

Recent Trends In Arrhythmia

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Abstract- Arrhythmia is a cardiac disorder. Arrhythmias are an abnormal heartbeat rhythm due to changes in heart's electrical system. Different kinds of arrhythmia are also studied. An abnormal heartbeat may be too fast or too slow or irregular. The study of treatment or medication which will depend on what is causing the arrhythmia and the new techniques were review for treating the different arrhythmias. To reduce the chances of arrhythmias patient should change their lifestyle and maintain their health good. Cardiac arrhythmia is a disease characterized by abnormal electrical conduction in the heart that results in ineffective pumping. Dysfunctional nodes in the conduction pathway or in the cardiac muscles lead to irregular heartbeat patterns that can potentially induce severe complications such as cardiac arrest. Radiofrequency ablation, the current gold-standard cardiac arrhythmia treatment procedure, has proven effectiveness but suffers from shortcomings due to instability between the RF tip and the target site.

Keywords: Arrhythmias, Pharmacological activities, History, Drug therapy.

1. INTRODUCTION

2.1 Arrhythmia :

Heart Arrhythmias (Heart rhythm problems) occur when the electrical impulses that coordinate heartbeats don't work properly, causing heart to beat too fast, too slow, or irregularly. Arrhythmias are an abnormal heartbeat rhythm caused by changes in heart electrical system. There are many different kinds of arrhythmias. Some may cause heart to skip or add a beat now and again but have no effect on general health or ability to lead a normal life. Other arrhythmias are more serious and life-threatening. Untreated, they can affect heart pumping action, which can lead to dizzy spells, shortness of breath, faintness or serious heart problems⁽³⁾

2.2 Symptoms -

Arrhythmias may not cause any signs or symptoms. In fact, doctor might find it have an arrhythmia before it does, during a routine examination. Noticeable signs and symptoms don't necessarily mean have a serious problem, however. Noticeable arrhythmia symptoms may include.⁽⁹⁾

1. A fluttering in your chest
2. A racing heartbeat (tachycardia)
3. A slow heartbeat (bradycardia)
4. Chest pain
5. Shortness of breath
6. Lightheadedness or dizziness
7. Sweating
8. Fainting (syncope) or near fainting.
9. Breathlessness (Dyspnea)
10. Dizziness
11. Palpitations
12. Syncope (Fainting, Or Nearly Fainting)
13. Weakness

2. HISTORY

Cardiac arrhythmias leading to sudden cardiac death is estimated to claim 2,50,000 lives annually or 25 lives per million people per week in United States. In more than 80%cases of sudden death is caused by abrupt onset of VT and may progress to VF, Family physicians and nurses working at primary, secondary and tertiary care hospital, are usually confronted with cardiac rhythm problems, which need to be high listened with regards to practical diagnosis and management, which is based not only on ECG but thorough history and physical examination indeed. In 1761, Morgagni recognized CHB as most ancient arrhythmia. Robert Adams was first to recognize atrial fibrillation as a sign of neutral stenosis in 1827. Ventricular fibrillation was first described by Erichson in 1842. In 1862, Panum induced ventricular

tachycardia. Cotton, 1867, described first supraventricular tachycardia. The construction of the string galvanometer by Einthoven in 1901, which allowed high-fidelity recording of the body surface ECG. which neither mechanical nor electrical activity was recorded provided crucial insights into re-entry as a mechanism for atrial and ventricular fibrillation, AV node re-entry and AV re-entrant tachycardia in hearts with an accessory AV connection. Mackenize (1902), described sick sinus syndrome and William Einthoven (1903) developed ECG. First ECG of ventricular tachycardia in man was published by Thomas Lewis in 1909. Paul Dudley white (1928) discovered WPW syndrome. The first intracellular potentials were recorded with micro-electrodes in 1949 by Coraboeuf and Weidmann. It is remarkable that interpretation of extracellular electrograms was still controversial in the 1950s and it was not until 1962 that Dower showed that the transmembrane action potential upstroke coincided with the steep negative deflection in the ECG. The mechanism of an arrhythmia to its successful therapy has been long; the studies of Mines in 1913 and 1914, microelectrode studies in animal preparation in the 1960s and 1970s, experimental and clinical demonstrations of initiation and termination of tachycardias by premature stimuli in the 1960s and 1980s, and finally catheter ablation at the end of the previous century, with success rates that approach 99% for supraventricular tachycardias.⁽⁵⁾

