Efficiency of the occlusion therapy with and without levodopa-carbidopa in amblyopic children- A tertiary care centre experience

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Abstract:

Objectives: To assess the role, efficacy and tolerability of levodopa-carbidopa in the management of small and older children with different types of amblyopia.

Methodology: Prospective randomised placebo controlled clinical study, in which 50 amblyopic patients between 5 and 20 years of age with visual acuity (V/A) < 20/40 were included, was carried on. After having attained the best possible refractive correction, patients were randomly divided into 2 groups. They were prescribed levodopa-carbidopa (10:1) (4-6mg/kg/day in 2-3 divided doses) or placebo, plus full-time occlusion of the sound eye, for a period of three months. Assessment of improvement in V/A, compliance and tolerance was done at follow up visits. Data was analyzed using computer software Ms-Excel and Epi-Info Version 6.0. The statistical significance was assessed by Chi-Square/Fisher's Exact Test.

Results: Visual acuity for the amblyopic eye improved significantly in both groups but there was significant improvement in group1 than group 2 (P = 0.0001). In a subgroup of patients older than 12 years, levodopa group showed statistically significant improvement in baseline V/A (P = 0.0001). In patients with severe amblyopia, each group showed significant improvement in baseline V/A ($p < 0.05$), but was significantly more in group1 (P = 0.0001). Compliance rates were similar among the groups and levodopa-carbidopa at a dose range of 4-6 mg/kg/day was well tolerated.

Conclusion: Levodopa-carbidopa can be used as an adjunct to conventional occlusion therapy in amblyopia particularly in older children and severe cases of amblyopia, and it is well tolerated.

Keywords: Amblyopia, Levodopa-carbidopa, Occlusion therapy.

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Introduction

Amblyopia affects approximately 2% - 2.5% of the general population [1] and it is the most frequent cause of unilateral visual impairment in childhood and school aged children. [2] Full time occlusion of the sound eye has been the most effective therapy of the amblyopia. [1, 3, 4, 50] It prevents the fixating eye from taking part in the act of vision, so that the patient is forced to use his amblyopic eye. There have been reports that part-time occlusion is as effective as full-time occlusion. [6] In a randomized trial, the Pediatric Eye Disease Investigator Group have compared full-time, or all but one hour per day, to six hours of patching per day in children with amblyopia and have found that both treatment protocols produced similar improvements in vision. [7] However, many older children and teenagers with amblyopia fail to achieve near normal visual acuity. Attempts have been made to treat amblyopia pharmacologically. Levodopa administration results in modest degree of improvement of visual acuity (2.7 lines) and contrast sensitivity (72%), [8] in older children and adolescents. [9] Even some studies concluded that a placebo controlled trial is necessary to determine whether levodopa can successfully augment occlusion therapy in the treatment of amblyopia. [10] The aim of this study was to assess the role, efficacy and tolerability of levodopa-carbidopa along with occlusion in the management of children with different types of amblyopia.

Materials and methods:

This study was in accordance with the ethical standards of Declaration of Helsinki and was approved by the Ethical committee of the institution. A written informed consent was taken from all the participants. Fifty cases that attended our institution were studied over a period of one year from November 2011 to October 2012. Patients between 5 and 20 years of age of either sex with different types of amblyopia (Anisometropic, Strabismic, Ametropic and Mixed anisometropic + strabismic), with best corrected visual acuity (BCVA) in the amblopic eye <20/40 were included in the study. Cases having any ocular cause for reduced visual acuity visible on examination, history of narrow-angle glaucoma, paralytic or restrictive strabismus, with history of dystonic reactions were excluded. All patients included were examined in our squint clinic after taking a detailed history regarding diminution of vision and strabismus. Clinical examination included measurement of body weight (kg), visual acuity of each eye by snellen's test-type, without and with glasses (if any), recording of the head posture, ocular movements of each eye, measurement of angle of deviation by Prism bar cover test (PBCT) for both near and distance(if any), Cycloplegic refraction using cyclopentolate hydrochloride 1% eye drops (Pentolate, Sunways (India) Private Limited, Mumbai, Maharashtra, India) / Atropine sulphate 1% eye ointment (Atrosulph Eye, Entod Pharmaceuticals Ltd, Mumbai, Maharashtra, India), intraocular pressure, dilated fundus examination to rule out a cause for reduced visual acuity other than amblyopia.

