Beta2-adrenergic agonist

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β_2-adrenergic agonists, also known as **β_2-adrenergic receptor agonists**, are a class of drugs used to treat asthma and other pulmonary disease states.

Uses

They act on the beta$_2$-adrenergic receptor thereby causing smooth muscle relaxation, resulting in dilation of bronchial passages, vasodilation in muscle and liver, relaxation of uterine muscle, and release of insulin. Due to some Beta-1 agonism is also results in contraction of the heart muscle.

Mechanisms of The Beta-2 Agonists

Beta-adrenergic receptors are coupled to the stimulatory G protein. The alpha subunit of the G protein activates adenylyl cyclase, which catalyzes the production of cyclic adenosine monophosphate (cAMP). In the lung, cAMP causes a decrease in the intracellular calcium concentration and, via activation of protein kinase A, both inactivates myosin light chain kinase and activates myosin light chain phosphorylase. In addition, beta-2 agonists open large conductance calcium-activated potassium channels and thereby tend to hyperpolarize airway smooth muscle cells. The combination of decreased intracellular calcium, increased membrane potassium conductance, and decreased myosin light chain kinase activity leads to smooth muscle relaxation and bronchodilation.

Potential Adverse Effects

Findings indicate Beta-2 stimulants, especially when they are given by parenteral or oral route, can induce adverse effects:

- tachycardia secondary to peripheral vasodilation and cardiac stimulation; tachycardia can be accompanied by palpitations.
- tremor, sweats, agitation.
- more severe effects, pulmonary edema, myocardial ischemia, cardiac arrythmia, are exceptional.

Asthma aggravation has been observed in patients using large dose of beta-2 stimulants, but it is not known if it results from spontaneous course of the disease or adverse effect of the drugs. The excipients, in particular sulphite, could contribute to the adverse effects. The possible loss of the **bronchodilator** activity of beta-2-mimetic could be attenuated by glucocorticoid intake.

Side Effects

Side-effects such as insomnia, anxiety, increased heart rate, and tremor occur in some patients.

Delivery

All β_2 agonists are available in inhaler form, either metered-dose inhalers, which aerosolize the drug, or dry powder, which can be inhaled.

Salbutamol (known as albuterol in the U.S.) also comes in a solution form for nebulization, which is more commonly used in inhalers than in emergency rooms[*citation needed*]. Salbutamol and terbutaline are also both available in oral forms. Nebuliser form is as effective as administering the drug intravenously.

In addition, several of these medications are available in intravenous forms, including both salbutamol and terbutaline. It can be used in this form in severe cases of asthma, but it is more commonly used to suppress premature labor because it also relaxes uterine muscle, thereby inhibiting contractions[*citation needed*].

Risks

On November 18, 2005, Food and Drug Administration (FDA) alerted healthcare professionals and patients that several long-acting bronchodilator medicines have been associated with possible increased risk of worsening wheezing in some people, and requested that manufacturers update warnings in their existing product labeling.

On June 29, 2006, Cornell University and Stanford University researchers reported that a meta-analysis they conducted found that "regularly inhaled beta-agonists (Orciprenaline/metaproterenol [Alupent], formoterol Foradil, fluticasone/salmeterol [Serevent, Advair], and salbutamol/albuterol [Proventil, Ventolin, Volmax, and others]) increased the risk of respiratory death more than twofold, compared with a placebo," while used to treat chronic obstructive pulmonary disease (COPD).[1]

On December 11, 2008, a panel of experts convened by the Food and Drug Administration (FDA) voted to ban the drugs Serevent and Foradil from use in the treatment of asthma. It was shown that, when these two drugs are used without steroids, they increase the risks of more severe attacks. The experts said that two other much more popular asthma drugs containing long-acting beta-agonists, Advair and Symbicort, should continue to be used.[2] The latter contains formoterol as contained in Foradil but also a steroid budesonide.

Types

They can be divided into short-acting and long-acting beta-adrenoceptor agonist (LABA) groups:

Short-acting beta$_2$ agonists

generic name (Trade Name)

- salbutamol (albuterol (US name), Ventolin)
- levosalbutamol (levalbuterol (US name), Xopenex)
- terbutaline (Bricanyl)
- pirbuterol (Maxair)
- procaterol
- metaproterenol (Alupent)
- fenoterol
- bitolterol mesylate
- ritodrine
- Isoprenaline

Long-acting beta$_2$ agonists

- salmeterol (Serevent Diskus)
- formoterol (Foradil, Symbicort)
- bambuterol
- clenbuterol

Ultra-long-acting beta$_2$ agonists

- indacaterol

References

1. ^ Ramanujan K. Common beta-agonist inhalers more than double death rate in COPD patients, Cornell and Stanford scientists assert. *Chronicle Online*. June 29, 2006. Available at: http://www.news.cornell.edu/stories/June06/Salpeter.COPD.kr.html. Accessed June 30, 2006.
2. ^ Harris G. F.D.A. Panel Votes to Ban Asthma Drugs. "The New York Times". December 11, 2008. Available at: http://www.nytimes.com/2008/12/12/health/policy/12fda.html?ref=health. Accessed January 19, 2009.