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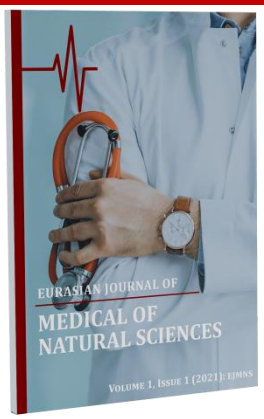

CLINICAL PHARMACOLOGICAL APPROACH TO RATIONAL DRUG TREATMENT OF BRONCHIAL OBSTRUCTIVE SYNDROME

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ABSTRACT

The article presents the fundamentals of clinical pharmacology of drugs used to treat broncho-obstructive and allergic diseases, and presents modern protocols for managing patients with this pathology.

INTRODUCTION

The use of the publications of the published series in the teaching process of medical and pharmaceutical universities will provide students with the latest information on the achievements of clinical pharmacology and pharmacotherapy. For doctors and pharmacists, this teaching aid can become a reference book containing information necessary for daily activities.

MATERIALS AND METHODS

Broncho-obstructive syndrome (BOS) or bronchial obstruction syndrome is a symptom complex associated with impaired bronchial patency of functional or organic origin. The term "broncho-obstructive syndrome" cannot be used as an independent diagnosis; it is a symptom complex of a disease, the nosological form of which should be established in all cases of bronchial obstruction.

BOS is formed due to the following main components:

1. Bronchial spasm;
2. Edema of the mucous membrane;
3. Release of viscous secretion and blockage of the bronchi;
4. Sclerotic changes in the bronchi.

RESULTS AND DISCUSSION

To eliminate the above mechanisms of bronchial obstruction, drugs with a bronchodilator effect are currently used, eliminating the inflammatory process in the bronchopulmonary system, affecting the secretion and transport of sputum.

I. Bronchodilators

1. Adrenergic receptor stimulants (adrenergic agonists)
2. Bronchospasm inhibitors (M-cholinergic receptor blockers)
3. Phosphodiesterase inhibitors (methylxanthine derivatives)

II. Anti-inflammatory drugs

1. Corticosteroid hormones
2. Anti-leukotriene drugs
3. Mast cell membrane stabilizers
4. Antibodies to immunoglobulin E (Anti – IgE).

III. Combination drugs

When using metered-dose inhalers with β2-agonists, the maximum number of inhalations is 8 per day (divided into 2-4 inhalations depending on the duration of action of the adrenergic agonists). When using other delivery methods, the doses and frequency of use are specified according to the attached instructions.

Indications for short-acting inhaled β2-agonists: relief of acute asthma symptoms, prophylactic use before exercise in case of bronchospasm of physical effort.

Indications for long-acting inhaled β2-agonists: long-term prevention of symptoms, especially at night, added to anti-inflammatory therapy, prevention of bronchospasm of physical effort.

Contraindications: hyperthyroidism, heart failure, arrhythmia, prolongation of the Q-T interval, hypertension, pregnancy, diabetes (for parenteral administration).

Exercise caution: when used in combination with other sympathomimetics, in hypoxia; keep in mind the possibility of hypokalemia when used in combination with theophyllines, corticosteroids, diuretics.

Side effects: tremor of the extremities, nervous excitement, headache, peripheral vasodilation, tachycardia, muscle twitching and myoclonus.

Among the side effects of adrenergic agonists, it is also worth noting:

- "rebound" syndrome - increased bronchospasm due to the β2-blocking effect of adrenergic agonist metabolites
- "lung closure" syndrome - caused by swelling of the bronchial mucosa as a result of increased capillary permeability due to excessive stimulation of β2 receptors and dilation of bronchial vessels [1].

It should be noted that in the development of tolerance to adrenergic agonists or increased bronchospasm against the background of their intake, in addition to the above syndromes, a decrease in the response of β2 receptors as a result of their dysregulation, as well as the phenomenon of "cold aerosol", high inhalation rate of the drug, the effect of solvents may be important.

Formoterol

Pharmacodynamic features - along with a long-term effect, formoterol has a rapid effect (high rate of development of the bronchodilating effect), which allows it to be used both for the prevention and relief of bronchospasm.

Indacaterol

A new selective β2-adrenergic receptor agonist of long action (within 24 hours) with a single dose. Indacaterol provides a stable significant improvement in lung function (an increase in the forced expiratory volume in the first second, FEV1) for 24 hours. The drug is characterized by a rapid onset of action (within 5 minutes after inhalation), comparable to the effect of salbutamol. The maximum effect of indacaterol is observed 2-4 hours after inhalation.

