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Health Canada Warning on Citalopram and Escitalopram—Its Effects on Prescribing in Consultation-Liaison Psychiatry

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Background: *Reports have suggested that citalopram and escitalopram may prolong the QTc interval, leading Health Canada to issue a warning to limit their dosages in 2012. Little is known about the effects of this warning and similar ones (e.g., by the Food and Drug Administration) on antidepressant prescribing in inpatients with acute medical illness, who are theoretically at high risk of QTc prolongation. The main objective of our study is to examine the effect of the Health Canada warning on citalopram/escitalopram prescribing patterns in the consultation-liaison (C-L) psychiatry setting.* **Methods:** *We performed a retrospective cohort study including 275 randomly selected inpatients with medical illness assessed by the psychiatric C-L team of a large Canadian academic hospital between 2008 and 2014. We grouped patients based on whether they were assessed by the C-L team before or after the citalopram Health Canada warning. Our primary outcome was change in citalopram/escitalopram prescribing patterns.* **Results:** *We found that of patients seen before the Health Canada warning, a significantly higher number were prescribed citalopram/escitalopram (44.1% vs. 22.3%, $\chi^2 = 14.835$, $p < 0.001$), even after controlling for confounders. However, the percentage of patients using a citalopram/escitalopram dose exceeding those recommended by the Health Canada warning was similar in both groups (8.9% vs. 12.1%, $\chi^2 = 0.233$, $p = 0.63$).* **Conclusions:** *Overall, C-L psychiatrists were less likely to prescribe citalopram/escitalopram following the Health Canada warning, which did not translate into safer dosing. Clinicians should not avoid prescribing citalopram/escitalopram appropriately in medically vulnerable inpatients when benefits outweigh disadvantages.*

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INTRODUCTION

Over the last 25 years, selective serotonin reuptake inhibitors (SSRIs) have emerged as first-line pharmacologic agents for depression and anxiety. This has been in large part due to their favorable side effect profile compared with tricyclic antidepressants, including less cardiac toxicity.[1] However, in recent years, reports have suggested that SSRIs, especially citalopram and escitalopram, may prolong the QTc

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interval.[2] In Canada, these concerns have led to a safety announcement in January/May 2012 regarding the association of citalopram/escitalopram with QTc interval prolongation and torsades de pointes, recommending that clinicians limit citalopram and escitalopram prescribing to 40 and 20 mg/d, respectively (or 20 and 10 mg/d, respectively, in patients with hepatic impairment and/or who are aged ≥ 65 y).[3,4] The Health Canada warning has an important effect on clinical practice: clinicians who have achieved positive patient outcomes from higher doses of citalopram/escitalopram are faced with the dilemma of adhering to the warning and potentially undertreating depression and anxiety by using insufficient doses or avoiding these medications.[5]

Although patients hospitalized for acute medical illness are theoretically at great risk for QTc prolongation and to a lesser extent, torsades de pointes,[6] to the best of our knowledge, no study has yet examined the effect of the Health Canada warning on antidepressant prescribing patterns and cardiac outcomes in this vulnerable population although a recent paper by Fabo et al.[13] examined the effect of the Food and Drug Administration warning on citalopram prescribing patterns in a sample of older adults hospitalized in psychiatry or medical wards. In this article, we hypothesize that (1) the warning has made C-L psychiatrists reluctant to prescribe citalopram/escitalopram in the acute medical setting, but (2) we did not expect that antidepressant prescribing changes would affect cardiac outcomes.

MATERIALS AND METHODS

Study Design and Population

We performed a longitudinal retrospective cohort study. We reviewed the records of 275 randomly selected inpatients with medical illness assessed by 3 psychiatrists and >30 psychiatry residents of the C-L team for depression or anxiety or both between July 1, 2008 and April 1, 2014 at the Jewish General Hospital (JGH) in Montreal, Canada. Patients were eligible to be included in our study regardless of their age and medication use (citalopram/escitalopram, other antidepressants, or no antidepressants), as long as they were admitted to a JGH medical/surgical ward during the aforementioned period and if the reason for consultation was anxiety or depression or both. The data collectors (A.D. and S.N.) had access to all the names of the 923 patients seen by C-L psychiatrists between July 2008 and April 2014. After screening the patients based on the aforementioned inclusion criteria, we entered their names into a list in an excel sheet, performed simple randomization, and chose the first 275 patients in this randomized list. Patients exposed to citalopram/escitalopram or other antidepressants included those who were started on an antidepressant at the time of the consultation (incidental users) as well as those who were already on an antidepressant and maintained on it by our team (prevalent users). Overall, 46% (41/89) of citalopram/escitalopram users had been newly prescribed these medications during their hospitalization. The follow-up period started from the time the patients were first seen by the C-L team and ended either (1) on day 30 after the assessment by the C-L team, (2) upon discharge from the hospital, or (3) upon death during the admission, whichever came first. In the event where the patients were discharged or died before the 30-day follow-up period, we recorded the latest data before discharge or death. Ethics approval was obtained from the JGH Research Ethics Office for this study.

Outcome Measures

Our primary outcome was change in antidepressant prescribing patterns, which was assessed by determining the proportion of patients receiving citalopram/escitalopram before and after the Health Canada warning. We also examined the percentage of patients exceeding the maximum daily dose recommended by the Health Canada warning (i.e., 20 mg and 10 mg for patients older than 65 years and 40 mg and 20 mg for patients younger than 65 years for citalopram and escitalopram, respectively) before and after the warning. Only the starting dose of citalopram/escitalopram was recorded. To obtain medication use and dosing information, patients' prescriptions during the 30-day follow-up period were all made available in the JGH's electronic medical record system and were thoroughly screened by the data collectors (A.D. and S.N.).

Our secondary outcome was a major adverse cardiac event occurring within the 30-day follow-up period across the entire cohort of patients. This included (1) ventricular arrhythmias (defined as accelerated idioventricular rhythm, premature ventricular contractions, monomorphic/polymorphic ventricular