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CASE REPORT

Ginkgo biloba precipitating epileptic seizures

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Abstract

Background: the herbal remedy *Ginkgo biloba* is promoted as a treatment for a variety of ailments including memory loss and dementia, poor concentration and mood, glaucoma, 'cerebral insufficiency' and 'peripheral circulatory disturbances'. It is gaining worldwide popularity, particularly as a potential treatment for dementia.
Case reports: two patients with well-controlled epilepsy presented with recurrent seizures within 2 weeks of commencing extract of *Ginkgo biloba*. The herbal remedy was discontinued and both patients are seizure-free several months later.
Discussion: *Ginkgo biloba* may have precipitated seizures in these two patients. This and other potential adverse effects should be highlighted on the packaging of the drug.

Keywords: Ginkgo biloba, *seizures*

Introduction

Two patients with well-controlled epilepsy presented with recurrent seizures within 2 weeks of commencing extract of *Ginkgo biloba*. The herbal remedy was discontinued and both patients are seizure-free several months later.

Case reports

Case 1

A 78-year-old man presented with three generalized tonic–clonic seizures in the preceding 12 h. Seven years previously he had been diagnosed with epilepsy attributed to cerebrovascular disease. The fits had been well controlled on sodium valproate, 1200 mg daily, his last seizure being 18 months earlier.

The only recent alteration to his medication was the addition, 2 weeks before admission, of *Ginkgo biloba* tablets, 120 mg daily, for the management of mild cognitive impairment (Mini-Mental State Exam 28/30). These had been purchased over the counter, and had not been discussed with his general practitioner. His other medications (temazepam, aspirin and ramipril) remained unchanged, and he was fully compliant with his anti-epileptic medication.

No systemic or infective cause for his recent cluster of seizures was found, nor was there evidence of a new stroke. The herbal remedy was discontinued, and he is seizure-free 8 months later. His dose of sodium valproate remains unchanged.

Case 2

The second patient, an 84-year-old woman with severe dementia (Mini-Mental State Exam 14/30), presented in status epilepticus. She was given intravenous diazepam in the emergency department, with abolition of her seizures 2 h after onset.

She had been free of seizures for 2 years on 1600 mg sodium valproate daily. *Ginkgo biloba*, 120 mg daily, had been prescribed by her psychiatrist 12 days previously. No alternative cause for her seizures was found, and her other medication (aspirin, rivastigmine and thioridazine) had been unchanged for 5 months.

The *Ginkgo biloba* was stopped on admission and, after three further seizures over the subsequent 48 h, she remains seizure-free 4 months later on the same dose of anti-epileptic medication.

Discussion

Ginkgo biloba may have precipitated seizures in these two patients. This herbal remedy is widely promoted and used to treat a diverse array of ailments, including memory loss and dementia [1], poor concentration and mood [2] and glaucoma [3], as well as 'cerebral insufficiency' and 'peripheral circulatory disturbances' [4]. It is currently among the top five prescribed medications in Germany [4], and is gaining worldwide popularity—particularly as a potential treatment for dementia: Coleman [5] reported that 55% of caregivers of patients with Alzheimer's disease had used at least one alternative medicine to improve the patient's memory, and that *Ginkgo biloba* was the most widely used. Furthermore, 70% of those using such herbal remedies do not reveal this to their pharmacists and physicians [6].

The postulated mechanisms of action of *Ginkgo biloba* include increased blood flow, antagonism of platelet-activating factor and prevention of membrane damage caused by free radicals [7]. Extracts are usually standardized in terms of the active ingredients, containing 24% ginkgo-flavone glycosides and 6% terpenoids. There are, however, no regulated manufacturing standards in place [1].

Also of concern is the public perception that such 'natural' remedies are free from adverse effects and do not interact with prescribed drugs. This is encouraged by marketing and sales practices: two preparations of *Ginkgo biloba* (Healthcraft's High Potency and Ginkyo Concentrated) available at a local supermarket contained information sheets which made no mention of either drug interactions or side effects. However, there are reports of serious adverse effects. Prolonged bleeding times have been attributed to the effects on platelet-activating factor [6], and *Ginkgo biloba* has been implicated in cases of spontaneous intracerebral and subdural haemorrhages [8–10].

There is some evidence in the scant literature to support the role of *Ginkgo biloba* in our two patients' seizures. Ginkgo toxin (4-O-methylpyridoxine), a known neurotoxin, may be present in the leaf and seed preparations; this has been implicated in cases of convulsions and loss of consciousness [11]. While the amount in commercial extracts is probably too low to be of clinical significance, Miller [7] recommends avoiding its use in epileptic patients and in those on medications known to lower seizure threshold.

Flavonoids of *Ginkgo biloba* have been shown to exhibit GABAergic activity, as partial agonists at benzodiazepine-binding sites [12]. There is some animal evidence that this may potentiate the epileptogenic actions of picrotoxin, a model GABA and chloride channel antagonist. Prior administration of ginkgo to mice resulted in more seizures being provoked by picrotoxin and reduced the protective effect of sodium valproate and carbamazepine [13, 14]. At least three studies have demonstrated alteration in electroencepholgraph activity after taking *Ginkgo biloba*, with a reduction in θ activity [15–17], although the clinical relevance of this is uncertain.

Both of our patients had excellent control of their seizures until commencing *Ginkgo biloba*, and both lost seizure-control within 14 days of starting it. We could not find an alternative explanation in either patient and, in light of the postulated mechanism outlined above, we believe the herbal remedy to be causative. The definitive test, in terms of re-challenge, has not been attempted in either patient.

Those most likely to take *Ginkgo biloba* are elderly people with dementia, often already on medications known to lower seizure threshold. This group has a higher incidence of epilepsy [18]. We wish to draw attention to the possibility that seizures may be precipitated by *Ginkgo biloba*: this and other potential adverse effects should be highlighted on the packaging of the drug. Physicians need specifically to ask if their patients are taking this or other herbal remedies, particularly where there is unexplained loss of seizure-control.

Key points

- Two patients with well-controlled epilepsy presented with recurrent seizures within 2 weeks of commencing extract of *Ginkgo biloba*; both became seizure-free when the herbal remedy was discontinued.
- Epileptic seizure and other potential adverse effects should be highlighted on the packaging of the drug.

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