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Is newer better? Propafenone *versus* quinidine for conversion of atrial fibrillation

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In this issue of "Cardiology Journal", Kosior et al. [1] report a randomized trial of propafenone *versus* quinidine for recent onset atrial fibrillation. They found that patients assigned to propafenone, as opposed to quinidine, had a greater chance of converting to sinus rhythm earlier after drug administration. Specifically, propafenone 600 mg orally was compared to quinidine 400 mg initially then 200 mg every two hours in combination with intravenous digoxin to prevent a rapid ventricular response due to the anticholinergic effect of quinidine. Major adverse events were not observed, and minor events, although relatively common, were not statistically significantly different in the two arms.

Several groups have popularized a 'pill in the pocket' approach [2] to conversion of atrial fibrillation; in essence, this means a loading dose of either propafenone (600 mg as used in this study) or flecainide. Success rates of 56% to 83% have been reported using this methodology; the percentage success has varied with duration of atrial fibrillation prior to treatment [3]. Patients with infrequent episodes that historically either last more than a few hours, or do not self-terminate, are candidates for this approach. This strategy obviates the need for the patient to come to the emergency room or even call his or her cardiologist. If the patient has infrequent episodes the 'pill in the pocket' regimen spares him the need to take a preventive antiarrhythmic drug twice (or more frequently) a day.

Concerns with the 'pill in the pocket' strategy, however, include the potential for proarrhythmia with a high dose of antiarrhythmic drug given outside the hospital. Patients should be free of structural heart disease, atrio-ventricular (AV) block, Brugada syndrome and coronary disease. One advantage of the Class IC agents, propafenone or flecainide, over quinidine is that significant QT prolongation is very rare. QTc prolongation is expected with quinidine [4] (and other Class IA agents such as procainamide or disopyramide) which block the I_{Kr} channel, in addtion to I_{Na} channels, and the absence of it in this study is in fact somewhat unexpected. Torsades des pointes is well recognized with these agents as opposed to the Class Ic agents. On the other hand, the Class Ic agents may in some cases produce a phenomenon of 1:1 atrial flutter.

One-to-one atrial flutter can occur due to slowing of the flutter cycle length (possibly after conversion from fibrillation to flutter, also favored by these drugs), and in the absence of sufficient AV nodal blocking effect, each atrial activation may conduct to the ventricles. AV nodal conduction is more rapid for a slower atrial arrhythmia due to AV nodal refractoriness properties. This is one of the main concerns with the use of IC agents in a 'pill in the pocket' strategy, and means that the first time the drug is administered it should be done so in a monitored setting. In Kosior et al. [1] study, slightly more patients experienced atrial flutter after propafenone than quinidine, as expected. In terms of other side effects, the absence of significantly greater gastrointestinal intolerance with quinidine (14% *vs*. 5%, p = NS) suggests a lack of power in this relatively small study.

Propafenone converted atrial fibrillation to sinus rhythm in a more timely fashion than quinidine, 83.3% *vs*. 54.3% at 8-hours after drug initiation.

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Does this favor widespread adoption of this in-patient strategy for conversion? It is not clear if the 8-hour cutoff was a preselected endpoint or if 24 hours or another time point was the initial objective. If not preselected, the finding of a difference at 8-hours is less important.

In many health systems, such patients with new onset atrial fibrillation would be treated with cardioversion and discharged, especially if the atrial fibrillation was recurrent, rather than a first onset, and as long as significant heart failure or other symptoms were absent. This approach may be more expeditious than the prolonged observation period necessary with a QT prolonging drug. The 'pill in the pocket'; approach, on the other hand, for eligible patients with recurrent atrial fibrillation is another strategy to minimize the need for hospitalization.

In cases where inpatient pharmacological conversion is required, additional intravenous options include the Ikr blocker Corvert® (ibutilide fumarate [Corvert]) which carries a non-trivial rate of torsades at 3.9% [5]. Under development are intravenous agents which block the predominantly atrial I_{Kur} channels and therefore do not prolong the QTc or cause torsades as often. Another caveat related to pharmacological conversion not stressed in this publication is the need for anticoagulation in cases where the atrial fibrillation duration is greater than 24–48 hours, or is uncertain. The authors limited the study to patients with atrial fibrillation less than 48 hours. In many cases there is a lack of reliability of the patient's history (due to asymptomatic atrial fibrillation in essence) or certainty that makes anticoagulation and a delayed cardioversion or alternatively a transesophageal echocardiogram necessary for early cardioversion (pharmacological or electrical).

In summary, the quinidine *vs*. propafenone publication expands our knowledge base and experience with these agents, confirms a tendency toward superiority of the newer agent and of course calls for more data on the safe and expeditious management of new onset, or recurrent, atrial fibrillation.

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