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Beta-Adrenergic Blockers

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Beta-adrenergic blockers (β-blockers) are an important class of drugs for the treatment of various heart diseases, including high blood pressure, insufficiency of blood flow to the heart muscle (angina pectoris), irregular heart beat (arrhythmias), thickened heart muscle (hypertrophic cardiomyopathy), and decreased ability of the heart to empty or fill normally (heart failure). β-Blockers can also be used to treat migraine headache and increased pressure of the eye (glaucoma). No other class of man-made drugs has had such widespread applicability in clinical medicine.

What Is a β-Blocker?

Hormones known as catecholamines (norepinephrine, epinephrine) activate or stimulate specific receptors on cell surfaces, known as adrenergic receptors. A receptor has a specific structure that allows a drug or hormone to bind to it, similar to a key fitting in a lock. The catecholamines are released from nerve endings of the sympathetic nervous system, an involuntary nerve network that enables the body to withstand stress, anxiety, and exercise. β-Adrenergic receptors are found in the heart, blood vessels, and the lungs, and can be stimulated by catecholamine binding, thus increasing the activity of cells in the body. β-Adrenergic receptor stimulation causes an increase in heart rate, heart muscle contraction, blood pressure, and relaxation of smooth muscle in the bronchial tubes in the lung, making it easier to exercise and expand the lungs.

When β-blocking drugs are given to patients through a vein or by mouth, they will block the access of catecholamines to their receptors (Figure) so that the heart rate and blood pressure are reduced, and the heart will pump with less intensity. This, in turn, will reduce the oxygen needs of the heart (Table). The effects of β-blockers are greatest when catecholamine levels and receptor numbers are high, as would occur during intense exercise, and are lessened when catecholamine levels are reduced, as during sleep. β-Blockers usually do not completely diminish the ability of the heart to respond to stress, but instead modify the heart's response to stress.

The β-Blocking Drugs

There are 16 β-blockers available in the United States for the treatment of heart disease. They all work to block the effects of catecholamines at receptor sites in the heart, but they differ somewhat in their ability to block receptors in the blood vessels and lungs. Selective β-blockers have their major actions on the heart; they are the drugs atenolol, metoprolol, betaxolol, bisoprolol, and esmolol. Some drugs are weak stimulators of the β-receptor while still blocking the major actions of catecholamines; they are acebutolol, carteolol, penbutolol, and pindolol. Some drugs block both the β-receptors in the heart and those in the blood vessels and have no stimulatory activity; they are nadolol, propranolol, sotalol, and timolol. Some β-blocking drugs block other catecholamine receptors that can cause a further opening of blood vessels; they are labetalol and carvedilol. Most β-blockers can be taken by mouth, and one, esmolol, is only available for intravenous use. Most of the drugs are broken down to inactive substances (metabolized) in the liver and must be used with caution in patients with liver disease. Those drugs that are not broken down in the liver must be used with caution in patients with kidney failure.

β-Blockers to Treat Heart Disease

β-Blockers are used to treat multiple diseases of the heart (see box). They work in all of these conditions by interfering with the effects of catecholamines.

Angina Pectoris

Angina pectoris is a discomfort caused by an inadequate supply of blood and

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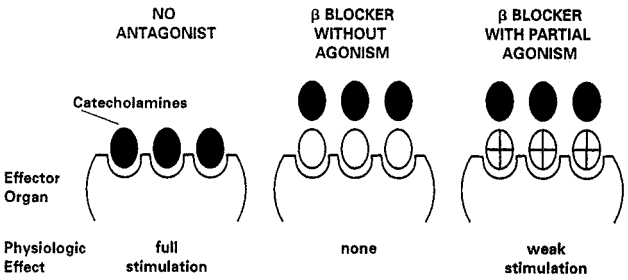

Physiological effects of β-adrenergic blocking drugs in the presence of circulating catecholamines. Reprinted with permission from Frishman WH. Pindolol: a new β-adrenoceptor antagonist with partial agonist activity. *N Engl J Med*. 1983;308:940–944.

oxygen to the heart muscle during exercise. It is a warning sign that the heart cannot function properly. β-Blockers reduce the increases in heart rate, blood pressure, and heart contraction that occur during exercise, thereby reducing the work of the heart and its need for oxygen. These effects allow the heart to perform for a longer period of time during exercise before symptoms develop. Essentially, the heart utilizes its limited oxygen supply more effectively, getting more miles per gallon, so to speak. To treat angina pectoris, β-blockers need to be taken daily and can be used in combination with other antianginal drugs, such as nitrates.

