CR016396 Executive Summary

Evaluating the Risk of Serious Ventricular Arrhythmia and Sudden Cardiac Death Among Users of Domperidone

This retrospective population-based study evaluated the combined risk of serious ventricular arrhythmia (SVA) and sudden cardiac death (SCD) in current users of domperidone compared with 1) current users of proton pump inhibitors (PPI's) and 2) current users of neither medication. It a case-control design nested in a cohort of Saskatchewan residents with at least one dispensing of domperidone or a PPI between 1990 through 2005, stratified on diabetes status and controlled for confounding by age, sex, calendar time, comorbidities, and concurrent medications.

Possible cases of SVA/SCD were verified by cardiologist review of electronic patient profiles, hospital record data, and vital statistics information, with exposure status masked. Up to four controls were matched to each case by the event date for the case, year of birth, sex, and diabetes status.

Conditional logistic regression was used to estimate the odds ratio of current domperidone exposure relative to nonuse (or, alternatively, to current PPI exposure), adjusted for possible confounding variables. Stratified analyses were performed in those with and without diabetes.

1,608 cases (49 SVA, 1,559 SCD) and 6,428 controls were identified from the 83,212 individuals in the cohort who remained after excluding those with a diagnosis of cancer. The cases and matched controls had mean age 79.4 years, 52.9% were female, and 22.2% had diabetes.

With nonusers of domperidone or PPI as the reference group, unadjusted odds ratios (OR's) for SVA/SCD were: Current domperidone users: 1.67; 95% CI: 1.37–2.04, current users of both domperidone and PPI: 2.09, 95% CI: 1.40–3.11. Past use of domperidone was not associated with increased risk of SVA/SCD. The increased risk of SVA/SCD in current domperidone users was attenuated somewhat in the adjusted analysis (OR: 1.59; 95% CI: 1.28–1.98). In the stratified analysis by diabetes status, the estimated OR was 1.27 (95% CI: 0.79–2.03) in diabetics and 1.69 (95% CI: 1.32–2.17) in non-diabetics. An unadjusted increased risk of 53% in current PPI users compared with nonuse decreased to an 11% increase in the adjusted analyses. In analyses using current PPI as the reference group, the adjusted OR for current domperidone use was 1.44, 95% CI: 1.12–1.86, and varied little by diabetes status.

In conclusion, a modestly increased risk of SVA/SCD was found with current use of domperidone in relation to nonuse of either study drug, as well as in relation to current PPI use. A change in the point estimate for this association toward the null in a model adjusting for multiple potential confounding factors suggests that accounting for other

such variables for which we did not have information from the SH database might further attenuate the magnitude of the association we observed. Steps to further evaluate this association include analysis by age, duration of domperidone use, and estimated dose.

This Study is based in part on de-identified data provided by the Saskatchewan Ministry of Health. The interpretation and conclusions contained herein do not necessarily represent those of the Government of Saskatchewan or the Saskatchewan Ministry of Health.

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