Dofetilide is safe and effective in preventing atrial fibrillation recurrences in patients accepted for catheter ablation

Yana Shamiss, Yaariv Khaykin*, Richard Oosthuizen, Denise Tunney, Bradley Sarak, Marianne Beardsall, Catherine Seabrook, Linda Frost, Zaev Wulffhart, Bernice Tsang, and Atul Verma

Southlake Regional Health Center, 105-712 Davis Drive, Newmarket, ON, Canada L4E 4M5

Received 1 April 2009; accepted after revision 7 September 2009; online publish-ahead-of-print 8 October 2009

Aims The aim of this study was to assess the safety and efficacy of dofetilide among patients refractory to other anti-arrhythmic drugs (AADs) and accepted for atrial fibrillation (AF) ablation.

Methods and results One hundred and twenty-seven of 454 patients (69% male, 58% paroxysmal, age 60 ± 10 years, AF duration 8 ± 7 years) scheduled for AF ablation between February 2004 and May 2008 were treated with dofetilide. Patients had failed 1.9 ± 1.1 AADs. Anti-arrhythmic drugs were stopped five half-lives before ablation and 3 months for amiodarone. Patients were followed for 15 ± 7 months with routine and symptom-driven monitoring. Success was defined as no further AF and partial success as a 50% reduction in frequency/duration of AF episodes. Thirty-six patients started dofetilide 158 ± 167 days before ablation: 9 had no improvement, 16 experienced partial success, 8 had no further AF, and 2 improved enough to forgo ablation. Seventy-one patients started dofetilide immediately following ablation, of which 14 had no improvement, 22 experienced partial success, and 32 had no further AF. Twenty patients started dofetilide 119 ± 153 days post-ablation, of which four had no improvement, seven experienced partial success, and nine had no further AF. Six patients discontinued dofetilide during initiation for QT prolongation.

Conclusion Dofetilide appears safe and effective in preventing AF in patients refractory to other AADs undergoing catheter ablation.

Keywords Dofetilide • Atrial fibrillation • Catheter ablation • Anti-arrhythmic drugs

Introduction

Atrial fibrillation (AF) is the most prevalent persistent cardiac arrhythmia observed in clinical practice.1,2 The prevalence of AF is estimated at 0.4% in the general population, but it is higher in men and increases with age and severity of heart failure or valvular disease.3 It can be associated with haemodynamic impairment, reduced quality of life, and high risk of thrombo-embolism.2 Conventional treatment approaches to AF include anticoagulation as well as either (i) restoration of sinus rhythm or (ii) allowing AF to persist while ensuring adequate ventricular rate control.

In many patients, AF is thought to be triggered by ectopic activity originating in the pulmonary veins (PVs) and other specialized anatomic areas.4 It is thought to be maintained by areas with non-linear myocardial fibre orientation.5 Consequently, ablation strategies have been developed to isolate or eliminate sources of atrial ectopy and modify the substrate thought to maintain AF. Catheter ablation is now indicated for symptomatic AF in patients who have demonstrated resistance to anti-arrhythmic drugs (AADs).

Dofetilide is a Class III AAD that selectively blocks the rapid component of the delayed rectifier potassium channels (I\textsubscript{Kr}).6,7 It is considered a ‘pure’ Class III agent since it selectively prolongs cardiac action potential duration without significant other electrophysiological or haemodynamic effects. By prolonging the refractory period and QT interval in a dose-dependent manner, it is...
used to treat both atrial and ventricular arrhythmias. Although amiodarone is the most commonly used non-selective Class III agent, it is associated with significant risk of toxicity affecting the thyroid, lungs, liver, and multiple other organ systems. Several large studies in populations with a recent myocardial infarction (MI), congestive heart failure (CHF), or structural heart disease suggest that dofetilide is effective at maintaining sinus rhythm, with an acceptable risk of adverse events, and does not increase mortality. The most recent treatment guidelines list dofetilide as an alternative first-line anti-arrhythmic agent in patients with persistent AF or recurrent paroxysmal AF and CHF for which the goal of rhythm maintenance is set. Moreover, it is a second-line alternative in patients with co-existing coronary artery disease, and an alternative in patients with hypertension. As such, dofetilide is an ideal agent to use in patients who have failed several other AADs.