3. OBJECTIVE

- ✓ To review about Arrhythmia and different kinds of arrhythmias.
- ✓ To study about anti-arrhythmic drugs.
- ✓ To study about treatment of different kinds of Arrhythmias.
- ✓ To study about recent drug therapies and technologies in arrhythmia.
- ✓ To get the knowledge about past (history) of arrhythmia.⁽⁴⁾

4. Causes Arrhythmias -

Arrhythmias are caused by a problem in your heart's electrical system. Following are the causes of arrhythmias :

4.1 Irritable heart cells – Sometimes heart cells begin to malfunction and start sending out electrical signals when they normally wouldn't. Signals from these malfunctioning heart cells interfere with the proper signals from the natural pacemaker within the heart. This 'confuses' heart and makes it beat irregularly.

4.2 Blocked signals – The electrical signals that tell heart to beat may get 'blocked'. This makes heartbeat very slowly.⁽⁵⁾

4.3 Tachycardia (a fast heartbeat) :

Tachycardia is when heart beats too fast, generally more than 100 beats per minute. Some forms of tachycardia are easily treated and not serious, while others can be life threatening. Forms of tachycardia are as follows:

- **Supraventricular tachycardia (SVT)** is a rapid heartbeat that starts in the collecting chambers of the heart, the atria, or the electrical pathway from the atria. Common types of SVT are atrial fibrillation.
- **Atrial flutter** is when an extra or early electrical signal travels around the atria in a circle instead of along the normal signal pathway. This 'overstimulation' causes the atria to contract quickly or 'flutter' at a much higher rate than normal. Atrial flutter is usually not life-threatening but can still cause chest pain, faintness or more serious heart problems.
- **Atrial fibrillation** is the most common form of SVT. It is when 'waves' of uncontrolled electrical signals, rather than the normal regulated signals, travel through the atria from the sinus node. When heart is in atrial fibrillation, it does not pump regularly or work as well as it should. It can cause a 'fluttering' heartbeat.
- **Paroxysmal supraventricular tachycardia (PSVT)** is when there is a 'short circuit' caused by an extra electrical connection or pathway in heart. It makes heart prone to episodes of sudden regular rapid heartbeats that may last for minutes or even hours.⁽⁸⁾

5. The treatments for arrhythmias-

The treatment will depend on what is causing the arrhythmia and how much it is affecting lifestyle. Treatments include:

- Medicines that slow down a very fast heartbeat or to thin the blood to reduce the chance of a clot breaking loose from heart and travelling through the blood to brain, causing a stroke.
- Implantable medical devices such as pacemakers, which use a small electrical current to stimulate the heart muscle to pump regularly or defibrillators that correct heartbeat.
- Other procedures such as cardiac ablation, a procedure that inactivates the areas of heart responsible for the abnormal electrical signals in heart or cardioversion, a procedure where heart is given a 'shock' to help restore a normal heartbeat.⁽⁶⁾

6. Diagnosis –

To diagnose a heart arrhythmia, doctor will review symptoms and medical history and conduct a physical examination

of patient. Doctor may ask about – or test for – conditions that may trigger arrhythmia, such as heart disease or problem with thyroid gland. Doctor may also perform heart-monitoring tests specific to arrhythmias. These may include:

