Asthma bronchiale therapy

Asthma is a chronic inflammatory disease of the airways characterized by increased reactivity of the airways to various stimuli. The inflammatory process increases *bronchial hyperresponsiveness*, resulting in *reversible bronchial obstruction*. The main clinical sign of acute attack is *dyspnea* caused by bronchoconstriction, edema, inflammation of the altered mucosa, and mucus plug. The classic auscultation phenomena are prolonged expiration, wheezing and whistling. Shortness of breath is accompanied by cough.

See the Asthma page for more information

Bronchodilators

Bronchodilators dilate the airways. If they affect inflammation or bronchial hyperreactivity, then weakly. It therefore operates at an early stage.

Beta2-sympathomimetics

Stimulating β2 receptors. They are mainly administered by inhalation. Their effect appears quickly and lasts 3-5 hours. These include **salbutamol , terbutaline , fenoterol.** Salbutamol and terbutaline are also distributed in tablet form. Their bronchodilator effect is fast and intense.

Parasympatholytics

They act as *competitive antagonists at M receptors in the bronchi*. . Quaternary ammonium bases are used as bronchodilators, which poorly penetrate the blood-brain barrier (they lack the central effects of atropine), and are less well absorbed from the gastrointestinal tract into the systemic circulation, so it is more advantageous to administer them by inhalation. Protects bronchi from cholinergic stimulation. The onset of the bronchodilator effect is delayed (the maximum effect is reached within 30–60 min) and its intensity is weaker than with β-mimetics. They are suitable for the treatment of acute symptoms in patients responding to β2-mimetics of tachycardia and tremor, but they are not able to stabilize asthma in the long term. **Ipratropium**, a s*uspension for inhalation, is used*.

Theophylline and derivatives (methylxanthines)

Theophylline together with caffeine and theobromine is an alkaloid present in coffee, tea, cocoa and the like. It has a relaxing effect on smooth muscle by inhibiting phosphodiesterase and affecting adenosine A2 receptors. The result is *plasma concentration*-dependent bronchodilation. The range of therapeutic concentrations is 5-20 mg / l. Signs of toxicity usually appear at plasma concentrations> 40 mg / ml.


Salbutamol (inhaler)

Pharmacokinetics

Theophylline is well absorbed and is metabolically biodegraded in the liver. Biological half-life 6-8 hours.

Side effects result from affecting the CNS, cardiovascular, gastrointestinal and kidney systems.

- *CNS:* psychomotor stimulation "doping" is of lower intensity than caffeine. Eliminates fatigue and drowsiness. In higher doses, it leads to insomnia, tremors, twitching and even convulsions of central origin.
- *Cardiovascular system:* positive chronotropic and inotropic effect, after high doses of tachycardia, tachyarrhythmia, palpitations. Vasoconstriction, rise in blood pressure.
- *GIT:* nausea, vomiting (possibly with an admixture of blood explained by intensive vasodilation of the vessels of the gastric mucosa) diarrhea.

Factors influencing the effect and toxicity of theophylline

- *age:* children between 1 and 9 years of age for high metabolism (approximately 1.40 ml / min / kg) require a relatively higher dosing regimen to achieve an effect; in contrast, in children <1 year of postnatal life, metabolism reaches very low levels; in the elderly, metabolism is reduced by more than 30% compared to young adults, symptoms of CNS and cardiovascular toxicity appear already in concentrations of 20-30 µg / l (dose reduction is necessary)
- *pathological condition:* cardiac decompensation, cor pulmonale, liver cirrhosis (for decreased blood flow to the liver), febrile conditions (virosis) reduce theophylline metabolism and carry the risk of toxicity
- *cigarette smoking:* due to enzyme induction, theophylline metabolism increases, the dose increases by approximately 1/3
- *drug interactions:* theophylline clearance is increased (up to 25%) in combination with rifampicin,

phenobarbital, phenytoin; on the contrary, it decreases (by 10-25%) in the presence of diltiazem, erythromycin, norfloxacin and verapamil

Drugs for preventive maintenance treatment

These drugs include long-acting bronchodilators and anti-inflammatory agents (corticoids, sodium cromoglycate).