After having attained the best possible refractive correction, the participants were randomized into one of the two groups. Group I included 25 cases and received occlusion therapy plus medical therapy in the form of Levodopa-carbidopa. Group II included 25 cases and received conventional occlusion therapy plus placebo in the form of Vitamin B-Complex (Polybion, Cradel, Merck Limited, Goa, India). Occlusion was 8-hours to all waking hours/day in the sound eye for 6 days a week and 1day for amblyopic eye in each group. Levodopa-carbidopa 100/10 combination (ratio 10:1) tablets (Syndopa, Sun Pharmaceutical limited, Inc, sikkim, India) were administered orally in a dose ranging from 4.1 to 6.6 mg/kg/day in 2-3 divided doses (1-3 tablets per day). The dose was adjusted as per the weight of the patients [Table 1]. Vitamin B-complex tablets were also administered orally as 1 tablet daily. The treatment regimen was given for 3 months.

All patients were prescribed with a time schedule to take the drugs and record of any potential adverse effect. Patients were followed in the squint clinic on 4^{th}, 8^{th}, and 12^{th} week. Assessment was done in terms of improvement in V/A using snellen's test-type, ocular alignment at distance and near using PBCT, evaluation of the compliance and adverse effects (if any). The BCVA thus recorded was converted to a logarithm of the minimal angle of resolution (logMAR) equivalent for analysis purposes. Each patient was contacted by phone calls at 1^{st}, 3^{rd}, 6^{th}, 10^{th} week and was questioned for occurrence of any adverse effect, reminder to continue medications and for proper occlusion.

Patient and parental interviews were used to assess the compliance to occlusion by eye patches. Patients wearing the patches for eight or more waking hours/day were considered compliant.

The descriptive statistics were calculated for case characteristics. The data was analyzed with the help of computer software Ms-Excel and Epi-Info Version 6.0.The outcome was reported as percentages and its statistical significance was assessed by Chi-Square / Fisher's Exact Test. *P*-value of < 0.05 was considered as statistically significant. All *P*-values reported were two tailed.

Results:

The baseline characteristics of the patients enrolled were summarized in [Table 2]. There was insignificant difference with regard to number of patients, age, gender, laterality and severity of amblyopia between the two groups.

After comparing best corrected visual acuity (BCVA) as mean logarithm of Minimum Angle of Resolution ± Standard Deviation (mean logMAR ± SD) (and its snellens equivalent), both for dominant and amblyopic eyes, of the patients in the two study groups at the baseline, 1st, 2nd and 3rd follow up (FU) visits, following points were revealed as summarized in [table 3]. The baseline BCVA as mean logMAR ± SD and its snellens equivalent for dominant eye as well as amblyopic eye in both the groups was similar and there was insignificant difference between the two groups for each eye (*P* = 0.950 and 0.113 respectively) [Table 3].

For the amblyopic eye, there was insignificant difference in mean logMAR at baseline between the two groups but there was a statistically significant difference between the two groups at all the three FU visits (*P* = 0.009, *P* = 0.0001 and *P* = 0.0001 respectively) [Table 3]. For the dominant eye, the mean logMAR ± SD (and its snellen equivalent) shows insignificant difference between the two groups at all the three FU visits (*P* = 0.55, *P*= 0.355 and *P* = 0.84 respectively) [Table 3].

There was a statistically significant improvement in V/A for the amblyopic eye both in group 1 {from 0.728 ± 0.27 (6/30) as pre-treatment mean logMAR to 0.106 ± 0.13 (6/7.5) at final visit (*P* = 0.0001)} and group 2 {from 0.606 ± 0.26 (6/24) to 0.394 ± 0.25 (6/15) (*P* = 0.001)} [Table 4 & Figure 1] while the difference in improvement between the two study groups at the end of treatment regimen was statistically significant (*P*= 0.0001) as seen in [Table 3]. Noticeably, there was significantly improvement in V/A in group1 than in group 2.

In comparing the improvement in mean logMAR ± SD (and its snellens equivalent) for amblyopic eyes among the subgroup of patients older than 12 years of age, we observed a statistically significant improvement (*P* = 0.0001) from 0.845 ± 0.30 (6/38 equivalent) at baseline to 0.164 ± 0.11 (6/9 equivalent) at final FU visit in the group 1 patients [Table 5]. On the other hand, the improvement in mean logMAR ± SD (snellens equivalent) from 0.733 ± 0.30 (6/30) to 0.667 ± 0.32 (6/24) among the older patients in group 2 was statistically insignificant (p = 0.17) [Table 5 & Figure 2].

