

The Resurgence of Flecainide

John Somberg^{a, b}

Over the last couple of years, there has been a marked increase in use of flecainide in the United States [1]. Sales of flecainide have dramatically increased. The increase in flecainide use has been to prevent recurrence of atrial fibrillation (AF) [2]. For prevention of AF, flecainide is very effective [2-6]. The recent American Heart Association/American College of Cardiology (AHA/ACC) guidelines for AF therapy list flecainide as a 2a indication with a level of evidence of A [7]. Given that there is no warning in the flecainide package insert against starting flecainide out of hospital, the use of flecainide can be very convenient for patients, unlike sotalol or dofetilide that instructs a 3-day hospital load. The side effect profile of flecainide is minimal unlike amiodarone that has side effects affecting every organ.

In fact, the use of flecainide is quite safe in patients with normal ejection fractions without structural heart diseases. The reason flecainide was of limited use was the results of the Cardiac Arrhythmias Suppression Trial (CAST) reported in 1991, which found that flecainide increased mortality in post myocardial infarction (MI) patients with ventricular premature beats [8]. The outcome was attributed to pro-arrhythmic action of flecainide in patients with the substrate for sustaining re-entrant ventricular arrhythmia. The surprising results of the CAST study dramatically changed medical practice. Ventricular premature contraction (VPC) suppression was out, and the use of Ic agents like flecainide markedly decreased. I can recall the concern of referring physicians when I prescribed flecainide for their young patients with symptomatic paroxysmal supraventricular tachycardia (PSVT) who had normal hearts. I always would receive calls with marked concern for pro-arrhythmia risk in light of the CAST study. A risk without supporting evidence in patients without structural heart disease.

Another concern with the prescribing of flecainide is that the drug can reduce concealed conduction at the atrioventricular (AV) node, causing 1:1 AV node conduction by slowing atrial rate [9]. Flecainide can also cause AF to organize to atrial flutter with 1:1 conduction causing a marked increase in ventricular rate with hemodynamic collapse [9, 10]. It is thus essential to co-prescribe flecainide with an AV node blocking

agent, beta blocker, verapamil, or diltiazem. Verapamil is negatively inotropic and can combine with the negative inotropic actions of flecainide. Diltiazem can increase flecainide blood levels by decreasing flecainide hepatic metabolism.

After four decades the specter of CAST has subsided, and the medical community has learned that the pro-arrhythmia risk of flecainide is not a problem given to patients with normal hearts. However, we must not forget that this is not the case for patients with ischemia, structural heart disease, conduction problems and patients post MI or with heart failure. These patients are at risk from flecainide, and its use should be avoided in patients at risk. Memories are short, and we must not forget the lessons of the CAST study and our understanding that antiarrhythmics such as flecainide are pro-arrhythmic in patients with the substrate for arrhythmias. This concern is not inconsequential since perhaps half of patients with AF have structural heart disease of the ventricles and are probably at increased arrhythmic risk from flecainide.

Acknowledgments

None to declare.

Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Data Availability

The author declares that data supporting the findings of this study are available within the article.

References

1. Flecainide: drug usage statistics, United States, 2013 - 2021. <https://clincalc.com/DrugStats/Drugs/Flecainide>.
2. Burnham TS, May HT, Bair TL, Anderson JA, Crandall BG, Cutler MJ, Day JD, et al. Long-term outcomes in patients treated with flecainide for atrial fibrillation with stable coronary artery disease. *Am Heart J.* 2022;243:127-

Manuscript submitted March 22, 2024, accepted April 3, 2024
Published online April 15, 2024

^aCardiology & Pharmacology, Rush University, Chicago, IL 60612, USA.
Email: johnsomberg1@comcast.net

^bEditor-in-Chief, Cardiology Research

doi: <https://doi.org/10.14740/cr1642>

139. [doi pubmed](#)
3. Muzzey M, Tellor KB, Ramaswamy K, Schwarze M, Armbruster AL. Flecainide is well-tolerated and effective in patient with atrial fibrillation at 12 months: a retrospective study. *Ther Adv Cardiovasc Dis.* 2020;14:1753944720926824. [doi pubmed pmc](#)
 4. Anderson JL, Gilbert EM, Alpert BL, Henthorn RW, Waldo AL, Bhandari AK, Hawkinson RW, et al. Prevention of symptomatic recurrences of paroxysmal atrial fibrillation in patients initially tolerating antiarrhythmic therapy. A multicenter, double-blind, crossover study of flecainide and placebo with transtelephonic monitoring. Flecainide Supraventricular Tachycardia Study Group. *Circulation.* 1989;80(6):1557-1570. [doi pubmed](#)
 5. Kirchhof P, Andresen D, Bosch R, Borggrefe M, Meinertz T, Parade U, Ravens U, et al. Short-term versus long-term antiarrhythmic drug treatment after cardioversion of atrial fibrillation (Flec-SL): a prospective, randomised, open-label, blinded endpoint assessment trial. *Lancet.* 2012;380(9838):238-246. [doi pubmed](#)
 6. Valembois L, Audureau E, Takeda A, Jarzebowski W, Belmin J, Lafuente-Lafuente C. Antiarrhythmics for maintaining sinus rhythm after cardioversion of atrial fibrillation. *Cochrane Database Syst Rev.* 2019;9(9):CD005049. [doi pubmed pmc](#)
 7. Joglar JA, Chung MK, Armbruster AL, Benjamin EJ, Chyou JY, Cronin EM, Deswal A, et al. 2023 ACC/AHA/ACCP/HRS guideline for the diagnosis and management of atrial fibrillation: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation.* 2024;149(1):e1-e156. [doi pubmed](#)
 8. Echt DS, Liebson PR, Mitchell LB, Peters RW, Obias-Manno D, Barker AH, Arensberg D, et al. Mortality and morbidity in patients receiving encainide, flecainide, or placebo. The Cardiac Arrhythmia Suppression Trial. *N Engl J Med.* 1991;324(12):781-788. [doi pubmed](#)
 9. Gavin JL, Peigh GS, Kim SS. Paroxysmal Atrial Fibrillation on Flecainide Therapy. *Eur J Intern Med.* 2020;81:89-90. [doi pubmed](#)
 10. Colangelo T, Johnson D, Ho R. Flecainide-Induced Atrial Flutter With 1:1 Conduction Complicated by Ventricular Fibrillation After Electrical Cardioversion. *Tex Heart Inst J.* 2021;48(2):e197099. [doi pubmed pmc](#)