

Effectiveness of intranasal corticosteroids

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Abstract. Intranasal corticosteroids (IC) are most commonly prescribed to treat allergic rhinitis (perennial and seasonal). There are now many IC available to treat rhinitis, all effective on nasal obstruction, rhinorrhea, sneezing, itching and post-nasal drip. IC are superior to oral antihistamines for the relief of all nasal symptoms; however, antihistamines are first line therapy if allergic conjunctivitis coexists. At present the data do not support the use of IC in the management of otitis media with effusion (OME), nasal polyposis and sinusitis, but when topical IC are administered together with antibiotic therapy they facilitate a more rapid improvement of symptoms.

Key words: Intranasal corticosteroids (IC), allergic rhinitis

Nasal obstruction represents a global health problem and one of the most common medical consultation (more than 40% of visits in northern Italy). Nevertheless, both doctors and patients seem to pay scant attention to nasal symptoms. The degree of impairment that can be experienced by an individual with nasal obstruction is frequently underestimated, while it can alter sleep pattern, school and sport performance and social life.

Nasal obstruction has a negative impact on the physiological functions of the nose such as pre-heating air temperature up to 32° C, humidification up to 98% and removal of particles bigger than 2 µm.

A right nasal airflow towards the bronchial tree could reduce the chronic secondary effects of nasal obstruction such as sinusitis, impaired development of facial bones, otitis media, nasal polyps and (mainly in allergic patients) bronchial asthma.

Causes of nasal obstruction

There are physiological and pathological causes of nasal blockage. The former are:

1. nasal cycle (rhythmical congestion-decongestion of the vasculature turbinate);

2. vasomotor reaction due to temperature variation (hot-cold) or different stimuli such as stress, fear and anger that stimulate hypothalamic reflexes.

Pathological causes of nasal blockage are:

1. infections (viral or bacterial rhinitis, rhinosinusitis);
2. mechanical obstruction (nasal polyposis);
3. allergic rhinitis (persistent or intermittent);
4. persistent inflammation (urban environmental pollutants).

Allergic rhinitis is one of the most common airway diseases, affecting 10-25% of the population under 30 years of age.

The availability of intranasal corticosteroids (IC) with high affinity for the glucocorticoid receptor, strong anti-inflammatory properties and minor side effects leads to a significant improvement of therapeutic strategies for the treatment of allergic rhinitis.

Characteristics of intranasal corticosteroids

There are six classes of IC available to treat rhinitis in Italy (Tab. 1).

Table 1. Recommendations for the use of intranasal corticosteroids

Beclomethasone dipropionate	>6 yrs 100 µg (in 2 doses)
Budesonide	>6 yrs 100-200 µg (1 or 2 doses)
Flunisolide	>5 yrs 100 µg (in 2 doses) >12 yrs 200 µg (in 2 doses)
Fluticasone propionate	>4 yrs 50 µg (once a day) >12 yrs 100 µg (once a day)
Mometasone furoate	>6 yrs 200 µg (in 1 or 2 doses)*
Triamcinolone acetonide	>6 yrs 220 µg (once a day)

* Mometasone furoate is approved from 3 years of age in the USA, UK, Australia

IC are safer than systemic corticosteroids; they have a high affinity for the glucocorticoid receptor and high drug concentrations can be achieved at receptor sites in the nasal mucosa. The profuse blood supply of the nasal mucosa (endothelial-windows) can lead to the absorption of intranasal steroids, whereas the swallowed portion is subject to first-pass deactivation in the liver before reaching the systemic circulation, leading to the minimal risk of systemic side effects.

The use of topical IC to treat allergic rhinitis reduces: eosinophils concentration in nasal mucus, mast cell secretion of cytokines and chemokines, sub-epithelial cell accumulation (Th2 lymphocytes, monocytes, eosinophils and basophils).

IC are effective in the early phase and in the late phase reaction of allergic inflammation: they therefore improve all nasal symptoms (sneezing, itching, rhinorrhea, nasal obstruction).

Side effects can be local or systemic. Mild local side effects such as nasal crusting, dryness and minor epistaxis occur, but the current intranasal preparations can be used on a long-term basis without causing mucosal atrophy. Local mycotic infections and perforation of the nasal septum have been rarely reported. Sneezing and stinging of the nasal mucosa soon after the administration of IC are reported as troublesome symptoms by 20% of children with allergic rhinitis.

Systemic side effects are rare, however the possible effect on growth for some, but not all, IC is of concern. Beclomethasone (100 µg/die) and Budesonide (400 µg/die) can reduce growth speed in the first year of treatment but do not affect final height (1).

Moreover the difference between measured height and expected height does not correlate with the length of the treatment.

Children receiving daily intranasal Mometasone for 1 year do not develop hypothalamic-pituitary-adrenal axis suppression (hypertension, high blood pressure, rash, cataract and glaucoma are extremely rare). The risk of side effects should be minimized by using the lowest dose to control symptoms and monitoring the total dose of inhaled and topical intranasal.

