EFFECT INHALED GLUCOCORTICOIDS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND BRONCHIAL ASTHMA

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Abstract. *An open comparative trial was designed to compare clinical efficacy of beclomethasone dipropionate (BDP) via non-freon metered dose inhaler (MDI) Easy Breathe or freon-containing MDI. The trial involved 30 patients not younger than 18 yrs with stable moderate to severe bronchial asthma (BA).*

Keywords: *bronchial asthma, beclomethasone dipropionate, bronchospasmolytic drugs, Beclazon, inhaled glucocorticoids*

The length of the disease exceeded 12 months and duration of previous therapy with inhaled steroids (freon-containing BDP) 1 000 to 1 500 mcg daily was at least 4 months. The trial duration was 6 months. The patients were randomised into 2 groups, 15 patients in each. Clinical signs, peak expiratory flow rate, need in short-acting β2-agonists were monitored. The study group patients were given non-freon BDP (Easy Breathe) instead of freon-containing BDP in the ratio 1 : 1. The control group patients continued treatment with freon-containing BDP. Then BDP daily doses were gradually reduced in both the groups while BA was controlled adequately. The daily dose was reduced by 500 mcg in average in 11 of 15 (73.3 %) non-freon BDP patients and in 6 (40 %) freon-containing BPD patients. So, BDP via MDI ECO Easy Breathe allows moderate to severe BA to be controlled with lower doses of the drug. This reduces a cost of the therapy, rate of potential adverse effects and results in improvement of quality of life of the patients.

nhaled glucocorticoids

Glucocorticoid hormones, used in the form of inhalations, have mainly a local effect, reduce or eliminate bronchospasm, help reduce swelling and inflammation of the airways. They are used for bronchial asthma, asthmatic, obstructive bronchitis along with other inhaled bronchospasmolytic drugs (ventolin, salamol, berotek, etc.).

There are currently three types of inhalation systems:

1. Metered dose inhaler (MRL) and MRL with spacer.
2. Powder inhaler (DRU).
3. Nebulizer.

In the nebulizer, the liquid is converted into a "fog" (aerosol) under the influence of compressed air (compression nebulizer) or ultrasound (ultrasonic nebulizer). When

using a nebulizer, the medicine penetrates well into the lower respiratory tract and acts more effectively. In nebulizers, the same substances are used as in other inhalers, but medicines for nebulizers are available in special bottles with a dropper or in plastic ampoules.

When prescribing drugs in the form of inhalation to children older than 3 years, the mouthpiece of the inhaler should be at a distance of 2-4 cm from the wide-open mouth. The valve is pressed during a deep breath, exhalation is done after 10-20 seconds. The duration of inhalation is 5 minutes. The minimum interval between inhalations is 4 hours. The duration of the use of inhaled corticosteroids at a full dose averages 3-4 weeks, the maintenance dose is prescribed for several months (up to 6 months or more).

The guide contains the following inhaled glucocorticoids:

Aldecin Syn.: Arumet; Beclason; Beklat; beclomethasone dipropionate; Bekodisk; Baconase; Becotid; Pliebecot 93

Beclazon 93, 135

Beclomet 137

Beconase 93, 138

Pulmicort 369

Flixotide Syn.: Cutiwait; Flixonase; Fluticasone 462

This text is an introductory piece.

Indications for the use of inhaled GCS are:

■ Bronchial asthma;

■COPD moderate and severe course (with a spirographically confirmed response to treatment).

Bronchial asthma Inhaled steroids are effective in patients with bronchial asthma of any age and severity. They have the following therapeutic effects:

■ reduce the severity of the clinical symptoms of the disease (the frequency of asthma attacks, the need for short-acting β2-agonists, etc.);

■ improve the quality of life of patients;

■ improve bronchial patency and reduce bronchial hyperreactivity to allergens (early and late asthmatic reaction) and non-specific stimuli (exercise, cold air, pollutants, histamine, methacholine, adenosine, bradykinin);

■ prevent exacerbations of asthma and reduce the frequency of hospitalizations of patients; ■ reduce the lethality of otasthma;

■ prevent the development of irreversible changes (remodeling) of the respiratory tract.

Inhaled glucocorticoids are indicated for patients with moderate and severe bronchial asthma. The effectiveness of their treatment is higher, the earlier they are prescribed. The necessity of using these drugs in patients with mild persistent asthma

is debatable. International consensus documents recommend the use of low-dose inhaled glucocorticoids or cromones or antileukotriene in these patients. The advantage of nonsteroidal drugs is the minimum number side effects. Apparently, inhaled glucocorticoids are indicated for patients with mild asthma with insufficient effectiveness of other drugs with anti-inflammatory activity. When using inhaled glucocorticoids, the following rules should be followed:

■ Start treatment with these drugs with the maximum dose (depending on the severity of the asthma) with its subsequent gradual decrease to the minimum required. Despite the rapid positive dynamics of clinical symptoms, the improvement in bronchial patency and bronchial hyperreactivity occurs more slowly. Usually, to achieve a lasting effect of therapy, at least 3 months are required, after which the dose of the drug can be reduced by 25%.

■ Treatment with inhaled steroids should be long-term (at least 3 months) and regular.

