**Introduction:**

Amiodarone is an antiarrhythmic characterized by substantial toxicity and prolonged half-life. Some of its adverse effects are potentially fatal. Its level should be monitored. It is used for atrial fibrillation and life-threatening recurrent ventricular arrhythmias which have not responded to alternative therapy in patients at risk for sudden death.

**Indications:**

Amiodarone is a class III antiarrhythmic agent approved for the treatment of life-threatening ventricular tachyarrhythmias. It is also used in prevention of recurrences of atrial fibrillation.**1**

**Pharmacodynamics/Kinetics:**

Absorption: Slow and variable

Onset of action: Oral: 2 days to 3 weeks; I.V.: May be more rapid

Peak effect: 1 week to 5 months

Distribution: Vd: 66 L/kg (range: 18-148 L/kg)

Protein binding: 96%

Metabolism: Hepatic via CYP2C8 and 3A4 to active N-desethylamiodarone metabolite; possible enterohepatic recirculation

Bioavailability: Oral: 35% to 65%

Half-life elimination: Terminal: 40-55 days (range: 26-107 days); shorter in children

Time to peak, serum: 3-7 hours

Steady-state plasma concentrations are reached in 50-300 days.

Excretion: Feces; urine (<1% as unchanged drug) **1**

**Dose:** Adults:Ventricular arrhythmias:Oral: 800-1600 mg/day in 1-2 doses for 1-3 weeks, then when adequate arrhythmia control is achieved, decrease to 600-800 mg/day in 1-2 doses for 1 month; maintenance: 400 mg/day; lower doses are recommended for supraventricular arrhythmias.**1**

**Indications for TDM:**

To evaluate amiodarone toxicity.

To assist in differential diagnosis: To distinguish between drug related adverse effects from disease symptoms.

To evaluate suspected drug-drug interaction: Amiodarone-phenytoin interaction resulting in decreased amiodarone plasma concentration.

To assess medication adherence: poor therapeutic response

To assess and monitor rhythm abnormalities.

**Therapeutic and Toxic Levels:**

Therapeutic Levels:

≤ 2.5 μg/ml

Possible Toxic level: > 2.5 μg/mL

Critical level: > 5 μg/mL 2

**Assay Parameters:**

Sample:

1 mL serum or plasma (0.5 mL minimum)

Container:

Red top (no additive) tube. Containers are laboratory and methodology specific.

Collection:

Routine venipuncture. Separate serum or plasma from cells as soon as possible. A consistent sampling time, ideally a trough level 30 minutes prior to next dose should be used to monitor patients on chronic therapy.

Storage Instructions:

Maintain sample at room temperature or refrigerate. 2

**Drug interactions:**

Amiodarone can potentiate effects of warfarin, elevating prothrombin time. It can elevate serum digoxin level, levels of other antiarrhythmic drugs including quinidine, procainamide, mexiletine, and propafenone. There are effects with anesthetics, β-blockers, or calcium channel blockers. Serum level of amiodarone is decreased by concomitant administration of cholestyramine or phenytoin and increased by cimetidine.**2**

**Analytical Methods:**

Primary and only methodology available for the analysis of amiodarone is high performance liquid chromatography (HPLC).

**HPLC:**

A) The sample is passed through a silica-C18 column, and after washing, the analytes are eluted with methanol. The determination is then accomplished by Reverse Phase(RP) HPLC using an octadecyl silica column and a mobile phase of methanol containing 0.0015% of ammonium hydroxide. The effect of ammonia concentration on the capacity factors of the analytes has been used for estimating the acid dissociation constants of the investigated secondary and tertiary amines in methanol.**3**

B) A rapid and reliable high-performance liquid chromatographic (HPLC) assay has been developed for the measurement of amiodarone**,** and its metabolite, N-desethyl-amiodaronein serum. The procedure involves addition of absolute ethanol to serum, previously adjusted to pH 6, followed by centrifugation. The supernatant is analyzed by reverse-phase HPLC with ultraviolet--visible detection.**4**

HPLC technique have the advantage of availability of test and cost and rapid results would give the edge over other analytical methods in Indian setup.

**Conclusion:**

Because of potential toxicity, the serum level of amiodarone should be monitored. The unpredictable relationship between dose and amiodarone concentration, and the presence of numerous clinically significant drug interactions support the need to individualize and maintain therapy using TDM. The accepted therapeutic range for amiodarone is ≤ 2.5 μg/mL when the drug is used for the treatment of ventricular tachyarrhythmias and fibrillation. Because amiodarone has a relatively longer half-life, sampling time in relation to dose ingestion is important for the interpretation of the drug concentration. Ideally samples for amiodarone measurements should be drawn 30 minutes before the next dose. HPLC is the method of choice for analysis of amiodarone sample in Indian setup.

**References:**

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