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Genetic variation in the CYP2D6 gene is associated with a lower heart rate and blood pressure in beta-blocker users

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Abstract

Several beta-blockers are metabolized by the polymorphic enzyme cytochrome P450 2D6 (CYP2D6). CYP2D6*4 is the main polymorphism leading to decreased enzyme activity. The clinical significance of impaired elimination of beta-blockers is controversial, and most studies suffer from inclusion of small numbers of poor metabolizers (PMs) of CYP2D6. In this study, the association between CYP2D6*4 and blood pressure or heart rate was examined in 1,533 users of beta-blockers in the Rotterdam Study, a population-based cohort study. In CYP2D6 *4/*4 PMs, the adjusted heart rate in metoprolol users was 8.5 beats/min lower compared with *1/*1 extensive metabolizers (EMs) (P < 0.001), leading to an increased risk of bradycardia in PMs (odds ratio = 3.86; 95% confidence interval 1.68-8.86; P = 0.0014). The diastolic blood pressure in PMs was 5.4 mm Hg lower in users of beta-blockers metabolized by CYP2D6 (P = 0.017) and 4.8 mm Hg lower in metoprolol users (P = 0.045) compared with EMs. PMs are at increased risk of bradycardia.

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