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Frequent Atrial Fibrillation in CYP2D6 Deficiency

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Genetic mutations which predispose to the development of atrial fibrillation (AF) have increasingly been identified, most of these directly encoding subunits of cardiac Na (+), Ca (++) and K (+) channels, but others encoding atrial natriuretic peptide and the renin-angiotensin-aldosterone systems.[1]

The hepatic cytochrome P450-2D6 (CYP-2D6) isoenzyme system metabolizes 25% of prescribed medications, including all class I and class III anti-arrhythmics commonly used in the treatment of AF with its activity severely impaired in 7-10% of Caucasians, 3-4% of Afro-Americans, and 1% of Asians resulting in their clarifications as poor metabolizers (PM's) effective metabolizers (EM), the status of most subjects, and very effective metabolizers (VEM) in 1-2%. PM status often requires doses of antiarrhythmic medications which are lower than those required in patients without this deficiency in order to avoid drug toxicity, and VEM patients often are inadequately treated by conventional antiarrhythmic doses.

Three investigations have reported larger percentages of CYP-2D6 deficient patients among these with AF. Jazwinska-Tarnawaska et al[2] demonstrated 11 PM subjects (26%) among 42 patients with AF, a frequency greater than that among other Caucasian populations (P<.02), and suggested that impaired CYP-2D6 activity might be more frequent among patients with AF.

Chow et al[3] identified 9 PM subjects (15%) among 60 Chinese patients with AF in Hong Kong, a higher percentage than the 1% reported in other Chinese populations (P<.01).

Martinez-Selles et al[3] among 40 Spanish subjects with PAF documented phenotypically PM status in 19, EM status in 16, and VEM status in 5. They expressed surprise that almost half of their subjects were PM, but did not report additional genetic details of their patients, and suggested phenotyping as potentially helpful in selecting the proper dose of antiarrhythmic medications. Twenty-one percent of their PM patients and 6.25% of their EM patient's demonstrated drug-induced adverse effects.

Paroxysmal atrial fibrillation (PAF) is 4-5 times more frequent among habitual endurance athletes than among other men of similar age who are similarly without other cardiovascular disease, a pattern which is considered to result from exercise-related myocardial remodeling and left atrial enlargement.[1] We recently observed an habitual marathon runner who fainted at age 81 after his only addition of propafenone (150mg), to the "Pill-in-a-Pocket" quinidine sulfate (600mg) which he had utilized successfully to treat PAF for 26 years and who was later found to demonstrate CYP-2D6 alleles 4 and 41, classifying him as a poor/intermediate 2D6 metabolizer. He is apparently the only endurance athlete with PAF who has undergone CYP-2D6 analysis. Since appropriate therapy for endurance athletes with AF has never been defined, CYP analysis of other athletes with AF would seem to be of potential benefit in determining their frequency of PM status as well their most appropriate therapy and evaluation of CYP-2D6 status in other non-athletic patients with AF helpful in determing the degree with which its deficiency is associated with this arrhythmia.

References:

1. Parvez B, Darber D. Lone AF-etiologic factors and genetic insights into pathophysiology. J Atr Fibrillation 2010;12:675-84.
2. Jazwinska-Tarnawska E, Orzechowska-Juzwenko K, Niewinski P, et al. The influence of CYP2D6 polymorphism on the antiarrhythmic efficacy of propafenone in patients with paroxysmal atrial fibrillation during 3 months propafenone prophylactic treatment. J Clin Pharmacol 2001;39:288-92.
3. Chow MS, White CM, Lau CP, Fan C, Tang MO. Evaluation of CYP2D6 oxidation of dextromethorphan and propafenone in a Chinese population with atrial fibrillation. J Clin Pharmacol 2001;41:92-6.
4. Martinez-Sells M, Castillo I, Montenegro P, Martin ML, Almendral J, Sanjurjo M. Pharmacogenetic Study of the Response to Flecainide and Propafenone in Patients with Atrial Fibrillation. Rev Esp Cardiol 2005;58(6):745-8.

Disclosures:
None

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