in phase 2, group I received citicoline plus patching and group II continued to receive only patching. **Outcome Measures:** Outcome was measured by the visual acuity in logMAR every month in phase 1 till plateau was achieved and then for 12 months in phase 2. **Results:** No significant difference was found in the mean visual acuities in these two groups in phase 1 till plateau was reached. In phase 2, for the initial four months, there was no significant difference in the visual acuities in these two groups, at the respective intervals. However, five months onward, up to 12 months, there was a significant difference in the visual acuities in these groups.The result was the same in younger patients (< seven years of age) as well as in older patients (> seven years of age). In phase 2, the mean proportional improvement in group I was significantly more than that in group II, at two months and onward, at the respective intervals. **Conclusion:** The improvement in visual acuity with citicoline plus patching was significantly more than that with patching alone, in one year of treatment.

Key words: Amblyopia, citicoline, patching

Access this article online
Website: www.ijo.in
DOI: 10.4103/0301-4738.128586
Quick Response Code:

Amblyopia is the most common cause of monocular visual impairment in children, young, and middle-aged adults.[1]

There is a consensus that amblyopia can be effectively treated in young children.[2-4] Although there has been, in the past, a general belief that treatment beyond a certain age is ineffective, it has been conclusively proved that 'age' is no bar, for the success of the treatment of anisometropic amblyopia.[5] Some believe that a treatment response is unlikely after the age of six or seven years, while others consider the age of nine or ten years to be the upper age limit for successful treatment.[6-10] However, there are many studies involving older children and adults with amblyopia, responding to treatment with patching.[11-24]

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.[25,26]

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.[27] It has also been shown to improve the learning and memory performance. There are few animal studies that have reported the enhancement of dopaminergic neurotransmission in the brain with citicoline (exogenous cytidine-5′-diphosphocholine). A study aimed at determining whether citicoline (50 mg/kg., twice daily) could influence retinal catecholamine levels in adult male Albino rabbits, has reported that, compared to vehicle-treated controls, citicoline-treated animals displayed a significantly higher retinal dopamine concentration and a tendency toward an increase in adrenaline concentration, while the noradrenaline concentration remained unchanged.[28]

Citicoline is an intermediate in the making of phosphatidylcholine, a phospholipid, in cell membranes. Citicoline activates the biosynthesis of structural phospholipids in the neuronal membranes, increases brain metabolism, and influences the levels of different neurotransmitters. It has been shown to increase acetylcholine, norepinephrine, and dopamine levels in the central nervous system. Citicoline is currently used in the treatment of Alzheimer's disease and stroke as a brain stimulator.

Citicoline is presently also tried in the treatment of amblyopia.[29,30] To the best of our knowledge, studies to evaluate the effect of citicoline in amblyopia have not been conducted in India. Therefore, the present study was conducted to find out the effectiveness of the addition of citicoline to patching in the treatment of amblyopia, in the age group of four to thirteen years.

Materials and Methods

The present study was carried out at Department of Ophthalmology, Dr. Vasantrao Pawar Medical College Hospital and Research Centre, Nashik; and Manishankar eye hospital and institute, Nashik The study was conducted between January 2006 and December 2009. Ethical clearance was taken from the Institutional Ethical Committee before the start of the study.

Department of Ophthalmology, [1]Department of Community Medicine, Dr. Vasantrao Pawar Medical College Hospital and Research Center, Nashik, [2]Consultant Ophthalmologist, Manishankar Eye Hospital and Institute, Nashik, Maharashtra, India

Correspondence to: Dr. Prachee Vasant Pawar, Department of Ophthalmology, Dr. Vasantrao Pawar Medical College Hospital and Research Center, Nashik, Maharashtra, India. E-mail: pawarprachi@rediffmail.com

Manuscript received: 13.12.12; Revision accepted: 17.05.13

The inclusion criteria were
- Patients of amblyopia from four to thirteen years of age
- Patients not suffering from any other ophthalmic morbidity
- Patients/Parents willing to participate in the study.