Indications for the use of indecaterol: long-term maintenance therapy of bronchial obstruction in patients with chronic obstructive pulmonary disease (COPD).

Indacaterol should be prescribed to patients [2]:

- with newly diagnosed COPD and who have not previously taken long-acting bronchodilators;
- receiving short-acting bronchodilators, ICS and other drugs that do not correspond to their stage of the disease according to the GOLD recommendations;
- for whom the appointment of tiotropium bromide does not provide control over the disease (exacerbations persist, the patient is not satisfied with the quality of the therapy, etc.). In this case, it is possible to replace tiotropium with indacaterol or add the latter to the existing treatment.

Aerosol systems for drug delivery:

- metered-dose inhalers (MDI), freon-free MDI, breath-activated MDI;
- combination of metered-dose inhalers with spacers;
- metered-dose powder inhalers (DPI): single-dose capsule, multi-dose reservoir, multi-dose blister;
- nebulizers: jet or compressor (convection, breath-activated, breath-synchronized), ultrasonic
- new types of inhalation systems: Respimat inhaler (Boehringer Ingelheim) is a liquid metered-dose inhaler, has a compact design and is equipped with a digital dose counter. Pulmonary deposition of aerosol during use reaches 45%, and oropharyngeal deposition ranges from 26 to 54%.

Parenteral administration. Euphyllin, when administered parenterally, produces a rapid effect (within 10-15 minutes), the duration of action is 4-6 hours:

- saturating dose - 5-6 mg/kg;
- maintenance dose - 10-12 mg/kg/day;
- with intravenous drip administration - 0.6 mg/kg/hour;
- in smokers, the dose is increased by 1.5 times;
- in case of renal and/or hepatic insufficiency, the dose of euphyllin is reduced to 2 mg/kg/day;
- the maximum daily dose of euphyllin is 2 g [3].

Oral administration (saturation regimen with oral theophylline forms)

- from the 1st to the 3rd day - 400 mg/day;
- from the 4th to the 6th day - 600 mg/day;
- from the 7th to the 9th day - 800 mg/day.

The rational maximum dose is 1000-1200 mg/day.

It is possible to use an individualized approach - a sequential (every 3 days) increase in the dose (in children, in adults with a body weight of less than 45 kg):

- 12 mg / kg / day (maximum 300 mg / day);
- 16 mg / kg / day (maximum 400 mg / day);
- 20 mg / kg / day (maximum 600 mg / day).

Indications: relief (parenteral forms) and prevention (oral forms) of asthma symptoms [4].

Contraindications: severe liver or kidney dysfunction, gastric ulcer or duodenal ulcer, chronic heart failure, hypoxemia, arterial hypertension, hyperthyroidism.

Side effects:

- cardiac (hypotension, tachycardia, arrhythmia);
- gastrointestinal (nausea, vomiting, abdominal pain, diarrhea); - neurological (headache, tremor, convulsions).

Prednisolone is the drug of choice. To relieve asthmatic status, intravenous administration of prednisolone is used at an initial dose of 0.5-1 mg/kg; if there is no effect, the dose of each subsequent administration can be increased by 1.5-2 times. For planned active therapy, average daily doses of prednisolone can range from 10 to 40 mg or more (10-20 mg/day - low-dose regimen, 20-40 mg/day - medium-dose regimen, more than 40 mg/day - high-dose regimen). The daily dose is taken in the morning or 2/3 of the dose in the morning and 1/3 in the afternoon. When the effect is achieved, the dose of glucocorticoids is slowly (by 0.5-1 tablet/week) reduced to a maintenance dose. The optimal maintenance dose of prednisolone is less than 10 mg/day.

Safe maintenance doses of prednisolone [5]:

- for men 7.5 mg/day;
- for women 5 mg/day. In the case of short-term treatment (up to 5-7 days), glucocorticoids can be discontinued quickly.

CONCLUSION

During the period of maintenance therapy with glucocorticoids, the following treatment regimens can be used:

- daily intake of a maintenance dose of glucocorticoid
- alternating - taking the drug every other day at a double dose
- intermittent - taking the drug for 4 days in a row, then a 3-day break.

Indications: inhaled GCS (ICS) (starting with mild persistent asthma) and oral, systemic forms (SGCS) (in severe asthma) are used only for the prevention of asthma attacks, parenteral forms - to relieve severe acute symptoms of asthma (resistant to traditional bronchodilator therapy). Oral GCS can be used for short-term administration (3-10 days): to quickly achieve an effect.

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