Amiodarone

2.0 Contact Hours
California Board of Registered Nursing CEP# 16140
American Medical Education Center

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Title: Amiodarone
Self Study Module 2.0 CONTACT HOURS

Suggestion: Read through these questions before the module as they will be the SAME questions on the required online exam.

Choose the Single Best Answer for the Following Questions and Place Answers on Form:

1. Antiarrhythmic drugs work by altering the action potential during the various stages of depolarization and repolarization.
   a. True
   b. False

2. The Depolarization Phase (Phase 0) is responsible for _____ on the ECG
   a. ST Segment
   b. P wave
   c. QRS Complex

3. The Plateau Phase (Phase 2) is responsible for ______ on the ECG.
   a. ST Segment
   b. P wave
   c. QRS Complex

4. Indications for Amiodarone use includes:
   a. Treatment of life-threatening recurrent ventricular tachyarrhythmia that is resistant to control by other antiarrhythmic drugs.
   b. Treatment for refractory sustained or paroxysmal atrial fibrillation and paroxysmal supraventricular tachycardia.
   c. Treatment for arrhythmias associated with Wolf-Parkinson-White Syndrome (WPW).
   d. First line of treatment for pulseless ventricular tachycardia and ventricular fibrillation.
   e. All of the above

5. During a code situation, IV Amiodarone dosage for ventricular fibrillation or pulseless ventricular tachycardia is _____ Amiodarone IV push.
   a. 150mg
   b. 300mg
   c. 350mg

6. The maximum cumulative dose of Amiodarone IV in a 24 hour period is 2.2 grams.
   a. True
   b. False
7. Amiodarone can increase QT intervals, hypokalemia or hypomagnesemia should be corrected before starting amiodarone therapy to prevent arrhythmias such as torsades de pointes.
   a. True
   b. False
8. Nursing implications for IV Amiodarone produces _________ decreasing vascular resistance, possibly causing hypotension.
   a. Vasoconstriction
   b. Vasodilation
   c. None of the above
9. Drug interactins with Amiodarone and Coumadin are:
   a. Prothrombin time
   b. Serum concentration
   c. Elevated plasma concentrations of Cyclosporine
10. It is important to educate male patients taking oral Amiodarone about signs and symptoms of:
    a. Leg pain
    b. Blurred Vision
    c. Epididymitis

Self Study Module 2.0 CONTACT HOURS

Objectives

At the completion of this program, the learners will:

1. Describe the five different phases of the cardiac action-potential cycle.
2. Identify the four different classifications of antiarrhythmic drugs.
3. List the major electrophysiologic actions of amiodarone.
4. Recognize situations in which amiodarone would be indicated, including those situations during a code in which ACLS guidelines are followed.
5. Identify IV and PO doses of amiodarone.
6. List three infusion precautions to be taken when administering IV amiodarone.
7. Identify three drug interactions to monitor when a patient is on oral amiodarone.
8. Discuss the contraindications for use of amiodarone.
9. Identify four adverse reactions of amiodarone therapy.
10. Identify three things that you would teach a patient who is going to be on long term amiodarone therapy.

INTRODUCTION:
Amiodarone, also known as Cordarone, was developed as a vasodilator in the early 1960’s. In the 1970’s experimental use of amiodarone as an antiarrhythmic began. It is now recognized as the most
effective antiarrhythmic for sudden cardiac death survivors, however, its role in preventing sudden cardiac death is still unclear.

The Food and Drug Administration in 1985, approved oral amiodarone for life-threatening ventricular arrhythmias. The IV form was not approved until 1995 for more rapid conversion of emergent ventricular arrhythmias. In 2000 the American Heart Association after several clinical trials, added amiodarone to its first line treatment modalities for the treatment of lethal cardiac rhythms and rapid atrial rhythms. In 2005 the American Heart Association continued to recommend amiodarone as its first line treatment for lethal cardiac ventricular rhythms and for rapid atrial rhythms with expert consultation. The most recent changes reflect concerns regards complications related to long-term use. The following review of cardiac cellular action potentials and antiarrhythmic drug classifications will help to clarify the actions and indications for the use of amiodarone.

**Review of Cardiac Cellular Action Potentials**

Antiarrhythmic drugs work by altering the action potential during the various stages of depolarization and repolarization. Action potential is a series of five phases that make up the depolarization-repolarization cycle of cardiac cells.