In the subgroup analysis of patients with severe amblyopia (mean logMAR > 0.5 or V/A < 6/18), there was highly significant improvement in mean logMAR ± SD (and its snellens equivalent) for amblyopic eye from 0.839 ± 0.23(6/38) at baseline to 0.114 ± 0.11(6/7.5) at final visit in group 1 (*P*=0.0001) [Table 6]. Group 2 also showed a significant improvement from 0.851 ± 0.18 (6/38) to 0.618 ± 0.21 (6/24) (*P* = 0.001) [Table 6]. In line, the difference in improvement of V/A for amblyopic eyes (as mean logMAR) between the two study groups in this subgroup of severe amblyopia was statistically significant (*P* = 0.0001) as shown in [Table 7]. The most common complaint of the patients of both the study groups was local itching and rash (by 6/50 patients) due to the patch applied to cover the sound eye. Nausea was reported by 2/25 patients (4%) from group 1. Other side effects were mild like headache, giddiness (1 patient each). None of the complaints were long lasting and both the regimens were well tolerated as none of the complaints were responsible for any non-compliance. Compliance rates were numerically better in the group receiving levodopa along with occlusion. But the difference between the two groups was statistically insignificant using Yates' corrected χ^2 (χ^2 = 0.30 and *P* = 0.60). Compliance with drug ingestion (levodopa/carbidopa in group 1 and placebo in group 2) was similar in both the groups.

Table 1. Dose adjustment as per weight

Dose adjustment according to weight of the patients		
Weight (kg)	**Syndopa 110 mg (tablets/day)**	**Levodopa Dose (mg/kg)**
15-20	1 tablet	6.66 - 5.00
21-24	1 tablet	4.70 - 4.10
25 - 30	1.5 tablets	6.00 - 5.00
31 - 40	2 tablets	6.45 - 5.00
41 - 50	2.5 tablets	6.09 - 5.00
51 - 60	3 tablets	5.88 - 5.00

Table 2. Baseline characteristics of the two groups

Baseline characteristics of the two study groups and their comparison				
	Group 1	**Group2**	**χ^2**	**p value**
Age (years):				
< 8	9(36%)	7(28%)	1.34	0.51
08- 12	8(32%)	12(48%)		
>12	8(32%)	6(24%)		
Gender:				
Male	14(56%)	13(52%)	0.08	0.77
Female	11(44%)	12(48%)		
Severity:			"yates corrected"	
Moderate (≤0.5 log MAR)	7(28%)	14(56%)	2.96	0.08
Severe (>0.5 log MAR)	18(72%)	11(44%)		
Laterality:				
Unilateral	19(76%)	19(76%)	0	1
Bilateral	6(24%)	6(24%)		
Causes/Types:				
Strabismic	5(20%)	4(16%)	0.41	0.3
Anisometropic	12(48%)	13(52%)		
Mixed (strabismic + anisometropic)	5(20%)	4(16%)		
Ametropic	3(12%)	4(16%)		

Table 3. Comparison between the two study groups at baseline and at 1st, 2nd & 3rd FU visits

Effect of treatment on the mean logMAR in both dominant and amblyopic eyes at baseline and at 1st, 2nd & 3rd FU visits					
follow-up visit	**LogMAR**	**Group 1, Levodopa / carbidopa + occlusion, n=25, mean ± (SD)**	**Group 2, Occlusion + placebo, n=25, mean ± (SD)**	**t-test**	***P* value**
Baseline	Dominant	0.138 ± (0.216)	0.142 ± (0.186)	-0.063	0.95
	Amblyopic	0.728 ± (0.270)	0.606 ± (0.262)	1.614	0.113
1st FU visit (month 1)	Dominant	0.100 ± (0.173)	0.128 ± (0.170)	-0.592	0.557
	Amblyopic	0.338 ± (0.181)	0.503 ± (0.240)	-2.732	0.009
2nd FU visit (month 2)	Dominant	0.079 ± (0.136)	0.116 ± (0.147)	-0.935	0.355
	Amblyopic	0.210 ± (0.157)	0.430 ± (0.239)	-3.836	0.0001
3rd FU visit (month 3)	Dominant	0.049 ± (0.092)	0.108 ± (0.139)	-1.767	0.84
	Amblyopic	0.106 ± (0.135)	0.398 ± (0.254)	-5.06	0.0001