Exclusion criteria in this study were
- Patients in whom citicoline was contraindicated, such as hypersensitivity to citicoline, history of epilepsy
- Not willing to participate in the study, after thorough discussion of treatment and its side effects with the family.

All the patients suffering from amblyopia were primarily screened for inclusion in the study. Subjects who fulfilled the inclusion criteria were selected for the study. The patients were randomly divided into two groups. The study was divided into two phases. In Phase 1, a complete history of the included patients was elicited including family, personal, and birth history. Visual acuity was tested with the Snellens chart. Dry retinoscopy and Wet retinoscopy were conducted followed by acceptance and prescription of the required glasses. Ophthalmic examination and slit lamp examination were performed for anterior segment examination. Dilated fundoscopy was carried out to rule out any retinal pathology.

The following tests were conducted:
- Complete refractive status of both eyes
- Binocular single vision by stereo charts and Worth four-dot test
- Cover test/uncover test for the amount of squint and type of squint, added vertical or oblique deviation
- Alternate cover test
- Extraocular movements
- Prism cover test
- Forced duction test as per the case, local or general anesthesia
- Dilated fundoscopy for the macular shift in cases of oblique overaction or eccentric fixation
- Direct ophthalmocopy for eccentric fixation in strabismic amblyopia
- Observation of result on initial patching therapy in strabismic cases.
- Color vision testing.

Following this, the patching therapy was started in both groups. The patients were followed at one month intervals and visual acuity was recorded. If there was no improvement in the visual acuity for three consecutive followups, then a plateau was considered. It was approximately corresponding to the maximum correction that could be achieved with patching. Once a plateau was achieved, the patient entered phase 2 of the study.

In phase 2, group I received citicoline in addition to continued patching. The doses of citicoline were 250 mg OD (for patients below five years) and 500 mg OD (for patients above five years). Group II continued to receive only patching. In both groups, the respective treatment was continued for six months in phase 2. At the end of this period citicoline was gradually tapered by giving half the dose daily for two months, half the dose on alternate days for another two months, and then discontinued. Patching was continued for 12 months in both groups.

The patients were followed at one month intervals for 12 months in phase 2. The visual acuity was recorded in every followup visit. Visual acuity was converted into the Logarithm of the minimum angle of resolution (LogMAR). The mean LogMAR visual acuity was calculated in both the groups. Proportional improvement in the visual acuity, adjusted for fellow eyes, was calculated using the following formula, suggested by Stewart C E *et al*.[31]

Proportional improvement = (VAas – VAae)/(VAas – VAfe)

Where VAas is the LogMAR visual acuity of an amblyopic eye at the start of the study (baseline); VAae is the LogMAR visual acuity of the amblyopic eye at the end of the respective interval; and, VAfe is the LogMAR visual acuity of the fellow eye at the end of the respective interval.

Age: 1, (maximum 6:1) schedule was followed for patching. For example, for a patient of five years, 5:1 schedule was followed (five days full-time patching for the better eye and one-day patching for the worse eye). For a patient of 10 years, 6:1 schedule was followed.

The analysis of variance (ANOVA) was used to test the significant difference between the mean LogMAR values. Differences in the proportional improvements were tested with a non-parametric test like the Mann Whitney U test. Other tests like Chi-square test and Z-test were also used at appropriate places. Analysis was done using SPSS 16.

Results

In the study period 165 patients were primarily screened for inclusion in the trial. Out of them, 134 patients were finally selected for inclusion in the study. Out of these, we could follow up 84 patients for one year in phase 2.

The distribution of the study subjects is shown in Table 1.

There was no significant difference in the baseline characteristics of patients in the two groups. The mean ages were 6.78 ± 1.53 and 6.68 ± 1.89 (P = 0.81). The mean visual acuity (LogMAR) in the amblyopic eyes were 0.78 ± 0.36 and 0.77 ± 0.35 (P = 0.90).

