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Case Report

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A Case of Extrapyramidal Side Effects Induced by Donepezil

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Abstract

A 78 year old man diagnosed with Alzheimer's Dementia was started on Donepezil and a few months later, experienced an acute episode of extrapyramidal symptoms that manifested as leg stiffness and bradykinesia. Various differential diagnoses were considered including Parkinson's disease, progression of dementia, acute vascular event and adverse reaction caused by Donepezil. He was advised to stop Donepezil whilst awaiting an MRI head and his symptoms resolved within a week of discontinuing Donepezil. His symptoms were attributed to the use of Donepezil, further supported by an MRI that showed changes consistent with Alzheimer's disease and no acute vascular change. This case generates interest given that the patient was psychotropic naïve and raises questions about acetylcholine-dopamine interactions in the brain which is explored in this report.

Keywords: *Extrapyramidal; Donepezil; Alzheimer's disease; Bradykinesia*

Case report

This is the case of a 78 year old man with a diagnosis of Mild dementia- Alzheimer's type, discharged from the community older persons mental health services in February 2019, on a stable dose of Donepezil 10mg OD, with no side effects. One morning, 9 months following initiation of Donepezil, the patient was not able to use his legs properly. He described feeling 'a bit vague and strange'. His wife noticed his legs going 'into spasms,' affecting his gait and walking almost 'robot like'. In retrospect, she had noticed that his gait had become more 'shuffling' few days prior. On examination by the geriatrician 3 weeks later, he was found to have hesitant speech, reduced blink rate and slow general movements. There was modestly increased tone on the right-hand side. There was some degree of bradykinesia evident on both sides, right slightly more than left. In conclusion, he was found to have mild but definite bilateral asymmetric extrapyramidal signs.

The history made diagnosis of Parkinson's Disease unlikely. It was considered that these symptoms could be secondary to Alzheimer's or adverse effects from Donepezil. Given the acute onset of symptoms, an MRI brain was arranged to rule out a vascular event and the patient was advised to discontinue Donepezil. Within a week of discontinuing Donepezil, there was significant improvement in physical symptoms and his mobility returned to normal. His memory had deteriorated slightly. Given the risk of further side effects with other medication of the same class, Memantine was prescribed. The patient had not reported adverse effects on Memantine since then.

Discussion

Although literature does contain a few case reports of Donepezil induced extrapyramidal symptoms, these have been associated with concomitant psychotropic medication or with Lewy Body dementia [1]. What renders this case unique is the lack of clinical signs of Lewy Body dementia (there have been no mobility problems since stopping the Donepezil, no falls, no sleep issues, no continence issues and no psychotic phenomena); and the lack of other significant co-morbidities and concomitant medication.

This case does raise the consideration of acetylcholine-dopamine interactions in the brain. Dopamine and Acetylcholine

are the two main neuromodulators involved in fine tuning the activity of the basal ganglia and there is evidence to show that they modulate each other's release [2]. Ach-rich nuclei within the pons region of the hindbrain which represent the only known cholinergic projections to midbrain Dopamine cells, seem to modulate neurotransmission in these dopamine systems, and Ach-containing interneurons in the striatum also provide a substrate for dopamine-acetylcholine interactions and modulate striatal output essential for the production of normal fluid movement [3].

The activation of acetylcholine receptors has been shown to result in both increase and decrease of dopamine activity in the basal ganglia suggesting a complex modulatory role.3 In this case, the Parkinson-like symptoms caused by the increase in acetylcholine would be in line with the theory behind the common use of anticholinergic drugs to improve Parkinsonism. However, there is some evidence in literature of donepezil improving some extrapyramidal symptoms such as tardive dyskinesia [4].

Overall, evidence suggest that dopaminergic and cholinergic systems operate in a fine dynamic balance and any disruption can often lead to neurological or psychiatric disorders.3 This is likely what would have happened in this psychotropic naïve patient.

Conclusion

Acetylcholine has complex modulatory actions- mAchR and nAChR subtypes have varying roles at multiple levels of the nigrostriatal and mesocorticolimbic dopaminergic systems, which makes finding a solution to restoring functional dopamine-acetylcholine interactions difficult.3 Further research into targeting selective Ach receptors in particular pathways would lead to improvements in the management of neuropsychiatric disorders linked to dysfunctional dopamine–acetylcholine interactions.

References

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