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Review Article

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Chemistry of Beta-blockers and their role in the Cardiovascular Disorders

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Abstract

Worldwide, in both advanced and growing countries cardiovascular disease (CVD) endures a prime root cause of death. Beta-blockers work by blocking the effects of epinephrine (adrenaline) and slowing the heart's rate, thereby decreasing the heart's demand for oxygen, thus; heart beats more slowly and pumps with less force. Due to this heart does not have to work hard and more efficiently reduces blood pressure. Beta-blockers have several properties like cardio selectivity, lipid solubility, intrinsic sympathomimetic activity and membrane stabilization. The benefits of Beta-blockers in patients as well as their antiarrhythmic effects with heart failure and ventricular dysfunction are clearly established. Beta-blockers also relax blood vessels through vasodilation. Pumping; blood more efficiently into relaxed blood vessels aids the heart to work better if it is damaged or affected by other conditions.

Keywords: Beta-blockers, Metoprolol, Bisoprolol, Atenolol.

Introduction

Beta-blockers were developed by Sir James Black at Imperial Chemical Industries in the United Kingdom in 1962. He awarded by Noble Prize in 1988 for his contributions to clinical medicine and pharmacology in the 20th century. Beta-blockers are one of the most widely prescribed classes of drugs to treat hypertension (high blood pressure) and are a mainstay treatment of congestive heart failure. It also helps to widen veins and arteries to improve blood flow. Beta- blockers are a class of medications that were predominantly used to manage abnormal heart rhythms and to protect the heart from a second heart attack after a first heart attack. Beta- blockers are also known as beta-adrenergic blocking agents. Beta- blockers are a class of drugs that works by blocking the neurotransmitters norepinephrine and epinephrine from binding to receptors. Long-term use of beta-

blockers helps manage chronic heart failure. Beta-blockers work by blocking the effects of epinephrine (adrenaline) and slowing the heart's rate, thereby decreasing the heart's demand for oxygen. Thus heart beats more slowly and pumps with less force. So heart does not have to work hard and is more efficient, which lower blood pressure. Examples of Beta-blockers are: Acebutolol (Sectral), Atenolol (Tenormin), Bisoprolol (Zebeta),Ccarvedilol (Coreg), Esmolol (Brevibloc), Labetalol (Normodyne, Trandare), Metoprolol (Lopresssor, Toprol-XL), Nadolol (Corgard), Propranolol (Inderal) etc. Secretion of melatonin lower by Beta- blockers thus; they may result in sleep changes and insomnia in some convalescets[1]. Beta-blockers remain very efficacious agents for treating heart failure, certain types of arrhythmia, hypertrophic obstructive cardiomyopathy, and in patients with prior myocardial infarction[2].

Classification of Beta-blockers:

They can be grouped into:

Non-selective (which block both Beta-1 and Beta-2 receptors such as nadolol, penbutolol, pindolol, propranolol, sotalol and timolol).

C**ardioselective** (only block Beta-1 receptors and include acebutolol, betaxolol, bisoprolol, esmolol and metoprolol) [3-5].

Some Beta-blockers are Alpha-1 receptors which produce vasoconstriction and uplift cardiac chronotropic; this means agonism at the insomnia Alpha-1 receptors leads to increased level of blood pressure and higher heart rate. In contrast, antagonism at the Alpha- 1 receptor leads to vasodilation and negative chronotropic, which leads to lower blood pressure and decreased heart rate.

Mechanism of Beta-blockers in Heart Failure

1. Upregulation of Beta- receptors and improved Beta-adrenergic signalling.
2. Reducing the hyperphosphorylation of calcium release channels of sarcoplasmic reticulum and normalizing their function.
3. Bradycardia (increased coronary blood flow and decreased myocardial oxygen demand).
4. Protection from catecholamine myocyte toxicity.
5. Suppression of ventricular arrhythmic.
6. Anti-apoptosis, Beta-2 receptors, which are relatively increases, are coupled to inhibitory G Protein and block apoptosis.
7. Inhibition of RAAS. When added to prior ACE-I or ARB, metoprolol augments RAAS inhibitors.