Table 2 shows the mean visual acuity at various intervals during treatment. In phase 1, both the groups received only the patching therapy. Therefore, no significant difference was found in the mean visual acuities in these two groups till the plateau was reached. The mean time taken to reach the plateau (no improvement in three consecutive assessments) was 8.28 months ± 1.09 in group I and 8.40 months ± 1.15 in group II. The range was seven to ten months in both the groups.

In phase 2, for the initial four months, there was no significant difference in the visual acuities in these two groups, in the respective intervals. However, at five months and onward, up to 12 months, there was a significant difference in the visual acuities in these two groups at the respective intervals. Thus, addition of citicoline showed a significant improvement in the mean visual acuities after five months. Group II, which received continued patching, showed some deterioration from the plateau, in the mean visual acuity, although marginal and statistically insignificant, after 12 months.

Table 3 shows the mean proportional improvement in the visual acuity, adjusted for fellow eye, with respect to the baseline values. In phase 1, there was no significant difference

Table 1: Distribution of the study subjects in the two groups

Characteristics	Group I	%	Group II	%	Total	%	*P*
Type of Amblyopia							
Strabismus	15	37.50	16	36.36	31	36.90	0.978
Anisometropia	14	35.00	15	34.09	29	34.52	
Combined	11	27.50	13	29.55	24	28.57	
Total	40	100.00	44	100.00	84	100.00	
Age							
4-5	3	7.5	2	4.55	5	5.95	0.52
5-6	7	17.5	9	20.45	16	19.05	
6-7	9	22.5	13	29.55	22	26.19	
7-8	8	20	7	15.91	15	17.86	
8-9	8	20	7	15.91	15	17.86	
9-10	3	7.5	3	6.82	6	7.14	
10-11	2	5	1	2.27	3	3.57	
11-12	0	0	1	2.27	1	1.19	
12-13	0	0	1	2.27	1	1.19	
Total	40	100	44	100	84	100.00	
Sex							
Male	17	42.50	17	38.64	34	40.48	0.72
Female	23	57.50	27	61.36	50	59.52	
Total	40	100.00	44	100.00	84	100.00	
Visual acuity (Amblyopic eye)							
≤ 20/200	15	37.50	13	22.73	25	29.76	0.64
> 20/200 to ≤ 20/120	7	17.50	10	22.73	17	20.24	
> 20/120 to ≤ 20/80	5	12.50	8	18.18	13	15.48	
> 20/80 to ≤ 20/60	8	20.00	6	20.45	17	20.24	
> 20/60 to ≤ 20/40	5	12.50	6	13.64	11	13.10	
> 20/40 to ≤ 20/20	0	0.00	1	2.27	1	1.19	
Total	40	100.00	44	100	84	100.00	
Mean visual acuity*	0.78±0.36		0.77±0.35		0.77±0.37		0.90
Visual acuity (Fellow eye)							
≤ 20/200	0	0.00	0	0.00	0	0.00	0.31
> 20/200 to ≤ 20/120	1	2.50	0	0.00	1	1.19	
> 20/120 to ≤ 20/80	4	10.00	3	6.82	7	8.33	
> 20/80 to ≤ 20/60	9	22.50	8	18.18	17	20.24	
> 20/60 to ≤ 20/40	11	27.50	16	36.36	27	32.14	
> 20/40 to ≤ 20/20	15	37.50	17	38.64	32	38.10	
Total	40	100.00	44	100	84	100.00	
Mean visual acuity*	0.27±0.24		0.24±0.21		0.25±0.22		0.85

*LogMAR

in the mean proportional improvements in these two groups. However, in phase 2 the mean proportional improvement in group I was significantly more than that in group II at two months, and onward up to 12 months, at the respective intervals. It showed that the mean proportional improvement even at the two- month interval was significantly more in group I (which received citicoline plus patching), as compared to Group II (which received patching alone).

Table 4 shows the visual acuity–wise distribution of patients at the end of phase II.

