Monitoring Anti-arrhythmic Medications in the Outpatient Setting: A Role for Pharmacists

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Michelle Musser, PharmD, BCPS

Disclosure

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:

- Suzanne M. Lifer: Nothing to disclose
- Michelle R. Musser: Nothing to disclose

Learning Objectives

- Discuss the monitoring parameters and patient education for commonly prescribed anti-arrhythmic medications.
- Discuss the role for pharmacists in the outpatient management of anti-arrhythmic medications including roles for clerical staff and pharmacy technicians.

Learning Objectives

- Discuss issues related to anti-arrhythmic medication management and possible solutions to these issues.
- Outline the current evidence related to the impact of pharmacist management of anti-arrhythmic medications.

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Antiarrhythmic Medications

Adverse effects and Monitoring

<table>
<thead>
<tr>
<th>Class</th>
<th>Drugs</th>
<th>Ion Block</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class Ia</td>
<td>Quinidine, Procainamide, Disopyramide</td>
<td>Sodium channels (intermediate)</td>
<td>Atrial and ventricular arrhythmias</td>
</tr>
<tr>
<td>Class Ib</td>
<td>Lidocaine, Mexiletine</td>
<td>Sodium channels (fast)</td>
<td>Ventricular arrhythmias</td>
</tr>
<tr>
<td>Class Ic</td>
<td>Flecainide, Propafenone</td>
<td>Sodium channels (slow)</td>
<td>Supraventricular arrhythmias and ventricular arrhythmias</td>
</tr>
<tr>
<td>Class II</td>
<td>Beta-blockers</td>
<td>Beta receptors</td>
<td>Atrial and ventricular arrhythmias</td>
</tr>
<tr>
<td>Class III</td>
<td>Amiodarone, Dofetilide, Sotalol, Ibutilide</td>
<td>Potassium channels</td>
<td>Atrial and ventricular arrhythmias</td>
</tr>
<tr>
<td>Class IV</td>
<td>Verapamil, Diltiazem</td>
<td>Calcium channels</td>
<td>Atrial and ventricular arrhythmias</td>
</tr>
</tbody>
</table>
Antiarrhythmic Medications

Antiarrhythmic medications play a critical role in the treatment of cardiac arrhythmias.

Vaughan Williams Class I antiarrhythmics, such as propafenone, and Class III antiarrhythmics, such as amiodarone, sotalol and dofetilide, are effective yet are associated with significant adverse drug events.

It is essential to perform periodic monitoring of laboratory and objective testing to:

- Prevent any unwanted adverse events.
- Ensure the safe and effective use of these medications.

Standardized monitoring protocols based on established guidelines exist for amiodarone and dofetilide.

- No formal guidelines exist for monitoring sotalol or propafenone.

Additional Considerations

- **Drug interactions**
  - CYP interactions
  - Other medications associated with QTc prolongation

- **Patient education**
  - Adverse effects to expect
  - Adverse effects to report
  - Communicate with health care provider regarding medication changes
  - Need for continued monitoring

Drug Dose adjustments Monitoring

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose adjustments</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propafenone</td>
<td>Use caution in renal impairment and hepatic dysfunction</td>
<td>ECG, Electrolytes</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Hepatic dysfunction</td>
<td>TSH/T4, Electrolytes, LFT</td>
</tr>
<tr>
<td>Sotalol</td>
<td>Renal impairment</td>
<td>ECG, Electrolytes, Scr</td>
</tr>
<tr>
<td>Dofetilide</td>
<td>Renal impairment</td>
<td>ECG, Electrolytes, Scr,</td>
</tr>
<tr>
<td></td>
<td>*Inpatient initiation</td>
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</tr>
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</table>

Outpatient Management

- Role of the pharmacist, pharmacy technicians, and clerical staff

Role of the pharmacist, pharmacy technicians, and clerical staff

- Drug interactions
  - CYP interactions
  - Other medications associated with QTc prolongation

- Patient education
  - Adverse effects to expect
  - Adverse effects to report
  - Communicate with health care provider regarding medication changes
  - Need for continued monitoring

- Establish standardized monitoring protocols based on established guidelines.

- Regular monitoring to prevent any unwanted adverse events.

- Ensure the safe and effective use of these medications.

- Consult with health care providers regarding medication changes.

