PHARMACOLOGY

بسم الله الرحمن الرحيم

FINAL | Lecture 2

Antiarrhythmic Drugs (Pt. 2)

وَلَقَدْ خَلَقْنَا الْإِنسَانَ وَنَعْلَمُ مَا تُوَسْوِسُ بِهِ نَفْسُهُ ۖ وَنَحْنُ أَقْرَبُ إِلَيْهِ مِنْ حَبْلِ الْوَرِيدِ

اللهم إنّا نعوذ بك من شرور أنفسنا ومن سيئات أعمالنا

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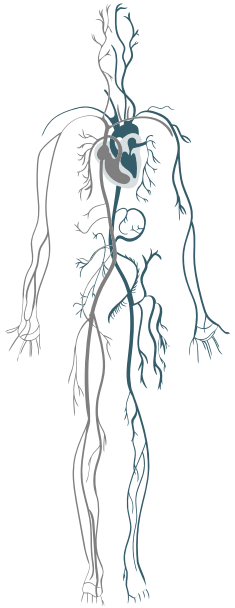

وَلِلَّهِ الْأَسْمَاءُ الْحُسْنَى فَادْعُوهُ بِهَا

المعنى: الذي أحاط علمه بالظواهر والبواطن، والإسرار والإعلان، فلا يخفى عليه شيء من الأشياء، يعلم ما كان وما هو كائن.

الورود: ورد اسم العليم (١٥٧) مرة، أما اسم العالم فورد (١٣) مرة، واسم علام الغيوب (٤) مرات.

الشاهد: ﴿إِنَّ ٱللَّهَ وَٰسِعٌ عَلِيمٌ﴾ [البقرة:١١٥]، ﴿عَٰلِمُ ٱلْغَيْبِ وَٱلشَّهَٰدَةِ﴾ [الأنعام:٧٣]، ﴿إِنَّكَ أَنتَ عَلَّٰمُ ٱلْغُيُوبِ﴾ [المائدة:١٠٩].

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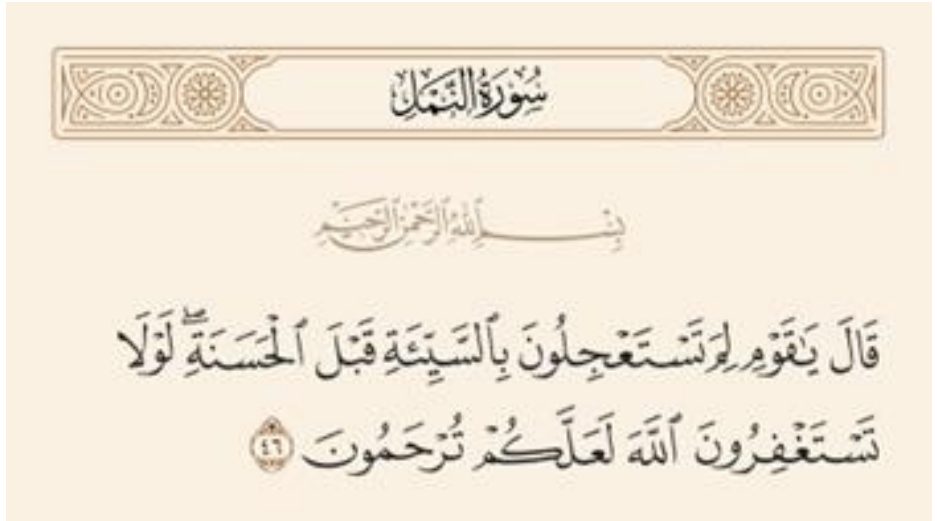
اضغط هنا لشرحٍ أكثر تفصيلًا



لا اله الا انت سبحانك اني كنت من الظالمين

Classification of Antiarrhythmic Drugs

Class	Description	Drugs
Class 1	Sodium Channel-Blocking Drugs	
	Subgroup 1A	Procainamide, quinidine, disopyramide
	Subgroup 1B	Lidocaine, mexiletine
	Subgroup 1C	Flecainide, propafenone
Class 2	β-Adrenergic blockers	Propranolol, esmolol, sotalol, nadolol, ..
Class 3	Drugs the prolong the effective refractory period by prolonging the action potential	Amiodarone, dronedarone, sotalol, dofetilide, ibutilide
Class 4	Calcium-channel blocking drugs	Verapamil, diltiazem
Unclassified	Various mechanisms	Adenosine, Ivabradine, Ranolazine, Vernakalant, Magnesium, Potassium

This slide is required.