To study the effect of age in the outcome, we have divided the study subjects in each group into two subgroups, one subgroup of young patients (age at start of phase 1 ≤ 7 years, Fig. 1) and the other of 'old' patients (age at start of phase 1 > 7 years, Fig. 2). At the end of the five months, in phase 2, the mean logMAR of the younger as well as older patients in group I was significantly less than that in Group II, showing significantly better improvement in the younger and older patients with citicoline along with patching ($P < 0.05$). This showed that the treatment of amblyopia with citicoline along with patching was equally effective in the seven-to-thirteen year age group.

No significant side effects, which could lead to withdrawal of the treatment, were recorded in both the groups. Only

Table 2: Mean visual acuity (LogMAR) in both the groups during follow up

Follow up	Mean visual acuity (LogMAR)			*P* value
	Group I	Group II	Total	
Phase 1 (Patching for both the groups)				
1 month	0.75±0.32	0.74±0.34	0.74±0.33	0.900
2 months	0.71±0.31	0. 70±0.35	0.70±0.32	0.900
3 months	0.69±0.31	0.68±0.31	0.69±0.31	0.900
4 months	0.64±0.30	0.64±0.32	0.63±0.31	0.953
5 months	0.58±0.30	0.57±0.30	0.57±0.30	0.954
6 months	0.55±0.31	0.55±0.29	0.55±0.30	0.900
7 months	0.52±0.30	0.53±0.30	0.53±0.30	0.900
Plateau	0.49±0.33	0.49±0.28	0.49±0.31	0.996
Phase 2				
	(Citicoline+Patching)	(Patching alone)		
1 month	0.47±0.33	0.49±0.28	0.48±0.30	0.854
2 months	0.44±0.31	0.48±0.27	0.46±0.27	0.502
3 months	0.42±0.31	0.48±0.27	0.45±0.26	0.455
4 months	0.39±0.31	0.48±0.29	0.42±0.27	0.150
5 months	0.36±0.30	0.49±0.29	0.43±0.27	0.035*
6 months	0.33±0.29	0.51±0.29	0.42±0.26	0.005*
7 months	0.30±0.26	0. 51±0.28	0.45±0.28	0.000*
8 months	0.29±0.25	0. 51±0.28	0.40±0.24	0.000*
12 months	0.29±0.24	0.51±0.30	0.40±0.23	0.000*

* Significant, LogMAR : Logarithm of the minimum angle of resolution

one patient in Group I had one episode of vomiting, which responded to the usual line of treatment.

Discussion

The present multicentric study was carried out to find out the effectiveness of the addition of citicoline to the conventional patching therapy for the treatment of amblyopia. This study has suggested that addition of citicoline, even after maximum improvement with conventional patching was achieved, can further improve the visual acuity.

Citicoline primarily acts by increasing the synthesis of phosphatidylcholine, the primary neuronal membrane phospholipid, thus enhancing the production of acetylcholine. Oral citicoline administration increases the plasma levels of choline and cytidine, the building blocks used to restore neuronal membrane integrity.[32] It is also postulated that citicoline facilitates the preservation of sphingomyelin, which promotes signal transduction in nerve cells.[33]

Citicoline may significantly impact the brain-remodeling activity. A study in rats has shown that citicoline treatment significantly increases the length and branch points of the dendrites, increasing the overall surface area occupied by neurons, which leads to an increased efficiency of sensory information processing. This mechanism of activity may potentially account for a significant portion of citicoline's neurorestorative functions.[34]

Campos *et al.*,[29] have also recorded that citicoline was effective in the treatment of amblyopia. They published the preliminary results of their study and stated that statistically significant improvement in visual acuity was found both for the amblyopic and sound eye in 46 of the 50 patients (92%). The behavior was different for normal and amblyopic eyes. The improvement remained stable for at least four months. Similarly Porciatti *et al.*,[35] recorded that visual acuity improved 1.4-1.5 lines in the amblyopic eyes and 0.4 lines in the normal eyes with citicoline. They also reported improvements in the contrast sensitivity and increase in the visually evoked potential. This study was conducted in adults with a mean age of 24.8 years. Ghosh S and Ghosh R, in a study on amblyopic

Table 3: Mean proportional improvement in the visual acuity, adjusted for fellow eye, with respect to the baseline values

