VIGABATRIN TREATMENT AND VISUAL PROBLEMS IN A PATIENT WITH LEARNING DISABILITY

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Introduction

Vigabatrin was licensed in Britain and the Republic of Ireland in 1989 and has proved to be a valuable drug for the treatment of epilepsy which is not satisfactorily controlled by other anti-epileptic drugs and for initial monotherapy in West's Syndrome.

However, since 1990, there have been reports of both symptomatic (Eke et al., 1997; Wilson and Brodie, 1997; Wong et al., 1997; Blackwell et al., 1997) and asymptomatic (Mackenzie and Klistorner, 1998) visual field defects in patients treated with this drug (usually in combination with other anti-epileptic drugs). The overall incidence, based on epidemiological studies is estimated to be 14.5/10,000 patients with epilepsy a year (Martinez and Noack, 1997). A specific pattern of bilateral concentric constriction of the visual field is seen which is predominantly nasal with temporal sparing (Eke et al., 1997; Harding et al., 1997; Mackenzie and Klistorner, 1998). In some cases, these defects improved after Vigabatrin was stopped, but in others it persisted (Eke et al., 1997; Wilson and Brodie, 1997).

We report on a patient with learning disability who presented with diplopia and blurred vision, after five years of Vigabatrin treatment. Ophthalmic examination revealed retinal epithelial atrophy around the macular area, with deposits.

Method

DH is a 39 year old left handed male. He was the third of 4 children and was the product...
of a normal, full term pregnancy and delivery. There were no complications during the neonatal, perinatal or post natal period. Developmental milestones were normal until the age of 2 years, when DH contracted Rubella encephalitis. He had severe status epilepticus which was uncontrolled for about 36 hours and was left with mild learning disability, right facial paresis, right hemiplegia and right hemianopia which have persisted to the present date.

DH attended a normal mainstream school until the age of nine years when he was transferred to a special school for children with learning disabilities where he stayed until the age of sixteen years. He has always lived with his parents who are his main carers. He does not smoke, drink or abuse any illicit substances. Psychological testing in 1997 (when DH was 36 years) using Raven’s Coloured Progressive Matrices gave an IQ equivalent of 60 (mild learning disability). At present, he requires minimal assistance with activities of daily living including personal care, dressing and feeding.

Between the ages of 3-20 years, DH continued to suffer from generalised tonic-clonic seizures and was initially treated with Phenobarbitone which had to be eventually discontinued because of severe behavioural problems. He was continued on Phenytoin (250mg. daily). At the age of 20 years, he started to have complex partial seizures with secondary generalisation and occasional myoclonic jerks. A combination of Carbamazepine slow release 1000mg. daily and Phenytoin 250mg. daily failed to control his seizures and in September 1992 Vigabatrin was added to the above regime. A total daily dose of 3g was successful in reducing his seizure frequency by over 50%. For the next 5 years, he did not have any significant visual symptoms. However, by September 1997, he started complaining of blurred vision and diplopia and was referred for an ophthalmological opinion.

Results

On examination, he had impaired visual acuity (6/12 - right eye and 6/18 - left eye) and a vertical nystagmus (with fast phase downwards). Fundus examination revealed retinal pigment epithelial layer changes around the macular area with white deposits. The veins also appeared attenuated and there was a question of whether the left optic disc was cupped.

A fluorescein angiogram showed retinal pigment epithelial atrophy which when reviewed by the Consultant Ophthalmologist was considered to be a drug induced toxic change. Electroencephalography showed a moderately severe bilateral, non-specific abnormality of cerebral activity with, in addition, an asymmetry, the record being of relatively lower amplitude over the left hemisphere.

Magnetic resonance imaging of the brain revealed extensive left hemisphere damage following rubella encephalitis.

In view of the damaged retinal pigment epithelium and the symptoms of blurred vision and diplopia, Vigabatrin was gradually tapered and stopped. His seizure frequency worsened. He was started on Lamotrigine and the fits are again under control. Following the withdrawal of Vigabatrin he no longer experienced blurring of vision and diplopia. His current medication is Lamotrigine 200 mg twice a day, Phenytoin 200 mg twice a day and Carbamazepine slow release 400 mg in the morning and 600 mg at night. Further ophthalmological examinations revealed that his measured visual acuities had improved but as expected the retinal pigment epithelial changes remained unchanged and were not expected to resolve.
Discussion

Preliminary data suggest that the visual field defects reported with the use of Vigabatrin might result from increased levels of GABA in the retina. Vigabatrin has been shown to cause microvacuolation in myelin sheaths in the white matter of rats, mice and dogs but not in monkeys or humans (Graham, 1989). Current evidence suggests that the onset of visual field defects varies from 1 month to several years after starting Vigabatrin. In most cases, visual field defects persisted despite discontinuation of treatment (Medicines Control Agency, 1998). Reported visual symptoms attributed to Vigabatrin toxicity include blurred vision, diplopia, photophobia, chromatopsia, nystagmus and visual field constriction (defects usually characterised by concentric, and predominantly nasal, visual field constriction with temporal sparing).

We are not aware of any report in Learning Disability of a patient presenting with retinal pigment epithelial atrophy following treatment with Vigabatrin. It is important to point out, however, that DH did not have a baseline pre-treatment ophthalmic assessment and, therefore, there is a possibility that we have assumed causality when there is only an association. This though seems unlikely in view of the growing body of literature implicating Vigabatrin in visual side effects. It should also be noted that DH’s other complaints - diplopia and blurring of vision, disappeared when Vigabatrin was withdrawn.

Routine ophthalmological screening of all patients taking Vigabatrin cannot be justified. However, it is essential that for epileptic patients being treated with Vigabatrin, specific questioning for visual symptoms, with confrontational testing of the visual field should be performed at baseline and during routine follow-up. Patients should also be instructed to report any new visual problems and if visual symptoms develop or abnormalities are found on visual field testing, then the patient should be referred to an ophthalmologist for further evaluation (Harding, 1998). Consideration should be given to discontinuation of Vigabatrin and where this is necessary, abrupt withdrawal should be avoided.

Summary

Vigabatrin is a valuable drug for many patients with epilepsy. However, its use needs to be evaluated in the context of its overall benefit:risk ratio in comparison with that of other antiepileptic drugs. It must be noted that all antiepileptic drugs pose some risk, as does uncontrolled epilepsy itself. In patients with learning disability, the development of visual symptoms may not be reported and there may be difficulties encountered with visual field testing. Conventional perimetry is seldom possible for patients with a developmental age of less than 9 years and alternative methods for testing visual fields should be used with which there may be poor compliance. Hence, if the use of Vigabatrin is considered for people with learning disability, the benefit:risk ratio should be sufficient to outweigh the lack of reporting of visual symptoms and the impossibility of visual field monitoring.

References


