REVIEW ARTICLE

Inhaled Glucocorticoids in Rhinosinusitis: A Few Pharmacological Aspects, We Must Know

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Abstract

Inhaled glucocorticoids are very effective for the management of seasonal and perennial allergic rhinitis. Various glucocorticoids are available for inhalation therapy with varying affinity for the receptors. Inhaled glucocorticoids have very low incidence of systemic side effects at the usual therapeutic doses. In this review we have discussed the pharmacokinetics, pharmacodynamics and adverse effects profile of the commonly available inhaled glucocorticoids.

Keywords: Atopy, Inflammation, Fluticasone, Beclomethasone, Ciclesonide, Flunisolide, Budesonide.

INTRODUCTION

Allergic rhinosinusitis is an IgE- mediated hypersensitivity disease of the mucous membranes of the nasal airways characterized by sneezing, itching, watery nasal discharge and sensation of nasal obstruction. It is subdivided based on exposure, into two types: (a) Seasonal: which is due to outdoor allergens, e.g. pollens, and (b) Perennial: caused by indoor allergens, e.g. as dust, mites, insects, animal dander.

Pathophysiology (Figs 1 and 2)

The major feature of atopy is production of IgE antibodies by human B lymphocytes in response to allergen. IgE further activates mast cells and basophils which start the cycle of metabolism of arachidonic acid by cyclooxygenase pathway. This reaction produces cytokines, interleukins, histamine, prostaglandin D2, leukotrienes. These chemicals are responsible for the clinical features of allergic rhinitis.

Mechanism of Action

The anti-inflammatory effects of glucocorticoids include inhibition of eicosanoid synthesis, modulation of cytokine and chemokine production, marked inhibition of accumulation of basophils, eosinophils and other leucocytes, and decreased vascular permeability. Glucocorticoids are not bronchodilators but they benefit by reducing hyper-

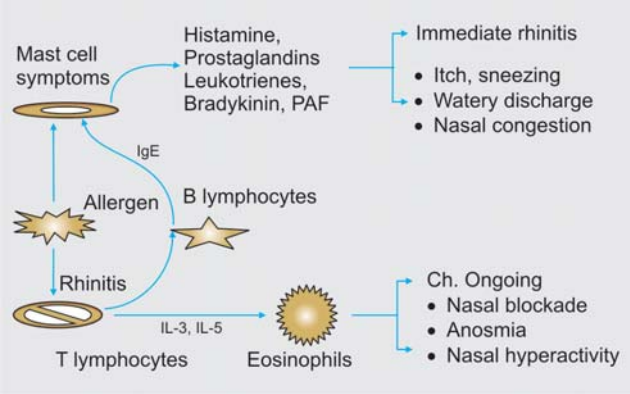

Fig. 1: Immediate and chronic allergic rhinitis

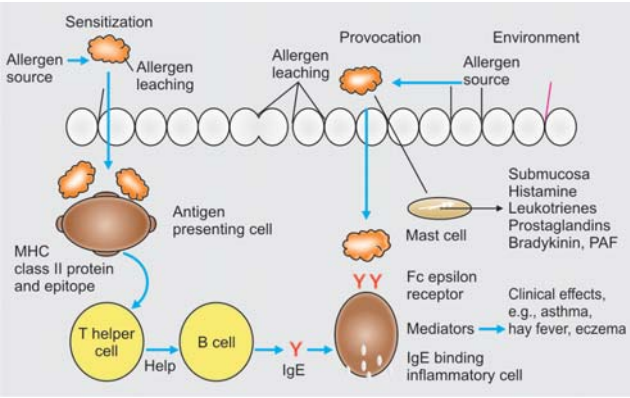

Fig. 2: Mechanism of allergy

reactivity, mucosal edema, and suppressing inflammatory response to antigen-antibody reaction or other trigger stimuli. Inhaled glucocorticoids target the drug directly to the relevant site of inflammation, thereby enhancing the therapeutic index of the drugs and diminishing the severity of side effects, without sacrificing clinical efficacy.

Various glucocorticoids available for inhalation therapy are: beclomethasone dipropionate, triamcinolone acetonide, flunisolide, budesonide, fluticasone propionate, ciclesonide and mometasone. These drugs differ markedly in their affinities for glucocorticoid receptors, e.g. fluticasone and budesonide has much higher affinity than beclomethasone. They are used prophylactically to control allergic rhinitis rather than in acute phase to reverse the symptoms as peak effect is seen after 4-7 days of inhalation and benefit persists for a few weeks after discontinuation. Highly potent drugs, e.g. fluticasone, flunisolide, and budesonide can be effective with as little as one or two puffs administered twice or even once daily. Patients may prefer it because of more convenient dosage regimen which provides them improved compliance and better control. Effective dose depends on the severity of the disease, particular steroid used, and device used for drug delivery, which determines the actually quantity of drug delivered.

Beclomethasone Dipropionate

Although, beclomethasone is mainly used for asthma but intranasal spray is equally effective in perennial rhinitis in the dosage of 50 μg in each nostril twice or thrice a day.

Budesonide

It has high topical: systemic ratio and is claimed to be better than beclomethasone. Its small fraction is absorbed in the systemic circulation, but it is rapidly metabolized without any significant side effects. It is effective in allergic rhinitis in the dosage of 200-400 μg per day. Initially two puffs in each nostril every morning and then tapered to one puff in each nostril. It may cause nasal irritation, sneezing, crusting, itching of throat, and dryness. It is contraindicated in presence of infection or nasal ulcers.

Fluticasone Propionate/Furoate

It has high potency, longer duration of action and negligible oral bioavailability and hence less systemic side effects however, higher dosages are absorbed in the lungs and may cause systemic side effects. It is effective in the dosage of 100-250 μg twice daily with maximum dose of 1000 μg per day.

Flunisolide

It is used for prophylaxis and treatment of seasonal and perennial rhinitis. It is available as 25 μg per actuation nasal spray, one spray in each nostril 2-3 times daily may be given.

Ciclesonide

It has high topical: systemic activity ratio. It is inhaled as prodrug which gets activated in the body by esterases in bronchial epithelial cells after cleavage. Its oral bioavailability is less than 1%. If this drug is absorbed in circulation then its active metabolite gets bound to serum proteins so that less drug is available for the receptors present in skin, eye, and bone thereby minimizing risk of causing cutaneous thinning, cataract, osteoporosis or temporary slowing of growth. It is used in the dosage of 80-160 μg once daily preferably in the evening.

TOXICITY OF INHALED STEROIDS

These inhaled drugs can reach circulation by direct absorption from lungs or by absorption from gastrointestinal tract after swallowing. These newer glucocorticoids have low oral bioavailability due to extensive first pass metabolism by liver therefore; they reach blood circulation mainly through absorption from lungs. The probability of adverse effects continues to increase at higher dose. Oropharyngeal candidiasis can occur which can be reduced by oral rinse after each use. These drugs can also cause dysphonia or hoarseness due to direct effect on vocal cords. The risk of osteoporosis and cataract increases on prolonged use. In children, they cause transient slowing of rate of growth.

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