*Action potentials* vary in different parts of the heart because cardiac cells depolarize at different speeds. The speed at which these cells depolarize depends on whether a fast or slow channel is present. The sodium current is drawn quickly into the cell through fast channels, while the slower calcium current passes through low channels. Fast channels dominate cardiac muscle cells so they depolarize rapidly. Slow channels dominate cardiac electrical cells (particularly those of the SA node and the central and proximal regions of the AV node) so they depolarize slowly. The action potentials reflect rapid sequence of voltage changes across cell membrane during cardiac cycle. There are five phases of the action potential: Phase 0, 1, 2, 3, 4.

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**Phases of Action Potential:**

**Phase 0  Depolarization Phase**

- When cardiac muscle cells (except the SA and AV nodes) rapidly depolarize.
- Begins when the cell receives an impulse
- Sodium moves rapidly into cell
- Potassium leaves cell
- Calcium moves slowly into cell
- Cell depolarizes; contraction begins
- Responsible for QRS complex on the ECG
- Cell’s negative electrical charge is changed positive as it is depolarized
**Phase 1  Early Repolarization**

- Represents the rapid repolarization of the cells
- Na+ channels partially close
- K+ leaving the cell
- Results in fewer positive electrical charges within the cell

![Graph showing repolarization phases](image)

**Phase 2  Plateau Phase**

- Represents when plateau in electrical activity is reached
- Repolarization continues relatively slowly
- Slow inward movement of Ca++
- Slow outward movement of K+
- Responsible for ST-segment on ECG
- Refractoriness: during phase 2, no stimulus can depolarize the cell
- Absolute refractory period: the interval during which the cells cannot be re-stimulated
- Begins during phase 1 and extends through the beginning of phase 3.

**Phase 3  Final Rapid Repolarization**

- Occurs when the plateau period ends and the cell rapidly completes its repolarization.
- K+ flows quickly out of the cell
- Entry of Ca++ and Na+ stops
- Cell becomes progressively more electrically negative and more sensitive to external stimuli
• Corresponds with T wave on the ECG
• Relative refractory period is when only very strong stimuli can depolarize the cell and this period

Phase 4  Return to Resting State

• The inside of the cell is negatively charged
• Potassium is high inside the cell
• Sodium is high outside the cell.
• Heart is "polarized" during this phase
• Ready for discharge
• Cell will remain in this state until reactivated by another stimulus

Antiarrhythmic Drug Classifications

Antiarrhythmic drugs are grouped into four different classes according to how they affect the heart’s electrical activity by altering cardiac action potentials. This grouping is referred to as the Vaughan Williams classification system.

<table>
<thead>
<tr>
<th>Classification of Antiarrhythmic Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Class I</strong></td>
</tr>
<tr>
<td>• fast flow of sodium into the cell</td>
</tr>
<tr>
<td>• decreases upstroke velocity of Phase 0</td>
</tr>
<tr>
<td>• increased length of refractory period</td>
</tr>
<tr>
<td>• diminishes spontaneous depolarization</td>
</tr>
<tr>
<td>• For treating dysrhythmias due to enhanced auto-motility and reentry mechanisms</td>
</tr>
<tr>
<td>• Quinidine, Lidocaine</td>
</tr>
</tbody>
</table>

| **Class II**                           |
| • Beta-adrenergic blockers             |
| • Reduces sympathetic stimulation of the heart|
| • Increases AV node conduction time and increases the length of refractory periods|
| • Effective in atrial dysrhythmias due to excessive adrenergic stimulation|
| • Inderal (propranolol), Lopressor (metoprolol) and Tenormin (atenolol) |
Class III
- Lengthens the action potential of the cardiac muscle cells
- Effective in preventing dysrhythmias
- Amiodarone

Class IV
- Calcium channel blockers
- Depresses the SA and AV nodes which results to increase AV – node conduction time and increased length of refractory period in the AV node
- Calan (verapamil)

Mechanism of Action
- Class III antiarrhythmic drug
- Blocks rapid sodium channels (similar to Class I antiarrhythmic drugs)
- Exerts a noncompetitive anti-sympathetic action (similar to Class II antiarrhythmic drugs)
- Prolonged administration causes lengthening of the cardiac action potential (similar to Class III antiarrhythmic drugs)
- Has negative chronotropic (heart rate) effect in nodal tissues (similar to Class IV antiarrhythmic drugs)
- Blocks myocardial potassium channels which contributes to the slowing of conduction and prolongation of refractoriness.
- Anti-sympathetic action and the blocking of calcium and potassium channels are responsible for the decreased conduction velocity in the sinus (SA) node and for the slowing of conduction and prolongation of refractoriness in the atrioventricular (AV) node resulting to of prolonged PR and QT intervals.
- Vasodilatory action causes decrease in the cardiac workload and in turn decreases myocardial oxygen consumption.

