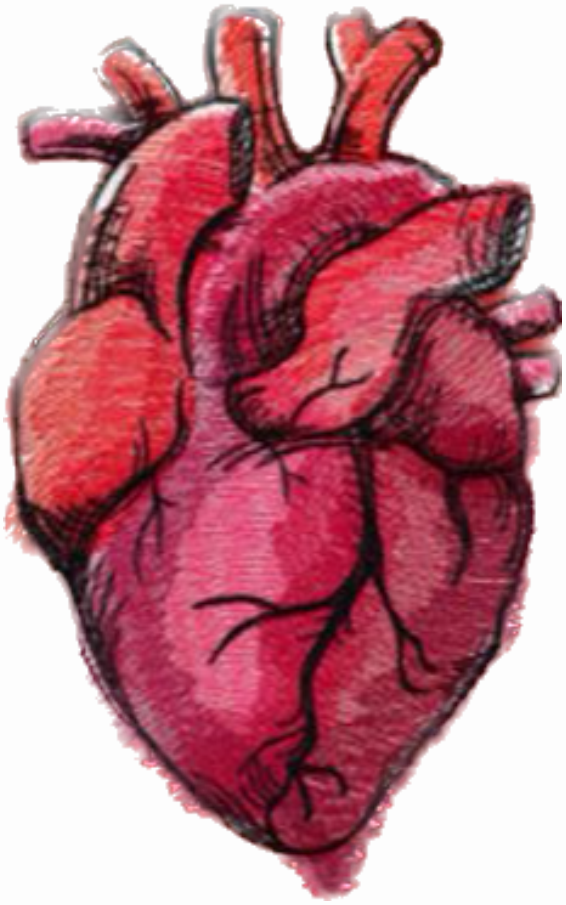
النادي الطبي

CARDIOVASCULAR SYSTEM



SUBJECT : Antiarrhythmics 1

LEC NO. : Summary L2

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وقل رب زدني علماً

Topic	Information
Arrhythmias	- The normal heart beats is regular. - Caused by abnormalities in the generation or conduction of the heart electrical impulses or both. - Causes: 1. Heart disorders: including congenital abnormalities of structure (e.g., accessory atrioventricular connection) and function (e.g., hereditary ion channelopathies). 2. Systemic factors: electrolyte abnormalities (particularly low potassium or magnesium), hypoxia, hormonal imbalances (e.g., hypothyroidism, hyperthyroidism), drugs and toxins (e.g., alcohol, caffeine). - ~~Video: Understanding Arrhythmias~~
Antiarrhythmic drugs	- Three Primary Indications for Treatment of Cardiac Arrhythmias: 1. Arrhythmias that decrease cardiac output (e.g., severe bradycardia, ventricular tachycardia or fibrillation). 2. Arrhythmias that are likely to precipitate more serious arrhythmias (e.g., atrial flutter may lead to sustained ventricular tachycardia). 3. Arrhythmias that are likely to precipitate an embolism due to creation of vascular stasis (e.g., chronic atrial fibrillation). - Non-pharmacological therapies: 1. DC cardioversion, implanting of a pacemaker, or defibrillator device (ICD). 2. Carotid sinus massage (increase vagal tone). 3. Surgical or catheter-mediated ablation of an ectopic focus, coronary bypass surgery. 4. Lifestyle modification (avoiding events that aggravate an arrhythmia - e.g., exertion, emotional stress, non-ideal diet).

Accessory atrioventricular connection, also known as accessory pathways or bypass tracts, are abnormal electrical connections between the atria and ventricles in the heart. These pathways can disrupt the normal electrical signals that regulate the heartbeat, leading to arrhythmias

HR ↑↓ thyroxine

Increase refractory period >increase QT interval >arrhythmias

1. **Delayed repolarization**: Potassium plays a crucial role in repolarizing cardiac cells after each heartbeat. When potassium levels are low, repolarization is delayed, prolonging the duration of the action potential. This can lead to the development of early afterdepolarizations (EADs) and trigger arrhythmias

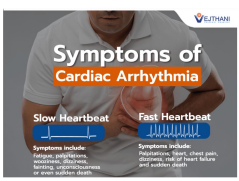
CO = SV x HR

filling ↓ وقت

Instead of coordinated contractions, the ventricles quiver ineffectively, leading to a loss of cardiac output and sudden cardiac arrest if not promptly treated.

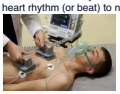
specific type of arrhythmia can induce other types.

Arrhythmias



to deliver a controlled electric shock to your heart in order to try and return your heart rhythm (or beat) to normal

Direct Current Cardioversion



Increase parasympathetic stimulation

involves gently massaging the carotid artery whilst monitoring your heart rhythm

ischemic heart tissue may be more susceptible to the formation of abnormal electrical pathways, further increasing the risk of arrhythmias.