Classification of Antiarrhythmic Drugs

- Antiarrhythmic drugs can **treat arrhythmias** but may also **induce them**, depending on factors such as **dose, electrolyte and acid-base balance, and interactions with other QT-prolonging drugs**, potentially leading to **polymorphic ventricular tachycardia**.
- Within each class or subgroup, **drugs are not identical**, and there **may be some differences between them**.
- In the presence of **hypokalemia or hypomagnesemia**, which can themselves cause arrhythmias, antiarrhythmic drugs **may fail to control the arrhythmia unless the electrolyte imbalances are corrected with potassium or magnesium supplementation**.

Sodium Channel-Blocking Drugs (Class 1)

- Subgroup 1A:
- Procainamide:
- It slows the upstroke of the action potential by blocking sodium channels, thus, slowing conduction, and prolonging the QRS duration in the ECG.
  - Anything that **slows ventricular conduction** will **prolong QRS duration**.
- It has direct depressant actions on SA and AV nodes that lead to suppression of the heart rate and conduction through AV node, which may be counter-balanced to a small extent by drug-induced vagal block.

Sodium Channel-Blocking Drugs (Class 1)

- Subgroup 1A:
- Procainamide:
- Procainamide has **antivagal, anticholinergic, and parasympatholytic effects**, which can **counteract bradycardia and influence conduction**, thereby **modifying SA and AV nodal activity**.
- It has **ganglion-blocking** properties, which reduces peripheral vascular resistance and may cause **postural** **hypotension**.

Procainamide Adverse Reactions:

1. Excessive action potential prolongation, QT-interval prolongation, and induction of torsades de pointes arrhythmia and syncope.
   - **Torsades** refers to a **twisting, polymorphic ventricular arrhythmia**. It can **progress to ventricular tachycardia, ventricular fibrillation, and, if untreated, death**.
2. Excessive slowing of conduction and development of new arrhythmias.
3. A lupus erythematosus-like syndrome consisting of arthralgia and arthritis (in one third of patients). Some patients may also have pleuritis and pericarditis; but rarely affecting the kidney.

Procainamide Adverse Reactions: SLE

- **Systemic lupus erythematosus (SLE)** is an autoimmune disease in which the immune system mistakenly attacks the body's own tissues, causing inflammation in organs such as the **kidneys, heart, blood vessels, liver, and joints**. This process involves the production of **autoantibodies** that target the body's cells and tissues.
- **Procainamide can induce a lupus-like syndrome** in some individuals. This condition **resembles SLE but typically does not affect the kidneys**, distinguishing it from classic lupus.

Procainamide Therapeutic Uses:

- It is no longer considered the first line treatment for any arrhythmia.
- It is effective against most atrial and ventricular arrhythmias
- It is the drug of second and third choice (**after** lidocaine and/or amiodarone) in most coronary care units for the treatment of sustained ventricular arrhythmias associated with acute myocardial infarction.

Sodium Channel-Blocking Drugs (Class 1)

- Subgroup 1B:
- Lidocaine:
- It is a rapid sodium channel blocker during phase 0 and phase 2, blocking sodium channels more quickly than procainamide, leading to decreased ventricular excitability.
- Its binding is use-dependent (the drug works more effectively when sodium channels are more active during the action potential); thus, the higher is the heart rate the more is the sodium channel blockade.

Lidocaine Therapeutic Uses:

- It is used via intravenous infusion.
- Ventricular tachycardia and ventricular fibrillation following acute myocardial infarction, cardiac surgery, and cardiac catheterization.

Lidocaine Contraindications:

1. Patients with Wolf-Parkinson-White (WPW) syndrome because it preferentially blocks the normal conduction pathway (AV node), leading to increased conduction through the accessory pathway and potentially causing arrhythmia and ventricular fibrillation.
2. Patients with severe heart block because it further depresses the His-Purkinje conduction system, and possibly other conduction pathways in the heart, potentially leading to complete heart block and asystole.

Lidocaine Adverse Reactions:

1. Hypotension, cardiovascular collapse (heart failure), bradycardia, cardiac arrest
   - **Hyperkalemia can impair AV conduction**, slowing electrical signaling in the heart, which may **lead to cardiac arrest**.
2. Light-headedness, unconsciousness due to low brain perfusion
3. Convulsions
4. Respiratory depression
5. Tennitus, visual disturbances, and vomiting.

- Mexiletine is an orally active analogue of lidocaine, as lidocaine cannot be given orally because it undergoes hydrolysis in the gut by intestinal mucosa.

Sodium Channel-Blocking Drugs (Class 1)

- Subgroup 1C:
- Flecainide:
- It is a potent **blocker** of **sodium and potassium channels** with **slow unblocking kinetics** (reversable, but slow unbinding).
  - Although it does block certain potassium channels, it does **not** prolong the action potential or the QT interval.
- It suppresses **premature** ventricular contractions.
- It has **no** antimuscarinic effects.