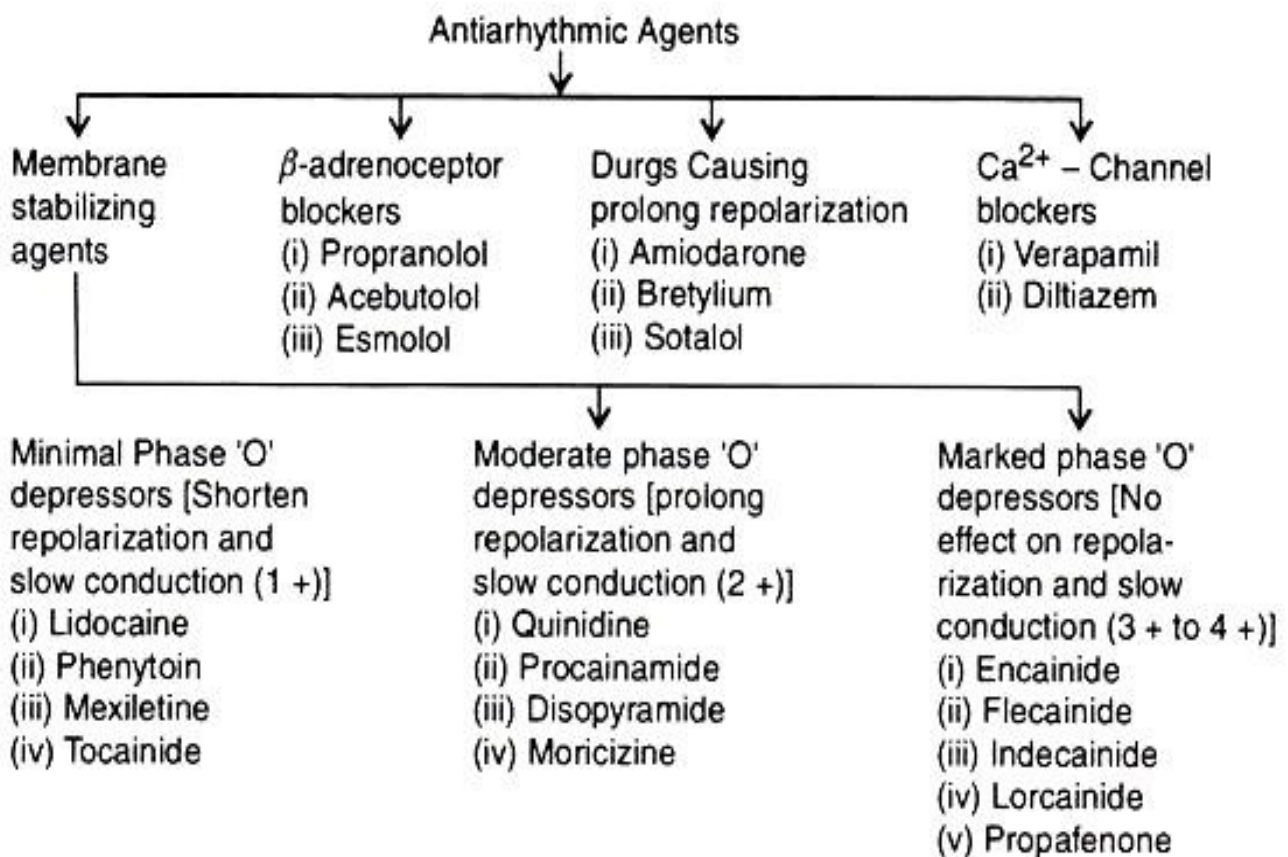
- **Electrocardiogram (ECG):** During an ECG, sensors (electrodes) that can detect the electrical activity of chest and sometimes to limbs. An ECG measures the timing and duration of each electrical phase in heartbeat.
- **Holter monitor:** This portable ECG device can be worn for a day or more to record heart’s activity as go about routine.
- **Event monitor:** For sporadic arrhythmias, available, attaching it to body and pressing a button when have symptoms. This lets doctor check heart rhythm at the time of symptoms.
- **Echocardiogram:** In this noninvasive test, a hand-held device (transducer) placed on chest uses sound waves to produce images of heart’s size, structure and motion.
- **Implantable loop recorder:** This device detects abnormal heart rhythms and is implanted under the skin in the chest area.

If doctor doesn’t find an arrhythmia during those tests, he or she may try to trigger arrhythmia with other tests, which may include:

- ❖ **Stress test:** During a stress test, patient will be asked to exercise on a treadmill or stationary bicycle while heart activity is monitored. If doctors are evaluating to determine if coronary artery disease may be causing the arrhythmia, and have difficulty exercising, then doctor may use a drug stimulate heart in a way that’s similar to exercise.
- ❖ **Tilt table test:** Doctor may recommend this test if patient had fainting spells. Heart rate and blood pressure are monitored as patient lie flat on a table. The table is then tilted as if patient were standing up. Doctor observes how patient’s heart and the nervous system that controls it respond to the change in angle.
- ❖ **Electrophysiological testing and mapping:** In this test, doctors’ thread thin, flexible tubes (catheters) tipped with electrodes through blood vessels to a variety of spots within heart. Once in place, the electrodes can map the spread of electrical impulses through heart.⁽¹³⁾

