Beta-blockers: Are they useful in arrhythmias?

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Introduction

Beta-blockers have been extensively used in the treatment of cardiovascular diseases for their anti-arrhythmic, anti-ischaemic and anti-hypertensive properties. Their pharmacological effect of competitively binding to the beta-adrenoceptors during activation of the sympathetic system result in their having a diverse mechanism of actions, with important differences between different beta-blocker drugs. The antiarrhythmic effect of beta-blockers is a result of their direct cardiac electrophysiological action such as reduced heart rate, decreased spontaneous firing of ectopic pacemakers, slowed conduction and increased refractory period of the atrioventricular (AV) node.[1,2] Other mechanisms include reduction of the sympathetic drive and myocardial ischaemia, improvement of baroreflex function, inhibition of cardiac apoptosis mediated via the activation of the beta-adrenergic pathway, inhibition of platelet aggregation, reduction of the mechanical stress imposed on the plaque, preventing plaque rupture, resensitization of the beta-adrenergic pathway and changes in myocardial gene expression.[2]

Due to these extensive anti-arrhythmic mechanisms, beta-blockers such as propranolol, metoprolol, atenolol, sotalol or timolol have been indicated in the management of many supra-ventricular and ventricular arrhythmias.

Beta-blockers in Arrhythmias

Beta-blockers are indicated in :

- Supraventricular arrhythmias
  - Sinus tachycardia
  - Supraventricular tachycardias
  - Wolff-Parkinson-White syndrome (WPW) with orthodromic AVRTs

Rate control for:

  - Atrial Flutter
  - Atrial Fibrillation (AF)
- Ventricular arrhythmias
- Conditions predisposing towards arrhythmias and sudden cardiac death
  - Acute myocardial infarction
  - Long QT Syndrome (LQTS)
  - Catecholaminergic polymorphic ventricular tachycardia

Beta-blockers are contraindicated in patients with asthma, symptomatic hypotension or bradycardia and severe decompensated heart failure.[3] Similarly, in patients in whom the benefit of therapy may outweigh the risk of untoward effects, chronic obstructive lung disease without bronchospastic activity and peripheral vascular disease are relative contraindications. [4]

In the context of these broad indications and contra-indications, the extent of use of beta-blockers varies according to arrhythmia, the associated clinical conditions and the consensus on the role of drug therapy for arrhythmias.

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Use of Beta-blockers in Supraventricular Arrhythmias

Sinus tachycardia - For sinus tachycardia with symptoms, beta-blockers have been effectively used to slow heart rate in individuals and are especially indicated in situations of anxiety, after myocardial infarction, in patients with heart failure and hyperthyroidism.

Supraventricular tachycardias AV node-dependant reentrant tachycardias (AVNRT/AVRT) respond well to administration of I.V. beta-blockers.[5] However, adenosine and verapamil are more effective in this regard.[6] Beta-blockers are however, fairly good in the prevention of these tachycardias on a long-term basis. However, beta-blockers have been ineffective and contraindicated in the treatment of multifocal atrial tachycardia is frequently associated with severe obstructive lung disease.[7]

Although beta-blockers have been effective in some patients with supraventricular arrhythmias in the presence of WPW, they may cause very serious adverse events. Beta-blockers, as well as digitalis and calcium channel blockers, do not block the accessory pathway and may even enhance conduction, resulting in a very rapid ventricular response which may lead to severe hypotension or cardiac arrest.[8]

For these reasons, beta-blockers are contraindicated when there are preexcited tachycardias in patients with WPW syndrome. They can be used only when these patients have narrow QRS tachycardias.

Atrial Flutter Beta-blockers have not been very effective for conversion of atrial flutter to sinus rhythm However, they are effective, to a certain degree, for ventricular rate control and are, therefore, indicated in stable patients.

Atrial Fibrillation (AF) Like for atrial flutter, beta-blockers are not effective in the prevention of most episodes of AF.

Only in specific settings, such as post-CABG, are they useful in this regard, especially when started preoperatively. The predominant role of beta-blockers in AF is for rate control, by virtue of their AV node-blocking action. For acute control of heart rate, especially in acute myocardial infarction complicated by AF, intravenous esmolol is the recommended agent.[8, 9] For long-term use, beta-blockade is a safe therapy to control heart rate in AF patients and antagonises the effects of increased sympathetic tone. In seven of twelve placebo-controlled studies, beta-blockers were effective in controlling resting heart rate. [7,10] The effect was drug specific, with sotalol, nadolol and atenolol being the most efficacious. Atenolol provided better control of exercise-induced tachycardia than digoxin alone. In general, the combinations of digoxin and beta-blockers have been more effective than either digoxin or beta-blocker alone and better than the combination of digoxin and calcium channel blockers.