- Communicate with health care providers regarding medication changes.

- Need for continued monitoring.
Blanchard Valley Medical Associates (BVMA) in Findlay, OH
- Private practice
- 15 physicians
- 5 clinical pharmacists

Physician referrals are primarily for amiodarone and sotalol.
- Approximately 150 patients enrolled

The pharmacist is responsible for:
- Ordering testing
- Coordinating monitoring
- Evaluating results
- Providing recommendations to the physician
- Reviewing results with patients at follow-up appointments

Recommended monitoring parameters to assess the safety and efficacy of antiarrhythmic medications:

<table>
<thead>
<tr>
<th>Amiodarone</th>
<th>Sotalol</th>
<th>Dofetilide</th>
<th>Propafenone</th>
</tr>
</thead>
<tbody>
<tr>
<td>LFTs</td>
<td>Chem-8</td>
<td>Chem-8</td>
<td>Chem-8</td>
</tr>
<tr>
<td>TFTs</td>
<td>Mg\textsuperscript{2}</td>
<td>Mg\textsuperscript{2}</td>
<td>Mg\textsuperscript{2}</td>
</tr>
<tr>
<td>EKG</td>
<td>EKG</td>
<td>EKG</td>
<td>EKG</td>
</tr>
<tr>
<td>PFTs</td>
<td>LFTs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CXR</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BVMA pharmacy secretary:
- Schedules all patients’:
  - Laboratory and objective testing
  - Follow-up office visit with pharmacist to review testing
- Assists with finding testing results

Technicians and/or other clerical staff could also complete these tasks

Possible Strategies for Improvement

Problem: Ordering and scheduling process is time consuming.

Solution: Order and schedule all upcoming testing at end of each appointment with pharmacist.
- Easier to do face-to-face
**Problem:** Minimize the amount of patients who only partially complete testing or complete all testing but do not schedule follow-up appointment with a pharmacist to review results.

**Solution:** Coordinate the execution of lab/objective testing and follow-up appointment with a pharmacist.

**Problem:** Difficulty finding/obtaining testing results completed off-site.

**Solution:** Require patients to obtain all testing on-site OR require patients to bring in all copies of testing completed off-site.

**Problem:** Need for more efficient way to follow-up with patients who do not complete testing as scheduled.

**Solution:** Create an electronic tracking system that can be queried monthly to identify patients who have not completed testing.  
- Utilize technology solutions

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**Current Evidence**

**Impact of Pharmacist Management**

**Studies that have examined adherence to recommended monitoring protocols in patients receiving amiodarone:**
- Usual care (management by a physician) is commonly not completed in accordance with recommended guidelines.

- Increasing adherence to monitoring protocols.
- Increasing identification of adverse events and drug interactions.

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**Impact of Pharmacist Management**

**Pharmacist-managed clinics for monitoring antiarrhythmic medications have provided improved care to patients by:**
- Increasing adherence to monitoring protocols.
- Increasing identification of adverse events and drug interactions.
### Trial Design Duration N

<table>
<thead>
<tr>
<th>Trial</th>
<th>Primary Outcome</th>
<th>Pharmacist Role</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Snider M, Kalbflesich S, Carnes CA, Clin Ther. 2009</td>
<td>Compliance with protocols at baseline and after enrollment</td>
<td>Conducted assessments, interviewed patients, provided education and counseling</td>
<td>Improved patient adherence to recommended testing protocols, helped identify AEs and clinically significant drug interactions</td>
</tr>
<tr>
<td>Spence MM, et al. J Manag Care Pharm. 2011</td>
<td>Rates of lab and PFT monitoring compared to usual care for patients on amiodarone</td>
<td>Ordered tests and procedures, generated testing reminder letters</td>
<td>Improved monitoring of lab and PFT testing</td>
</tr>
<tr>
<td>Sanoski CA, et al. Pharmacotherapy. 1998</td>
<td>Review rationale and development of amiodarone clinic</td>
<td>Interviewed patients, screened for drug interactions, provided education, coordinated lab test scheduling</td>
<td>Improvement in adherence after enrollment, improved outcomes by detecting drug related toxicity and facilitating proper dose adjustments</td>
</tr>
</tbody>
</table>