The epinephrine, catecholamines, and norepinephrine attach to Beta-1 receptors and rise cardiac automaticity and conduction pace.Beta-1 receptors also activate the release of renin, and as a result of this, blood pressure increases. In contrast, attaching to Beta-2 receptors causes relaxation of the smooth muscles along with increased metabolic effects such as glycogenolysis. Beta-blockers vary in their specificity towards different receptors, and accordingly, the results, produced depend on the type of receptor(s) blocked as well as the organ system involved. To some degree, few Beta-blockers also bind to Alpha-receptors allowing them to induce different clinical results when used in specific settings. Once Beta-blockers bind to the Beta-1 and Beta-2 receptors, they inhibit these effects. Thus, the chronotropic and inotropic effects on the heart undergo inhibition and as a consequence of it the heart rate decreases. Beta-blockers also lower down blood pressure via several mechanisms, including reduced cardiac output and decreased renin. The weak chronotropic and inotropic effects results in less oxygen demand thus; angina corrected after use of Beta-blocker. Medications of Beta-blocker also prolong the atrial refractory periods and have a potent antiarrhythmic effect[6].

How do Beta - blockers chemistry work?

Beta-blockers subvert processes by setting on to Beta-receptors and preventing the chemical messengers from binding to their receptors. This slows the heart rate. Improves the conduction of electrical signals in the heart, relaxes blood vessels and lower down blood pressure.

Propranolol

It is one of the original medicines of the Beta-blocker. Propranolol sold under the brand name **Inderal**. Its molecular formula is $C_{16}H_{21}NO_2$. It is used to treat high blood pressure, hypertension, irregular heartbeats, migraine, myocardial infarction etc.[7-8]. Propranolol also is an effective and safe drug for treating migraine headaches, anxiety disorders and infantile hemangiomas [9-10]. It is in the WHO list of essential medicine. It was the 53rd most commonly prescribed medication in the US in 2018.

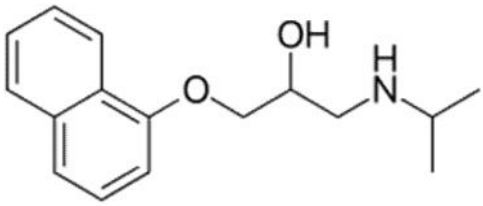

Fig.1. Structure of Propanolol

Mechanism: Propranol ⟶ Inhibits
Vasomotor Conduction ⟶ Decrease
Sympathetic Discharge ⟶ Vasodilation
⟶ Decrease blood pressure

Atenolol

It is a selective Beta-1 receptor antagonist. A drug belonging to the group of beta blockers, primarily used in the cardiovascular diseases. Its trade name is Tenormin. Its molecular formula is $C_{14}H_{22}N_2O_3$. It is a white crystalline powder having a melting point of 146°-148°C, freely soluble in methanol, soluble in DMSO and acetic acid and sparingly soluble in 96% alcohol. It is found in vascular smooth muscle and the heart. Blocking the positive inotropic, chronotropic actions of endogenous catecholamines such as isoproterenol, norepinephrine and epinephrine. It is used to treat high blood pressure and heart-associated chest pain. It, however, does not seem to improve mortality in those with high blood pressure. Other uses include the prevention of migraines and treatment of certain irregular heartbeats.

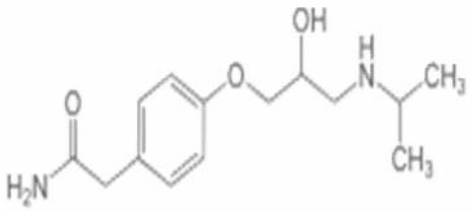

Fig.2.Structure of Atenolol

Metoprolol

Metoprolol is sold under the name Lopressor, Toprol XL. Its molecular formula is $C_{15}H_{25}NO_3$. The active substance metoprolol is employed either as metoprolol succinate or as metoprolol tartarate. The tatarate is an immediate - release formulation and succinate is an extended- release formulation. It is used to treat high blood pressure, chest pain due to poor blood flow to the heart and several conditions, involving an abnormal heart rate.