7. Drug Therapy of Arrhythmias :-

8.1 Classification of Drugs :



Flow Chart

8. Pharmacologic Management of Arrhythmias –

Understanding the mechanisms by which individual antiarrhythmic agents work requires a detailed understanding of the cardiac action potential (AP). The AP of the ventricular myocyte has 5 phases (0 to 4) and is the standard model of the cardiac AP. At baseline (phase 4, also known as the resting membrane potential), the intracellular environment is negatively charged, compared with that of the extracellular space (-96 mV). This phase is associated with cardiac diastole. The AP is the result of synchronized influx and efflux of multiple cations and anions. Briefly, this gradient is the sum of 3 main factors:

- 1) An ATPase sodium/potassium (Na/K) pump.
- 2) The plasma membrane's impermeability to negatively charged intracellular proteins, which prevents their efflux; and

For simplicity's sake and the purposes of this discussion, we will mention only those ion channel activities that are relevant to the drugs discussed in this review.

During phase 0 (rapid depolarization), fast sodium (Na^+) channels open, which results in rapid inward conductance of Na^+ and a rapid influx of Na^+ ions into the cell, rendering the intracellular space positive relative to the extracellular milieu. Recovery of the resting membrane starts during phase 1 but is most pronounced during phase 3, when positive currents, primarily in the form of K ions, leave the cell through the delayed rectifier K^+ channels (rapid repolarization).

Figures 1 and 2 demonstrate the correlation between these currents and the surface measurements of these activations as shown by the P, QRS, and T waves. The sodium dependent (inward current) depolarization of ventricular cells can best be thought of as the QRS complex on the surface electrocardiogram. For this reason, any drug that affects this inward sodium current can also affect the QRS. If it delays the influx of Na^+ , the QRS is widened; conversely, any agent that delays potassium efflux (and a return to the baseline state) delays the recovery phase or repolarization. For ventricular cells, this delay manifests itself electrocardiographically as a longer QT interval. According to the Singh and Vaughan Williams classification of antiarrhythmic agents,¹ there are 5 main classes: class I agents, which are Na^+ -channel blockers; class II agents, which are antisympathetic nervous system agents, most of which are β -blockers.⁽¹⁾

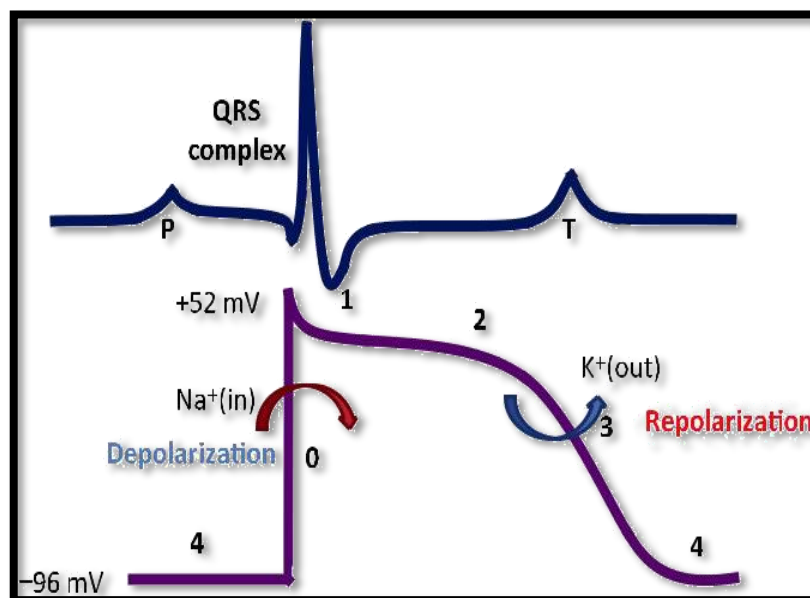


Figure 1: The phases of the cardiac action potential.

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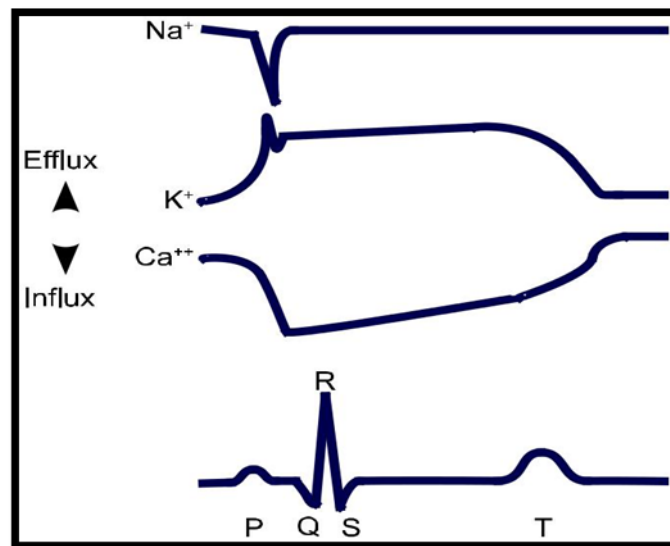


Figure 2: The Electrocardiogram and relative ion flow in cardiac cells.