Table 4. Effect of treatment

Effect of treatment on the mean logMAR for amblyopic eyes at baseline and at final (3 month) FU visits				
logMAR	**Baseline (mean ± SD)**	**Final (3month) FU visit**	**t-test**	***P* value**
Group 1, n=25	0.728 ± 0.27	0.106 ± 0.14	11.89	0.0001
Group 2, n=25	0.606 ± 0.26	0.398 ± 0.25	6.981	0.001

Table 5. Effect of treatment in patients older than 12 years

Effect of treatment on the mean logMAR at baseline and at final FU visit for amblyopic eyes in the subgroup of patients older than 12 years in each study group				
Mean logMAR,(> 12 years)	**Baseline, (mean ± SD)**	**Final visit, (Mean ± SD)**	**t test**	***P* value**
Group 1, n=8	0.845 ± 0.30	0.164 ± 0.11	7.25	0.0001
Group 2, n=6	0.733 ± 0.30	0.667 ± 0.32	1.58	0.17

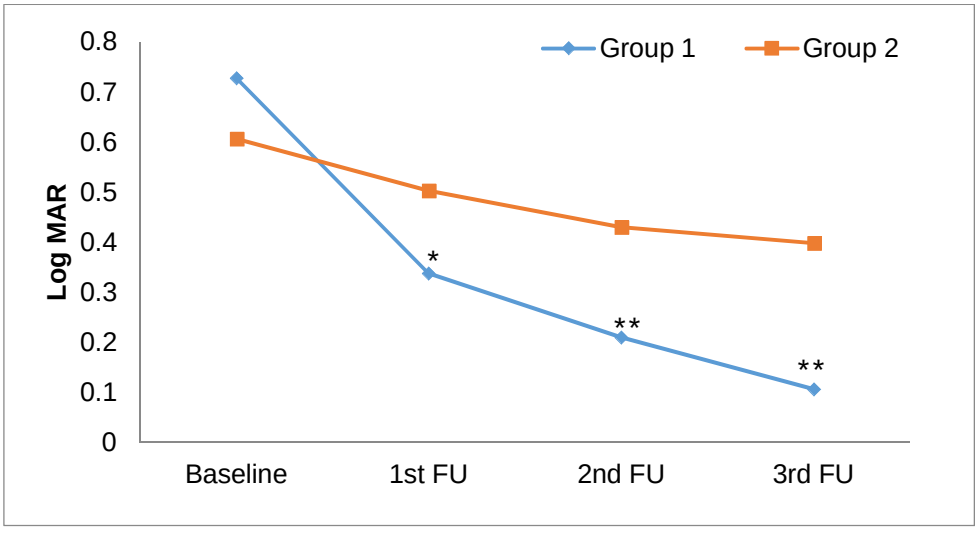
Table 6. Effect of treatment in patients with severe amblyopia

Effect of treatment on the mean logMAR for amblyopic eyes at baseline and at final (3 month) FU visit in the subgroup of patients with severe (> 0.5) amblyopia in each study group				
Mean logMAR > 0.5	**Baseline, (mean ± SD)**	**Final visit, (Mean ± SD)**	**Paired t-test**	**p value**
Group 1, n=18	0.839 ± 0.23	0.114 ± 0.11	14.52	0.0001
Group 2, n=11	0.851 ± 0.18	0.609 ± 0.23	4.32	0.001

Table 7. Difference between the two study groups regarding improvement of BCVA in patients with severe amblyopia