Follow up	Mean Proportional improvement in visual acuity (w. r. t. baseline)		*P* value
	Group I	Group II	
Phase 1			
Baseline	0.00	0.00	1.0000
Month 1	0.06	0.06	1.0000
Month 2	0.14	0.13	0.8223
Month 3	0.18	0.17	0.8858
Month 4	0.27	0.25	0.6192
Month 5	0.39	0.38	0.8934
Month 6	0.45	0.42	0.6551
Month 7	0.51	0.45	0.1178
Plateau	0.57	0.53	0.2989
Phase 2			
Month 1	0.61	0.53	0.3035
Month 2	0.67	0.55	0.0351*
Month 3	0.71	0.55	0.0088*
Month 4	0.76	0.55	0.0003*
Month 5	0.82	0.53	0.0002*
Month 6	0.88	0.49	0.0000*
Month 7	0.94	0.51	0.0000*
Month 8	0.96	0.51	0.0000*
Month 12	0.96	0.49	0.0000*

* Significant

Table 4: Visual acuity at the end of phase 2

Visual acuity	Group I		Group II		Total		*P* value
	No.	%	No.	%	No.	%	
≤ 20/200	0	0	0	0.00	0	0.00	0.000
> 20/200 to ≤ 20/120	0	0	2	4.55	2	2.38	
> 20/120 to ≤ 20/80	0	0	10	22.73	10	11.90	
> 20/80 to ≤ 20/60	3	7.5	17	38.64	20	23.81	
> 20/60 to ≤ 20/40	21	52.5	10	22.73	31	36.90	
> 20/40 to ≤ 20/20	16	40	5	11.36	21	25.00	
Total	40	100	44	100	84	100	
Mean visual acuity (LogMAR)	0.29±0.24		0.51±0.30		0.40±0.23		0.000

LogMAR: Logarithm of the minimum angle of resolution

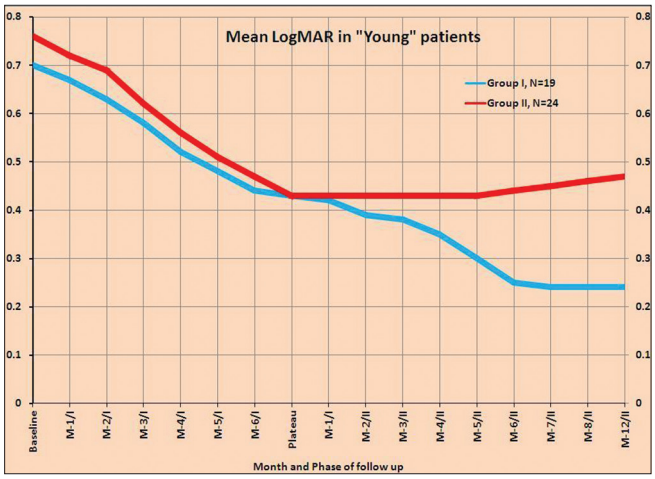

Figure 1: Mean LogMAR of "young" patients during the study (age, at start of phase 1 ≤ 7 years)

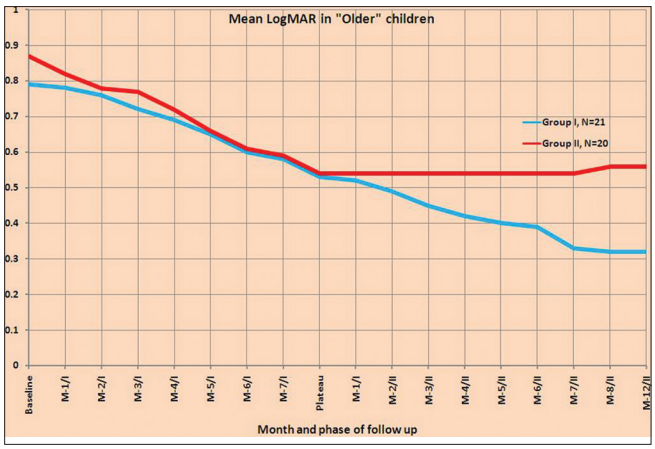

Figure 2: Mean LogMAR of "Older" patients during study (age, at start of phase 1, >7)

patients, in the age group of 10 to 18 years, reported that 71% of the patients had shown visual improvement with citicoline.[36]

Our findings were in contrast with the findings of Michela Frenisa *et al*.,[30] who have reported that addition of CDP-choline to patching therapy was not found to be more effective than patching alone after a 30-day treatment. They have reported that adding CDP-choline to patching stabilized the effects obtained during the treatment period.