9.1 Use Dependence and Reverse-Use Dependence –

Use dependence and reverse-use dependence are most often associated with Na^+ channel blocking drugs. These drugs block open inactivated sodium channels, and they show little affinity for the channels in their resting state. With each AP, they block the channels, and, during each diastolic interval, they dissociate from their ligands. When the heart rate increases, the diastolic interval shortens, and the dissociation time decreases. Therefore, steady-state Na^+ channel blockade increases.

Reverse-use dependence can be thought of as the opposite, wherein the drug more avidly binds to the channel during the resting phase. Most potassium channel-blocking drugs are reverse-use dependent. In general, drugs that prolong repolarization have a decreased effect on depolarizing tissue, because they tend to bind during the resting phases of the ion channel.³ This increases the likelihood that the drug will bind to the channel at times of slower heart rates, during which the ion channel is more often in the resting phase. Reverse-use dependent drugs tend to be effective in the prevention of arrhythmia⁽¹⁴⁾

10. Sodium Channel Blockade: Flecainide, Propafenone, and Disopyramide –

At the onset, it is crucial to note that most antiarrhythmic drugs are extremely promiscuous, binding to multiple channels. For this reason, predicting their effects on the AP or by means of electrocardiography can be confusing without an understanding of each drug's various actions. Furthermore, because sodium channel blockade leads to slowing of myocardial conduction, it can be proarrhythmic in patients who have any type of structural heart disease—in this population, these agents should be used only with great caution.

• Flecainide -

Flecainide is a class I antiarrhythmic agent with a very potent Na⁺ channel blockade effect that also blocks the Ca²⁺ current and the delayed rectifier K⁺ current. It shortens the AP duration in Purkinje cells, consequent to the blockage of late-opening Na⁺ channels (blocking this current lessens the influx of positive current during the entire AP, thus truncating its duration); but flecainide prolongs the AP duration in the ventricular cells because of the blockage of the delayed rectifier K⁺ current. In atrial tissue.

• Adverse effects –

- ❖ The most common noncardiac adverse effect of flecainide is dose related blurred vision.
- ❖ Flecainide increases the capture thresholds of pacemakers—that is, the amount of current required to electrically capture cardiac tissue. Therefore, capture thresholds should be remeasured in individuals with pacemakers after the steady-state flecainide dosage is changed.
- ❖ It includes hallucination, confusion, and paresthesia.

• Propafenone –

Propafenone is a Na⁺ channel blocker that also blocks K⁺ channels. It was originally manufactured as a β-blocker, and it maintains significant levels of such activity. Propafenone is used in the treatment of SVT, including AF. It may also be used for ventricular arrhythmias, with modest efficacy.

Adverse effects –

- ❖ It includes acceleration of the ventricular response in patients with atrial flutter, an increased risk of ventricular tachycardia (VT), exacerbation of heart failure.
- ❖ The adverse effects of beta-adrenergic blockade, such as bradycardia and bronchospasm.
- ❖ Other include hypersensitivity reactions, agranulocytosis.

• Disopyramide –

The electrophysiologic effects of disopyramide include Na⁺ channel blockade with minimal prolongation of the AP.