Dofetilide is currently FDA-approved but not Health Canada’s Health Protection Branch (HPB)-approved and thus is not marketed in Canada. The US FDA has approved dofetilide for conversion of AF and atrial flutter to normal sinus rhythm (NSR), but not for paroxysmal AF. Dofetilide has also been approved in the USA for maintenance of NSR in patients with AF/atrial flutter of >1 week duration who have been converted to sinus rhythm. Dofetilide is available in Canada only via Special Access Programme (SAP). Special Access Programme provides access to non-marketed drugs for practitioners treating patients with serious or life-threatening conditions when conventional therapies have failed. The SAP authorizes a manufacturer to sell a drug that cannot otherwise be sold or distributed in Canada. Concerns of pro-arrhythmia associated with dofetilide have prompted the manufacturer to develop evidence-based treatment guidelines requiring US institutions and prescribers to complete educational programmes before using the drug.

As there are little data systematically assessing the utility of oral dofetilide in patients refractory to other AADs and meeting guideline criteria for catheter ablation of AF, the goal of this study was to evaluate the safety and efficacy of oral dofetilide treatment in this population.

Methods

Data were retrospectively collected for patients receiving dofetilide at a single Canadian tertiary care centre. Of the entire cohort of 454 patients referred and accepted for PV antrum isolation according to current clinical practice guidelines,14 guided by intracardiac echocardiography (ICE) and circular mapping between February 2004 and May 2008, 127 were treated with dofetilide. Several clinical conditions lead to initiation of dofetilide therapy: (i) patients received dofetilide if they continued to have AF recurrences >30 s despite adequate therapy with a Class 1C anti-arrhythmic agent (flecainide 200 mg/day, propafenone 450 mg/day or greater), sotalol (160 mg/day or greater) continued for at least 1 month, or amiodarone (200 mg/day or greater) following a 10 g load; (ii) patients with a high prior burden of AF leading to amiodarone initiation, who had no AF while on amiodarone therapy, but had to stop the drug at least 3 months prior to catheter ablation; (iii) patients who did not tolerate therapy with a Class 1C anti-arrhythmic agent, sotalol, or amiodarone. A collaborative dofetilide initiation and dosing programme was jointly developed by the Heart Rhythm Program and the Department of Pharmacy at our institution. The entire cardiology staff, including nurses, pharmacists, and physicians, received in-service training on the use of dofetilide given by a PharmD (Y.S.). A teaching kit was developed, which included lecture material and select references. The department of pharmacy ensured that all new staff were certified. A list of all certified staff was kept at the department. All patients were initially seen by the electrophysiologist (A.V., Y.K., Z.W. or B.T.) who suggested dofetilide initiation, followed by a separate pre-assessment visit with a nurse practitioner (M.B. or L.F.) and an arrhythmia clinic nurse (C.S.). Dofetilide initiation was restricted to the electrophysiology service. Medication was ordered by a single pharmacist for all patients (D.T.). All patients received medication education on discharge by a dofetilide trained cardiac pharmacist. All cardiac pharmacists were trained to answer phone calls from community prescribers and pharmacists on potential drug interactions, adverse drug reactions, indications, and restrictions on the use of dofetilide. A treatment pathway including a list of admission orders (Appendix) was developed to facilitate this process.

Dofetilide initiation procedure

Amiodarone was discontinued at least 3 months before ablation in all patients, and all other anti-arrhythmic agents were stopped five half-lives prior to ablation. Dofetilide could be started in anticipation of ablation (Group I), immediately following ablation (Group II) to prevent early AF recurrences during the 3-month blanking period, or after the 3-month blanking period following ablation (Group III) to suppress recurrent AF in patients deemed ablation failures.

Amiodarone was stopped 4–6 weeks prior to dofetilide initiation and all other AADs were stopped five half-lives prior to dofetilide initiation. Patients were admitted to the hospital for continuous telemetry for 3 days during dofetilide initiation. Starting dose was selected based on the creatinine clearance and QTc/QTc measurements. Patients were given 500, 250, or 125 μg twice daily based on calculated creatinine clearance of >60, 40–60, or 20–40 mL/min, respectively. Dosage was reduced if QTc increased by >15% from baseline or exceeded 500 ms after the first dose to reduce the risk of pro-arrhythmia. If QTc increased beyond 500 ms any time after the second dose, dofetilide was discontinued. Patients who remained in AF after five doses were electrically cardioverted and monitored for an additional 24 h.