Use of beta-blockers in Ventricular Arrhythmias

Beta-blockers are effective in the control of ventricular arrhythmias related to sympathetic activation, including stress-induced arrhythmias, AMI, perioperative and in heart failure,

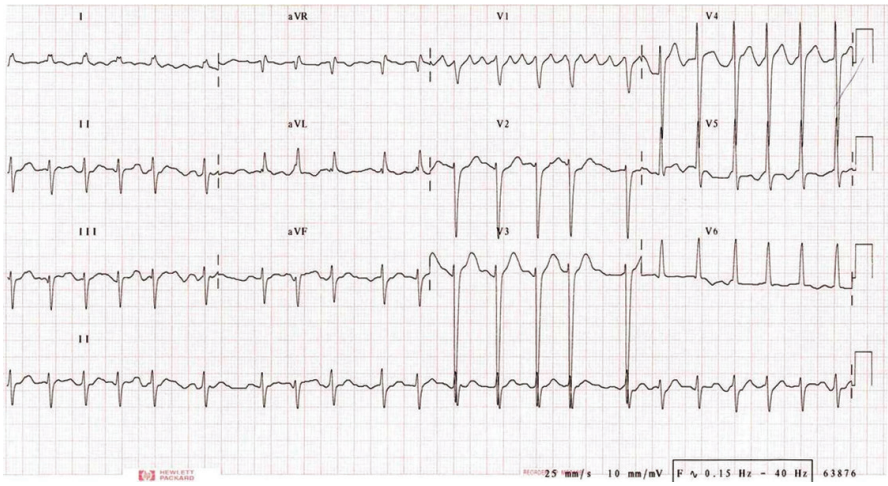

Fig. 1 : Atrial Fibrillation with rapid ventricular rate, left axis deviation and left ventricular volume overload

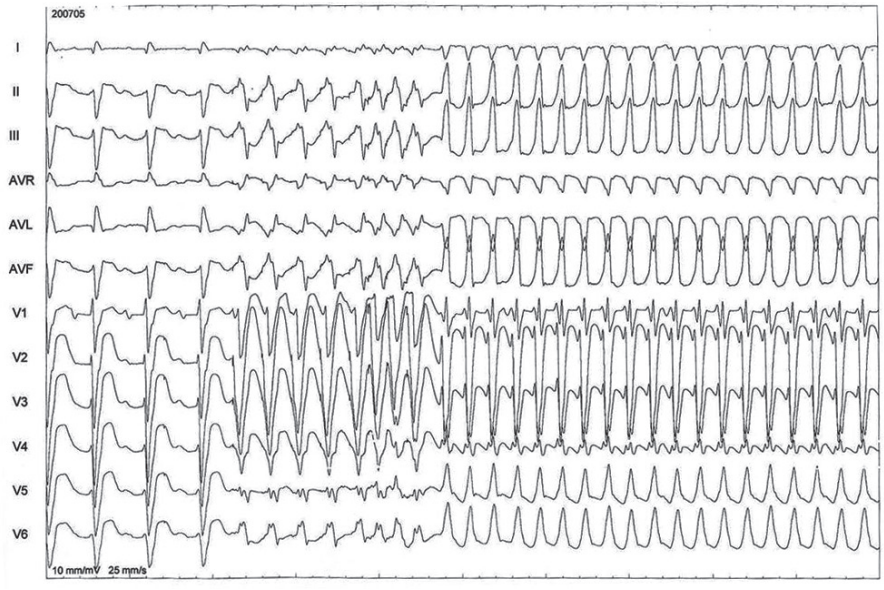

Fig. 2 : Monomorphic scar VT in a patient with old MI and IVCD

including the prevention of sudden cardiac death. Beta-blockers have proven to be very effective to prevent arrhythmias leading to sudden cardiac death in different conditions, including acute and chronic myocardial ischaemia, heart failure and cardiomyopathies.[11,12]

Use of Beta-blockers in Conditions Predisposing Towards Arrhythmias and Sudden Cardiac Death

