

Visual evoked potentials (VEP) and visual acuity improvement after cytidine 52 - diphosphocholine (CDP-Choline) therapy in amblyopic patient

Melhora do potencial evocado visual (PEV) e da acuidade visual em paciente amblíope tratado com citidina difosfato colina

Regina Halfeld Furtado de Mendonça ¹, Eliana Lucia Ferreira ¹

ABSTRACT

Citicoline may be used in many neurological disorders. Combined treatment of citicoline with patching in amblyopia has previously been researched. The purpose of this paper is to illustrate the effect of citicoline in non-patching amblyopic patient. A 11-year-old amblyopic boy underwent complete ophthalmological examinations, including VEP with flash and pattern stimulus. Two averages of 100 sweep were performed for flash stimulus. Pattern reversal stimulus obtained with high contrast was performed with 60', 30' and 15' checks stimuli. The VEP was repeated 90 days later after a therapy with citicoline and vitamin and the results compared with the responses of the previous recording session. The visual acuity (VA) was 0,7 in the RE and 1,0 in the LE. The VEP pattern amplitude was normal in both eyes. Delayed in latency was detected for all spatial frequency stimulus (SFS) in the RE. Delay in latency was detected only for high SFS in the LE. After the treatment, the VA was 1,0 in both eyes. The latency was normalized with low SFS on the RE and with high SFS on the LE. The flash VEP was normal before and after the therapy. In conclusion, the citicoline demonstrated that it was effective in the treatment of amblyopic eye without patching. The VA and the VEP latency improvement demonstrated that the citicoline enhance the transmission of the electric impulse from retina to visual cortex. Further research is required to understand the immediate and long-term effect of coline treatment in amblyopic patients.

Keywords: Amblyopia; Cytidine diphosphate choline; Evoked potentials, visual; Case reports

RESUMO

A citicolina pode ser utilizada em vários problemas neurológicos. O tratamento combinado de citicolina e oclusão na ambliopia já foi previamente relatado. O objetivo deste estudo é ilustrar o efeito da citicolina em paciente amblíope sem o tratamento oclusivo. Um menino de 11 anos de idade foi submetido a um exame oftalmológico completo incluindo PEV do tipo flash e do tipo padrão reverso. Para o PEV tipo flash, foram analisadas duas médias de 100 estímulos cada uma. Para o PEV do tipo padrão reverso, foram utilizados estímulos de alto contraste de 60', 30' e 15'. O PEV foi repetido 90 dias depois do tratamento com citicolina e vitaminas e os resultados comparados com os exames antes do tratamento. A acuidade visual era de 0,7 no olho direito e 1,0 no olho esquerdo. A amplitude do PEV era normal em ambos os olhos. Era presente um aumento da latência a todas as frequências espaciais de estimulação (FEE) no olho direito e somente à alta FEE no olho esquerdo. Após o tratamento, a acuidade visual era de 1,0 em ambos os olhos. A latência se normalizou à baixa FSS no olho direito e à alta FSS no olho esquerdo. O PEV tipo flash era normal antes e depois do tratamento. Em conclusão, a citicolina demonstrou ser eficaz no tratamento de olhos amblíopes sem oclusão. A melhora da acuidade visual e da latência do PEV demonstraram que a citicolina restaura a transmissão elétrica do impulso da retina ao cortex visual. Pesquisas futuras são necessárias para entender o efeito imediato e a longo prazo da citicolina no tratamento de pacientes amblíopes.

Descritores: Ambliopia; Citidina difosfato colina; Potenciais evocados visuais; Relatos de casos

¹ Universidade Federal de Juiz de Fora (UFJF) - Juiz de Fora (MG) Brasil.

Study carried out at Universidade Federal de Juiz de Fora (UFJF) - Juiz de Fora (MG) Brasil.

Interest conflict - None

Recebido para publicação em 20/10/2011 - Aceito para publicação em 2/3/2012

INTRODUCTION

Amblyopia therapy is one of the most cost-effective methods of restoring vision, and treatment should be undertaken aggressively⁽¹⁾. It is a common condition, which can affect up to 5% of the general population⁽²⁾. Amblyopic patients, or their parents, often want to know the potential for success before committing to treatment⁽³⁾.

Amblyopia is a developmental disorder that generally results in decreased visual acuity and is associated with strabismus, anisometropia, or form deprivation⁽³⁾. New vision screening technologies that allow early detection of anisometropia provide ophthalmologists with an opportunity to provide early intervention, perhaps retarding, or even preventing, the development of amblyopia⁽⁴⁾.