Flecainide

- Adverse Effects:
- It may cause severe exacerbation of arrhythmia in patients with preexisting ventricular tachyarrhythmias and those with a previous myocardial infarction and ventricular ectopy.
- It may increase mortality rate.
- Therapeutic Uses:
  - It is used for patients with normal hearts who have supraventricular arrhythmias but not as first line.
    - Supraventricular → Either SA or AV node

Sodium Channel-Blocking Drugs (Class 1)

- Propafenone:
- It possesses weak β-blocking activity.
- It does not prolong the action potential.
- Its sodium channel-blocking kinetics are similar to those of flecainide.
- It is used primarily for supraventricular arrhythmias.
- The most common adverse effects are a metallic taste (also seen with metronidazole) and constipation.
- Arrhythmia exacerbation can also occur.

β-Adrenergic-Blocking Drugs (Class 2)

- **β-Adrenergic blocking agents (Class II)** exert a **greater effect on the atria than on the ventricles** because they **depress SA node activity and slow AV nodal conduction.**
- As a result, **not all atrial impulses are transmitted to the ventricles.** For example, if the atrial rate is approximately **130 impulses per minute**, a proportion of these impulses may be **blocked at the AV node** due to the **reduced conduction velocity.**

β-Adrenergic-Blocking Drugs (Class 2)

- Actions in the electrical activity of the heart:

1. Negative chronotropic effect → bradycardia.
2. Slowing of AV nodal conduction and prolonging its refractory period and prolong PR interval.

- They are effective in both supraventricular and ventricular arrhythmias (β-blockers are beneficial in patients with **extrasystoles**).

β-Adrenergic-Blocking Drugs (Class 2)

- They improve survival following myocardial infarction due to suppression of arrhythmias, because they reduce the heart's O_2 demand, which helps **limit** the ischemia.
- In patients with MI, β-blockers are given without question to **reduce the heart's oxygen demand** and to **suppress cardiac arrhythmias**. Lowering oxygen demand **helps limit ischemia.**
- By increasing the AV nodal refractory period, they slow ventricular response rates in atrial flutter and fibrillation.
- In atrial fibrillation and flutter, reducing the atrial rate or slowing conduction through the AV node prevents ventricular fibrillation, as not all impulses will be conducted due to the prolonged refractory period.
- They also reduce ventricular ectopic beats, those precipitated by catecholamines (Smokers!).

β-Adrenergic-Blocking Drugs (Class 2)

- Esmolol is particularly useful against **acute perioperative arrhythmias** because it has a short duration of action and can be given parenterally.
- The non-selective β-blockers (propranolol, nadolol) are more **effective** subgroup of β-blockers for prevention and treatment of **cardiac arrhythmias**.

β-Adrenergic-Blocking Drugs (Class 2), Adverse Reactions:

1. Sinus bradycardia
2. Depression of myocardial contractility, leading to heart failure
3. They can **mask the early adrenergic symptoms of hypoglycemia**—especially tachycardia, sweating and anxiety—and may **delay recovery from hypoglycemia** because β-blockers inhibit sympathetic responses. As a result, patients may not perceive the typical warning signs, leading to **prolonged hypoglycemia**, which can cause neurological injury. Therefore, **non-selective β-blockers are not recommended in insulin-dependent diabetics**.
4. Fatigue, depression (specific for β-blockers that cross BBB like propranolol), exercise intolerance and sexual dysfunction

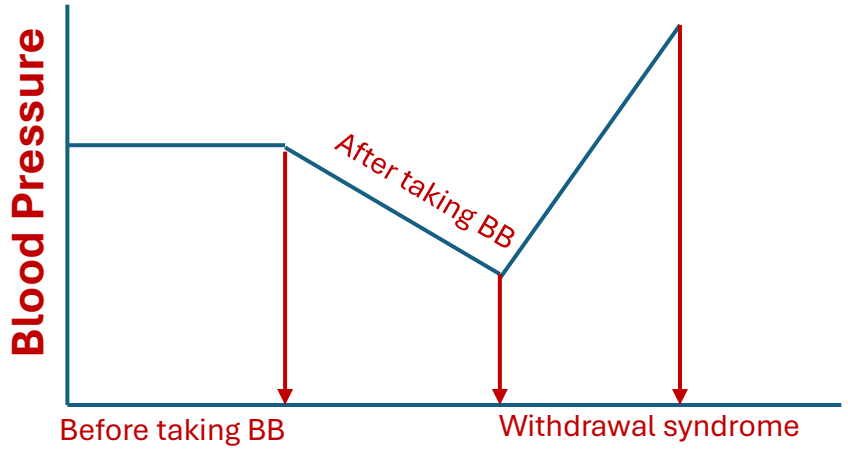
β-Adrenergic-Blocking Drugs (Class 2), Adverse Reactions:

5. A small increase in body weight and triglycerides and a decrease in HDL. These effects are not seen with vasodilating β-blockers (labetalol and carvedilol), are also referred to as **mixed alpha-beta blockers**. These medications are commonly used in managing **hypertension**, and carvedilol is also used in **heart failure (HF)** patients.

