Pain with Donepezil

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Abstract

An 85-year-old lady with a 4-year history of Alzheimer’s dementia was started on a dose of 5 mg of Donepezil. Improvements were noted in her overall mental state with an associated reduction in the level of carer stress but with mild and transient subjective gastrointestinal complaints. Therefore, the dose was cautiously increased to 10 mg. But within 10 days of the increase, she reported bilateral leg pain severe enough to cause her mental state to deteriorate significantly. Pain induced by Donepezil undermined the efficacy of the drug, resulted in increased carer stress and worsening cognition not reversed by the change of medication to another cholinesterase inhibitor.

Keywords: Donepezil, pain, dementia, elderly

Case report

An 85-year-old lady with a 4-year history of Alzheimer’s dementia, glaucoma and hypertension, controlled with Timolol 0.5% eye drops and Candesartan 3mg, respectively, was started on a dose of 5 mg of Donepezil. Improvements were noted in her mood, cognition, and confidence in daily living skills. In view of subjective gastrointestinal complaints, Donepezil was cautiously increased to 7.5 mg while ongoing significant improvements were continued to be observed in her overall mental state and Mini Mental State Examination scores. The patient and family noted decreased grumpiness and improved sleep pattern, with considerable reduction in the carer stress. Donepezil was then increased to 10 mg but, within 10 days of the increase in dose, she experienced bilateral leg pain, which was continuous, severe in the morning and reducing in severity by evening, associated with food and drink refusal, insomnia, decreased mobility and an overall deterioration in her mental state. Detailed neurological examination and investigation revealed no identifiable cause of this pain. Donepezil was stopped with advice for pain and carer stress to be diarised. A marked reduction in pain and restitution of the sleep pattern was noted, albeit the patient became increasingly grumpy, short-tempered with an increase in the level of carer stress. Alternative cholinesterase inhibitor therapy with Galantamine unfortunately did not show as good a response and did not alleviate the care stress to the level experienced with Donepezil.

Discussion

The common adverse effects of Donepezil include transient gastrointestinal disturbance which generally resolves without the need for dose modification or change of medication [1]. Dose-related adverse effects are generally associated with peripheral cholinergic activity, seen during the maintenance phase of therapy, and reportedly more frequently with Donepezil than other cholinesterase inhibitors [2]. Pain as an adverse effect has seldom been reported. Non-specific pain poorly localised and not serious enough to require any dose modification or discontinuation of the medication has been recorded [3-5]. We believe that this is the first case report of pain as an unusual adverse drug reaction arising with the use of Donepezil which undermined the efficacy of the medication, increased the carer stress and was not reversed on withdrawal of the drug and change of medication to another cholinesterase inhibitor.

We suspect Donepezil to have contributed to pain in view of:

(i) The temporal association between the symptom emergence and the administration of Donepezil, particularly with the increase in dosage.
(ii) Symptom reduction on withdrawal of Donepezil.
(iii) Lack of recurrence of the symptoms on initiation of alternative cholinesterase inhibitor.

Cholinesterase inhibitors can have significant interactions with other drugs that are metabolised by the hepatic cytochrome system and therefore need to be used with caution [2].
Candesartan is associated with myalgia and is metabolised by the same cytochrome P450 isoenzyme 3A4 as Donepezil, which led us to suspect Donepezil of potentiating the adverse effect of Candesartan. However, at this stage, it remains a hypothesis.

Key points
- Donepezil needs to be used with care; and pain as an adverse effect needs to be considered.
- Further research into interactions between Candesartan and Donepezil and the role of cytochrome P450 isoenzyme 3A4 is warranted.

Conflicts of interest
None.

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None.

It was not just a heatwave! Neuroleptic malignant-like syndrome in a patient with Parkinson’s disease

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Abstract
Neuroleptic malignant-like syndrome (NMLS) is a rare but life threatening and important complication because of the withdrawal of long-term L-Dopa therapy in Parkinson’s disease patients. In this case report, we review the pathophysiology, clinical features and treatment of this curable condition.

Keywords: neuroleptic malignant-like syndrome, Parkinson’s disease, apomorphine, elderly

Case report
A 76-year-old woman with advanced idiopathic Parkinson’s disease was admitted to hospital with aspiration pneumonia. She was treated with intravenous antibiotics and all regular medications including L-Dopa preparations were given through a nasogastric feeding tube at the correct doses and times. Later in the admission, she experienced florid dyskinesias and painful dystonias. Consequently, total daily L-Dopa was slowly reduced from 1,250 to 875 mg, and the dopamine agonist cabergoline introduced.