Patients were not given dofetilide if measured QTc was >440 ms at baseline or if they had severe renal dysfunction defined as creatinine clearance <20 mL/min. Drugs known to inhibit the cationic transport system and reduce renal excretion of dofetilide such as cimetidine, verapamil, and ketoconazole were discontinued. Patients with congenital or acquired long-QT syndrome were not considered for dofetilide treatment.

Atrial fibrillation ablation procedure

The ablation approach has been described previously. In brief, a 64-element linear phased array ICE probe (Siemens-AcuNav) was placed in the left atrium. It was used to guide transseptal punctures, position the circular mapping catheter, monitor for complications, and assess tissue overheating by monitoring for microbubble formation in patients treated using an 8 mm tip catheter. Double transseptal access to the left atrium was established under fluoroscopic and ICE guidance from the left femoral vein. The left atrium was instrumented with a decapolar fixed diameter deflectable circular mapping catheter used to roam the PV antra in search of high-frequency, PV-like potentials. It was followed by the ablation catheter used to ablate atrial myocardiunm exhibiting any such potentials.
Irrigated or 8 mm tip catheters were used for ablation. Power was titrated between 30 and 50 W with the temperature held <40°C with irrigated tip catheters or 55°C with 8 mm tip catheters. Endpoint of elimination of PV-like potentials in the area spanning from the interatrial septum anterior to the right PVs, across PV ostia and the posterior wall, to the ridge between the left PVs and the left atrial appendage was achieved in all patients. Additionally, for 47 patients still in AF at the end of the procedure, areas exhibiting complex fractionated electrograms were ablated. In those who developed organized atrial tachyarrhythmias at the end of the procedure, we attempted to map the source or the circuit using a combination of three-dimensional electroanatomical mapping and entrainment techniques. Patients persisting in an atrial tachyarrhythmia were converted to sinus rhythm using a biphasic transthoracic shock.

All patients received oral anticoagulation therapy for at least 1 month before and 3 months after ablation. It was continued indefinitely for those with CHADS-2 embolic risk score >1. Anticoagulation was bridged to subcutaneous low molecular weight heparin 4 days prior to the procedure followed by a pre-ablation transoesophageal echocardiography to rule out left atrial thrombus. During ablation, activated clotting time was maintained between 350 and 400 s. Patients presenting for ablation in AF were treated with half-dose low molecular weight heparin for 3 days following ablation and restarted their oral anticoagulation with double the usual dose of warfarin administered on the day of ablation.

Follow-up and outcomes

Patients were followed for 15 ± 7 months with routine and symptom-driven ambulatory monitoring. Specifically, 24 h Holter monitoring was carried out at 1, 3, 6, 9, and 12 months and loop event recorders were given to patients for a 2-week period whenever symptoms were reported.

Success was defined as no further symptomatic or asymptomatic AF (>30 s in duration). A significant improvement was defined as ≥50% reduction in the frequency or duration of AF episodes.

Statistical analysis

All continuous variables are expressed as mean ± SD, and a value of P < 0.05 was considered statistically significant.

Results

A total of 127 patients refractory to or intolerant of other AADs were accepted for AF ablation and received dofetilide. Table 1 illustrates baseline characteristics of the study cohort.

Seventy-seven patients had previously taken amiodarone, 53 had failed flecainide, 33 had failed propafenone, and 82 had failed sotalol. Patients had failed an average of 1.9 ± 1.1 AADs prior to consideration for dofetilide.

Of the 77 patients in our cohort who were previously treated with amiodarone, 48 (62%) stopped it due to gastrointestinal (GI) irritation, toxicity, or an allergic reaction and 29 (38%) discontinued amiodarone in preparation for ablation.

Of the 29 patients who discontinued amiodarone in view of ablation, 10 (34%) patients had no AF while on amiodarone and 19 (66%) were previously refractory to amiodarone. All 29 patients had symptomatic documented AF between amiodarone withdrawal and dofetilide initiation.

