## Dose-Dependent Bradycardia With Citalopram in an Elderly Patient

**To the Editor:** Selective serotonin reuptake inhibitors (SSRIs) are the first line of treatment of depression and anxiety. They are preferred over other antidepressants because of their safety and tolerability. Despite their generally favorable side effect profile, adverse reactions related to the cardiovascular system have been reported, including QT prolongation, torsade de pointes, and ventricular arrhythmias.[1] The dose response of cardiovascular side effects with SSRIs has not been previously investigated. We report a dose-dependent bradycardia associated with use of citalopram.

***Case report.*** Mr A, a 66-year-old man, was diagnosed with panic disorder according to *DSM-IV-TR* criteria. He complained of a 6-month history of panic attacks peaking in 5 minutes accompanied by shaking, palpitations, sweating, and an impending sense of doom at a frequency of 2 to 3 attacks a day. These were followed by anticipatory anxiety. He reported a new onset of difficulty with driving due to the fear of panic attacks and also reported being uncomfortable in grocery stores. He reported of some concerns about his memory, particularly short-term memory, and some difficulty with names of people that he had known for a long time. He denied any functional decline. He scored 4/15 on the 15-item Geriatric Depression Scale (GDS-15)[2] and 29/30 on Mini-Mental State Examination.[3] A score above 5 on the GDS-15 is typically considered indicative of depression. His past medical history included hyperlipidemia, right rotator cuff surgery, and nicotine dependence. His medications included simvastatin 20 mg daily, aspirin 81 mg daily, and alprazolam 0.25 mg 3 times a day.

The patient was started on 10 mg/d of citalopram. He was seen for a follow-up visit 2 months later wherein he reported improvement in anxiety. His panic attacks were less frequent, now at a frequency of once or twice a week. He also reported improvement in mood, appetite, and sleep. He was able to drive without the fear of having panic attacks but was unable to shop without being on guard.

His citalopram was increased to 20 mg/d. He reported feeling light-headed and dizzy and called the clinic 2 days after the increase in dose. Mean heart rate over several recordings in the subsequent 48 hours was 47 beats per minute (bpm). He complained of a sensation of something moving inside his body. Citalopram was reduced to 10 mg/d. His subjective feelings of lightheadedness resolved within a day, and the mean heart rate over several readings in the next 48 hours was 71 bpm.

All of the blood pressure and heart rate values were confirmed from the electronic memory of a home blood pressure monitoring kit and also at his visits to the clinic. At this point, he was having panic attacks at a frequency of 3–4 per week. His heart rate and blood pressure were closely monitored. His mean heart rate was stable at 72 bpm over the next week.

We attempted a rechallenge of the 20 mg dose of citalopram after a month for better control of panic symptoms. This resulted in a prompt return of bradycardia, with his mean heart rate dropping to 53 bpm. His dose was again reduced to 10 mg/d, and he continues to be treated with 10 mg/d of citalopram with good control of panic disorder.

Although SSRIs are the first-line of treatment of depression in older adults, they need to be used with caution. Several uncommon side effects have been reported with their use in elderly including akathisia,[4] gastrointestinal bleeding,[5] and hip fractures,[6] which may be unique to their use in the elderly.

SSRIs have fewer anticholinergic and antihistaminergic properties when compared with tricyclic antidepressants. This translates to fewer cardiotoxic side effects, but nevertheless the elderly are at higher risk of developing these side effects when compared to young adults.

Several mechanisms have been proposed for the cardiotoxicity of SSRIs. In animal studies, fluoxetine is found to have cardiodepressant and vasodilatory properties.[7] Fluoxetine and citalopram also have antiarrythmic and proarrythmic properties.[8] Bradycardia induced by SSRIs could be explained by their propensity to inhibit sodium and calcium channels in the heart, which has been demonstrated to cause bradycardia in isolated hearts of rats, rabbits, and guinea pigs exposed to SSRIs such as citalopram and fluoxetine.[1] Another study demonstrated that citalopram inhibited L-type calcium channel current in rat cardiomyocytes in tissue culture, thus causing cardiotoxic effects.[9] In patients receiving both SSRIs and β-blockers, SSRIs increase the levels of β-blockers by inhibiting cytochrome P450 enzymes, thus further increasing the potential for bradycardia.[8] We checked for drug interactions between citalopram and simvastatin and found none.

Induction of bradycardia in this patient goes along with other published studies of adverse reactions of the SSRIs, in which hypotension and bradycardia were more often reported in older adults.[10] We assessed the development of bradycardia with citalopram using the Naranjo et al criteria.[11] The onset of bradycardia with increased dose of citalopram and its resolution with decreased dose suggests a causal relationship. This relationship is further strengthened by the reemergence of bradycardia upon rechallenge with the increased dose of citalopram. The Naranjo et al probability scale revealed a highly probable adverse reaction. In this case, the bradycardia was dose related with 10 mg/d of citalopram being well tolerated, suggesting that careful monitoring of adverse reactions can let clinicians continue the use of citalopram at lower doses for the treatment of panic disorder.

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