Henderson, E., Whatley, J., & Huffman, A. (2018). Acute inability to mobilise resulting from probable donepezil-induced myoclonus. *Age and Ageing*. https://doi.org/10.1093/ageing/afy093

Acute inability to mobilise resulting from probable donepezil-induced myoclonus: a case report

Abstract

Donepezil is a commonly prescribed cholinesterase inhibitor in Alzheimer's dementia. We present a case of probable donepezil-induced generalised myoclonus causing total inability to mobilise in a 93 year old woman.

Case report

A 93 year old woman living independently and mobilising with a stick, presented to hospital via her GP 'off legs'. She was unable to mobilise due to the onset of frequent uncontrollable jerking movements of her limbs which were of sudden onset. She had recently been diagnosed with Alzheimer's disease and had a background of hypertension. There was no history suggestive of seizures. She was taking donepezil 10mg daily, sodium docusate and calcium supplements.

Neurological examination was normal with the exception of prominent multifocal myoclonic jerks, non-synchronously affecting all four limbs at rest. Investigation revealed no evidence of systemic infection or biochemical abnormality. CT head showed generalised cerebral atrophy and small vessel disease, but no acute pathology. A collateral history revealed that donepezil 5mg had been commenced 6 weeks previously which had been increased to 10mg, 7 days prior to admission.

In the absence of other causes of myoclonus a working diagnosis of donepezil-induced myoclonus was made. Donepezil was discontinued and over the following 48 hours the myoclonus diminished and then resolved.

Discussion

Donepezil hydrochloride is an acetylcholinesterase inhibitor licensed in the UK for the management of mild to moderately severe Alzheimer's disease. Whilst it is generally well tolerated, side effects are reported in approximately 5% of patients, with the most common being gastrointestinal upset [1]. Muscle spasms are less common, occurring in 0.1 to 1% of patients, but myoclonus is not listed as a recognised side effect [1].

This is the first report of donepezil induced myoclonus at a therapeutic dose (10mg). Notably the myoclonus caused significant impairment to daily function and ability to walk. A literature search limited to English language and humans was performed with the search strategy (donepezil OR Aricept OR Cholinesterase Inhibitors/adverse effects) AND (myoclon*) on Medline and Embase on 15.02.18, yielding 24 articles. Previous cases have described myoclonus occurring with donepezil overdose [2] and in conjunction with memantine use [3,4]. Myoclonus was described in a patient on memantine and donepezil 5mg, which worsened upon treatment with trimethoprim [3]. Upon cessation of memantine, the myoclonus ceased. Another case describes the emergence of prominent myoclonic jerks when memantine was added to donepezil which subsequently resolved on discontinuation of memantine [4]. In addition, data from a French phamacovigilance database reported myoclonus potentially having resulted from the use of cholinesterase inhibitors [5]. However, in this aggregated data causality cannot be reliably established.

Conclusion

Myoclonus can be classified according to the aetiology, clinical presentation or physiological source. The most common drug causes of symptomatic myoclonus are opiates, antidepressants, antibiotics and antipsychotics. This case illustrates the emergence of severe, disabling myoclonus occurring with up-titration of donepezil at therapeutic dose, which resolved on discontinuation of the drug, strongly

suggesting a causal association. The case highlights the importance of careful examination to elicit an unusual cause of acute inability to mobilise and the necessity for consideration of potential drug toxicity. We highlight the importance of a rare but disabling complication of cholinesterase treatment which has previously been reported only after overdose or in conjunction with memantine prescription.

Conflicts of interest

None declared

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