Thirty-six patients were started on dofetilide 158 ± 167 days immediately following ablation (Group II), and 20 were started on dofetilide 119 ± 153 days post-ablation because of recurrent AF (Group III). Six patients [83% female, baseline QTc of 439 ± 9 ms and 83% with mild-to-moderate left ventricular (LV) dyssynchrony] discontinued dofetilide during initiation due to excessive prolongation of their QT interval (Table 2). Female gender (P = 0.016), baseline QTc duration >429 ms (P < 0.0001), and mild-to-moderate LV dysfunction (P = 0.016) were significant predictors of dofetilide discontinuation during inpatient initiation.

Of the 36 patients in Group I who started dofetilide before ablation, three stopped it prior to ablation (one for ventricular bigeminy, one for bradycardia, and one due to ineffectiveness). Within Group I, 9 patients reported no improvement, 16 had a significant improvement, 8 had no further AF prior to undergoing ablation. While two of these patients felt well enough on dofetilide

### Table 1 Baseline characteristics of patients treated with dofetilide

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60 ± 10</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>69%/31%</td>
</tr>
<tr>
<td>Paroxysmal AF</td>
<td>74 (58%)</td>
</tr>
<tr>
<td>Persistent AF</td>
<td>34 (27%)</td>
</tr>
<tr>
<td>Permanent AF</td>
<td>19 (15%)</td>
</tr>
<tr>
<td>LA size (mm)</td>
<td>43 ± 6</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>&gt;60: 80 (63%), 40–60: 30 (24%), 20–40: 17 (13%)</td>
</tr>
<tr>
<td>Heart disease (CAD, CHF, CM, RHD, or LVH)</td>
<td>40 (31%)</td>
</tr>
<tr>
<td>Hypertensive disease</td>
<td>63 (50%)</td>
</tr>
<tr>
<td>Renal function (creatinine clearance)</td>
<td>96 ± 35 mL/min</td>
</tr>
<tr>
<td>Failed sotalol prior to dofetilide initiation</td>
<td>82 (65%)</td>
</tr>
<tr>
<td>Failed propafenone prior to dofetilide initiation</td>
<td>33 (26%)</td>
</tr>
<tr>
<td>Failed flecainide prior to dofetilide initiation</td>
<td>53 (42%)</td>
</tr>
<tr>
<td>On amiodarone prior to dofetilide initiation</td>
<td>77 (61%)</td>
</tr>
<tr>
<td>QT interval prior to initiation</td>
<td>415 ± 32 ms</td>
</tr>
<tr>
<td>QT interval at discharge</td>
<td>456 ± 25 ms</td>
</tr>
</tbody>
</table>

### Table 2 Incidence of excessive QTc interval prolongation/Torsade de pointes

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Study group (N = 127)</th>
</tr>
</thead>
<tbody>
<tr>
<td>QTc prolongation, n (%)a</td>
<td>6 (4.7)</td>
</tr>
<tr>
<td>After first dose</td>
<td>3 (2.4)</td>
</tr>
<tr>
<td>Subsequent doses</td>
<td>3 (2.4)</td>
</tr>
<tr>
<td>Torsade de pointes, n (%)b</td>
<td>0 (0)%</td>
</tr>
</tbody>
</table>

aQTc >15% above baseline after first dose or >500 ms following any dose (>350 ms in patients with ventricular conduction abnormalities). Uncorrected QT interval used when HR < 60 bpm.
bWhile being dosed within our program.
to forgo catheter ablation altogether, the other six chose to proceed with ablation as a means to discontinue chronic anti-arrhythmic drug therapy.

Of the 71 patients in Group II who started dofetilide at ablation, three stopped it (one for pro-arrhythmia concerns, one for GI upset, and one for an allergic reaction). Within Group II, 14 had no improvement, 22 had a significant improvement, and 32 had no further AF during the follow-up period.

Of the 20 patients in Group III who started dofetilide during follow-up for AF recurrences beyond the 3-month blanking period and were considered ablation failures, 8 failed flecainide, 3 failed propafenone, and 9 failed sotalol between their ablation and dofetilide initiation. Within Group III, four had no improvement, seven had a significant improvement in the reported frequency and severity of AF, and nine had no further AF while on dofetilide.