There is clear evidence demonstrating that the benefit derived from beta-blocker treatment in the reduction in sudden cardiac death (SCD) in many of the high-risk subgroups. [7,11,12]

Acute myocardial infarction

For the prevention of VF, i.v. beta-blockers are indicated in patients with ventricular arrhythmias. Beta-blockers increase the threshold for VF during acute ischaemia and a decrease in VF was demonstrated in some placebo-controlled trials with metoprolol, atenolol and propranolol very early after onset of symptoms.[7,13] After acute myocardial infarction, the efficacy of beta-blockers is related to a reduction in all-cause mortality and sudden cardiac death and their use is recommended in all patients for the primary prevention of sudden cardiac death.

Scar VT is typically monomorphic (Figure). This is more common in patients with a large scar due to an old MI and consequent LV dysfunction. These VTs may lead to VF and cardiac arrest. Beta-blockers, often in conjunction with amiodarone, help prevent recurrence of such VTs. They are also used in patients who have received implantable defibrillators .

Long QT Syndrome (LQTS) Based on the available data, beta-blockers are indicated in LQTS patients. However, there is a lack of prospective, placebo-controlled studies assessing the efficacy of beta-blockers in LQTS patients. In one of the largest retrospective analyses conducted in LQTS patients (233 patients), all symptomatic for syncope or cardiac arrest, mortality 15 years after the first syncope was 9% for the patients treated by antiadrenergic therapy (beta-blockers and/or left cardiac sympathetic denervation) and close to 60% in the group not treated or treated with miscellaneous therapies.[14] The mechanism of benefit is by prevention of adrenergic-mediated torsade de pointes; the QT interval itself remains unaffected.

Catecholaminergic polymorphic ventricular tachycardia

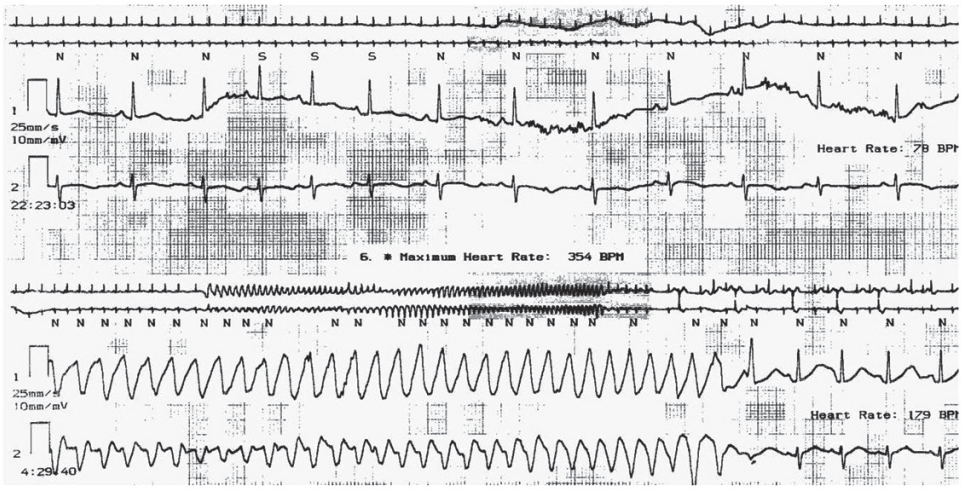

Fig. 3 : Long QT syndrome in a 12 year old girl. Torsades de pointes and prolonged QT interval were observed during 24-hour ambulatory recording

This rare clinical entity is characterised by adrenergically induced polymorphic ventricular tachycardia in the absence of structural cardiac abnormalities and a familial history of syncope and SCD occurs in approximately one third of the cases. The arrhythmias are reproducible during exercise stress test or during isoproterenol infusion. At the present time beta-blockers is the only therapy that may be effective.[7,15]

Conclusion

The arrhythmogenic effects of sympathetic stimulation and the antiarrhythmic effects of beta-blockers have been extensively reviewed in recent years. Taking into consideration the present consensus on its indications and contraindications, and the evaluation of combinations of beta-blockers with other antiarrhythmic therapies, beta-blockers have a definitive role to play in the treatment of supraventricular arrhythmias. With the available clinical study findings and anecdotal evidence, beta-blockers are clearly indicated in the primary and secondary prevention of SCD in different clinical settings. Therefore, beta-blockers are of substantial importance in the management of arrhythmias by drug therapy.

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