There are few limitations of this study, which must be documented. This was not a double-blind study rather it was an open study. This could have resulted in observer or investigator bias. Second, we have analyzed only those subjects whose follow-up data was available up to one year in phase 2. Therefore, there was a problem of attrition, which may have affected the results. No imputation methods have been used to fill the missing values. Nevertheless, this study has shown that the addition of citicoline to patching therapy can significantly improve the visual acuity in amblyopic patients.

References

1. Attebo K, Mitchell P, Cumming R, Smith W, Jolly N, Sparkes R. Prevalence and causes of amblyopia in an adult population. Ophthalmology 1998;105:154-9.
2. Pediatric Eye Disease Investigator Group. A randomized trial of atropine vs patching for treatment of moderate amblyopia in children. Arch Ophthalmol2002;120:268-78.
3. Neumann E, Friedman Z, Abel-Peleg B. Prevention of strabismic amblyopia of early onset with special reference to the optimal age for screening. J PediatrOphthalmol Strabismus1987;24:106-10.
4. Scott WE, Dickey CF. Stability of visual acuity in amblyopic patients after visual maturity. Graefes Arch ClinExpOphthalmol 1988;226:154-7.
5. Patwardhan NA. Is age relevant for the success of treatment of anisometropic amblyopia? Indian J Ophthalmol 2007;55:469-70.
6. Quah BL, Tay MT, Chew SJ, Lee LK. A study of amblyopia in 18-19 year old males. Singapore Med J 1991;32:126-9.
7. Epelbaum M, Milleret C, Buisseret P, Dufier JL. The sensitive period for strabismic amblyopia in humans. Ophthalmology 1993;100:323-7.
8. Flynn JT, Schiffman J, Feuer W, Corona A. The therapy of amblyopia: An analysis of the results of amblyopia therapy utilizing the pooled data of published studies. Trans Am OphthalmolSoc 1998;96:431-53.
9. Simons K, Preslan M. Natural history of amblyopia untreated owing to lack of compliance. Br J Ophthalmol 1999;83:582-7.
10. Assaf AA. The sensitive period: transfer of fixation after occlusion for strabismic amblyopia. Br J Ophthalmol 1982;66:64-70.
11. Kupfer C. Treatment of amblyopia exanopsia in adults; a preliminary report of seven cases. Am J Ophthalmol 1957;43:918-22.
12. Brown MH, Edelman PM. Conventional occlusion in the older amblyope. Am Orthopt J 1976;26:34-6.
13. Sen DK. Results of treatment in amblyopia associated with unilateral high myopia without strabismus. Br J Ophthalmol 1984;68:681-5.
14. Oliver M, Neumann E, Chaimovitch Y, Gotesman N, Shimshoni M. Compliance and results of treatment for amblyopia in children more than 8 years old. Am J Ophthalmol1986;102:340-5.
15. Wick B, Wingard M, Cotter S, Scheiman M. Anisometropic amblyopia: Is the patient ever too old to treat? Optom Vis Sci 1992;69:866-78.
16. Noda S, Hayasaka S, Setogawa T. Occlusion therapy of Japanese children with anisometropic amblyopia without strabismus. Ann Ophthalmol 1993;25:145-7.
17. Tsubota K, Yamada M. Treatment of amblyopia by extended-wear occlusion soft contact lenses. Ophthalmologica 1994;208:214-5.
18. Woodruff G, Hiscox F, Thompson JR, Smith LK. Factors affecting the outcome of children treated for amblyopia. Eye (Lond) 1994;8:627-31.
19. Simmers AJ, Gray LS. Improvement of visual function in an adult amblyope. Optom Vis Sci 1999;76:82-7.
20. Mintz-Hittner HA, Fernandez KM. Successful amblyopia therapy initiated after age 7 years: Compliance cures. Arch Ophthalmol 2000;118:1535-1.
21. Pediatric Eye Disease Investigator Group. A prospective, pilot study of treatment of amblyopia in children 10 to<18 years old. Am J Ophthalmol 2004;137:581-3.
22. Mohan K, Saroha V, Sharma A. Successful occlusion therapy for amblyopia in 11- to 15-year-old children. J PediatrOphthalmol Strabismus 2004;41:89-95.
23. Park KH, Hwang JM, Ahn JK. Efficacy of amblyopia therapy initiated after 9 years of age. Eye (Lond) 2004;18:571-4.
24. Magoon EH, Garuda S. Visual acuity plasticity in amblyopes between age 10 and 14. In: Scott A, editor. Proceedings of the Jampolsky Festschrift. San Francisco, Calif: Smith-Kettlewell Eye Research Institute; 2000.
25. Campos EC, Frenisa M. Medical treatment of amblyopia: Present

