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Successful intervention to mitigate an acetylcholinesterase inhibitor-induced rhinorrhea prescribing cascade: a case report

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SUMMARY

What is known and objective—A prescribing cascade is often treated by discontinuing both medications. We describe an intervention to mitigate a prescribing cascade while continuing a clinically necessary medication without negatively impacting the patient.

Case Summary—A 77 year-old woman experienced probable acetylcholinesterase inhibitor-induced rhinorrhea and subsequently self-medicated with diphenhydramine which led to worsening cognitive function. We reduced the dose of the acetylcholinesterase inhibitor and discontinued the diphenhydramine. The symptoms of rhinorrhea were subsequently reduced without negatively impacting cognition.

What is new and conclusion—This was the first prescribing cascade intervention that did not require discontinuation of both medications, which may be emulated in future cases of a prescribing cascade.

Keywords

Prescribing Cascade; Drug-induced adverse event; Elderly; Clinical pharmacy

WHAT IS KNOWN AND OBJECTIVE

A prescribing cascade occurs when a drug-induced adverse event (DIAE) is misinterpreted as a new medical condition resulting in the prescription of a new, potentially unnecessary medication.⁽¹⁾ Case reports have previously described the negative impacts of prescribing

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Conflicts of Interest

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cascades in older adults.(2–9) Currently there are a limited number of case reports that have described a successful intervention to mitigate a prescribing cascade by discontinuing the medication contributing to the DIAE.(2–5) However, the initial medication may not be able to be discontinued depending on the patient and medication in question. We describe a case of acetylcholinesterase inhibitor-induced rhinorrhea, subsequent self-medication using an over-the-counter (OTC) product, and the intervention to reduce these symptoms without negatively impacting cognition or function in a patient with dementia.

DETAILS OF THE CASE

A 77-year-old woman presented to the geriatric assessment clinic with a history of memory loss over four years, having difficulty remembering names, cooking meals, managing finances, and administering medications. Her past medical history was significant for tricuspid valve regurgitation, coronary artery disease, gastroesophageal reflux disease, hyperlipidemia, osteoarthritis, ovarian cancer, and a history of a fall-related vertebral fracture. Her current medications included atenolol, multivitamin, fish oil, furosemide, glucosamine/chondroitin, fiber, simvastatin, calcium/vitamin D, and vitamin C. She was diagnosed with dementia of mild severity, likely to due to Alzheimer's disease, based on a detailed clinical assessment and assigned a clinical dementia rating (CDR) of 1, indicating mild severity.(10) The Short Blessed Test (SBT) score was 2 which is consistent with normal cognition.(11) She tolerated the initial therapy of donepezil 5mg per day and was subsequently titrated to 10mg per day four weeks later.

At her 6-month follow-up, she continued to have issues with short-term memory supported by a worsening Short Blessed Test (SBT) score of 11, in which a score of 10 or greater is consistent with dementia.(11) Her only complaint was a 'runny nose' during this follow-up visit. She was also started on aspirin, mirtazapine, and Vitamin B6 since her initial visit to the geriatric assessment clinic. Using a medication reconciliation tool to confirm a complete medication history,(12) the patient also identified as self-medicating with over-the-counter (OTC) oral diphenhydramine, without any benefit to the rhinorrhea symptoms. Upon further investigation, this patient had no history of allergic rhinitis, and she noted that these symptoms had started only started within the previous few months.

We determined that rhinorrhea may have been related to the cholinergic adverse effects of donepezil, and the worsening cognitive issues were likely due to dementia progression and possibly the anticholinergic adverse effects of diphenhydramine. As the team determined that donepezil was a clinically important medication for this patient, donepezil was decreased to 5mg per day, a dose the patient had previously tolerated, instead of being discontinued. The patient was also educated to discontinue diphenhydramine as it was likely not beneficial for rhinorrhea and potentially worsened cognition.

At the follow-up visit, the patient remained off diphenhydramine and continued donepezil 5mg per day. The rhinorrhea remained present but described as less bothersome and more tolerable compared to treatment with donepezil 10mg per day. Her cognition was stable with a SBT score of 10. The patient was continued on donepezil 5mg per day beyond this follow-up visit.

WHAT IS NEW AND CONCLUSION

We suspected that rhinorrhea was related to the acetylcholinesterase inhibitor based on temporality, plausibility, and an adverse drug reaction probability scale score of 6 (probable).(13, 14) Moreover, the lack of improvement in rhinorrhea, despite the use of diphenhydramine, suggested that symptoms were drug-induced and not due to environmental causes.(14)

This DIAE was confirmed after the dose reduction of donepezil led to a subsequent improvement in rhinorrhea symptoms. As the patient's cognition and functionality may have benefited from the use of donepezil, we did not want to discontinue that medication. Therefore, the dose was reduced as rhinorrhea secondary to acetylcholinesterase inhibitors is likely dose dependent. A meta-analysis of randomized control trials by Whitehead and colleagues, identified statistically significant higher rates of rhinitis in donepezil 10mg per day (7.9%) compared to 5mg per day (4.7%; $p<0.05$) and placebo (4.8%; $p<0.05$) confirming this as a dose dependent adverse outcome.(15)

The patient was able to continue on a therapeutic dose of donepezil with diminished rhinorrhea.(16) At the 12-month follow-up visit, her dementia symptoms and her SBT score were slightly improved based on a CDR of 0.5 and SBT score of 10. Thus the reduced dose of donepezil may have proven effective for the cognitive symptoms, while avoiding the future negative adverse outcomes of diphenhydramine including worsening cognition and falls.(17, 18)

This case report serves as a reminder of the necessity of performing a complete medication history to identify potentially harmful medications including OTC products, ensure medication causes for new symptoms are ruled out, and intervene on medications used to treat adverse events of other medications (i.e., prescribing cascade).

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