Indications
- Treatment of life-threatening recurrent ventricular tachyarrhythmia that is resistant to control by other antiarrhythmic drugs.
- Treatment for refractory sustained or paroxysmal atrial fibrillation and paroxysmal supraventricular tachycardia.
- Treatment for arrhythmias associated with Wolf-Parkinson-White Syndrome (WPW).
- First line of treatment for pulseless ventricular tachycardia and ventricular fibrillation.
- Used for rate control of rapid atrial arrhythmias in-patients with impaired left ventricular function when Digoxin has proven ineffective. With the new guidelines, the use of amiodarone for atrial rhythms is done so with the consultation of an expert. For a more complete understanding of its use during a code situation or a pre-code situation, a review of the current ACLS guidelines is suggested.

Dosage and Administration

Note:
- A 0.2 micron filter is required for the infusion (a filter is not required for the loading dose)
- All infusions must be delivered using the drugs guardrails option in our IV infusion pumps
- Check drug compatibility before infusing with another drug
Non-Code Situation: IV Amiodarone dosage and administration:

1. **Loading Dose:** 150 mg of amiodarone in 100ml of D5W (premixed from pharmacy)  
   Infuse over 10 minutes (15 mg/minute.)

2. **Maintenance Dose:**
   - 450mg of amiodarone is added to 250ml of D5W (premixed from pharmacy)
   - First 6 hours: Infused at 1mg/min (60 mg/hr) x 6 hours
   - After 6 hours the infusion is decreased to maintenance infusion of 0.5mg/hr (30 mg/hr)
   - After the first 24 hours, the maintenance infusion rate is 720mg/24 hours (0.5 mg/minute)
   - This infusion should be continued for 48 to 96 hours, or until the patient’s ventricular arrhythmias are stabilized or per MD order

3. The initiation of IV amiodarone is intended for the critical care areas only and in some cases in Cardiac Telemetry and PCSU with 1:3 patient status. Please refer to the hospital guidelines for on IV Amiodarone for more.

**CODE situation: IV Amiodarone dosage and administration**

1. IV push 300 mg of amiodarone for ventricular fibrillation or pulseless ventricular tachycardia.
   
   **Note:** Use filtered needle when drawing the medication from the ampule

2. Consider repeating with 150 mg IV push in 3 to 5 minutes if there is no response.
3. The **maximum cumulative dose is 2.2 gm IV in 24 hour period.**

Wide-complex (stable) tachycardia, amiodarone can be administered as follows:

1. **Rapid infusion:** 150 mg IV over 10 minutes.
2. **Repeat rapid infusion:** (150 mg IV) every 10 minutes as needed.
3. **Slow infusion:** 360 mg IV over 6 hours (1mg/min.)
4. **Maintenance infusion:** 540 mg IV over 18 hours (0.5 mg/min).

**Infusion Precautions:**

- When Amiodarone is added to normal plastic infusion bags 10% of the medication can be absorbed into the plastic after 2 hours. The initial bolus can be placed in a plastic bag. The maintenance infusion needs to be mixed in a glass bottle of D5W unless the **non-absorbable plastic bags** are available. (premixed by Pharmacy).
• Prepared solutions should not be kept hanging for >24 hours.

• Care must be taken when increasing the concentration of the IV infusion.

• Concentrations >3 mg/ml have been associated with a high incidence of peripheral vein phlebitis.

• If high concentrations are needed, administration via central venous access is recommended.

• If breakthrough episodes of life-threatening ventricular tachycardia or ventricular fibrillation occur, the rate of the maintenance infusion may be increased.

• Infusions for >three weeks have not been studied.

• Transition to oral therapy is recommended at the earliest possible time.

• If a patient has already been taking oral amiodarone and an IV infusion is started, a different IV dosage schedule will be required because the drug is already at therapeutic blood levels.

• Amiodarone can increase QT intervals, hypokalemia or hypomagnesemia should be corrected before starting amiodarone therapy to prevent arrhythmias such as torsades de pointes.