Heart Attack

A heart attack occurs when there is either no or a limited amount of blood flow being supplied to a part of the heart muscle and that part of the heart muscle dies. During a heart attack, catecholamine levels are high, and this can worsen the situation by making the heart work harder and extending the injury. By interfering with the effects of catecholamines on heart rate, blood pressure, and contractility, the amount of injury can be contained. During a heart attack, β-blockers can be given by mouth or through the vein.

Effects of Catecholamines and β-Blockers on the Heart and Blood Vessels

	Heart Rate	Heart Contraction	Blood Pressure
Catecholamines	↑	↑	↑
β-Blockers	↓	↓	↓

After a Heart Attack

β-Blockers have been shown to reduce the risk of a new heart attack and/or death occurring in survivors of a previous heart attack. The drugs should be started by mouth as soon as a patient is stable after a heart attack and maintained indefinitely.

Arrhythmias

β-Blockers are effective in treating heart rhythm problems (arrhythmias). They work to normalize the rhythm or slow down a rapid heart rate.

Heart Failure

β-Blockers can be used with other heart failure treatments to relieve the symptoms of heart failure, such as shortness of breath or weakness. The drugs improve heart function and reduce the risk of death in patients with heart failure.

Hypertrophic Cardiomyopathy

In this condition, the heart muscle is thickened, and its normal function is impaired. β-Blockers can improve heart function and relieve the symptoms of shortness of breath, chest pain, and lightheadedness.

Dissection

The tear of a major artery (dissection) is a life-threatening condition usually caused by longstanding high blood pressure. β-Blockers can reduce the extent of the tear and prevent a recurrence. They are often relied on for very strict blood pressure control in these patients.

High Blood Pressure

By blocking the effects of catecholamine on the heart and blood vessels, the long-term use of β-blockers reduces blood pressure. The drugs are considered a first-line treatment for high blood pressure, and they can be used in combination with other blood pressure-lowering drugs to maximize effect.

Other Conditions

β-Blockers can be used during surgery to reduce the stresses on the heart brought on by activated catecholamines. The drugs have also been used to reduce the heart rate with an overactive thyroid gland, to reduce increased pressure in the eye (glaucoma) when used as eye drops, to prevent and/or reduce migraine headaches by interfering with the effects of catecholamines on blood vessels, and to reduce muscle tremors caused by catecholamines.

Diseases for Which β-Blockers Are Useful

- High blood pressure (hypertension)
- Angina pectoris (insufficient blood to the heart)
- Heart Attack (injury to the heart muscle)
- Arrhythmias (heart rhythm irregularity)
- Dissection of an artery (torn blood vessel)
- Heart failure
- Migraine headache
- Glaucoma (high pressure in eye)
- Muscle tremor (shaking of limbs)

What Side Effects Can I Expect?

β-Blockers are extremely well tolerated and have been used for over 30 years in some patients. Because β-blockers interfere with effects of catecholamines, some patients notice muscle fatigue, especially with vigor-

ous physical activity. Patients with asthma should not take β-blockers because they can interfere with the passage of air into the lungs. In some patients, heart rate and blood pressure may be reduced too much, causing lightheadedness and fainting. The drugs should be used with caution in diabetic patients taking insulin who have problems with excessive blood-sugar lowering and lightheadedness. Selective β-blockers may avoid this latter problem. As with all antihypertensive drugs, male penile erectile dysfunction (impotence) can be seen, but the drugs can be used with Viagra (Pfizer, Inc). The drugs should not be used if a patient has severe mental depression.

What Precautions Do I Need to Take?

- Never stop taking your prescribed β-blockers abruptly without informing your healthcare provider. Try not to miss any doses.
- If you develop excessive fatigue, mental depression, lightheadedness, fainting, or excessive shortness of breath, inform your healthcare provider.
- If you are prescribed new medicines or herbal remedies, inform your healthcare provider.

Additional Information

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