The suggested regimen in children is to use a once daily dose, preferably administered in the morning.

The administration of IC can be particularly effective on symptoms and minimize side effects following simple recommendations:

- use nasal devices delivering fixed doses
- shake the nasal device before use
- lean the head forward
- direct the spray towards the external side of the nose (in this way most of the spray is spreaded on turbinates and not on nasal septum).

In addition to the effectiveness in the treatment of nasal symptoms, IC are easy to administrate and require only one or two daily doses. These properties could enhance patient's adherence to treatment; nevertheless adherence remains a problem in the paediatric population.

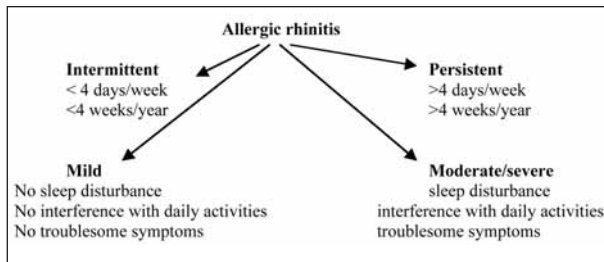
Intranasal corticosteroids in upper respiratory inflammatory diseases

Allergic rhinitis

Allergic rhinitis is one of the most important and common causes of chronic illness, affecting between 10% (6-7 yrs) and 20% (16-20 yrs) of Italian population.

In childhood its prevalence is increased in males. Symptoms are defined as seasonal and perennial in the 20% and 40% of the patients, respectively. Rhinitis, such as asthma, is usually subdivided into intermittent and persistent, mild and severe (Table 2).

Based on the most important symptoms, patients with allergic rhinitis are classified in sneezers/runners and blockers. The first line treatment is different in

Table 2. Classification of allergic rhinitis

sneezers and in blockers patients (eg. intranasal steroids can be used as monotherapy in patients with prevalent nasal obstruction) (Table 3).

Although the use of IC in allergic rhinitis is increasing, few data are available to evaluate their efficacy and safety in paediatric patients. However current evidence points (2-4) to suggest the following indications:

1. IS are more effective than oral antihistamines on nasal obstruction, rhinorrhea, sneezing, itching and post-nasal drip. However "Allergic Rhinitis and its Impact on Asthma" (ARIA) guidelines (5) recommend antihistamines alone in the treatment of mild intermittent rhinitis.
2. There is no difference on efficacy treatment of rhinitis among IS.
3. IS and oral antihistamines were found to have no differences in improving eye symptoms (itching, conjunctivitis)
4. IS are more effective than antileukotrienes, alone or in association with oral antihistamines, to reduce eosinophilic nasal inflammation due to pollens inhalation and to control symptoms.
5. Patients with allergic rhinitis treated with IC have lower risk for asthma and sinusitis than untreated patients, despite uncontrolled rhinitis.

Table 3. Clinical differences between Sneezers and Blockers patients

	Sneezers/runners	Blockers
Nasal obstruction	variable	severe
Nasal itching	+++	+
Rhinorrhea	watery, anterior	mucous, posterior
Ocular symptoms	++	+-
Diurnal rhythm	worse during day	worse during night

6. Patients with rhinitis and asthma treated with IC have lower risk for Emergency Department (ED) admissions and hospitalizations for asthma than untreated patients.

Otitis media with effusion

Scientific publications analysed by Evidence Based Medicine (EBM) on otitis media with effusion (OME) are scanty and controversial. However, it has been shown that:

- oral steroids (OS) and IC, alone or in association with antibiotic therapy, induce a more rapid OME remission;
- there is no evidence of long term (>3 months) efficacy of OS or IC with or without antibiotic to treat OME with or without deafness (6);
- there are no differences of efficacy and side effects between IC or OS.

Nasal polyposis

Nasal polyposis is considered as inflammatory disease and the best therapeutical approach consists in the use of OS or IC (7). The efficacy of treatment relies on their early use or immediately after surgery.

Budesonide (BUD) aqueous nasal spray significantly reduces nasal polyposis compared with placebo.

There are no significant differences in efficacy between BUD 250 µg once a day and BUD 100 µg once a day over an 8 weeks treatment period.

The efficacy of macrolides, associated with steroids, is still debatable.

Sinusitis

Anatomic changes can alter nasal ventilation and drainage. This factor along with mucous-ciliary clearance and nasal immunity impairment may induce a mucosal inflammation, especially in atopic patients. Mild sinusitis can recover spontaneously in most patients, while severe sinusitis needs antibiotic therapy and topical treatment.

EBM shows that antibiotic associated with mometasone furoate nasal spray 400 µg twice a day is more effective on nasal symptoms than antibiotic alone.

Conclusions

The efficacy of IC is widely recognized; however, their effectiveness can be limited in attempting to minimize side effects, especially in paediatric patients.

A careful evaluation of cost-benefit ratio has to be considered in order to establish whether or not an early treatment of allergic rhinitis with IC may prevent the onset of asthma.

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