■ The combination of long-acting (β2-adrenergic agonists, antileukotriene drugs or long-acting theophylline drugs with inhaled steroids is more effective than increasing the dose of the latter. The use of such therapy allows you to reduce the dose of topical glucocorticoids. In recent years, fixed combinations of drugs have been introduced into clinical practice: FP / salmeterol, BUD / formoterol, which are indicated for moderate and severe bronchial asthma

■ The use of inhaled steroids can reduce the dose of tableted glucocorticoids It has been established that 400-600 mcg / day BDP is equivalent to 5-10 mg prednisolone It should be remembered that the clinical effect is clearly manifested on the 7-10th day of using inhaled glucocorticoids With their simultaneous use with tablet preparations, the dose of the latter can begin to be reduced no earlier than this period.

■ With a stable course of bronchial asthma, inhaled glucocorticoids are used 2 times a day. Esonide in patients with mild to moderate bronchial asthma in the remission phase can be used once. With exacerbation, the frequency of administration is increased to 2-4 times a day. This technique allows you to achieve higher compliance.

■ High doses of inhaled glucocorticoids may be used instead of systemic steroids to treat and prevent asthma exacerbations.

Chronic obstructive pulmonary disease

Inhaled steroids do not affect the progressive decrease in bronchial patency in patients with COPD. High doses of these drugs can improve the quality of life of patients and reduce the frequency of exacerbations of moderate to severe COPD. The reasons for the relative steroid resistance of airway inflammation in COPD are the subject of research. It is possible that it is due to the fact that glucocorticoids increase the lifespan of neutrophils by inhibiting their apoptosis. The molecular mechanisms

underlying glucocorticoid resistance are not well understood. In recent years, there have been reports of a decrease in the activity of histone deacetylase, which is a target for the action of steroids, under the influence of smoking and free radicals. This may reduce the inhibitory effect of glucocorticoids on the transcription of "inflammatory" genes. Recently, new data have been obtained on the effectiveness of combined drugs (salmeterol + FPiformoterol + BUD) in patients with moderate and severe COPD. It has been shown that their long-term (within 1 year) administration improves bronchial patency, reduces the severity of symptoms, the need for bronchodilators, the frequency of moderate and severe exacerbations, and also improves the quality of life of patients compared with monotherapy with inhaled glucocorticoids (long-acting β2-adrenomimetics and placebo.

Side effects of inhaled glucocorticoids

Oropharyngeal candidiasis(less often - candidiasis of the esophagus)

According to different authors, it occurs in 5-25% of patients. It is manifested by a burning sensation in the mouth and whitish rashes on the mucous membranes. It has been established that its development is directly proportional to the dose and frequency of taking inhaled glucocorticoids.

Prevention of candidiasis:

■ mouth rinsing after each inhalation;

■ use of a metered-dose aerosol spacer or powder inhalers;

■ the use of inhaled steroids in smaller doses and with a lower frequency of administration (in the phase of remission of bronchial asthma).

It is observed in 30-58% of patients. Depends on the dose of steroids and the type of dosing device. Due to the deposition of the drug in the larynx and the development of steroid myopathy of its muscles. It often develops in people whose profession is associated with increased voice load (singers, lecturers, teachers, announcers, etc.). For the treatment of dysphonia use:

■ replacement of DI with powder ones;

■ Reducing the dose of inhaled steroids (in remission).

Irritation of the upper respiratory tract

Manifested by cough and bronchospasm. Often caused by propellants contained in MDIs. Prevention of this complication:

■ use of fast-acting β2-agonists before inhaled glucocorticoids;

■ use of a spacer;

■ replacement of DI with powder ones.

Systemic side effects of inhaled glucocorticoids

Suppression of the hypothalamic-pituitary-adrenal system

Manifested by a decrease in the secretion of endogenous cortisol. Typically, this side effect is seen with high doses of BDP, TAA, FLU, BUD (>1500 mcg/day in adults

and >400 mcg/day in children) and AF (>500-750 mcg/day in adults and >200 mcg/day in children).

To prevent the systemic action of inhaled glucocorticoids, it is recommended to use their minimum required dose. The use of these drugs must be combined with long-acting β2-agonists, theophylline or leukotriene antagonists.

Steroid osteopenia and osteoporosis

A few studies have shown a decrease in the functional activity of osteoblasts in patients receiving high doses of inhaled glucocorticoids. However, most studies have not yet provided convincing evidence for the development of osteoporosis and bone fractures in adults and children taking these drugs for a long time (1-6 years), which was confirmed in a recently published meta-analysis. However, in some observations, a significant relationship was found between the cumulative dose of inhaled steroids and a decrease in the density of the lumbar vertebrae and hips in patients with bronchial asthma, especially in women. A small number of studies have shown a lesser effect on bone tissue of BUD and AF than BDP when using CFC-containing DIs.

Thus, the results of the works cited above do not completely exclude the potential for the development of osteopenic syndrome in patients taking high doses of inhaled glucocorticoids for a long time. Probably, the risk group includes elderly patients, postmenopausal women, patients suffering from endocrine diseases (thyroid pathology, hypogonadism), having bad habits (smoking, alcoholism) and low physical activity. Prevention of this possible side effect is recommended with the help of calcitonin preparations, calcium salts (Ca + 2 content 1500 mcg / day) and vitamin D3 (400 IU / day). In women, in the absence of contraindications, estrogen replacement therapy can probably be prescribed. Equally important is the normalization of physical activity and the rejection of bad habits.

Skin bleeding

It is due to its thinning due to a decrease in the production of the main substance by skin fibroblasts. It develops more often in elderly patients receiving high doses (> 1000 mcg / day) of inhaled glucocorticoids. Often combined with a decrease in cortisol secretion. This complication, as a rule, does not represent a significant clinical problem, but may be an indicator of the systemic effect of steroids.

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