Levodopa as Treatment for Adults with Amblyopia

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Levodopa is a medication used in treatment for Parkinson’s disease, which is associated with low levels of a chemical called dopamine in the brain. Levodopa is turned into dopamine in the body and therefore increases levels of this chemical. Levodopa was used as a treatment of amblyopia alone or in combination with classical treatment of occlusion. Visual acuity is improved after treatment with oral Levodopa. When used as an adjunct to the occlusion therapy, Levodopa can be associated with long-term improvement in the vision, and may have also better compliance for patching. Levodopa stimulates the brain plasticity in adult age and can be used in treatment for amblyopia. Patients have also an increase of the visual acuity after orthoptic treatment for amblyopia and when Levodopa is administered, the vision increases much more. Contrary to the classical conception, according to which amblyopia cannot be treated after 10-12 years of age and it is untreatable in adults, studies about treatment with Levodopa in amblyopic eyes, may allow the improvement of the visual acuity in adults, as well.

Keywords: Levodopa, amblyopia, adult, visual acuity

Recognizing the incomplete effectiveness of conventional amblyopia therapy, clinicians have sought alternatives. One such ancillary treatment is Levodopa, which is used to supplement dopamine deficiency in brains of adults with Parkinson’s disease and children with dopamine-responsive dystonia [1]. Although there is no evidence of a deficiency of dopamine in amblyopic brains, levodopa has been used by some clinicians for amblyopia treatment since 1995 on an investigational basis [2,3]. Since the discovery of its effectiveness in Parkinson’s treatment in the 1960’s [4], Levodopa is known more commonly as L-Dopa. In Parkinson’s treatment, this line of treatment is based on the replacement of the neurotransmitter dopamine in the Central Nervous System, a molecule that is able to cross the blood-brain barrier is required, thus the need for L-Dopa [5]. Dopamine in itself is not able to cross this barrier, but levodopa uses a transporter to reach its target [5,6].

Several reports indicate that Levodopa either alone or in combination with occlusion, can be useful to improve vision in the amblyopic eye [1,7-11] 0.5 to 2mg/kg/dose thrice a day is considered a safe and effective dose. When combined with 25% Carbidopa, conversion of Levodopa to dopamine is prevented in the peripheral circulation, which reduces the systemic side effects of levodopa. So far, occlusion amblyopia in patients treated with levodopa and occlusion therapy has not been reported. Visual acuity gained from the treatment with oral Levodopa is reported to have a high incidence of regression. However, when used as an adjunct to the occlusion therapy, levodopa can be associated with long-term improvement in the vision, and may have better compliance to patching [12]. The aim of the study was to identify the efficacy of Levodopa using in treatment for patients with amblyopic eyes, treated before with occlusion or exercises at sinoptophore.

Experimental part

Materials and methods
The study is a prospective, observational study on 5 eyes from 4 adults patients treated for different forms and degrees of amblyopia, in Second Ophthalmology Clinic from Prof. Dr. Nicolae Oblo Emergency Hospital in Iasi. The age of patients was between 28 and 47 years old. The study was approved by the Ethics Committee of Prof. Dr. Nicolae Oblo Emergency Hospital, based on the doctoral study protocol, after signing by patients the informed consent, with detailed explanations of side effects and contraindications of the drugs. All the cases were monitored in relation to surgery, stimulation of perception (by occlusion and/or exercises at sinoptophore) and Levodopa treatment. The patients had been previously treated either by surgical treatment or by alternate occlusion. These four patients have been receiving Levodopa, 2mg/kgbw for 6 weeks.

The patients underwent a complete ophthalmologic examination, consisting of the following functional explorations: slit-lamp examination of anterior pole of the eyeball (with Haag Streit BERN slit-lamp); visual acuity (Snellen optotype); objective refraction (MRK 3100 Huvitz ophthalmometer/keratometer); direct and indirect ophthalmoscopy; cover-test examination and prism examination for strabismus; orthoptic and binocular vision examination at sinoptophore. Visual acuity (VA) was determined at the beginning of the study, then after 1 month, 3 months, 6 months, 1 year, and 1 year and 6 months. The crucial element of the progress of amblyopia was the visual acuity. The values of corrected visual acuity (cc) were taken into consideration. The analysis of the visual acuity was made for each case, using the linear regression line, regression equation, and correlation coefficient R².
Results and discussions

Progress of vision

One patient had mixed amblyopia – strabismic and refractive (case 1), one patient was with deprivation amblyopia (case 2) and two cases had anisometropic amblyopia (cases 3 and 4). The progress of the visual acuity was monitored in 5 amblyopic eyes, divided into:

-1 eye with mild amblyopia (VA = 0.7) - 20%
-2 eyes with severe amblyopia (VA = 0.1 and 0.12) - 40%
-2 eyes with serious amblyopia (VA under 0.1) – 40%

The study presents 1 patient with bilateral amblyopia and 3 patients with unilateral amblyopia. We monitored the progress of the visual acuity at 1 month after treatment, 3 months, 6 months, 1 year, and 1 year and 6 months (table I).

