# *L3. Antiarrhythmic Drugs*

## *1-WHAT IS ARRHYTHMIA?*

***An Abnormality in the :***

- ***rate ..... high= tachycardia***

***low = bradycardia***

- ***regularity ..... extrasystoles***
- ***site of origin ... ectopic pacemakers***
- ***or disturbance in conduction***

## *2-Therapeutic use &Rationale of antiarrhythmic drugs*

***1-The ultimate goal is to restore normal rhythm & conduction***

***2- drugs are used to prevent more serious & lethal arrhythmias.***

## *Antiarrhythmic drugs are used to :*

***1-↑ or ↓ conduction velocity***

***2-Alter the excitability of cardiac cells by changing the effective refractory period.***

***3-Suppress abnormal automaticity***

# 3-CLASSIFICATION

# OF

# ANTIARRHYTHMIC DRUGS

## (Vaughn Williamsclassification)

| CLASSI | CLASS II | CLASSIII | CLASSIV |
|---|---|---|---|
| • Na+ channel blockers (membrane stabilizing drugs) and it's subclassified into: | • β- adrenoceptor blockers<br>• e.g proranlol,Atenolol | • drugs that prolong action potential duration<br>• e.g Amodarone,Ibutilide | • calcium channel blockers<br>• e.g Verampil , Diltiazem |

**1A**

- Block potassium channels
- moderate NA channel blockade ↑ *ESR*
- e.g QUINIDINE ,PROCAINAMIDE

**1B**

- Shorten action potential duration
- weak NA channel blockade ↓ *ESR*
- e.g Lidocaine, Mexiletine

**1C**

- have no or little effect on action potential duration
- stronge NA channel blockeade → ESR
- e.g flecainide, propafenone

**FIRST CLASS I**

Mechanism:

- **Blocking the rapid inflow of Na+ ions ,decreasing the rate of rise of depolarization ( slope of Phase O )**
- **Suppress abnormal automaticity by decreasing the slope of phase 4 , which is generated by pacemaker currents**. that's mean decreased the action potential of SA node by unknown mechanism done by this drug

Clinical uses :

- **At high concentration they have local anaesthetic effect**
- **-Ve inotropic effect ( cardiac depression )**

Sub-classification:

**1A** 1st e.g: QUINIDINE :

**it's a drug that has:**

1-antiartthamic effect by:**Block potassium channels >leading to prolongation of actionpotential duration & refractory period of both atrial & ventricular tissues.**

2-anticholiergic effect by:**Increase conduction through the A.V. node, May lead to high ventricular rate in atrial flutter <remove the vagal inhibitory effect but before doing the effect may some impulses escape and reach to A.V**

**Can be prevented by administration of a drug that slow A.V. conduction such as digoxin, β blocker calcium channel blockers.(either as prophylactic or combination with quinidine).**

3- Depress cardiac contractility

4- α-adrenergic blocking: **Effect which cause vasodilatation and reflex sinustachycardia .This effect is seen more after i.v.dose.**

## ECG changes:

**1-Prolongation of P-R & Q-T interval.**

**2-Widenes QRS complex**

## Clinical uses :

**1-In almost all types of arrhythmias**

**Common uses: atrial flutter & fibrillation**

**Can be used for ventricular tachycardia**

**2-To maintain sinus rhythm after D.C cardioversion**

## Adverse effects:

**1-GIT:anorexia, nausea, vomiting, diarrhea**

**2-CARDIAC:quinidine syncope:**

- episodes of fainting

- (due to torsades de pointes developing at therapeutic plasma levels )

- may terminate spontaneously or lead to fatal ventricular fibrillation

**N.B** torsades de pointes: Torsade de pointes is an uncommon and distinctive form of polymorphic ventricular tachycardia (VT) characterized by a gradual change in the amplitude and twisting of the QRS complexes

**3- Anticholinergic adverse effects:**

**4-Cinchonism:( tinnitus , headache & dizziness) ,Hypotension .**

**5-At toxic Cons :can precipitate arrhythmia and produce asystole ( cardiac arrest ) if serum concentrations exceed 5 µg/ml or in high potassium levels ( > 5mmol/L).**