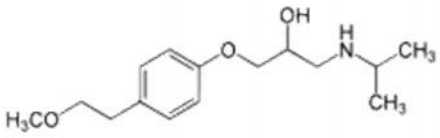

Fig.3. Structure of Metoprolol

Acebutolol

It is sold under the name ***Sectral***. Acebutolol is a selective Beta-1 receptor antagonist used to treat hypertension and irregular heart rhythm (premature ventricular contractions, or PVCs). Molecular formula of it is $C_{18}H_{28}N_2O_4$. Molecular weight of acebutolol is 336.4g/mol. It is the ether that is the 2-acetyl - 4- (butanoyl amino) phenyl ether of the primary hydroxyl group of 3-(propan-2-ylamino) propane-1, 2diol). It is operated by loosen down blood vessels and decelerating heart rate to better blood flow and lower down blood pressure. Acebutolol is used in high-risk patients of acute myocardial infarction.

As it is a selective Beta-1 receptor antagonist, activation of Beta-1 receptors by epinephrine increases the heart rate and blood pressure, and the heart consumes more oxygen. Acebutolol blocks these receptors, lowering the heart rate and blood pressure. Acebutolol then reverse the effect of epinephrine. In addition Beta- blockers prevent the release of rennin, which is hormone produced by the kidneys which lead to constriction of blood vessels.

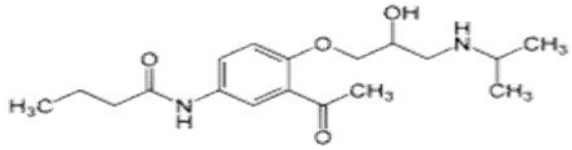

Fig.4.Structure of Acebutolol.

Labetalol

Its molecular formula is $C_{19}H_{24}N_2O_3$. Its trade name is Normodyne. It was patented in 1966 but in 1977, it came into medical use. It was the first drug that has both Alpha and Beta- adrenergic receptor blocking properties. It is available as a generic medicine and used to decrease blood pressure. It was developed to potentially fix the compensatory reflux issue that occurred when blocking a single receptor subtype, i.e., vasoconstriction after stopping beta-receptors or tachycardia after stopping alpha-receptors. Because the reflex from blocking the single receptor subtypes acted to prevent the lowering of blood pressure, it was postulated that weak blocking of both alpha- and beta - receptors could work together to decrease blood pressure.

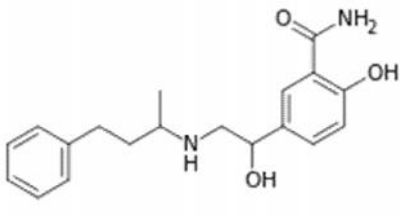

Fig.5. Structure of Labetalol

Carvedilol

It is sold under the name Coreg. Its molecular formula is $C_{24}H_{26}N_2O_4$. It is used to treat high blood pressure, congestive heart failure and left ventricular dysfunction. It improves the workload of the heart, exercise-induced high heart rate and high heart rate upon standing. It also widens blood vessels which help to decrease blood pressure. Carvedilol in addition to its non-selective Beta- receptor blockage has additional Alpha-1 receptor blockage activity. This property is clinically useful because Beta-blockers that block the Alpha-1 receptor have a more specific clinical effect in the treatment of hypertension[11].

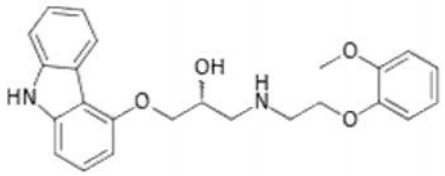

Fig.6. Structure of Carvedilol

Nebivolol

Its molecular formula is $C_{22}H_{25}F_2NO_4$, used in the treatment of high blood pressure and heart failure. As other Beta-blockers, it is generally a less preferred treatment for high blood pressure. It may be used by itself or with other in blood pressure medication. It is taken orally. It was patented in 1983 but came into medical use in the year 1997. It is available as generic medicines in the United Kingdom. In 2018, it was the 197th most commonly prescribed medicines in the United States, with more than 2 million prescriptions.

