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EDITORIAL

The ocular side effects of vigabatrin (Sabril): information and guidance for screening

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Background

Vigabatrin (Sabril) is an antiepileptic drug indicated for the treatment of partial epilepsy, which is only licensed as first line/monotherapy for the treatment of infantile spasms (West's syndrome). In 1997, three cases of severe, symptomatic, persistent visual field constriction associated with vigabatrin treatment were described.[1] This led to the recommendation that vigabatrin therapy should only be initiated by an epilepsy specialist and in clinical situations where all other antiepileptic therapies had not been effective or tolerated. A NICE Technology Appraisal in 2004 found that there was no convincing evidence for superiority of seizure control by vigabatrin compared with alternative therapies in either partial seizures or West's syndrome. However, the risk of visual field constriction attributable to vigabatrin (VAVFC) must be balanced against the adverse effects of alternative therapies, and of uncontrolled epilepsy, and vigabatrin therapy remains an important option in this group. Overall, it appears that the use of vigabatrin as an antiepileptic drug is declining.[2]

Clinical features

Patients with VAVFC are usually asymptomatic of the field loss unless the defect encroaches within the central field.[3] Visual field loss can exist in the absence of any demonstrable fundal pathology observed clinically. However, optic nerve head pallor and retinal nerve fibre layer atrophy[4] have been demonstrated in subjects taking vigabatrin. VAVFC (best detected by static perimetry in subjects over 9 years of age) is characteristically bilateral, concentric, and predominantly nasal, and has an estimated prevalence of 30–40%.[5–7] In a minority of patients, VAVFC has been so severe that it limited their ability to perform a variety of activities of daily living.

Electrophysiology

Electrophysiological testing may reveal a normal VEP response, ERG abnormalities (increased photopic β-wave latency, reduced β-wave amplitude, and reduced oscillatory potentials)[8,9] and a reduced Arden Index on EOG testing.[5,8,10] Field-specific VEP responses have shown promise in detecting VAVFC in subjects unable to produce reliable perimetry such as children.[11]

Risk factors

Men on vigabatrin have an increased risk of developing VAVFC of approximately twofold compared with women.[7,8]

The prevalence of VAVFC rises steeply at cumulative doses between 1 and 3 kg[12] with a cumulative risk plateau at 5 kg.[13] The majority of cases occur after a year of treatment.

Children present a particular problem as accurate assessment of visual impairment is difficult, but the prevalence of VAVFC in paediatric patients has been estimated to be 29%.[13]

Prognosis

The vast majority of studies indicate that VAVFC does not reverse on cessation of the drug, and may worsen with continued use.[14] Progression of VAVFC after stopping vigabatrin has not been reported to date.

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Screening recommendations

- A baseline visual field should be obtained before starting treatment.
- Visual field examination should be undertaken with Humphrey 120 point, Octopus 07, or Goldmann perimetry (III4e and I4e or I2e stimuli, as appropriate).
- Perimetry should be repeated every 6 months for 5 years. It can then be extended to annually in patients who have no defect detected.
- If VAVFC is detected, it is advisable to conduct a confirmatory field test within 1 month before considering cessation of vigabatrin.
- If the drug is discontinued, perimetry should be repeated at a future date to monitor the field loss.

In subjects unable to perform perimetry (typically children under 9 years and approximately 20% of adults with epilepsy[9]), field-specific VEPs may detect an absent peripheral response but the diagnostic accuracy of field-specific VEP testing requires further validation.

Discussion with patients and carers

- It is the responsibility of the prescribing doctor to discuss with the patient, or the patient's relatives or carers, the risks of VAVFC.
- As the degree of field loss may be severe enough to limit driving and even daily activities, the potential risk needs to be assessed against the potential benefit of seizure control.
- Patients should be alerted to report any abnormalities in their vision, and must be informed of any abnormalities in visual field tests.
- Patients should be advised that VAVFC can worsen if the drug is continued, although it may remain static, particularly if the duration of treatment is greater than 5 years or the cumulative dose is greater than 5 kg.

Conclusions

There are still many unanswered questions concerning the relation between vigabatrin and visual field defects. Evaluation of the clinical situation is difficult when it comes to assessing the potential risk to the patient, particularly where children are concerned. It is a matter for the prescribing paediatrician or neurologist to weigh up the dangers of potential side effects against seizure control and to instigate screening for VAVFC. Accurate visual field monitoring will enable a more informed decision on whether to initiate or continue treatment with vigabatrin.

The unabridged guideline is available at http://www.rcophth.ac.uk/docs/publications/published-guidelines/Vigabatrin_Guidelines_March_2008.pdf

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