Class I Antiarrhythmic Drugs
Mechanism of Action
Act by blocking voltage-sensitive Na+ channels. They bind more rapidly to open or inactivated Na+ channels than to channels that are fully repolarized. These drugs have use dependence (or state dependence) property as they show a greater degree of blockade in tissues that are frequently depolarizing, enabling them to block cells that are discharging at an abnormally high frequency without interfering with the normal beating of the heart.
Effects and Subdivisions
- Have proarrhythmic effects, particularly in patients with reduced left ventricular function and atherosclerotic heart disease. - Class I drugs are further subdivided into three groups according to their effect on the duration of the cardiac action potential.
Binding to Fast Na Channels
- Bind to and block the fast Na channels in non-nodal tissue (e.g., myocytes of the atria and ventricles, His-Purkinje system). - Blocking fast Na channels: Decrease slope of phase 0, leading to a decrease in the amplitude of action potential. Decrease velocity of action potential (transmission within the heart) (decrease conduction velocity). - Important mechanism for suppressing tachycardias caused by abnormal conduction (e.g., reentry mechanisms). - Reentry mechanisms can be interrupted by decreasing abnormal conduction.

The degree of sodium channel blockade depends on the frequency of depolarization of the cardiac tissue.

During fast heart rates or in tissues with frequent depolarization, such as during tachycardia or in diseased cardiac tissue, Class 1 antiarrhythmics bind more readily to sodium channels and have a stronger effect. This is because the channels are more likely to be in the open or inactivated state, making them more accessible to the drug.

phase 0

phases 1 & 2 & 3

phase 4

↑HR → Channels more accessible to → the drug. Normal heart rate.

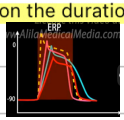
↓ VF

Increase refractory period >increase QT interval >arrhythmias

drug's ability to promote an arrhythmia.

This can prolong the action potential duration and refractory period, which is intended to suppress abnormal rhythms. However, in certain conditions, this action can actually promote the development of arrhythmias.

extra



electrical impulse circulates repeatedly around a circuit within the heart, causing the heart to beat in an abnormal rhythm

Class IA Antiarrhythmic Drugs

- They have concomitant class III activity (K channel blockers). — Increase refractory period >increase QT interval >arrhythmias
- They can cause arrhythmias that can progress to ventricular fibrillation.

Drugs

1. Quinidine (prototype)
2. Procainamide
3. Disopyramide

Mechanism of Action

- Na channel effects:

intermediate rate of association with Na channels

- Intermediate speed of binding and dissociation from voltage-gated Na channels. Slows the upstroke of action potential and conduction.

- K channel effects:

- Blocks K channels, leading to decreased K efflux, slowing repolarization, increased effective refractory period (ERP), and action potential duration (QT prolongation).

- Other effects:

It's not a mechanism of action
It's only a side effect

- Anticholinergic activity increases sinoatrial rate and atrioventricular conduction, decreases myocardial contractility.

Subdivisions

Stimulation of alpha-adrenergic receptors leads to vasoconstriction

- Quinidine: Mild α-adrenergic blocking and anticholinergic actions.
- Procainamide: No α-adrenergic blocking and less anticholinergic activity than quinidine.
- Disopyramide: No α-adrenergic blocking and more anticholinergic activity than quinidine. Produces a greater negative inotropic effect and causes peripheral vasoconstriction.

Therapeutic Uses

- Quinidine: Atrial, AV junctional, and ventricular tachyarrhythmias.
- Procainamide: Acute atrial and ventricular arrhythmias (not often used; replaced by electrical cardioversion or defibrillation and amiodarone).
- Disopyramide: Ventricular tachyarrhythmias, atrial fibrillation/flutter (not first choice).

Contraindications

Proarrhythmic effect

- Patients with atherosclerotic heart disease or systolic heart failure.

Negative Inotropic Effects: Class 1a antiarrhythmic drugs can exert negative inotropic effects on the heart, meaning they decrease the strength of cardiac muscle contraction. In patients with systolic heart failure, where the heart's pumping ability is already compromised, further reduction in contractility can worsen cardiac function and lead to worsening heart failure symptoms.

Side Effects

- Large doses of quinidine may induce cinchonism symptoms (blurred vision, tinnitus, headache, disorientation, psychosis).

Class IB Antiarrhythmic Drugs

Drugs

- Lidocaine
- Mexiletine

Class 1b antiarrhythmics primarily exert their effects by selectively blocking sodium channels in depolarized or ischemic cardiac tissue. This preferential blockade of sodium channels in ischemic myocardium reduces abnormal automaticity and stabilizes cell membranes, which can be beneficial in managing arrhythmias associated with acute ischemia or infarction. In contrast, Class 1a antiarrhythmics have a broader spectrum of sodium channel blockade and can prolong action potential duration, which may exacerbate ischemia-related arrhythmias.

