RESPONSE TO IDEBENONE AND MULTIVITAMIN THERAPY IN LEBER’S HEREDITARY OPTIC NEUROPATHY

RESPUESTA A LA IDEBENONA ASOCIADA A MULTIVITAMINOTERAPIA EN NEUROPATÍA ÓPTICA HEREDITARIA DE LEBER

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ABSTRACT

Objective: To ascertain the efficacy of idebenone and multivitamin treatment in Leber’s hereditary optic neuropathy (LHON).

Method: Two patients diagnosed of unilateral LHON were treated with megadoses of idebenone, vitamin C and riboflavin for one year. They were examined clinically before, during and after treatment.

Results: No improvement of visual function was observed. Despite the idebenone treatment, in both cases the second eye became involved.

Conclusions: Despite previous reports of visual recovery with idebenone in patients with LHON, our experience shows that an effective treatment for Leber’s disease remains to be found (Arch Soc Esp Oftalmol 2007; 82: 377-380).

Key words: Idebenone, multivitamins, Leber’s hereditary optic neuropathy, hereditary neuropathy.

RESUMEN

Objetivo: Determinar la eficacia del tratamiento con idebenona y multivitamínico en la neuropatía óptica hereditaria de Leber (NOHL).

Método: Dos pacientes diagnosticados de NOHL, fueron tratados con idebenona, vitamina C y riboflavina durante un año. Ambos fueron evaluados clínicamente antes, durante y después del tratamiento.

Resultado: Ninguno de los dos pacientes experimentó mejoría visual y ambos sufrieron afectación en el segundo ojo.

Conclusiones: A pesar de casos publicados en la literatura de recuperación visual con idebenona en pacientes con NOHL, nuestra experiencia indica que este tratamiento no es efectivo para la enfermedad de Leber.

Palabras clave: Idebenona, multivitaminas, neuropatía óptica hereditaria de Leber.
INTRODUCTION

Leber’s hereditary optic neuropathy (LHON) is a disease caused by the mutation of mitochondrial DNA (mtDNA.) Males are mainly affected and it usually begins at 15 to 35 years of age, with a loss of central and painless unilateral vision, and the second eye was involved in weeks or months, sometimes in association with neurological alterations. The eye fundus (EF) reveals a circumpapillary telangiectatic microangiopathy and swelling of the peripapillary nerve fibers layer subsequently progressing to an optic atrophy. So far, no efficient treatment is available, although several possibilities have been suggested. The case of two patients suffering from LHON treated with idebenone and vitamins is described herein.

CASE REPORTS

Case 1

In March 2001, a 30-year-old male went to the doctor’s office reporting loss of vision in the right eye (RE) with a 10-day progression. Visual acuity (VA) of count fingers at 50 cm in the RE and 1 in the left eye (LE), with abolition of chromatic vision and relative afferent pupillary defect (RAPD) in the RE. The EF is shown in figure 1. The results of biochemical, hematologic and serologic analyses and the brain magnetic resonance (MR) were not relevant. The mtDNA study detected the G11778A mutation in the homoplasmy. Megadoses of methylprednisolone (methylprednisolone sodium succinate injection. 8 ml to 14 ml vial with attached diluent and preservative. Sanofi Aventis Laboratories. SAU. Barcelona) were administered. Subsequently, idebenone [6(hydroxy-decyl-ubiquinone), Takeda Italia Farmaceutici Laboratories, SpA, Rome, Italy) 270 mg/d, vitamin C (ascorbic acid, Redoxon, with 500 mg tablets, Laboratorios Bayer Hispania, Barcelona) 700 mg/d and riboflavin (becoyme C forte, multivitamin complex with thiamine 15 mg, riboflavin 15 mg, nicotinamide 50 mg, pyridoxine 10 mg, calcium pantothe 25 mg, biotin 150 mg, cyanocobalamin 10 mg, ascorbic acid 200 mg, Laboratorios Bayer Hispania, Barcelona] 15 mg/d, were administered for one year. Eleven months after treatment began, the patient experienced visual loss in the LE, remaining stable to date, with VA hand movements in the RE and counting fingers at 20 cm in the LE. EF (fig. 2).

Case 2

In October 2003, a 19-year-old female with a family history LHON went to the doctor’s office reporting loss of vision in the LE with a 4-day progression. VA was 1 in the LE and count fingers at 40 cm in the LE, with a reduction in chromatic

Fig. 1: Swelling of nerve fibers in the RE papilla with pallor in the temporal area. LE papilla with normal appearance (case 1).

Fig. 2: Bilateral optic atrophy (case 1).

Fig. 3: Gray scale of Humphrey 30-2’s visual field, RE: reduction of peripheral sensitivity; LE: global defect of the field with greater central density (case 2).
vision and RAPD in the LE. Visual field (fig. 3). EF (fig. 4). The FAG revealed the absence of contrast leak from the optic disk, the results of biochemical, hematologic and serologic analyses were normal and the brain MRI revealed a signal increase and the reduction in the left optic nerve thickness. The mtDNA study detected the G11778A mutation in the homoplasmia. Megadoses of methylprednisolone were administered, as well as idebenone 270 mg/d, vitamin C 860 mg/d and riboflavin 9.6 mg/d, for one year. Four months after the beginning of treatment, the patient experienced a loss of vision in the LE which has remained stable to date, with VA counting fingers in both eyes. EF (fig. 5).

**DISCUSSION**

The loss of vision caused by LHON tends to stabilize, although cases have been described reporting spontaneous visual recovery related to the age at the time of onset and the type of mutation. Of the different mutations involved, 11778, present in our patients, has the worse prognosis. Both cases confirmed the characteristic LHON findings in the eye fundus and the FAG allowed discarding a real papillary edema in patient no. 2. The computed tomography (CT) and MR revealed no findings specific to this disease, and the alterations present in patient no. 2 are related to the progression towards optic atrophy.

Approximately 15 mtDNA mutations have been described in relation to the LHON. The most frequent mutations are G11778A, G3460A and T14484C, so-called primary mutations since they entail a genetic risk for the LHON individual expression (1). Both patients presented mutation 11778 in homoplasmia, which means that their mtDNA had mutated. Considering the fact that certain mitochondrial cytopathies may respond to treatments which increase the production of mitochondrial energy, the use of the coenzyme Q has been tried. In such cases, idebenone is used. Idebenone is a coenzyme Q precursor quinoline that stimulates the formation of ATP and protects the mitochondrial membrane against lipid peroxidation (2,3). Some authors have described a clinical improvement after administering this treatment, whether on its own or in combination with vitamins B2 and C (2-4). In 1992, Mashima published the case of a patient suffering from LHON, 11778 mutation in homoplasmia, and after a 7-month treatment with idebenone the patient recovered VA in both eyes (3). Two other authors, Cortelli (2) and Carelli (4) published similar findings, adding vitamins in both patients with 11778 and 14484 mutations, respectively, with recovery of the associated neurological symptoms. Based on the above findings, some authors have suggested the possibility of this therapy accelerating or promoting visual recovery in such patients (5). In our cases, vision could not be recovered and the second eye was involved during treatment. However, since there are cases with spontaneous visual recovery in patients suffering from LHON, we cannot discard this possibility in the cases published. Finally, our experience could not prove the therapeutic success of the idebenone and multivitamin treatment.

**REFERENCES**


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