There were two significant events associated with dofetilide treatment. One patient had an allergic reaction during initiation and one patient discontinued the drug during follow-up for symptomatic ventricular bigeminy presumed associated with dofetilide.

No patient developed Torsade de Pointes (TdP) while medicated according to the dosing algorithm implemented by our program. Two patients reported episodes of TdP when their dose was increased in the setting of recurrent AF by emergency room physicians with no experience in dofetilide dosing. However, both patients ultimately resumed their prior dofetilide dose and had no further pro-arrhythmic events. There were no sudden cardiac deaths, episodes of ventricular fibrillation, or other serious adverse events reported. No association between dofetilide dose and clinical success was seen in this study.

Nine of 10 patients previously controlled on amiodarone were still controlled on dofetilide. Fourteen of 19 (74%) patients who were previously refractory to amiodarone were controlled or had a significant improvement in AF while on dofetilide before ablation. Of the 82 patients who previously failed or were intolerant of sotalol, 62 (76%) had no AF or experienced a significant improvement in AF while on dofetilide. Of the 33 patients who failed or were intolerant to propafenone, 24 (73%) had no AF or had a significant improvement in AF while on dofetilide. Of the 53 patients who failed or were intolerant to flecainide, 38 (72%) had no AF or had a significant improvement in AF while on dofetilide.

Of the 25 patients who failed or were intolerant of sotalol and were started on dofetilide pre-ablation, 8 (32%) had no AF and 11 (44%) had a significant improvement in AF prior to undergoing ablation. Of the 11 patients who failed or were intolerant of propafenone and were started on dofetilide pre-ablation, 2 (18%) had no AF and 3 (27%) had a significant improvement in AF prior to undergoing ablation. Among patients who were started on dofeti-

lide prior to ablation, 15 had previously failed or were intolerant of flecainide. Of these, 3 (20%) had no further AF and 5 (33%) had a significant improvement in AF while on dofetilide pre-ablation. Of the 20 patients who were refractory or intolerant of either Class 1C drug and were started on dofetilide pre-ablation, 4 (20%) had no further AF and 8 (40%) had a significant improvement in AF prior to ablation. Of the 13 patients who failed both a Class 1C drug and sotalol and were started on dofetilide pre-ablation, 3 (23%) patients had no AF and 6 (46%) had a significant improvement in AF prior to undergoing ablation.

In total, dofetilide was discontinued in 6 of 127 patients (5%). Of the 121 patients who received dofetilide beyond the initiation period, none experienced a significant adverse outcome provided the dose achieved during initiation remained the same. Of these, 94 (78%) had either no AF recurrences (49, 52%) or experienced a significant improvement in frequency and duration of AF episodes (45, 48%).

Discussion

This is the first study systematically evaluating the use of dofetilide in a large cohort of patients referred and accepted for AF ablation who were previously intolerant or failing other anti-arrhythmic drugs including amiodarone or who were previously controlled on amiodarone but stopped it in preparation for ablation. Amio-
darone was stopped only 4–6 weeks prior to initiation of dofeti-

lide instead of the recommended 3 months. The findings suggest that provided judicious use and a clearly defined treatment plan, dofetilide can be used in these patients, with little risk of significant adverse events and with considerable clinical efficacy. Amiodarone, considered by some to be the gold standard of medical therapy for AF, was discontinued for intolerance in 62% of the patients who were on it in our cohort and was ineffective in 66% of the patients who were able to tolerate it. Dofetilide on the other hand was toler-

ated by 95% of the patients and effective in 52% of the patients treated. Of the Group I patients in whom dofetilide was used pre-

ablation, dofetilide as a second- or third-tier therapy was effective in 24% of the patients and had partial efficacy beyond that achieved on baseline therapy in another 48% where other drugs failed or were not tolerated by the patients. Furthermore, 74% of the patients previously refractory to amiodarone, 76% of those pre-

viously refractory to sotalol, 60% of those who were previously refractory to a Class 1C drug, and 69% of those who were pre-

viously refractory to both sotalol and a Class 1C drug were con-

trolled or experienced a significant improvement with dofetilide prior to undergoing ablation.

