

## Toxic Interaction Between Fluoxetine And Donepezil: A Case Of Cholinergic Toxidrome

*To the Editor:* Donepezil is a reversible inhibitor of the enzyme acetylcholinesterase used to treat mild-to-moderate dementia. It is metabolized by CYP 450 isoenzymes 2D6 and 3A4. We present a patient who developed cholinergic toxicity from donepezil after starting fluoxetine.

Mr. K is a 65 yo male with schizoaffective disorder, bipolar type. He was admitted to an inpatient psychiatric unit due to increased agitation, fecal incontinence, and new behaviors of smearing feces and repeatedly placing his fingers in his rectum. His vitals were 129/56; 107, 20, 96.1. Physical exam was notable for excessive salivation, lacrimation, and fecal incontinence. He drooled excessively and periodically used a small towel and shoved deep into in his mouth. He made eye contact and nodded periodically in response to questions but was otherwise unable to meaningfully engage in interview. Complete blood count and chemistry panel were within normal limits.

The patient was restarted on all of his outpatient medications including

fluoxetine 20mg daily and donepezil 10mg nightly. Records indicated that he had been on donepezil for the last 3 years and that fluoxetine was added 2 weeks prior to admission. Due to concern for a cholinergic toxidrome, donepezil and fluoxetine were discontinued. Within 48-hours the patient's symptoms improved. He drooled less and no longer placed towels into his mouth. His diarrhea improved and ceased entirely which resulted in less preoccupation with his rectum. He became less agitated and was able to respond verbally to simple questions and able to communicate his needs to staff.

### Discussion

The cholinergic toxidrome is well known by the mnemonic SLUDGE (salivation, lacrimation, urination, diarrhea, GI distress, and emesis). To our knowledge this is the first reported case in the literature of a drug-drug interaction between donepezil and fluoxetine. We are aware of two published cases reporting possible interaction between donepezil and paroxetine.<sup>1</sup> This report cautions against the concomitant use of donepezil and other SSRIs that inhibit CYP450 2D6 including fluoxetine. It is well documented that fluoxetine is a potent inhibitor of CYP450 2D6 which can lead to elevated drug levels of medications

metabolized by this system.<sup>2</sup> It is highly probable that combining donepezil with fluoxetine led to elevated serum levels and adverse effects. According to the package insert, frequent side effects of donepezil include fecal incontinence, irritability and aggression; drooling is an infrequent side effect. The fact that Mr K's symptoms resolved when the medications were discontinued, we surmise that symptoms of cholinergic toxicity were due to increased levels of donepezil after recent addition of fluoxetine to his medication regime. This information, coupled with the knowledge that elderly adults metabolize medications slowly and are often more sensitive to side effects than younger patients, leads us to caution against using fluoxetine in combination with donepezil.

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### References

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