

Cholinesterase inhibitors and affective symptoms: a case report on long-term donepezil use in Alzheimer's and late onset of manic symptoms

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Cholinesterase inhibitors, possibly have a role in the treatment of disorder involving the neuro cognition. Cholinesterase inhibitors like donepezil has been approved by Food and Drug Administration for mild moderate and sever dementia in Alzheimer s disease. Here we present a case report of a 92 year-old Caucasian female with Alzheimer's dementia with no personal or family history of psychiatric disorder presented with symptoms of pressured speech, flight of ideas, grandiosity, paranoia, and she endorsed euphoric mood. Weeks prior to presentation, patient had depressive symptoms. Patient received Donepezil 10mg daily and memantine 10mg twice daily for many months. Behavioral symptoms had been unsuccessfully treated with quetiapine 25mg PO three times daily. Donepezil was discontinued with all other medications unchanged. Behavior rapidly improved with resolution of affective symptoms. Donepezil is associated with the early mania and rare cases of late onset mania. Exact mechanism is still unclear. This case report hopes to add to the literature and to make consultation psychiatrists aware of this possible adverse effect of this class of medications.

Keywords:

affective and manic symptoms causes, cholinesterase block
cholinesterase inhibitor and affective symptoms, donepezil and mania

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Introduction

Cholinesterase inhibitors possibly have a role in the treatment of disorders involving neurocognitive impairment like frontotemporal lobar degeneration, Huntington's disease, multiple sclerosis, epilepsy, delirium, traumatic brain injury, sleep-related disorders, Down's syndrome, vascular dementia, and certain psychiatric disorders (e.g. schizophrenia and bipolar disorder). Cholinesterase inhibitors like donepezil have been approved by the Food and Drug Administration for mild, moderate, and severe dementia in Alzheimer's disease. The development of affective symptoms has been documented during clinical trials, and also several cases of mania and bipolar symptoms during the early phase of treatment have been published. Here we present a case report of an old-aged woman with [1,2] Alzheimer's disease, moderate dementia without any pre-existing psychiatric illness treated for several months with donepezil, and with late onset of bipolar symptoms. Long-term use of cholinesterase inhibitors like donepezil and the emergence of late onset of bipolar illness should prompt a search for the secondary causes.

Methods

Literature review, research studies, case reports, and case series included structured searches of PubMed, Medline, and Google and other publications on the subject of

acetylcholine, acetylcholinesterase inhibitor, donepezil and mood disorder, affective symptom associated with these class of drugs, cholinergic system in the cerebral cortex, and hippocampal formation.

Case report

A 92-year-old White woman with Alzheimer's dementia with no personal or family history of psychiatric disorder presented for evaluation with the members of her family. On examination, she presented as hyperactive, had pressured speech, flight of ideas, grandiosity, paranoia, and she endorsed euphoric mood. Collateral information from her daughter revealed that weeks before presentation, patient had depressive symptoms, but the behavior had recently changed as the patient was no longer sleeping and demonstrated increased level of activity and participation in goal-directed activities. Patient had also been increasingly irritable, aggressive, and violent. For treatment of cognitive deficits, patient had been prescribed donepezil 10 mg daily and memantine 10 mg twice daily for many months. Behavioral symptoms had been unsuccessfully treated with quetiapine 25 mg, oral, three times daily. There had been no significant changes in laboratory values or neuroimaging. On admission, donepezil was discontinued with all other medications unchanged. Behavior rapidly improved with resolution of affective symptoms. She was discharged 5 days later at baseline mental status as per her family.

Discussion

Alzheimer's disease certainly involves the substantial loss of the element of the cholinergic system, especially in the cerebral cortex and other areas of brain (it has been noted in several different studies, hippocampal formation plays an important role in the process of control attention, memory, and learning) [2-4].

While considering the use of cholinesterase inhibitors in the treatment of neurocognitive impairment in Alzheimer's disease, new experimental evidence showed direct interaction of donepezil with the nicotinic receptors and this adds a new insight into the mechanism of this drug. This interaction leads to the increase in the level of acetylcholine (pathologically low in the Alzheimer's disease patients) [1]. There is a proposed mechanism also that cholinesterase inhibitor might also induce parallel nicotinic receptor desensitization, which also leads to the adaptive brain processes. It also acts as a potent agonist of the σ receptor, and has been shown to produce specific anti-amnesic effects in animals, through their interaction. This biochemical alteration leads to the shift in the balance of acetylcholine and serotonin, and ultimately serotonin predominance, resulting in the late onset of bipolar symptoms [1-5].

Conclusion

Cholinesterase inhibitors like donepezil act through several different mechanisms. There is mounting evidence presented by a number of trials, case report, and case series reports that donepezil is associated with the early mania and rare cases of late-onset mania. The exact mechanism is still unclear, but it interacts with various other neurotransmitters, which eventually lead to the secondary alteration in these network-producing manic-like symptoms [1-3,5]. The current case report hopes to add to the literature and to make consultation psychiatrists aware of this possible adverse effect of this class of medications.

Conflicts of interest

There are no conflicts of interest.

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