state and perspectives. Strabismus 2006;14:71-3.

26. Chatzistefanou KI, Mills MD. The role of drug treatment in children with strabismus and amblyopia.Paediatr Drugs 2000;2:91-100.
27. Secades JJ, Frontera G. CDP-choline: Pharmacological and clinical review. Methods Find ExpClinPharmacol 1995;17 Suppl B: S1-54.
28. Rejdak R, Toczołowski J, Solski J, Duma D, Grieb P. Citicoline treatment increases retinal dopamine content in rabbits. Ophthalmic Res 2002;34:146-9.
29. Campos EC, Schiavi C, Benedetti P, Bolzani R, Porciatti V. Effect of citicoline on visual acuity in amblyopia: Preliminary results. Graefe's Arch ClinExpOphthalmol 1995;233:307-12.
30. Fresina M, Dickmann A, Salerni A, De Gregorio F, Campos EC. Effect of oral CDP-choline on visual function in young amblyopic patients. Graefes Arch ClinExpOphthalmol2008;246:143-50.
31. Stewart CE, Moseley MJ, Fielder AR. Defining and measuring treatment outcome in unilateral amblyopia. Br J Ophthalmol 2003;87:1229-31.
32. D'Orlando KJ, Sandage BW. Citicoline (CDP-choline): Mechanisms of action and effects in ischemic brain injury. Neurol Res 1995;17:281-4.
33. Adibhatla RM, Hatcher JF, Dempsey RJ. Citicoline: Neuroprotectivemechanisms in cerebral ischemia. J Neurochem 2002;80:12-23.
34. Rema V, Bali KK, Ramachandra R, Chugh M, Darokhan Z, Chaudhary R. Cytidine-5-diphosphocholine supplement in early life induces stable increase in dendritic complexity of neurons in the somatosensory cortex of adult rats. Neuroscience 2008;155:556-64.
35. Porciatti V, Schiavi C, Benedetti P, Baldi A, Campos EC. Cytidine-5'-diphosphocholine improves visual acuity, contrast sensitivity and visually-evoked potentials of amblyopic subjects. CurrEye Res 1998;17:141-8.
36. Ghosh S, Ghosh RK. Amblyopic management in older age group. A ray of hope. Paper presented in 69th All India Ophthalmic Conference Proceedings, Ahmedabad 2011. (Internet). Available from: http://aioseducation.org/PDF/pps/awfp/awfp10.pdf. [Accesed on 1 Jun 2013].

Cite this article as: Pawar PV, Mumbare SS, Patil MS, Ramakrishnan S. Effectiveness of the addition of citicoline to patching in the treatment of amblyopia around visual maturity: A randomized controlled trial. Indian J Ophthalmol 2014;62:124-9.

Source of Support: Nil. **Conflict of Interest:** None declared.