To the Editor: Many patients with an implantable cardioverter-defibrillator (ICD) require concomitant antiarrhythmic drug (AAD) therapy at some point. Sotalol and especially amiodarone have been shown to reduce the number of ventricular tachycardia (VT)/ventricular fibrillation (VF) episodes and high-energy shocks therapies delivered by the ICDs (1). However, these drugs are frequently not tolerated or are ineffective (2).

Dofetilide, a selective I\textsubscript{Kr}-blocking agent, was as efficacious as sotalol in preventing the induction of sustained VT in patients with ischemic heart disease in 1 study (3). Dofetilide appears to be safe, as the mortality rate was not increased with dofetilide in patients with recent myocardial infarction and impaired left ventricular function (4).

The aim of this cohort study was to assess the efficacy and tolerability of dofetilide in patients with ICDs who have frequent VT/VF and who either failed or did not tolerate conventional AAD therapy.

The study included all defibrillator patients from our center who were placed on dofetilide for frequent VT/VF defined as either electrical storm (≥3 episodes of VT/VF within 24 h) or an average ≥1 symptomatic episodes of VT/VF or appropriate shock per month. These patients did not tolerate or failed a mean number of 2.7 ± 1.0 AADs (range 2 to 5) alone or in combination, including amiodarone in all but 1 patient.

The primary end point was the total number of VT/VF episodes. Secondary end points were mortality, number of total shocks, appropriate shocks, electrical storm, hospitalization, and drug discontinuation. The patients served as their own controls: the "on-dofetilide" treatment period was compared with an equivalent duration of a "pre-dofetilide" treatment period just prior to initiating dofetilide, when the patients had been treated with other AADs. Continuous variables are expressed as mean or median as appropriate. For statistical comparisons, paired Student t test, Wilcoxon signed ranked test, and chi-square test were used as appropriate.

Eighteen patients were included in the study. All but 1 patient was male, most patients had a history of coronary artery disease, their average left ventricular ejection fraction was 30%, and all received the ICD for secondary prophylaxis. In the 90 days preceding dofetilide initiation, patients had a median of 11 VT/VF episodes and 1.5 shocks from the ICD.

Amiodarone was ineffective in 2 patients; it had to be discontinued because of side effects in 13 patients, and in another 2 patients because the defibrillation threshold was high. Sotalol was used in 14 patients. Other AADs included quinidine, procainamide, mexiletine, propafenone, flecainide, and azimilide.

The mean dose of dofetilide was 778 ± 410 \( \mu \)g/day. The QT\textsubscript{c} (QT interval corrected for heart rate) significantly increased on dofetilide compared with baseline (494 ± 45 vs. 461 ± 48, \( p = 0.001 \)). No patient required a reduction of the dofetilide dose due to side effect or excessive QT\textsubscript{c} prolongation. No patient developed torsade de points VT.

All patients continued to take a beta-blocker while on dofetilide. Dofetilide as a sole antiarrhythmic drug was effective in 9/18 (50%) of the patients (“responders”). Three patients were restarted on low-dose amiodarone, whereas mexiletine was added in 5 patients, and 1 patient was given both amiodarone and mexiletine.

Electrical storm occurred in fewer patients taking dofetilide than prior to dofetilide (5 of 18 patients vs. 13 of 18 patients, \( p = 0.018 \)), and the number of electrical storm episodes was reduced (\( p = 0.005 \)) (Table 1). The number of VT/VF episodes was also reduced (\( p = 0.007 \)).

Patients were followed for 15.5 ± 12.9 months (range 1 to 39 months) (Table 1). On dofetilide, there was a tendency toward reduced number of VT/VF episodes, reduced number of shocks from the ICD, and reduced number of electrical storm episodes. Fewer patients experienced electrical storm on dofetilide (8 of 18 patients vs. 15 of 18 patients, \( p = 0.035 \)). Both all-cause hospitalization and hospitalization for electrical storm were reduced by dofetilide. One patient required radiofrequency ablation of VT. One nonarrhythmic death occurred that was unrelated to dofetilide.

In the subgroup of the 9 responders, the number of VT/VF episodes, total shocks, appropriate shocks, appropriate anti-tachycardia pacing, electrical storm, and hospitalizations were significantly reduced both during short-term and medium-term follow-up.

Dofetilide-based antiarrhythmic therapy was well tolerated and moderately effective for electrical storm and/or frequent VT/VF in patients who did not tolerate or failed amiodarone-based antiarrhythmic therapy.

Effective arrhythmia control was achieved in 50% of patients, whereas the other 50% of patients required further intervention at some point during the follow-up. Overall, an approximately 40% reduction was observed in the number of VT/VF episodes on dofetilide-based therapy compared with conventional AAD therapy (mainly amiodarone). However, the unknown natural course of frequent VT/VF episodes could significantly affect our findings. The 40% reduction in the number of VT/VF episodes is less than what was observed with amiodarone in the OPTIC (Optimal Pharmacological Therapy In Cardiovascular Defibrillator Patients) trial, but our study used a different patient population (1). Even this modest 40% reduction in the number of VT/VF episodes translated into fewer hospitalizations.

ICD patients with frequent episodes of VT, especially after failure or intolerance of amiodarone, should be considered for an
ablation procedure (5). However, 30% to 100% of the patients had to continue an AAD after ablation. This was a small, retrospective, single-center cohort study. There was no control group. The effects of dofetilide could be confounded by the concomitant use of other AADs and amiodarone washout.

Dofetilide could be considered as an adjuvant antiarrhythmic therapy for patients with an ICD and frequent VT/VF if the findings of this study are confirmed in a randomized controlled trial.

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Please note: Dr. O’Connell is the president of Resolve Radiologic, a radiology software design company.

REFERENCES


Table 1

<table>
<thead>
<tr>
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<th>Medium-Term (15 Months)</th>
<th>Short-Term (3 Months)</th>
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<tbody>
<tr>
<td></td>
<td>Pre-Dofetilide</td>
<td>Post-Dofetilide</td>
</tr>
<tr>
<td>VT/VF episodes</td>
<td>21 (7.70, 75)</td>
<td>9 (3.75, 39.5)</td>
</tr>
<tr>
<td>Total shocks</td>
<td>5 (1, 15)</td>
<td>1.5 (0, 6.5)</td>
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<tr>
<td>Appropriate shocks</td>
<td>2 (0, 9.25)</td>
<td>0.5 (0, 5)</td>
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<tr>
<td>Appropriate ATP</td>
<td>8.5 (1.75, 70.25)</td>
<td>2 (2, 31.25)</td>
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<tr>
<td>Inappropriate shocks</td>
<td>0 (0, 0.25)</td>
<td>0 (0, 0)</td>
</tr>
<tr>
<td>Inappropriate ATP</td>
<td>0 (0, 0.25)</td>
<td>0 (0, 0)</td>
</tr>
<tr>
<td>Nonsustained episodes</td>
<td>17 (0.75, 55)</td>
<td>1.5 (0, 42.75)</td>
</tr>
<tr>
<td>Electrical storm episodes</td>
<td>1.5 (1, 6)</td>
<td>0 (0, 1)</td>
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<tr>
<td>Hospitalization (all-cause)</td>
<td>2 (1, 2)</td>
<td>0 (0, 1)</td>
</tr>
</tbody>
</table>

Values are given as median (25th, 75th percentiles), except as indicated.

ATP = anti-tachycardia pacing; VF = ventricular fibrillation; VT = ventricular tachycardia.