## Drug interactions:

**Increase concentration of digoxin:**

- **Displace digoxin from plasma proteins**
- **Decrease digoxin renal excretion**

## Root of administration :

**Given orally rarely given I.V.**

**1A** 2nd e.g. Procainamide:

## As compered to quinidine :

**1- less toxic on the heart...**

**2- can be given I.V.**

**3- more effective in ventricular than in atrial arrhythmias**

**4- Weak anticholinergic**

**5-No α-blocking actions**

## Clinical usese:

**1-Therapeutic : In atrial and ventricular arrhythmias**

**2-Second choice( afterlidocaine ) in ventricular arrhythmias after acute myocardial infarction.**

## Adverse effects:

**1-In long term therapy causessystemic lupus erythematosus SLE (in 5-15% )**

**2-Hypotension**

**3-Torsades de pointes**

**4-Hallucination & psychosis.**

## 1B 1st e.g. LIDOCAINE

**Clinical usese:**

**1- FirstDrug of choice for treatment of ventricular arrhythmias in emergency as in :**

**cardiac surgery , acute myocardial infarction**

**2- NOT effective in atrial arrhythmias**

**3- NOT effective orally (3% bioavailability)**

**Root of administration :**

**- GIVEN I.V. bolus or slow infusion**

**Adverse effects:**

**1-hypotension**

**2-Neurological adverse effects (paresthesia, tremor, dysarthria (slurred speech), hearing disturbances, confusion and convulsions )**

**3-T1/2 = 2hrs**

## 1B 2nd e.g MEXILETENE

**Clinical usese:**

**1- ventricular arrhythmia**

**2- digitalis-induced arrhythmias**

**3- chronic pain e.g. diabetic neuropathy and nerve injury**

**Root of administration :**

**Given orally**

**Adverse effects:**

**1- nausea , vomiting**

**2- neurological**

**3- arrhythmias & hypotension**

**4- t1/2 = 10 hr**

**1C** 1st e.g.FLECAINIDINE

**Clinical usese:**

**1-Supraventricular arrhythmias in patients with normal hearts**

**2- Wolff-Parkinson-White syndrome:Pre-excitation of the ventricles due to an accessory pathway known as the Bundle of Kent.**

**This accessory pathway is an abnormal electrical communication from the atria to the ventricles**

**3- Ventricular arrhythmias{ very high risk of proarrhythmia }**

**4- Reserved for resistant arrhythmias.**

**Adverse effects:**

**1- CNS : dizziness, tremor, blurred vision, abnormal taste sensations, paresthesia**

**2- Arrhythmias**

**3- heart failure due to -ve inotropic effect**

**1C** 2nd e.g. PROPAFENONE:

**- Chemical structure similar to propranolol**

**- has weak beta-blocking action**

**- cause metallic taste and constipation**

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## 2nd CLASS

Mechanism:

**block$\beta_1$- receptors in the heart → reduce the sympathetic effect on the heart causing :**

**- decrease automaticity of S.A. node and ectopic pacemakers**

**- prolong refractory period ( slow conduction ) of the A.V node this help prevent re-entry arrhythmias**

Clinical uses :

**1-Atrial arrhythmias ( with emotion, exercise thyrotoxicosis )**

**2-WPW**

**3- digitalis-induced arrhythmias**

**4-To reduce the incidence of post myocardial infarction arrhythmias**

## Class 3

Prolong the action potential duration & refractory period(Prolong phase 3)

### 1-AMIODARONE

-Prolong action potential duration and effectiverefractory period

-Has an additional action of classes ( 1, 2 and 4 )

-vasodilating effect

-( α- and β-adrenoceptor &calcium channel blocking effects )

#### Clinical uses

1-Serious ,resistant ventricular arrhythmias

2-Maintenance of sinus rhythm after D.C. cardioversion of atrial flutter and fibrillation

3-Resistant supraventricular arrhythmias e.g: WPW

#### Adverse effect

1-bradycardia & heart block, heart failure

2- pulmonary fibrosis

3- hyper- or hypothyroidism

4-photodermatitis ( in 25%) and skin deposits

5- Bluish discoloration of the skin

6- tremor, headache, ataxia, paresthesia

7- constipation

8- corneal microdeposits

9- hepatocellular necrosis

10- peripheral neuropathy

#### Pharmacokinetics

extremely long t1/2 = 13 - 103 DAYS

#### Drug Interactions:

reduce clearance of several drugs e.g.

quinidine, warfarin, procaiamide, flecainide

### 2-Ibutilide

Given by a rapid I.V. infusion -

-Acute conversion of atrial flutter or atrial fibrillation to normal sinus rhythm.