• Adverse effects –

- ❖ Precipitation of glaucoma
- ❖ Constipation
- ❖ Dry mouth
- ❖ Urinary retention (especially in men with prostatism)⁽¹²⁾

Sodium channel blockers

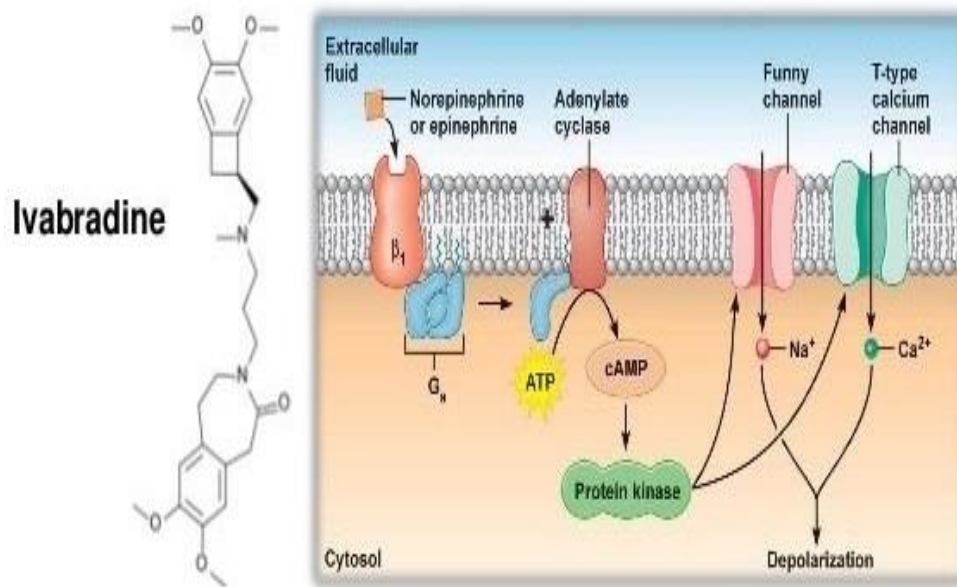


Fig.3

10.1 Potassium Channel Blockade: Amiodarone, Dofetilide, Sotalol, and Dronedarone:

• **Amiodarone** –

Amiodarone is the most effective drug presently available for sinus-rhythm maintenance in patients with AF. It blocks the inactivated Na⁺ channels, and it decreases the Ca²⁺ current and outward and the inward rectifier K⁺ current. It also has a noncompetitive adrenergic blocking effect. It blocks potassium channels and prolongs myocardial repolarization. Adverse effects –

- ❖ Pulmonary fibrosis
- ❖ Corneal microdeposits (asymptomatic)
- ❖ Optic neuritis (rare)
- ❖ Hepatic dysfunction
- ❖ Peripheral neuropathy

• **Dofetilide** –

Dofetilide is a potent, pure K⁺ blocker with no extracardiac pharmacologic effect. It is safe in patients with structural heart diseases. Its potassium blockade is reverse-use dependent and the risk of torsades de pointes is therefore greatest during bradycardia.

• **Adverse effects** –

- ❖ Its only significant toxicity relates to QT prolongation and torsades de pointes.
- ❖ There is a risk of torsades de pointes in 1% to 3% of patients taking dofetilide.

• **Dronedarone** –

Dronedarone is a modified analogue of amiodarone and has the pharmacologic ability to block multiple ion channels, including the L-type calcium current, the inward sodium current, and multiple potassium currents. It also has sympatholytic effects.

Dronedarone is generally less efficacious than amiodarone, and its half-life of 1 to 2 days is shorter than that of amiodarone. It has no risk of thyroid or pulmonary toxicity.

• **Adverse effects** –

- ❖ The FDA released a warning about a number of reports of hepatic toxicity related to dronedarone administration.

❖ The agency notified healthcare providers and patients about rare but severe cases of liver damage, including 2 cases of acute liver failure that led to liver transplantation. As a result, the FDA has added a new warning and adverse-effect section to dronedarone labeling.⁽⁹⁾

11. Treatment of Arrhythmias –

Non-drug interventions are being used increasingly to treat arrhythmias and they are reviewed below:

11.1 Radiofrequency ablation:

Radiofrequency ablation represents a major advance in the arrhythmias, particularly supra-ventricular tachycardias. Success rates are high (approximately 90 percent) with a low complication rate. The procedure destroys the aberrant conduction pathways present in certain arrhythmias, preventing future arrhythmias and obviating the need for long-term anti-arrhythmic drugs.

RF ablation is frequently the first-line option in the management of arrhythmias such as AV nodal re-entry tachycardia or AV re-entry tachycardia including Wolff-Parkinson White syndrome, AF, atrial flutter and ventricular tachycardia.

11.2 Direct current cardioversion:

Cardioversion refers to the process of restoring the heart's normal rhythm, usually in patients with atrial flutter or AF. This can be done chemically using drugs such as amiodarone, flecainide, sotalol or verapamil. It is more commonly achieved by the application of a controlled electric shock across the chest wall to override disordered conduction and allow the sinus node to regain control of heart rate. The patient is briefly anaesthetized while the shock is delivered.