Compatibility:

The following medications cannot be infused in the same IV line as Amiodarone without precipitation occurring. It is recommended that amiodarone be infused into an IV line in which no other medication is being given.

• Aminophylline
• Sodium Bicarbonate
• Heparin

• Cefamandole Nafate (Mandol)
• Cefazolin Sodium (Ancef)
• Mezlocillin Sodium (Mezlin)

Oral Therapy

• Initial PO daily dose of oral therapy: 800 mg-1600 mg/day x 1-3 weeks until a therapeutic response is achieved.
• Then reduced to 600-800 mg/ day after 1 - 4 weeks.
• Maintenance dose: 400 mg/day.
• Oral dose is supplied in 200 mg tablets.
• The absorption takes 3 to 7 hours after the oral dose for maximum plasma concentrations to be reached.
• Therapeutic effects on abnormal rhythms are not seen before 2 - 3 days and may take 1 - 3 weeks.
• The time to reach therapeutic levels may be shortened by using a loading –dose regimen.

Pharmacokinetics

• Amiodarone concentrates in the body in adipose tissue, liver, spleen, and the lungs
• Metabolized in the liver
Main route of elimination is via hepatic excretion into the bile.
Mean half-life is 53 days
Antiarrhythmic effects may persist for weeks or months after the medication is stopped.

Drug Interactions

Hemodynamic and electrophysiologic interactions have been observed when amiodarone is being given along with

1. Propranolol (Inderal)
2. Diltiazem (Cardizem)
3. Verapamil

Oral administration of amiodarone over 2 weeks impairs metabolism of

1. Dilantin (phenytoin)
2. Decadron (dextromethorphan)
3. Methotrexate

Caution should be observed when giving Amiodarone with the following drugs due to drug to drug interactions:

1. Drugs that may cause prolongation of QT interval: Flecainide, Procainide, Quinidine, Lidocaine
2. HIV Protease Inhibitors
3. Histamine H1/H2 Receptor Antagonists
4. Statins
5. Rifampizin
6. St John’s Wort
7. Cardiac Glycosides
8. Gapapentin
9. Phenytoin
10. Macrolides
11. Azoles (antifungal)
12. Fluoroquinolones
13. Disopyridamole
14. Drugs with P-glycoprotein-mediated clearance
15. Dietary supplements/Herbal supplements that affect hepatic microsomal enzymes
Table 1. Summary of Drug Interactions with Amiodarone

<table>
<thead>
<tr>
<th>Drug</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coumadin</td>
<td>↑ prothrombin time</td>
</tr>
<tr>
<td>Digoxin</td>
<td>↑ serum concentration</td>
</tr>
<tr>
<td>Quinidine</td>
<td>↑ serum concentration</td>
</tr>
<tr>
<td>Procainamide</td>
<td>↑ serum concentration</td>
</tr>
<tr>
<td>Norpace</td>
<td>↑ QT prolongation which could cause arrhythmias</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>May cause hypotension, bradycardia, decreased cardiac output</td>
</tr>
<tr>
<td>Tambocor</td>
<td>↓ Dose of Tambocor needed to maintain therapeutic plasma concentrations.</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>Oral: Sinus bradycardia noted in a patient receiving oral amiodarone who was given Lidocaine for local anesthesia.</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>Persistently elevated plasma concentrations of Cyclosporine resulting in ↑ creatinine, despite reduction in dose of Cyclosporine.</td>
</tr>
<tr>
<td>Questran</td>
<td>↑ enterohepatic elimination of amiodarone and may reduce serum levels.</td>
</tr>
<tr>
<td>Tagamet</td>
<td>↑ serum amiodarone levels</td>
</tr>
<tr>
<td>Dilantin</td>
<td>↓ serum amiodarone levels</td>
</tr>
</tbody>
</table>

Contraindications
- Cardiogenic shock
- Marked bradycardia
- Marked sinus bradycardia
- Second- or third-degree AV block
- Hypotension
- Pregnancy
- Breast-feeding mothers

Adverse Effects

There are many adverse effects from long-term oral use of amiodarone. However, the adverse effects are usually outweighed by its benefits for a patient with life-threatening arrhythmias who is at risk for sudden cardiac death. The following is a systems review of adverse effects of long-term therapy including nursing management and patient education.