For unilateral amblyopia (strabismic and refractive), caused by the presence of a esodeviation of 35 DP and of a compound myopic astigmatism (case 1), VA did not improve either after the surgery of strabismus combined with the optical correction, or after the occlusive treatment (1 hour/day, two times a day) or orthoptic treatments (macular stimulation). VA is in RE = 1 wc, and in LE = 0.02 cc (with correction -3 cyl -0.75/59). The binocular vision is absent. The visual acuity increases in LE to 0.04 cc after the classical treatments (one month of treatment), and after starting the treatment with Levodopa (2mg/kgbw/day for 6 weeks), the visual acuity increases to 0.06 cc (at 3 months), 0.1 cc (at 6 months), when the stage I of BV is reached, and to 0.16 cc at 1 year, respectively 0.2 cc at 18 months (fig. 1). The statistical analysis reveals an increase of VA: \( y = 0.0323x - 0.033, R^2 = 0.8571 \).

For deprivation unilateral amblyopia, caused by congenital cataract in RE (case 2), the visual acuity was phm (perceives hand movements) before the surgical intervention. After 1 month, the visual acuity increases, VA-RE= 0.05 cc (-1 sf). VA-LE= 1 wc. We proceeded to occlusive treatment and macular stimulation (at sinoptophore), and the visual acuity increases to 0.1 cc. The patient accepted to follow the medication with Levodopa 2mg/kgbw/day, for 6 weeks. At 6 months: VA-RE increases to 0.16 cc, and then to 0.2 cc (at 1 year), respectively to 0.3 cc (at 18 months). The statistical analysis reveals an increase of the visual acuity: \( y = 0.0486x - 0.02, R^2 = 0.9175 \) (fig. 2).

For bilateral anisometropic amblyopia, there is a significant increase of visual acuity after treatment with Levodopa (case 3). The visual acuity increases in RE (which suffers from severe amblyopia caused by a high hyperopia, of +6 D) from 0.1 cc (before the treatment) to 0.2 cc. After the classical treatments (occlusions and macular stimulation) VA increased to 0.3 cc - after one year of Levodopa medication (fig. 3). Statistical analysis reveals a significant increase of the visual acuity: \( y = 0.0454x + 0.0527, R^2 = 0.9483 \).

For severe unilateral anisometropic amblyopia, there is an increase of the visual acuity after Levodopa treatment (case 4). The visual acuity increases in the amblyopic eye, LE (which suffers only from moderate hyperopia, of +3.5 D) from 0.12 cc (before treatment) to 0.16 cc after the classical treatments, and to 0.3 cc (at 1 year and 6 months), after medication (fig. 4). Statistical analysis reveals a significant increase of the visual acuity: \( y = 0.038x + 0.0587, R^2 = 0.9542 \).

Calculating a mean of the multiplication coefficient of initial VA, we see that the multiplication mean of VA increased on average 4.39 times in cases who received Levodopa, almost two times higher, in comparison with
the average increase of 2.29 times a VA for the cases who did not receive Levodopa.

The brain plasticity is active limited at cellular and molecular level. Reducing of plasticity is produced by structure (inhibition-mielin), perineural and functional (excitation/inhibition equilibrium in local neuronal channels [13,14]. Many children treated with patching for amblyopia have an incomplete effectiveness of conventional amblyopia therapy. One such ancillary treatment is oral levodopa, which is used to supplement dopamine deficiency in brains of adults with Parkinson’s disease and children with dopamine-responsive dystonia [2,3]. Levodopa improves visual acuity and neuroplasticity of the brain in treatment of amblyopic eyes, both for children and adults patients [15-19]. Levodopa-Carbidopa is used for treatment of amblyopia, 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) [20].

Several studies have used levodopa as a pharmacological agent alone or in combination with standard occlusion therapy. These studies have used this agent for a period varying from 1 day to 7 weeks [8], with doses varying from 0.5 mg/kg to 8.3mg/kg per day [21, 22]. In our study, Levodopa was used 2mg/kgbw, for 6 weeks.

Other study underline that there is a lack of efficacy for levodopa in children 7 to 12 years of age with residual amblyopia from anisometropia, strabismus, or both, after a period of treatment with patching [23]. Our study underlines that after macular stimulation by orthoptic exercises and levodopa treatment visual acuity was improved. We observed an increasing of visual acuity after 3 months of levodopa treatment, and the visual improving remain long time after treatment. Levodopa treatment is a possible treatment for increasing of quality of vision and in the same time of quality of life. Young patients need more possibilities of treatment for socio-professional integration [24].

This study is limited by the small sample size, and the fact that it does not include a follow up examination of the patients more than 18 months. Another limitation is missing of placebo group for comparation. The difficulty for study was patient’s acceptance for levodopa treatment, and impossibility of observation in ambulatory.

Conclusions

Contrary to the classical conception, according to which amblyopia cannot be treated after 10-12 years of age and it is untreatable in adults, the results of the study show that the treatment with Levodopa, which stimulates the brain plasticity in adult age, may allow the improvement of the visual acuity in adults, as well. At amblyopic eye cortical connections are in stand-by, and can be stimulated. Treatment with Levodopa can relocked the blocked connection for amblyopic eye and is recommended for adult patients with amblyopia.

References


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