The Novel Antiarrhythmic Drug Dronedarone: Comparison with Amiodarone

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ABSTRACT

Dronedarone is a noniodinated benzofuran derivative that has been developed to overcome the limiting iodine-associated adverse effects of the commonly used antiarrhythmic drug, amiodarone. It displays a wide cellular electrophysiological spectrum largely similar to amiodarone, inhibiting the potassium currents $I_{Kr}$, $I_{Ks}$, $I_{K1}$, $I_{KACH}$, and $I_{sus}$, as well as sodium currents and L-type calcium currents in isolated cardiomyocytes. In addition, dronedarone exhibits antiadrenergic properties. In vivo, dronedarone has been shown to be more effective than amiodarone in several arrhythmia models, particularly in preventing ischemia- and reperfusion-induced ventricular fibrillation and in reducing mortality. However, an increased incidence of torsades de pointes with dronedarone in dogs shows that possible proarrhythmic effects of dronedarone require further evaluation.

The clinical trials DAFNE, EURIDIS, and ADONIS indicated safety, antiarrhythmic efficacy and low proarrhythmic potential of the drug in low-risk patients. In contrast, the increased incidence of death in the dronedarone group of the discontinued ANDROMEDA trial raises safety concerns for patients with congestive heart failure and moderate to severe left ventricular dysfunction. Dronedarone appears to be effective in preventing relapses of atrial fibrillation and atrial flutter. Torsades de pointes, the most severe adverse effect associated with amiodarone, has not yet been reported in humans with dronedarone. Unlike amiodarone, dronedarone had little effect on thyroid function and hormone levels in animal models and had no significant effects on human thyroid function in clinical trials.

In conclusion, dronedarone could be a useful drug for prevention of atrial fibrillation and atrial flutter relapses in low-risk patients. However, further experimental studies and long-term clinical trials are required to provide additional evidence of efficacy and safety of dronedarone.

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