Pattern VEPs have been used to identify amblyopes and monitor their acuity and progress during amblyopia therapy⁽³⁾. From a prognostic point of view, the study of the VEP and especially the latency appears important⁽⁵⁾ in amblyopic patients. It must be emphasized that the degree of improvement of the VA in most of the cases depends on the severity of the delay of the VEP latency before treatment⁽⁵⁾.

We know that the treatment of amblyopia should start as soon as possible but in many cases the patient presents too late for the usual therapy to be effective. A major goal in adult plasticity has been to reinstate juvenile-like plasticity in the adult visual cortex using pharmacologic and genetic interventions, with the expectation that this will guide clinical therapies for amblyopia⁽⁶⁾. Despite the discovery of multiple manipulations that can successfully enhance adult plasticity, none of these have been translated into therapies for amblyopia⁽⁶⁾.

More studies are necessary to standardize treatment guidelines in cases of resistant amblyopia. Treatment with atropine drops or ointment, instilled in the nonamblyopic eye, is not always effective. Coline has been demonstrated to improve vision in amblyopic eye but the therapeutic success in the clinical management of amblyopia remains unproven⁽⁷⁾. Some authors pointed out that coline combined with patching contributes to obtaining more stable effects than patching alone⁽⁸⁾. It is important to emphasize that poor compliance with treatment protocols has a significant risk factor for treatment failure⁽⁹⁾.

Cytidine 5'-diphosphocholine, CDP-choline, or citicoline may be used in many neurological disorders such as cerebral vascular disease, head trauma (HT), cognitive disorders, neurological deficits, so-called post-concussional syndrome, acute ischemic cerebral vascular disease, treatment of senile cognitive impairment, degenerative diseases (e.g., Alzheimer disease)⁽¹⁰⁾. Citicoline has also been shown to be effective in Parkinson disease⁽¹⁰⁾, as well as in amblyopia and glaucoma^(10,11).

As amblyopic treatment should start as soon as possible usually in earlier childhood, we need a standardized treatment guideline proving the efficacy and safety of the therapy. In this study, we illustrate how visual acuity and visual evoked potentials improve in an amblyopic patient treated with citicoline.

CASE REPORT

An 11-year-old amblyopic boy underwent complete ophthalmological examinations, including full-field electroretinography (ERG), pattern electroretinography (PERG) and visually evoked cortical potentials with flash and pattern stimulus. Surface active electrodes were used for recording PERG. Contact lens electrodes (ERG-jet®) were used for ERG using the ISCEV standard (rod response, combined rod-cone response, oscillatory potentials, cone response and 30

Hz flicker). Pattern and flash VEPs were recorded using techniques based on those previously described using the "Biomedica Mangoni®" system⁽¹²⁾.

For the flash VEP, the stimuli were presented in a dimly illuminated room and two averages of 100 sweeps were recorded. The stimulus strength was +0.25 U.L.ott with a frequency of 1 Hz with a background of 20 cd/m².

For the pattern VEP, the patient was seated 1 meter from a 17-inch monitor (19.5°). Mean luminance of the display was 80 cd/m². Check contrast was 90%. The patient underwent a clinical protocol with three check sizes: large checks sizes of 60' (low spatial frequency stimulus), medium checks sizes of 30' (medium spatial frequency stimulus) and small checks sizes of 15' (high spatial frequency stimulus).

The responses were amplified 50,000 times with a ½ amplitude bandpass of 1-50 Hz with a 50 Hz notch filter in place. Two averages of 100 epochs of the responses were recorded monocularly from the amblyopic and sound eye respectively for each of the three check sizes. Fixation was monitored by an observer and data collected only when the patient was looking at the pattern.

Pattern and flash VEPs were repeated 90 days later after a therapy with citicoline (163 mg) and vitamin (vitamin A 264 mcg - vitamin E 3.3 mg - vitamin C 20 mg and vitamin B6 0.4 mg) and the results compared with the responses of the previous recording session. The parents had provided written consent.

RESULTS

Before the treatment the best corrected visual acuity was 0,7 in the right eye (with -9.00 dioptre of spherical refractive error and -4.50 dioptre of cylindrical refractive error) and 1,0 in the left eye (with -7.75 dioptre of spherical refractive error and -2.00 dioptre of cylindrical refractive error). In the ocular motility examination the patient had exophoria and an intermittent exotropia. The full-field ERG and the PERG were normal. The VEP pattern amplitude was normal in both eyes. Delay in latency was detected for all SFS in the right eye. Delay in latency was detected only for high SFS in the left eye. After the treatment, the best corrected visual acuity was 1,0 in both eyes. The latency was normalized for low SFS on the RE and for high SFS on the LE (Figure 1).