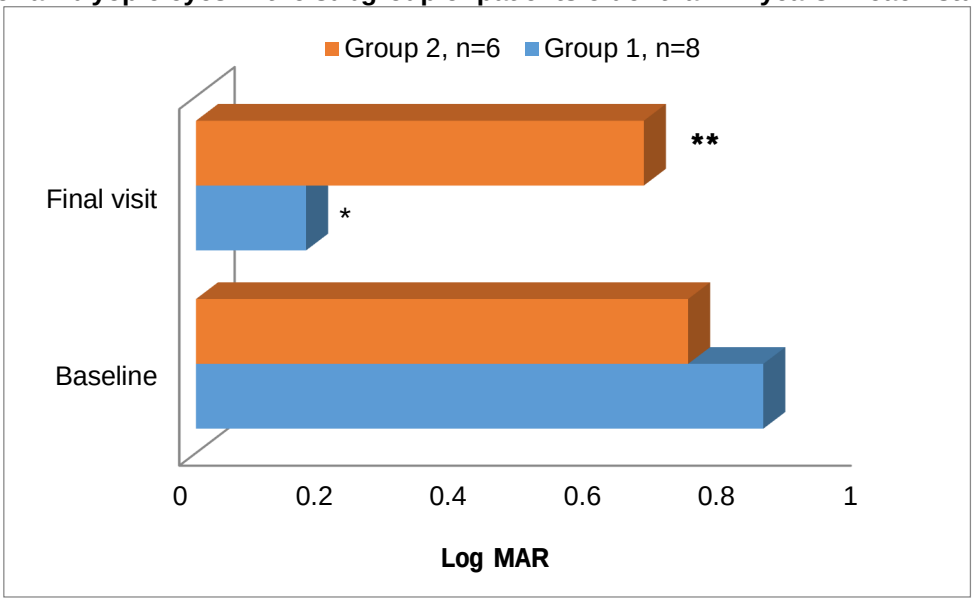
Effect of treatment on the mean logMAR for amblyopic eyes at baseline and at final (3 month) FU visits in the subgroup of patients with severe (> 0.5) amblyopia				
LogMAR	**Group 1, Levodopa/carbidopa + occlusion, n=18**	**Group 2, occlusion + placebo, n=11**	**Mann-Whitney test**	***P* value**
Baseline, (mean ± SD)	0.839 ± 0.23	0.851 ± 0.18	91	0.74
Final visit, (mean ± SD)	0.114 ± 0.11	0.609 ± 0.23	0	0.0001

Figure1. Line diagram showing Improvement for the amblyopic eyes in the two study groups regarding mean logMAR at baseline, and at 1st, 2nd and 3rd FU visits



***P-value <0.01, **P-value <0.001 (Statistically significant difference between groups)**

Figure 2. Line diagram showing Effect of treatment on the mean logMAR at baseline and at final FU visit for amblyopic eyes in the subgroup of patients older than 12 years in each study group



***P-value <0.001, **P-value >0.05**

Discussion

Occlusion therapy of the sound eye is considered as the standard treatment of amblyopia [(1)] so this study used occlusion therapy in all the cases. Visual evoked potential (VEP) abnormalities (phase-misalignment and reduced signal-to-noise ratios) associated with amblyopia improved after occlusion therapy of the sound eye. [(11)] Several studies have used levodopa as a pharmacological agent alone [(12-14)] or in combination [(15-19)] with standard occlusion therapy. These studies have used this agent for a period varying from 1 day to 7 weeks [(12, 13, 23, 24)] with doses varying from 0.5 mg/kg to 8.3mg/kg per day [(8, 10, 16, 21-23)] in different age groups. The present study used levodopa-carbidopa (ratio 10:1) in a dose range of 4.1 to 6.6 mg/kg/day for 12 weeks. The purpose of this study was to assess the role, efficacy and tolerability of this drug in addition to the occlusion therapy in the management of amblyopia in children. The baseline characteristics including demographic data, severity of amblyopia, laterality and mean baseline logMAR were insignificantly different in two groups. There was a significant improvement of mean logMAR at 1st, 2nd and 3rd / final FU visit in both the groups but showing significantly more improvement in the group using levodopa-carbidopa in addition to occlusion therapy. Similar results were reported by Leguire *et al* [(8)] who evaluated the tolerability and efficacy of levodopa/carbidopa combined with occlusion therapy for childhood amblyopia between 6-14 years of age. At the end of 3 weeks treatment regimen, there was a significant improvement in visual acuity by 2.7 lines and in mean contrast sensitivity by 72% in the amblyopic eye and the placebo group improved in visual acuity by 1.6 lines in the amblyopic eye, concluded that at an average of 0.48/0.12 mg/kg Levodopa / carbidopa, is well tolerated and, when combined with part time occlusion, is effective in improving visual function in amblyopic children. This is contrary to a report by Rashad *et al* [(23)] who observed that Mean logMAR at the three follow-up visits (months 1, 3, and 12) was similar in the occlusion group and the pharmacological enhancement group.