Although prior studies have shown dofetilide to be effective in terminating acute episodes of AF and in long-term prevention of AF, its widespread use has been hindered by the risk of TdP. Atrial fibrillation is associated with reduced quality of life and mor-

bidity, but is not directly life-threatening, so the risk of a serious pro-arrhythmia with treatment would indeed be discouraging.

However, the results of this study suggest that dofetilide can effectively treat AF refractory to other AADs and, more impor-

antly, no sudden cardiac death occurred in 127 patients being con-

sidered for ablation for AF. Although previous studies have reported episodes of TdP without a defined dose titration sche-

dule, our experience suggests that with conservative patient selec-

tion and careful monitoring, dofetilide could be used safely in this patient population. Two patients who did experience TdP did so in the setting of inappropriate dofetilide dose adjustment by unquali-

fied medical personal. Both were able to resume their titrated dofetilide dose with no further pro-arrhythmic effect.

Risk factors for Torsade de pointes

Torsade de Pointes is the primary concern with dofetilide treatment. Episodes of TdP while on dofetilide have been documented with a prevalence rate between 0.3 and 4.8%, depending on the patient population and the dosing algorithm. Since the majority of cases
have occurred during dofetilide initiation, FDA mandates initiating
dofetilide in a hospital setting on telemetry. Pedersen et al. studied risk factors and predictors of TdP on dofetilide using data
from the two Danish Investigations of Arrhythmia and Mortality on dofetilide (DIAMOND) studies. Female gender, no MI within
8 weeks, NYHA III or IV, and baseline QTc duration were significant
predictors of TdP in patients treated with dofetilide. Our data
appears consistent with these risk factors since female gender,
mild-to-moderate LV dysfunction, and QTc duration >429 ms
were all identified as significant predictors of dofetilide discontinu-
ation during inpatient initiation for excessive QT prolongation.

Role of dofetilide in pharmacotherapy of atrial fibrillation patients
This study suggests that dofetilide should be considered for manage-
ment of AF in patients accepted for catheter ablation following
failure of or intolerance to other anti-arrhythmic agents. It appears
to be safe in this population with a conservative dosing algorithm
and is associated with a low risk of TdP. Occasionally, the drug was
used at doses inconsistent with guidelines, given in combinations
with interacting drugs, or uptitrated by non-certified practitioners
resulting in temporary reversible complications. Prudent patient selec-
tion, compensation for renal function, hospitalization for initiation,
monitoring of the QTc interval, and an expectation to withdraw
patients demonstrating contra-indications, all contribute to safety in
AF management with dofetilide before and after catheter ablation.

Limitations
The findings of the study are limited by the fact that this was a ret-
rospective study. On the other hand, the entire cohort of patients
accepted for catheter ablation at our centre was included in the
analysis suggesting that reported outcomes are generalizeable.

Dofetilide was started within 4–6 weeks following cessation of
amiodarone therapy in some of the patients. Thus, greater efficacy of
dofetilide in this population may be attributable to a combined effect
of amiodarone and dofetilide. At the same time, the study illustrates
safety of starting dofetilide within a shorter time span of amiodarone
discontinuation than is recommended by the current guidelines.

Patients in the study were started on dofetilide at various times—
before, immediately after ablation, and remote from ablation in
patients who failed ablation. They were monitored intermittently
rather than continuously leaving some concern over asymptomatic
AF recurrences. That said, this was a highly symptomatic group of
AF patients and based on current evidence, the role of catheter abla-
tion is to reduce AF symptoms since little is known about its effect on
longevity or prevention of embolic events. In this setting, any treat-
ment that would render AF less symptomatic would be viewed as ben-
eficial even with a residual risk of asymptomatic AF burden. A 50% 
reduction in AF burden while not a ‘hard outcome’ was clearly per-
ceived by the patients and reported on as a noticeable clinical
improvement. Furthermore, as a regional centre, all of these patients
were followed by our group and all AF recurrences were reported to
the arrhythmia clinic suggesting low likelihood of missing important
outcomes in some of these patients.

Conclusion
Dofetilide appears safe and effective in the treatment of AF in
patients who have previously failed or did not tolerate other
AADs and in those who were previously on amiodarone with a
judicious dosing algorithm. No patient in this cohort had TdP on
the titrated dofetilide dosing regimen. Dofetilide should be con-
sidered in patients accepted for catheter ablation of AF.