- A potential adverse effect of β-blockers is the **worsening of heart failure** if they are started during acute decompensation or if the dose is increased too rapidly. They have **cardioprotective effects when initiated at low doses**. Therefore, β-blocker therapy should be started **only in clinically stable patients**, with **slow and careful dose titration**.

β-Adrenergic-Blocking Drugs (Class 2), Adverse Reactions:

6. Acute withdrawal leads to sudden onset of tachycardia and exacerbation of ischemic symptoms (known as withdrawal syndrome or rebound effect). This is due to upregulation of β-receptors. This can be prevented by gradual tapering of dose rather than abrupt discontinuation of the drug.



Additional Figure

Drugs the Prolong the Effective Refractory Period by Prolonging the Action Potential (Class 3)

- These drugs **prolong action potential duration**, by **blocking potassium** channels in **phase 3** of the cardiac cycle, which **increases** the **effective refractory period**.
- Amiodarone (contains **iodine** in its structure):
- Used **orally** or **intravenously** to treat **ventricular arrhythmias**, as well as **supraventricular arrhythmias** such as atrial fibrillation.
  - In atrial arrythmatices use smaller dose than ventricular Arrhythmias.
- It has a broad spectrum of adverse effects.
- Dronedarone, an analog that lacks iodine atoms, used for the treatment of atrial flutter and fibrillation.

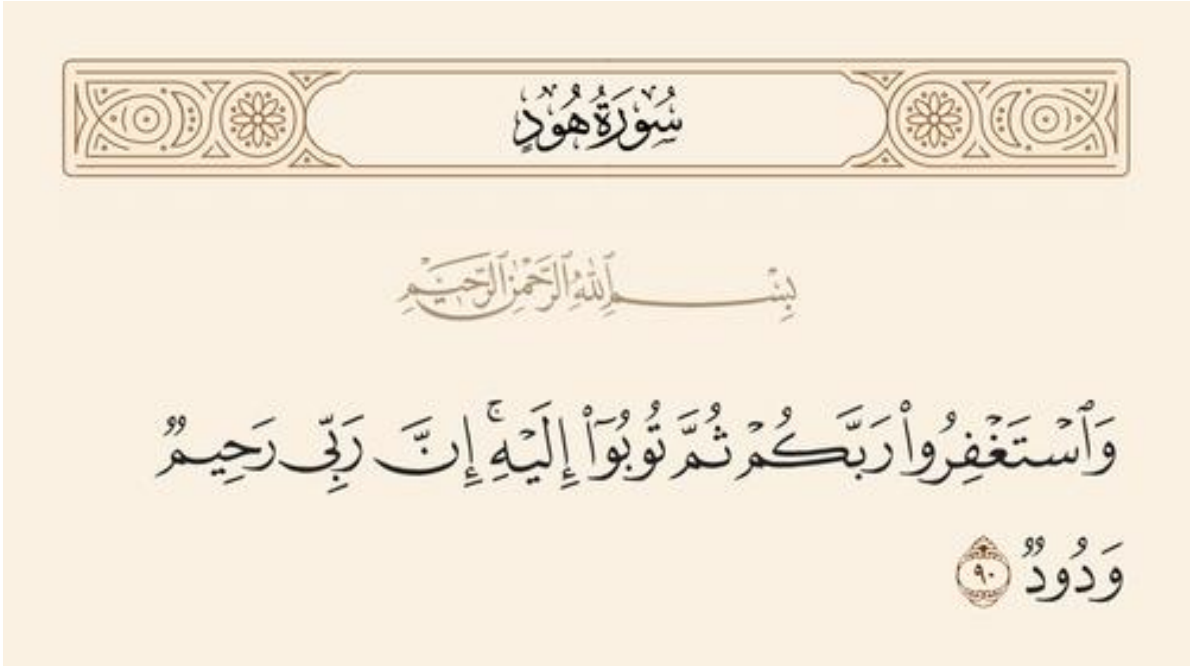
PHARMACOLOGY QUIZ LECTURE 2

رسالة من الفريق العلمي


سُورَةُ هُودٍ

بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

وَأَنِ ٱسْتَغْفِرُوا۟ رَبَّكُمْ ثُمَّ تُوبُوٓا۟ إِلَيْهِ يُمَتِّعْكُم مَّتَٰعًا حَسَنًا إِلَىٰٓ أَجَلٍ
مُّسَمًّى وَيُؤْتِ كُلَّ ذِى فَضْلٍ فَضْلَهُۥ ۖ وَإِن تَوَلَّوْا۟ فَإِنِّىٓ أَخَافُ
عَلَيْكُمْ عَذَابَ يَوْمٍ كَبِيرٍ ﴿٣﴾


سُورَةُ هُودٍ

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Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
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