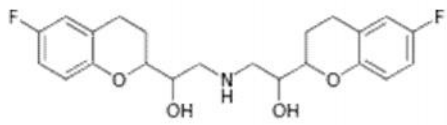

Fig.7. Structure of Nebivolol

What beta-blockers do?

Small proteins called beta receptors sit on the outer surface of many cells. Beta-blockers are of three main types. Beta-1 receptors are found almost exclusively in heart cells. Beta-2 receptors reside mostly in lung and blood vessel cells; though heart cells also have some Beta-3 receptors are found on fat cells. The job of beta-receptors is to latch into chemical messengers released by the nervous system. In response to these messengers, the heart beats faster, blood vessel constricts, the airways relax, and the kidneys increase the production of a protein that boosts blood pressure. Beta- blockers subvert these processes by setting onto beta receptors and preventing the chemical messengers from binding to the receptors. This slows the heart, improves the conduction of electric signals in the heart, relaxes blood vessels and lowers blood pressure.

Conclusion

Beta-blockers are a group of drugs that are part of the standard therapeutic armamentarium (equipment and techniques available to a medical practitioner) for several cardiovascular conditions. In the context of acute myocardial infarction, early administration of intravenous Beta-blockers reduces the incidence of ventricular fibrillation and can decrease infarct size. However, it is still necessary to show whether this translates into an improvement in long-term morbidity and mortality. Beta-blockers were discovered as anti-anginal drugs in the 1960s and are currently widely used in heart failure, arrhythmias, and ischemic heart disease.

References

1. Fares A. Night-time exogenous melatonin administration may be a beneficial treatment for sleeping disorders in beta blocker patients. J Cardiovasc Dis Res. Jul 2011; 2 (3):153-55.
2. Sripal Bangalore MD, M H A Franz H. Messerli MD, John B.Kostis MD, Cark J.Pepine MD Cardiovascular Protection Using Beta-Blockers: A Critical Review of the Evidence Journal of the American College of Cardiology 14 August 2007; 50 (7): 563-572.
3. Gorre F, Vandekerckhove H. Beta-blockers: focus on the mechanism of action. Which beta-blocker, when and why? Acta Cardiol. Oct 2010; 65(5):565-70.
4. Machackova J, Sanganalmath SK, Elimban V, Dhalla NS. Beta-adrenergic blockade attenuates cardiac dysfunction and myofibrillar remodelling in congestive heart failure. J Cell Mol Med. March 2011; 15(3):545-54.
5. Rehsia NS, Dhalla NS. Mechanisms of the beneficial effects of beta-adrenoceptor antagonists in congestive heart failure. Exp Clin Cardiol. Winter; 2010; 15(4): e86-95.
6. do Vale GT, Ceron CS, Gonzaga NA, Simplicio JA, Padovan JC. Three Generations ofBeta-blockers: History, Class Differences and Clinical Applicability. Curr Hypertens Rev. 2019; 15(1):22- 31.
7. Hardison S, Wan W and Dodson K M, “The use of propranolol in the treatment of subglottic hemangiomas : a literature review and meta-analysis”. International Journal of Pediatric Otorhinolaryngology, 2016; 90:175-180.
8. Stenen SA, Vanwijik A H, Var der Heijden G A, Van Westrgebeb R, De Lange J and De Jongh A, “Propranolol for the treatment of anxiety disorders: Systematic review and meta- analysis”. Journal of Psychopharmacology (Oxford England), 2016; 30(2): 38-139.
9. Srinivasan A V, “Propranolol: 50- year historical perspective” Annals of Indian Academy of Neurology, 2019; 22(1): 21-26.

10. Cizmarikova R, Habala L,Valentova J and Markuliak M, “Survey of pharmacological activity and pharmacokinetics of selected Beta-adrenergic blockers in regard to their stereochemistry”. Applied Sciences, 2019; 9(4): 625.
11. Weir MR. Beta-blockers in the treatment of hypertension: are there clinically relevant differences? Postgrad Med. May 2009; 121(3):90-8.

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