The present study showed an improvement in mean logMAR for amblyopic eyes among the patients >12 years of age in both the groups but was statistically significant in group 1 patients rather than group 2. These findings were different from that reported by Dadeya *et al* [(22)] who reported that levodopa improved V/A

significantly only in patients younger than 8 years. This difference may be explained by the smaller sample size and/or smaller dose of levodopa (0.5 mg/kg) and type of amblyopia (only strabismic amblyopia included) in their study than the present study. The statistical methods used included the percentage of eyes achieving at least two lines of improvement, and found them to be 100% in patients younger than 8 years and 60% in patients older than 8 years. Our study used the mean logMAR for group comparison and included all the three types of amblyopic patients.

Further, the present study showed significant improvement in V/A for amblyopic eye in a subgroup of patients with severe amblyopia (mean logMAR > 0.5 or V/A < 6/18) in both the study groups, but there was significantly more improvement of V/A in group 1 than group 2 in patients with severe amblyopia. This suggests that addition of levodopa to occlusion can lead to a better visual outcome of severe amblyopia similar to that of mild to moderate amblyopia. Mohan *et al* [18] reported that there was no correlation between baseline visual acuity and treatment effect. This can be explained by their subgroup distribution. They included the levodopa alone group and the levodopa with occlusion group. They did not include a subgroup of occlusion alone. The present study results showing more improvement of severe amblyopia in the levodopa group can be explained by better patient co-operation with levodopa-occlusion. This is supported by Pandey *et al* [21] who considered levodopa to be an important adjunct to conventional occlusion therapy because it may improve patient compliance for occlusion by improving visual acuity in the amblyopic eye.

The results of the present study can be explained by the fact that Dopamine is a neurotransmitter that does not cross blood-brain barrier and Levodopa is an intermediate in the biosynthesis of dopamine that can cross the blood–brain barrier where it is converted to dopamine. Carbidopa is a peripheral decarboxylase inhibitor that prevents peripheral breakdown of levodopa. Concomitant administration, thus, allow more levodopa to cross the blood-brain barrier. This allows reduction in the dose of levodopa required for the desired effect by about 75%. [25] These effects are explained in terms of general role of dopamine both in retina and in the central visual pathway. For the retinal mechanism of action, two reports have suggested that increased dopamine levels lead to shrinkage in the size of the receptive field, thereby improving visual acuity.[12,16] For cortical mechanism, it has been hypothesized that increased dopamine levels produce a reduction in the size of the suppression scotoma, thereby, improving visual acuity. In a single dose administration, dopamine changes the volume of cortical activation measured by functional MRI.[26,27] Both improved visual acuity and VEP amplitudes have been reported following both single dose and 1 week of levodopa administration. [12, 28]

References:

1. Von Noordon GK, Campos EC. Amblyopia. In: Von Noorden GK, Campos EC, editors. Binocular vision and ocular motility - theory and management of strabismus. 6th ed. London: Mosby Publishers; 2002. p. 246-8, 282-6.
2. Ohlsson J, Villarreal G, Sjostorm A, Cavazos H, Abrahamsson M, Sjostrand J. Visual acuity, amblyopia, and ocular pathology in 12- to 13-year-old children in Northern Mexico. J AAPOS, 2003; 7:47-53.
3. Jingyun Wang. Compliance and patching and atropine amblyopia treatments. Vision Research, 2015; 114:31-40.
4. EWH Tang, BCY Li, IYL Yeung, KKW Li. Occlusion therapy in amblyopia: an experience from Hong Kong. Hong Kong Med J, 2014; 20:32-6.
5. Tsirlin I, Colpa Linda, Goltz HC, Wong AMF. Behavioral Training as New Treatment for Adult Amblyopia: A Meta-Analysis and Systematic Review. Investigative Ophthalmology & Visual Science, 2015; 56:4061-75.
6. Singh I, Sachdev N, Brar GS, Kaushik S. Part-time occlusion therapy for amblyopia in older children. Indian J Ophthalmol, 2008; 56:459-63.
7. Holmes JM, Kraker RT, Beck RW, Birch EE, Cotter SA, Everett DF, et al. A randomized trial of prescribed patching regimens for treatment of severe amblyopia in children. Ophthalmology, 2003; 110:2075-87.
8. Leguire LE, Walson PD, Rogers GL, Bermer DL, McGregor ML. Longitudinal study of levodopa/carbidopa for childhood