So the VEP pattern became completely normal in the sound eye. The flash VEP was normal before and after the therapy.

DISCUSSION

The accepted treatment for anisometropic amblyopia consists first of correcting the refractive error. However if VA has not improved, actively treating amblyopia is necessary⁽⁴⁾. Treatment options include atropine penalization, patching or contact lenses⁽¹⁾. Combined treatment with atropine and optical therapy is also possible⁽¹³⁾.

By age 4, when most children undergo traditional screening, amblyopia has usually already developed⁽⁴⁾. Although the prevalence of anisometropic amblyopia does not increase after age 3, the depth of amblyopia does⁽⁴⁾. Studies have demonstrated that anisometropic amblyopic patients older than 6 years have a significant relative risk of treatment failure⁽⁹⁾. Considering the age (an 11-year-old boy) and the anisometropic amblyopia (spherical refractive error difference: -1,25 dioptre and cylindrical refractive error difference of -2,50) of the present case, we can consider that the treatment with coline and vitamin was really very effective, confirming that the correlation between age and treatment response is unclear⁽⁴⁾.

Amblyopia may be considered a consequence of suppression in cases where strabismus is not alternated (5). In the present case the patient had exophoria and an intermittent exotropia (the left eye was the dominant eye).

In the present study, the VEP pattern amplitudes were normal and latencies delayed for all SFS in the amblyopic eye before treatment. Contrasting with our findings studies have demonstrated that the amblyopic eye has reduced amplitudes of the VEP with normal or mildly delayed latencies (14).

Anisometropic amblyopia is associated primarily with abnormal parvocellular rather than magnocellular visual system function (15). In the present study, the flash VEP was normal before and after therapy. In fact the magnocellular layers may be relatively undamaged in amblyopia (16).

Parvocellular pathways tend to reflect foveal visual function and account for the relatively greater defects in central rather than peripheral visual function observed in amblyopic individuals (15). Delay in latency was detected for high SFS in amblyopic and sound eye in the present case. The VEP abnormalities are related to the loss of high spatial frequency contrast sensitivity and can be marked in anisometropic amblyopes (17). In cases with normal or nearly normal VEP latencies, the treatment shows satisfactory improvement of visual acuity (5). After the treatment, the latency was normalized for high SFS in the sound eye and remained delayed in the amblyopic eye although there was improvement of the visual acuity.

The reduced response in amblyopic eye may be correlated with decreased contrast sensitivity or contrast gain, or deficits in high SFS mechanisms (14). This information can explain why the latency was normalized only to low SFS on the amblyopic eye in the present study.

Nowadays new techniques for preschool vision screening have become increasingly commonplace, allowing early detection of amblyopia (4). Technology that identifies amblyopic children with anisometropic refractive error prior to the age of 4 years enables early treatment, reducing the proportion and depth of amblyopia (4). This will allow ophthalmologists the opportunity to intervene with treatment and attempt to prevent amblyopia or retard its further development (4). The clinical profile of patients with anisometropic amblyopia may be useful in predicting responses to therapy, but compliance with treatment has a major effect on response to therapy (9).

As evidenced by the toxicological tests conducted, citicoline is a safe drug that has no significant systemic cholinergic effects and is a well tolerated product (10). Citicoline demonstrated that it was also effective in the treatment of amblyopic eye also without patching. Few studies demonstrated VEP improvement in adults with amblyopia after citicoline treatment, but the mean age was 24,8 years (18). The visual acuity and the VEP latency improvement demonstrated that the citicoline enhanced the transmission of the electric impulse from retina to visual cortex. Further research is required to understand the immediate and long-term effect of coline treatment in amblyopic patients.

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Autor correspondente:

Dra. Regina Halfeld Furtado de Mendonça
 Universidade Federal de Juiz de Fora (UFJF)
 Faculdade de Educação Física e Desportos
 Grupo de Pesquisa em Inclusão, Movimento e Ensino à Distância
 Campus Universitário s/nº - Martelos
 CEP 36036-900 - Juiz de Fora (MG), Brasil
 Fone: (32) 2102-3283
 E-mail: regina.halfeld@uab.ufjf.br