11.3 Defibrillation:

Defibrillation is performed to correct life-threatening fibrillations of the heart, which could result in cardiac arrest. It should be performed immediately after identifying that the patient is experiencing a cardiac emergency, has no pulse and is unresponsive. The process similar to DC cardioversion, using the delivery of an electric shock to the myocardium via the chest wall.

11.4 Pacemakers:

Pacing is employed on a temporary or permanent basis to correct bradycardia. The most common indication for temporary pacing is post-myocardial infarction (MI) with the development of new bundle branch block with first degree heart block or symptomatic bradycardia in anterior MI or second-degree Av block in an anterior MI.

11.5 Internal cardioversion defibrillators:

Internal cardioversion defibrillators (ICDs) are implanted in high-risk patients to prevent sudden cardiac death due to malignant ventricular tachycardias. National Institute for Clinical Excellence guidance recommends that ICDs should be considered in the following:

- For secondary prevention in patients with cardiac arrest due to VT or ventricular fibrillations, or spontaneous sustained VT with hemodynamic compromise (including syncope), or sustained VT in presence of left ventricular systolic dysfunction.
- For primary prevention post-MI in patients with non-sustained VT on 24-hour tape and positive VT stimulation tests and left ventricular systolic dysfunction.

The devices are implanted and monitor the cardiac rate and rhythm in a similar manner to permanent pacemakers. However, on sensing a VT, the device will initially deliver anti-tachycardia pacing impulses at a rapid rate (faster than the arrhythmia) to try to regain control of cardiac rhythm and then slow the heart rate down in a controlled manner. If this fails, the device will discharge an internal electric shock (at a higher voltage than for DC cardioversion) to terminate the arrhythmia and return the heart to sinus rhythm. This can be an unpleasant experience for the patient, and additional anti-arrhythmic drugs may be required to ensure episodes occur infrequently and to reduce the number of inappropriate shocks.⁽¹⁰⁾

12. Marketed Formulations of Arrhythmias (U.S. FDA approved) :-

Sr. No.	DRUGS	GENERIC NAME	BRAND NAME
1.	Amiodarone	Amiodarone systemic	Pacerone, Nexterone
2.	Verapamil	Verapamil systemic	Calan, Calan SR
3.	Propranolol	Propranolol systemic	Inderal
4.	Dofetilide	Dofetilide systemic	Tikosyn
5.	Lidocaine	Lidocaine systemic	Dentipatch, UAD Caine
6.	Mexiletine	Mexiletine systemic	Mexitil
7.	Quinidine	Quinidine systemic	Cardioquin, Quin-G
8.	Disopyramide	Disopyramide systemic	Norpace, Norpace CR

13. Recent development in treatment of Arrhythmia –

- Atrial and ventricular arrhythmias are associated with substantial morbidity and mortality and thus are a significant economic burden for healthcare systems.
- Currently available pharmacological agents have limited efficacy or the risk of relevant side effects, such as drug toxicity and proarrhythmic potential.
- Recent scientific developments have added new aspects and approaches to this field meriting a fresh review of treatment options.
- These include novel ion-channel blockers (e.g., dronedarone, celivarone, vernakalant, ranolazine), non-ion channel blockers (e.g., GsMtx4) such as gap junction modulators (rotigaptide) and drugs antagonizing the angiotensin system (ACE-inhibitors, angiotensin 2 receptor blockers), which appear to have various effects on cardiac electrophysiology.
- Special emphasis is placed on new antiarrhythmic drugs (e.g., dantrolene) targeting molecular, proarrhythmic and structural remodeling.
- Finally, new developments in the prevention of thromboembolic complications of atrial fibrillation are discussed.⁽¹¹⁾

CONCLUSION –

In above decision of pharmacology and drug therapy of cardiac arrhythmia. Some research papers and review articles related to the different types of arrhythmias and its management, treatment and new technologies were studied. New techniques also developed for the treatment of different kinds of arrhythmias.

From the above study of arrhythmia, can be concluded that arrhythmia is an abnormal cardiac disorder but in some frequent cases it is severe and can cause sudden death. If in case it is not treated by medication of an anti-arrhythmic drugs, it can be treated by using non-interventions of drugs that means by using newly developed techniques.

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