amblyopia. J Pediatr Ophthalmol Strabismus, 1993; 30:354-60.
9. 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.
10. Repka MX, Kraker TR, Beck RW, Atkinson SC, Bacal DA, Bremer DL, et al. A pilot study of levodopa dosage as treatment for residual amblyopia in children 8 to <18 Years old. Arch Ophthalmol, 2010; 128:1215-7.
11. Kelly JP, Tarczy-Hornoch K, Herlihy E, Weiss AH. Occlusion therapy improves phase-alignment of the cortical response in amblyopia. Vision Res, 2015; 114:142-50.
12. Gottlob I, Charlier J, Reinecke RD.Visual acuities and scotomas after one week levodopa administration in human amblyopia. Invest Ophthalmol Vis Sci, 1992; 33:2722-8.
13. Gottlob I, Wizov SS, Reinecke RD. Visual acuities and scotomas after 3 weeks' levodopa administration in adult amblyopia. Graefes Arch Clin Exp Ophthalmol, 1995; 233:407-13.
14. Wu X, Liu S, Xu H, Huang P, Xu H, Ming X, et al. A preliminary report of the effect of levodopa and carbidopa for childhood amblyopia. Yan Ke Xue Bao, 1998; 14:238-41.
15. Leguire LE, Rogers GL, Walson PD, Bermer DL, McGregor ML. Occlusion and levodopa-carbidopa treatment for childhood amblyopia. J AAPOS, 1998; 2:257-64.
16. LeguireLE, Walson PD, Rogers GL, Bermer DL, McGergor ML. Levodopa/carbidopa treatment for amblyopia in older children. J Pediatr Ophthalmol Strabismus, 1995; 32:143-51.
17. Procianoy E, Fuchs FD, Procianoy L, Procianoy F. The effect of increasing doses of levodopa on children with strabismic amblyopia. J AAPOS, 1999; 3:337-40.
18. Mohan K, Dhankar V, Sharma A. Visual acuities after levodopa administration in amblyopia. J Pediatr Ophthalmol Strabismus, 2001; 38:62-7.
19. Bhartiya P, Sharma P, Biswas NR, Tandon R, Khokhar SK. Levodopa-carbidopa with occlusion in older children with amblyopia. J AAPOS, 2002; 6:368-72.
20. Leguire LE, Komaromy KL, Nairus TM, Rogers GL. Long-term follow-up of L-dopa treatment in children with amblyopia. J Pediatr Ophthalmol Strabismus, 2002; 39:326-30.
21. Pandey PK, Chaudhuri Z, Kumar M, Satyabala K, Sharma P. Effect of levodopa and carbidopa in human amblyopia. J Pediatr Ophthalmol Strabismus, 2002; 39:81-9.
22. Dadeya S, Vats P, Malik KP. Levodopa/carbidopa in the treatment of amblyopia. J Pediatr Ophthalmol Strabismus, 2009; 46:87-90.
23. Rashad MA. Pharmacological enhancement of treatment for amblyopia. Clin Ophthalmol, 2012; 6:409-16.
24. Leguire LE, Rogers GL, Bremer DL, Walson PD, McGregor ML. Levodopa/carbidopa for childhood amblyopia. Invest Ophthalmol Vis Sci, 1993; 34:3090-5.
25. Yeh KC, August TF, Bush DF, Lasseter KC, Musson DG, Schwartz S, et al. Pharmacokinetics and bioavailability of Sinemet CR: a summary of human studies. Neurology, 1989; 39(11 Suppl 2):25-38.
26. Algaze A, Leguire LE, Roberts C, Ibinson JW, Lewis JR, Rogers G. The effects of L-dopa on the functional magnetic resonance imaging response of patients with Amblyopia: A Pilot Study. J AAPOS, 2005; 9:216-23.
27. Yang CI, Yang ML, Huang JC, Wan YL, Jui-Fang Tsai R, Wai YY, et al. Functional MRI of amblyopia before and after levodopa. Neurosci Lett, 2003; 339:49-52.
28. Basmak H, Yildirim N, Erdinç O, Yurdakul S, Ozdemir G. Effect of levodopa therapy on visual evoked potentials and visual acuity in amblyopia. Ophthalmologica, 1999; 213:110-3.