1550062

Variation in the Cyp2d6 Genotype Is Not Associated With Carvedilol Dose Changes in Patients with Heart Failure

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Carvedilol is the standard of care for heart failure (HF) patients. Carvedilol is partially metabolized by the highly polymorphic enzyme, CYP2D6. To reach an effective dose while avoiding adverse drug reactions (ADR), testing of CYP2D6 genotype prior to carvedilol initiation should be considered. The objectives were to determine CYP2D6 metabolic genotypes in an Israeli cohort of HF patients and investigate the relationship between genotype, carvedilol dose, and number of ADRs in order to consider CYP2D6 genotyping prior to treatment initiation.Descriptive and inference statistics were performed followed by correlation and regression analyses. 93Patients on carvedilol were CYP2D6 genotyped and classified as poor, intermediate, extensive, or ultra-rapid metabolizers. UM, n=6, 6.5%; IM n=11, 11.8%; EM n=70, 76.3%; PM n=5, 5.4%. The initial carvedilol dose increased significantly according to patients clinical needs in each of the four genotype groups.Twenty-two patients experienced adverse events(ADRs). There were not significant differences among the dose and the number ADRs after 3, 12 and 60 months following initiation of carvedilol treatment in each genotype group. There were no statistically significant differences in carvedilol doses among those treated with 4 medications compared with those treated with 5 or more concomitant drugs. Twenty-two patients were also treated with 2D6 inhibitors (amiodarone, n=19; antidepressants, n=4). Regression analyses revealed that genotype group affiliation and number of adverse drug reactions were not predictive of carvedilol dose changes. Patient weight was the only significant predictors for the carvedilol dose. CONCLUSIONS:No relationship was found between carvedilol dose and patient CYP2D6 genotype and number of adverse drug reactions in an Israeli cohort. Therefore, the recommendation of CYP2D6 genotyping prior to carvedilol initiation should be questioned.