- Causes QT interval prolongation , so it precipitates torsades de pointes.

## Class 4 calcium channel blockers

**Drugs: Verapamil , Diltiazem**

Main site of action ( A.V.N & S.A.N )

(causing slow conduction & prolong effective refractory period ).

Clinical uses: -

1- atrial arrhythmias

2- supraventricular arrhythmias

e.g. WPW

NOT effective in ventricular arrhythmias

## MISCELLENIOUS ANTIARRHYTHMIC DRUGS "class5"

### ADENOSINE

naturally occurring nucleoside-

half-life= less than 10 sec-

**Mechanism:**

- In cardiac tissues

Binds to type 1 (A1) receptors which are coupled to Gi- proteins , activation of this pathway cause :

1- Opening of potassium channels (hyperpolarization)

2- Decrease cAMP which inhibits L-type calcium channels (↓ calcium influx ) causing

3-decrease in conduction velocity (negative dromotropic effect ) mainly at AVN.

-In cardiac pacemaker cells ( SAN) , inhibits pacemaker current, which ↓ the slope of phase 4 of pacemaker action potential ( ↓ spontaneous firing rate {negative chronotropic effect})

**Clinical uses:**

-First drug of choice in paroxysmal supraventricular tachycardia

-preferred over verapamil ( saferand does not depress contractility )

-given 6 mg I.V. bolus followed by 12 mg ifnecessary

**Adverse effects:**

-Flushing in about 20% of patients

-Shortness of breath andchest burning in 10% of patient (brochospasm)

-AV block ( contraindicated in heartblock)

-Rarely: hypotension, nausea, paresthesias

### DIGITALIS

## BRADYARRHYTHMIAS

### ATROPINE

**can be used in sinus bradycardia after myocardial infarction and in heart block**

**in emergency heart block isoprenaline may be combined with atropine**

## NONPHARMACOLOGIC THERAPY OF ARRHYTHMIAS

**- Implantable Cardiac Defibrillator (ICD)**

**- can automatically detect and treat fatal**

**- arrhythmias such as ventricular fibrillation**

**Questions:.**

**1) A patient with a long history of cardiovascular disease develops worsening ventricular arrhythmias. Which of the following drugs is most likely to be the cause of the arrhythmia?**

**(A)Quinidine**

**(B)Propanolol**

**(C)Dobutamine**

**(D)Methyldopa**

**2) A patient is admitted into the emergency room and manifests ventricular tachycardia following an acute myocardial infarction(MI). This arrhythmia is life threatening and must be controlled immediately . Which of the following drugs would be best to quickly control the condition?**

**(A) Dobutamine.**

**(B) Digitalis.**

**(C) Quinidine**

**(D) Lidocaine.**

**3) A women Who is undergoing an endocrine work-up to diagnose the cause of a large multinodular goiter develops atrial fibrillation . Which of the following would be best to treat this arrhythmia?**

**(A) Verapamil.**

**(B) Propanolol**

**(C) Digitalis.**

**(D) Bretylium.**

**4) A 57-year –old man with atrial flutter is initially treated with Quinidine to control the arrhythmia. He is released from the hospital, and while his condition improves, sporadic arrhythmias continue . which of the following drugs might be used as an adjunct to Quinidine in the treatment of the atrial flutter?**

**(A) Digitalis.**

**(B) Lidocaine.**

**(C) Procainamide.**

**(D) Propanolol**

**Answers:**

**1-(A)**

**2-(D)**

**3-(B)**

**4-(A)**