1. **Cardiac** (ASHSP, 2009)
   - Worsens existing arrhythmias and cause new arrhythmias
   - 2-5% of patients have progression of ventricular tachycardia to ventricular fibrillation, SVT, torsades de pointes, atrial fibrillation and nodal arrhythmia
   - Increased resistance to cardioversion
   - Hypotension
   - New or worsening of heart failure in 3% of patients
   - Flushing and edema in 1-3% of patients on PO
   - Cardiac arrest, shock in 2.9% of patients on IV

2. **Pulmonary**
   - Pulmonary toxicity in about 10-17% of patients who take PO amiodarone (American Society of Health-Systems Pharmaceutics (ASHSP), 2009)
   - Pulmonary interstitial pneumonitis (or alveolar pneumonitis) and pulmonary fibrosis in 10-17% of patients (ASHSP, 2009)
   - ARDS & lung edema in 2% of patients (ASHSP, 2009)
     - Signs and symptoms: exertional dyspnea, dry cough, fever
     - Clinical manifestations: high erythrocyte sedimentation rate (ESR), pulmonary fibrosis on chest x-ray

3. **Endocrine**
   - Hypo/hyperthyroidism in less than 3% of patients
   - Inhibits peripheral conversion of T4 to T3
   - Monitoring of thyroid panel

4. **Skin**
   - Photosensitivity is seen in 50% of patients on long-term amiodarone therapy
   - Blue-gray skin discoloration in about 10%
   - Sunlight protection is advised such as application of sun block, wearing of hat and long sleeves when going outside and avoid prolonged sun exposure
5. **Vision**
   - Corneal microdeposits are found in about 90-100% of patients on long-term amiodarone therapy
   - Corneal microdeposits does not affect visual acuity, however patient would see halos which disappears after 6-12 months after cessation of intake of amiodarone

6. **Neurological**
   - Ataxia, tremors, dizziness, muscle weakness, abnormal gait, paresthesia, sleep disturbance and headache which are dose related

7. **Gastrointestinal**
   - Nausea, anorexia, and constipation
   - PO amiodarone is taken with meals to lessen these GI adverse effects
   - Increase fiber consumption to prevent constipation
   - Caution patients about stopping the drug without consulting a physician

8. **Liver**
   - Elevated liver enzymes (3-20% of patients with abnormal liver function tests results)
   - 1-3% non-specific hepatic disorders (AHFSP, 2009)
   - Baseline liver function test must be done prior to starting oral Amiodarone
   - Monitor liver function tests and thyroid functions tests regularly

9. **Hematologic**
   - Spontaneous ecchymosis in 1-3%
   - Thrombocytopenia
   - Petechiae

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**Nursing Management & Patient Education**

**Nursing Implications:**

1. IV amiodarone produces vasodilation decreasing vascular resistance, and thus possibly causing hypotension.
2. Amiodarone also has a slightly negative inotropic response, which decreases myocardial contractility thus may decrease cardiac output and pulmonary artery pressure.
3. Notify the physician if hypotension occurs.
4. For hypotension, recommended treatment is to stop amiodarone and infuse 100-500 ml of fluid.
5. Make sure when started your Amiodarone drip that you program it under drug guardrails.
6. Monitor patient closely. ECG should be monitored continuously during IV therapy or initiation of oral therapy.
7. Assess signs and symptoms of pulmonary toxicity and ARDS.
8. Assess patient for signs of thyroid dysfunction and ophthalmic problems such as photophobia, and decrease in visual acuity
9. Monitor liver and thyroid functions.
Patient/Family Teaching: (Deglin & Vallerand, 2009)

1. Instruct patient to take oral amiodarone exactly as directed. If a dose is missed, do not take at all. Consult health care professional if more than two doses are missed.
2. Educate the patients about the side effects.
3. Inform patient to wear protective clothing and sunblock usually during and for 4 months after therapy.
4. Inform patients that a possible drug side effect is the bluish discoloration of the face, neck and arms which is reversible over several months.
5. Educate male patients about the signs and symptoms of epididymitis (pain and swelling of the scrotum) which may occur. Notify healthcare professional if this occurs.
6. Before any surgical procedure, healthcare professional should be notified of the medication regimen.
7. Emphasis on the importance of the following exams: chest x-ray, pulmonary function tests every 3-6 months and ophthalmic exams after 6 months of therapy and then annually or depending upon the health professional’s recommendations.

References


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