Corticoids are the most important in terms of prevention. There is a decrease in exacerbations of asthma attacks, a reduction in bronchial hyperactivity and chronic symptoms, an improvement in lung function.

Beta2-mimetics with prolonged effect

Fluticasone (inhaler)

- Due to their high fat solubility, they are contained in a higher concentration in the smooth muscle cell membrane,
- *inhalation:* **salmeterol** and , **formoterol,**
- *oral* (tbl, syrup): **clenbuterol**, **prokaterol**, prolonged- release **salbutamol**
- they have proved particularly useful in the treatment of night attacks and as a prevention of exercise-induced asthma,
- combined with anti-inflammatory drugs.

Sustained-release theophylline

Long intervals between doses (12-24 hours) will increase patient compliance.

Corticosteroids

They do not have a bronchodilator effect , but they strongly suppress the inflammatory response, eg by inhibiting the release of arachidonic acid from cell membranes, thus preventing the formation of prostaglandins and leukotrienes– mediators of inflammation. They prevent the migration and activation of cells involved in inflammatory processes, and reduce the hyperresponsiveness of the bronchi. They increase the sensitivity of β-adrenergic smooth muscle receptors to β2 mimetics.

Systemic (overall) administration

As a short-term shock cycle (5-7 days) – **maximum therapy** to manage persistent severe asthma. The cycle is usually the beginning of long-term treatment of patients with destabilized asthma or is used in the event of a sudden deterioration of the patient's clinical condition. Another variant of use is long-term oral corticosteroid therapy (daily or alternative - ie one dose every day) in patients with severe disease. Oral administration is preferred to parenteral administration. The side effects of this treatment need to be controlled.

Hydrocortisone , prednisone , methylprednisolone , triamcinolone are used .

Side effects : mineralocorticoid (hypertension), glucocorticoid (steroid diabetes), resulting from anti-inflammatory and antianabolic effects (slow healing of wounds, risk of dissemination of infection, herpes infections, osteoporosis, growth retardation in children, mucosal atrophy), attenuation of pituitary-suppression endogenous corticoid secretion), thrombosis, gastric and duodenal ulcer, cataract

Topical administration (aerosols)

Fat-soluble corticoids are used: **beclomethasone , budesonide , fluticasone.**

They are given as two breaths 4 times a day or 4 breaths twice a day (for milder asthma), which corresponds to a dose of 10-15 mg prednisone / day. High doses of 8-12 breaths / day are intended to replace systemic administration. The effect comes in 3-7 days.

Side effects: oropharyngeal Candidiasis, dysphonia. They can be prevented by using an inhalation attachment and rinsing the mouth. The risk of systemic side effects by absorption of topical corticosteroids is minimal.

Sodium cromoglycate

Sodium cromoglycate has a weaker anti-inflammatory effect, selectively inhibits cells and mediators of asthmatic inflammation, and inhibits the early and late stages of the allergic reaction. Its full effect develops after 4-6 weeks of treatment. Administration is by inhalation. **Nedocromil sodium** has a similar effect.

Treatment of acute attack

1. 1.Inhaled β2-mimetics with a short-term effect of 2-4 doses every 20 minutes in the first hour, ev. combination with inhaled anticholinergics. *Alternative:* oral β2-mimetics or theophylline with short-term effect (slower onset of action, side effects).

2. Higher doses of β2-mimetics (4-8 doses) in more severe seizures.
3. In case of insufficient response: corticoids usually systemically orally (basic dose corresponds to 40-60 mg prednisone).

Links

References

- {{Institute of Pharmacology, Faculty of Medicine, Charles University in Hradec Králové. Selected chapters from clinical pharmacology for bachelor study: Asthma therapy [online]. © 2001. [feeling. 2010-07-04]. < https://www.lfhk.cuni.cz/farmakol/predn/bak/kapitoly/astma-bak.doc/ >.}}

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