Mechanism of Action

Unlike class 1b
Mainly given to ischemic myocarium patients

- Na+ channel blockade: Binds primarily to channels in the inactivated state. Useful for arrhythmias in ischemic myocardium due to enhanced binding. Decreases velocity of action potential transmission within the heart. Shortens phase 3 repolarization and action potential duration.

لا يعتبر من MOA

- Neither drug contributes to negative inotropy.

Work mainly on ischemic tissue

Limited Negative Inotropic Effects**: Class 1b antiarrhythmic drugs generally have minimal negative inotropic effects on the heart. This is beneficial in patients with ischemic heart disease, where preserving myocardial contractility is important for maintaining cardiac output and preventing further ischemic damage.

Therapeutic Uses

Give the amiodarone more priority than Lidocaine for ventricular fibrillation or ventricular tachycardia (VT).

For acute treatment
- Lidocaine: Alternative to amiodarone for ventricular fibrillation or VT. Used in combination with amiodarone for VT storm.

For chronic treatment
- Mexiletine: Chronic treatment of ventricular arrhythmias often in combination with amiodarone.

Adverse Effects

in acute state → high dose → more common occuring of SEs

- Lidocaine: CNS effects include nystagmus (early toxicity indicator), drowsiness, slurred speech, paresthesia, agitation, confusion, convulsions.

Repetitive,uncontrolled movement of eyes

in chronic state → low dose → less common occuring of SEs.

- Mexiletine: Nausea, vomiting, dyspepsia.

Class IC Antiarrhythmic Drugs

Drugs

- Flecainide
- Propafenone

Mechanism of Action

- Suppress phase 0 upstroke in Purkinje and myocardial fibers,(slowing conduction in all cardiac tissue*)
- Automaticity is reduced by an increase in the threshold potential.*

↑ threshold → ↓ firing

Therapeutic Uses

- Flecainide: Maintenance of sinus rhythm in atrial flutter or fibrillation, treating refractory ventricular arrhythmias.
- Propafenone: Restricted mostly to atrial arrhythmias, rhythm control of atrial fibrillation/flutter and paroxysmal supraventricular tachycardia, prophylaxis in patients with AV reentrant tachycardias.

Contraindications

Class 1 → avoided in case of heart failure.
Class 1 A+C → avoided in case of SHD + ASHD
Class 1 B → Given in case of ischemic myocardium

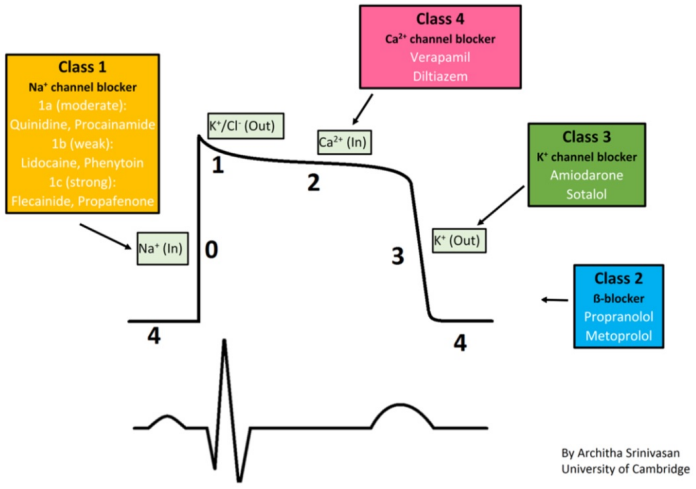
- Avoided in patients with structural heart disease (left ventricular hypertrophy, heart failure, atherosclerotic heart disease) due to negative inotropic and proarrhythmic effects.

Adverse Effects

Class one is avoided in case of heart failure
Class one(a+b) is avoided in case of Structural heart disease and atherosclerotic heart disease
Class one (b)given in case of ischaemic myocardium

- Flecainide: Blurred vision, dizziness, nausea.
- Propafenone: Blurred vision, dizziness, nausea, bronchospasm (avoided in asthma).

Antiarrhythmic drugs



CLASSIFICATION OF DRUG	MECHANISM OF ACTION	COMMENT
IA	Na^+ channel blocker	Slows Phase 0 depolarization in ventricular muscle fibers
IB	Na^+ channel blocker	Shortens Phase 3 repolarization in ventricular muscle fibers
IC	Na^+ channel blocker	Markedly slows Phase 0 depolarization in ventricular muscle fibers

Antiarrhythmic Drugs

Class Ia

1 Double Quarter Pounder

Disopyramide

Quinidine

Procainamide

Class Ib

with Lettuce, Mayo

Lidocaine

Mexeletine

Class Ic

Fries Please!

Flecainide

Propefanone

Class II

Beta blockers? Lol

Propanolol

Atenolol

Metoprolol

Class III

This is SAD

Sotalol

Amiodarone

Dofelitide

Class IV

I and V in Class IV?

Diltiazem

Verapamil