

## **Antidepressant-related seizures**

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### **Abstract**

A 58-year-old female had absence seizures after a recent intraparenchymal haemorrhage. Laboratory studies, electrocardiogram and computerised tomography brain were unremarkable. Episodes coincided with the commencement of Fluoxetine, resulting in a diagnosis of Fluoxetine-related absence seizures. Fluoxetine was ceased and Levetiracetam was increased, leading to seizure resolution. Cautious prescription of antidepressants is advised in patients, especially those predisposed to seizure.

**Keywords:** Seizures; Antidepressants; Intracerebral hemorrhage; Fluoxetine

### **Antidepressant-related Seizures**

A 58-year-old female presented to the emergency department with absence seizures on a background of a recent intraparenchymal haemorrhage five months earlier for which she was commenced on Levetiracetam for six months. Since then, she had discrete episodes of unconsciousness with eyes rolled back and prodromal abdominal fullness and nausea. This lasted one minute with complete recovery within five minutes. Episodes occurred once a week but had increased to four to five episodes a day in the past ten days. There was no tonic clonic activity, incontinence, or tongue biting. She denied chest pain, palpitations and syncopal episodes.

Past medical and surgical history includes left parietal lobe intraparenchymal haemorrhage, type 2 diabetes mellitus, hypertension, gastro-oesophageal reflux disease, total abdominal hysterectomy, cholecystectomy and appendectomy. Her medications included Fluoxetine 20mg once daily, Levetiracetam 500mg twice daily, Perindopril/Amlodipine 5/5 and Ryzodeg 70/30 8 units twice daily with meals. Neurological exam revealed no new focal neurological signs apart from ongoing right upper limb paraesthesia and weakness, dysarthria and left visual neglect consistent with her previous haemorrhagic stroke.

Laboratory studies, electrocardiogram and cardiac monitoring were normal. Computerised Tomography (CT) brain was unremarkable except for chronic left parietal gliosis at the site of previous haemorrhage. Differential diagnoses included transient ischaemic attack, cardiogenic syncope and metabolic and electrolyte disturbances such as hypoglycaemia and hyponatraemia. These were excluded with relevant tests.

It was noted that the increased seizure frequency coincided

with the commencement of Fluoxetine ten days earlier. A diagnosis of Fluoxetine-related absence seizures was made. The patient was admitted to the medical ward. Treatment involved ceasing Fluoxetine as the patient was already on the lowest possible dose and hence, reducing her dose was not an option. Her Levetiracetam dose was also increased to 750mg mane and 500mg in the afternoon. Follow up with neurology was organised. No further seizures were noted.

### **Discussion**

Antidepressants are common medications indicated in depression, anxiety, mood disorders, eating disorders and chronic pain. In Australia, 27.6 million prescriptions for antidepressants were dispensed in 2018-19 [1]. Seizure is an infrequent but serious consequence of antidepressant treatment which lowers the seizure threshold in susceptible patients.

Existing literature suggests that the overall incidence of antidepressant-related seizures ranges from 0.1-0.4% [2]. Older antidepressants include tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs). TCAs at therapeutic doses possess high epileptogenicity (0.4-2%) [2]. Newer antidepressants have a better tolerability profile and include selective serotonin reuptake inhibitors (SSRIs), serotonin/norepinephrine reuptake inhibitors (SNRIs), bupropion, mirtazapine and reboxetine. SSRIs are less epileptogenic (0-0.4%) which is relatively similar to the incidence of first seizure in the general population (0.07-0.09%) [2].

Most antidepressant drugs, in particular TCAs, exhibit a proconvulsive effect at supratherapeutic doses (4-30%) [3]. This is due to local anaesthetic, antimuscarinic and antihistaminergic action influencing neurochemical pathways that promote neu-

ronal excitation [2]. However, there is debate about seizure risk with antidepressants at therapeutic doses. Therapeutic doses are postulated to have anticonvulsive effects due to increased circulating monoamines [2]. In contrast, in patients susceptible to seizures due to predisposing risk factors, therapeutic doses may unmask a seizure diathesis [2]. Potential risk factors include a history of seizures, epilepsy or a family history of epilepsy. Other risk factors are intracranial pathology, multisystem illness, electrolyte and metabolic disturbances, withdrawal states, drug interactions, rapid dose escalation, advanced age and renal impairment. The timing of antidepressant-related seizures can vary, with most occurring during the first few weeks of treatment, after rapid dose escalation or during overdose. Treatment involves ceasing the antidepressant and commencing an anticonvulsant medication.

Our patient had a recent haemorrhagic stroke which predisposed her to seizures. To the best of our knowledge, this is the first report of antidepressant-related seizures in a patient with previous haemorrhagic stroke. There is a 5-20% risk of seizures after stroke, with haemorrhagic stroke carrying a higher risk [4]. In haemorrhagic stroke, acute seizures may occur due to cerebral irritation by products of blood metabolism, including haemosiderin; while in the long term, a permanent lesion is thought to promote seizure activity. To manage seizure risk after haemorrhagic stroke, a short-term prophylactic anticonvulsant can be trialled for six months. After this period, the need

for long-term prophylaxis should be evaluated periodically. Physicians should exercise caution when prescribing antidepressants in patients, especially those with predisposing risk factors for seizure. For patients with significant predisposition to seizures, psychotherapy and other non-pharmacological measures remain important options in depression treatment. Seizure risk needs to be carefully balanced against the impaired function and distress caused by depression. If antidepressant treatment is necessary, antidepressants with low seizure risk should be given at the lowest effective dose with slow dose titration. Stringent monitoring is crucial to prevent iatrogenic complications of antidepressant treatment.

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