### Sample Table

<table>
<thead>
<tr>
<th>Interval</th>
<th>ALT</th>
<th>TSH</th>
<th>T4</th>
<th>PFT</th>
<th>CXR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Months 1–6</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Months 7–12</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td></td>
</tr>
</tbody>
</table>
| Months 1–12 | * | * | * | * | *

*Monitoring rates significantly higher in the pharmacist–managed group compared to usual care (p<0.05)*

### Adverse Events Identified

<table>
<thead>
<tr>
<th>Event</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total events</td>
<td>77</td>
</tr>
<tr>
<td>44% of patients had at least 1 event*</td>
<td>44</td>
</tr>
<tr>
<td>38% of visits</td>
<td>29</td>
</tr>
<tr>
<td>40 events required physician contact</td>
<td>40</td>
</tr>
<tr>
<td>77 events</td>
<td>77</td>
</tr>
<tr>
<td>11 events detected by medication reconciliation</td>
<td>11</td>
</tr>
<tr>
<td>21 clinically significant drug interactions</td>
<td>21</td>
</tr>
</tbody>
</table>

*Event requiring further assessment, intervention, and/or follow-up

**Completion of Testing**

<table>
<thead>
<tr>
<th>Before referral</th>
<th>After Initial Visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>59% of patients</td>
<td>98.5% of patients</td>
</tr>
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</table>

*Testing had to be completed within 10% of the timeframe in the monitoring protocols.

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Completion of Testing

<table>
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<tr>
<th>Before referral</th>
<th>After enrollment</th>
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<tbody>
<tr>
<td>23% of patients</td>
<td>90% of patients</td>
</tr>
</tbody>
</table>

- Significant improvement in patient’s completing required testing (p<0.001)

<table>
<thead>
<tr>
<th>Trial</th>
<th>Design</th>
<th>Duration</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Johnson SG, et. al. J Pharm Pract. 2010</td>
<td>Retrospective, longitudinal cohort study</td>
<td>8 years</td>
<td>905</td>
</tr>
<tr>
<td>Tafreshi J, Chui MA, Riley AB. Am J Health-Syst Pharm. 2009</td>
<td>Retrospective chart review</td>
<td>1 year</td>
<td>200</td>
</tr>
</tbody>
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Trial Design Duration N

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<tbody>
<tr>
<td>Johnson SG, et. al. J Pharm Pract. 2010</td>
<td>Adherence to recommended monitoring before and after implementation of a centralized amiodarone monitoring service (AMS)</td>
<td>&gt;Initiated TSH/ALT monitoring &amp; Ordered CXR/ECG monitoring with physician authorization</td>
<td>&gt;Improved adherence to ALT and ECG monitoring, but not TSH and CXR monitoring &amp; Fewer amiodarone related adverse effects</td>
</tr>
<tr>
<td>Tafreshi J, Chui MA, Riley AB. Am J Health-Syst Pharm. 2009</td>
<td>Monitoring completed before and after implementation of amiodarone clinic</td>
<td>&gt;Audited patient records &amp; Analyzed clinical outcomes &amp; Recommended testing and dose adjustments</td>
<td>&gt;Improved monitoring after implementation of amiodarone clinic which allowed for early detection of adverse events</td>
</tr>
</tbody>
</table>

Adverse Event Type | AMS Cohort | Control Cohort
Liver-related      | 3          | 9          |
Thyroid-related    | 15         | 31         |
Pulmonary-related  | 3          | 10         |
Cardiac-related    | 0          | 1          |
Total (p=0.0362)   | 21         | 51         |

- *Significantly higher monitoring rates in AMS cohort than control cohort
Significant improvement in monitoring after referral
- Few patients had all recommended lab tests performed and no patients had current PFTs prior to referral
- Previously unrecognized adverse events detected in 23 patients (19%) enrolled

Previously unrecognized adverse events detected in 23 patients (19%) enrolled

Which of the following is NOT a required component of amiodarone monitoring?
- a) Liver function
- b) Renal function
- c) Thyroid function
- d) Pulmonary function

Which of the following is a required component of sotalol monitoring?
- a) Liver function
- b) Renal function
- c) Thyroid function
- d) Pulmonary function

The pharmacist can assist with which of the following tasks in antiarrhythmic management?
- a) Ordering testing
- b) Coordinating monitoring
- c) Evaluating laboratory and objective testing
- d) Providing recommendations to the physician
- e) All of the above
References


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