Conflicts of interest: none declared.
### Appendix

## Dofetilide Admission Orders

**Dofetilide in patients accepted for AF ablation**

**Guidelines for Completing Pre-Printed Orders**

1. Please use a ballpoint pen and press firmly.
2. Where appropriate, draw a line through orders not needed and initial.
3. Where tick-boxes are offered, only tick orders that are to be pursued.

**Charting Codes**

- SS: slip sent
- SMO: slip made out
- <: order attended to and copies in appropriate place
- COPIED: all orders copied and completed

| Diagnosis: | 1. Admit to telemetry bed: Dr. |
| DATE (mm/dd/yyyy): | TIME: |
| Height: cm | Weight: kg |
| NON-DRUG ORDERS | 1. Dofetilide | med PO Bid. |
| | a) Call Dr. | or ACNP to |
| | b) Hold a.m. dose until reviewed by MD or |
| | c) Hold dofetilide if QTc > 500ms vs QT and |
| | call MD or ACNP. |
| | warfarin daily, as ordered by MD or ACNP. |
| | Target INR: |
| | 3. Night sedation qhs PRN. |
| | 4. Acetaminophen 650 mg PO q4h PRN. |
| | 5. Dimenhydrinate 25-50 mg PO or IV q4h PRN. |
| | 6. Laxative daily PRN. |
| | 7. Saline lock. |
| | Pharmacists to see prior to D/C. |
| Baseline QTc: | Expected discharge date (after 6th dose): |
| (mm/dd/yyyy) | Discontinue the following, if currently prescribed: |
| | Verapamil |
| | Ketoconazole |
| | Cimetidine |
| | Trimethoprim/Sulfamethoxazole |
| | Prochlorperazine |
| | Meperidine |
| | Hydrochlorothiazide/timelurene |
| | Hydrochlorothiazide |

**Physician (print):** (sign):
# Dofetilide Initiation Protocol

## Dofetilide Orders

**THIS IS NOT A NOMOGRAM**
FOR USE BY THE ARRHYTHMIA SERVICE STAFF ONLY

<table>
<thead>
<tr>
<th>STEP 1:</th>
<th>STEP 2:</th>
<th>STEP 3:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong>&lt;br&gt;QT or QTc: __________</td>
<td><strong>Initial Dose based on Creatinine Clearance</strong></td>
<td><strong>2-3 hrs after the FIRST dose check QTc</strong></td>
</tr>
</tbody>
</table>

### Action

- **Greater than 440 msec**
  - Creatinine clearance
  - If increase in QT or QTc: ACTION

- **Dofetilide contraindicated**
  - Dofetilide dose
  - Actual New Dose

- **Less than or equal 440 msec:**
  - greater than 50 mL/min:
  - less than or equal 15%: continue same dose

- **see Step 2**
  - 500 mcg twice daily

- **msec = milliseconds**
  - 40 to 60 mL/min:
  - greater than 15% or > 500 msec: decrease dose by half

  - 250 mcg twice daily

- **If HR < 60 BPM use QT.**
  - > 500 msec: stop dofetilide

- **Otherwise use QTc**
  - 20 to 40 mL/min:

  - **125 mcg twice daily**
  - **no further down titration based on QTc is recommended.**

  - less than 20 mL/min:

  - **If at anytime after the second dose the QTc is**

  - **Dofetilide contraindicated**
  - > 500 msec dofetilide should be discontinued.

Creatinine clearance:

\[
(\frac{140 - \text{age} \times \text{Wt(Kg)}}{\text{Gender} \times 1.2 \times (0.85 \text{ women})}) \times \text{Serum creatinine}
\]

**Dofetilide Indication:**

- [ ] Class 1C drugs contraindicated

**Medication Intolerance:**

- [ ] Sotalol
- [ ] Amiodarone
- [ ] Beta blockers + 1C drugs

**Medication Ineffectiveness:**

- [ ] Sotalol
- [ ] Amiodarone
- [ ] Beta blockers + 1C drugs
- [ ] Amiodarone contraindicated peri-procedure
References


