Expert Opinion

Central & Peripheral Nervous Systems

Nasal decongestants in the treatment of chronic nasal obstruction: efficacy and safety of use

Desiderio Passàli[†], Lorenzo Salerni, Giulio Cesare Passàli, Francesco Maria Passàli & Luisa Bellussi

[†]ENT Clinic University of Siena Medical School, Policlinico 'Le Scotte' viale Bracci, 53100 Siena, Italy

Nasal decongestants are the most powerful drugs in the reduction of nasal obstruction. Despite their large use, local and systemic adverse reactions are frequent. The authors focus on the pharmacology of these kinds of drugs in light of the most recent knowledge on nasal pathophysiology. The ultrastructural anatomy of nasal mucosa explains the complexity of the possible interactions between the sympathomimetics and imidazoles derivates, and the submucosal layer. Nasal obstruction is one of the most frequent clinical problems that otorhinolaryngologists encounter daily, both in adults and children. All possible predisposing conditions to nasal obstruction are documented along with the better ways to diagnose them through nasal functionality tests. Active anterior rhinomanometry, acoustic rhinometry and the determination of mucociliary transport time represent, together with nasal endoscopy, the gold standard for an accurate diagnosis and the follow-up of the patient to cure. An updated review of the most significant works in this field and the best treatment protocol to avoid adverse effects, such as rhinitis medicamentosa, are reported.

1. Introduction

The nasal respiratory function is one of the most important, and among the most complex activities by which our body is supplied with the quantity of air suitable for its needs. In the nose, the air is filtered, heated and humidified, and thus adapted for passing through the delicate pulmonary alveolar structures.

Nasal patency, the conditioning of air and defence activity, are connected with the complex structure of the nasal mucous membrane and submucosa, which is particularly rich of arteriovenous anastomotic shunts capable of modifying inspired air. The arteriolar flow and the repletion of the cavernosa is regulated by the sympathetic and parasympathetic nervous system. Studies conducted with the electron microscope and the microcorrosion technique have shown that the turbinates microcirculation consists of a subepithelial capillary bed, with more or less aggregated vessels, a second intermediate bed with rectilinear vessels and a deeper bed made up of venous sinusoids, arterioles and arteriovenous anastomoses [1]. The arterioles and the arteriovenous anastomoses are referred to as resistance vessels, and the venules and venous sinusoids as capacitance vessels. Their repletion or depletion is regulated by the autonomic nervous system. The sympathetic nervous system acts on the α-1, α-2 and β-receptors by releasing noradrenalin which induces vasoconstriction. The parasympathetic system, through the release of acetylcholine, stimulates glandular secretion and causes vasodilation.

informa
healthcare

The autonomic nervous system is controlled by the Vidian nerve which reaches the sphenopalatine ganglion formed by the conjunction of two nerves: the nervus petrosus superficialis major, which carries parasympathetic fibres that cause vasodilation and secretion, and the nervus petrusus profundus, which carries sympathetic fibres that instead cause secretion and constriction.

The inhalation of cold air produces arteriolar vasoconstriction, whereas if the air is warm there is vasodilation. In order to undergo these essential transformations, inhaled air is conveyed in such a way as to follow a particular pathway. Once inhaled air penetrates the nasal fossa, the nasal valve, the inferior nasal turbinate and the other lateral nasal wall structures apply movement which carries it upwards and backwards to the middle nasal meatus, and then downwards to the choanae. Laminar flow provides movement of air along this path, reducing resistance and thus heat loss. During expiration, the air does not follow a fixed path and produces eddies in the middle nasal meatus causing the condensation of existing water, and thus allowing considerable energy saving along with the yielded heat.

Along with ventilation, mucociliary clearance is as important and essential for the delicate nasal homeostasis. By means of mucociliary transport, the potentially harmful inhaled particles are deposited on the mucus which lines the nasal walls. From there they are transported to the pharynx by mucociliary transport. Good ventilation and the presence of a proper quantity and quality of nasal secretion are the necessary conditions for normal ciliary activity.

It is obvious that in situations resulting in nasal obstruction, breathing mostly takes place through the mouth, normal nasal functions are impaired, and thus morphostructural changes are induced leading to pathological events.

Nasal obstruction is one of the most frequent clinical problems that otorhinolaryngologists encounter daily, both in adults and children. Although chronic nasal obstruction is not immediately life threatening for the patient, it is nevertheless marked by a negative impact on their social and working life. Moreover, it is important to keep in mind that the nose and the other facial structures are not merely contiguous anatomical entities, but are part of a system of inter-related, collaborating and interdependent organs. The nasal cavity, rhinopharynx, Eustachian tube, middle ear and oropharynx are part of a system referred to as the rhinopharyngotubal unit.

Nasal obstruction, besides limiting the quantity of air intended for pulmonary respiration and thus reducing the oxygen supply to the entire organism, impairs the normal aeration of the nasal sinuses and middle ear causing CO_2 accumulation. This, in turn, stimulates sinus pH reduction and the production of mucus that cannot be drained due to the oedema constricting the sinus and tube ostia, promoting stasis of secretions, and thus providing fertile ground for proliferation of germs [2].

The side effects of long-standing breathing through the mouth, which, as already mentioned, does not provide air with the physical requirements suited for the lower airways, are rhinosinusitis and rhino-otitis, as well as respiratory tree inflammations, such as pharyngitis and laryngitis (i.e., the upper and lower airways are affected in the complex picture of the rhinobronchial syndrome) [3]. Hence, all the pathologies resulting in nasal obstruction allow the onset of other pathologies that affect nearby and distant organs, producing increasingly marked alterations of the homeostasis of the entire organism.

Among the pathologies responsible for more or less complete and continued, or occasional, nasal obstruction, specific and aspecific vasomotor rhinitis are the conditions with greater epidemiological impact. Even a common cold of short duration may be characterised by nasal obstruction caused by oedema and congestion of the turbinates. In this pathology, frequent side effects are otitis and sinusitis due to direct spreading of germs, and impaired passage of secretions through oedematous ostia.

Analysis, based on the incidence at different ages of pathological conditions marked by the presence of nasal obstruction, shows that, within the forms susceptible to medical treatment, specific vasomotor rhinopathy and acute rhinitis are the most frequent in both adults and children (Table 1).

In the absence of any evident deviations of the septum, irreversible hypertrophy of inferior turbinates, polyps or tumours of the nasal fossae and paranasal sinuses, or conditions exclusively requiring a surgical approach, nasal breathing may be improved by medical treatment that serves to decongest the mucosa and reduce the volume of turbinates.

2. Nasal decongestants

The decongestion of nasal mucosa and, in particular, of paranasal sinuses ostia, is the fundamental treatment for restoration of the physiology of the nasal and paranasal sinuses [2].

Decongestants are constituted by a wide range of substances available alone, or in combination with other substances for both topical and systemic use. Sympathomimetic drugs represent the most important category in this medicinal class, both from the usage viewpoint and, unfortunately, for their side effects, which require some precautions for a correct and safe use.

Nasal decongestants may be divided into two groups:

- Sympathomimetic amines: primary aliphatic (e.g., tuaminoeptano); phenolic (e.g., adrenaline, hydroxyamphetamine and phenylephrine); and nonphenolic (e.g., ephedrine and phenylpropanolamine).
- Imidazoline derivatives (e.g., naphazoline, oxymetazoline, tetryzoline, tramazoline, xylometazoline and clonazoline).

The efficacy of topical nasal decongestants (sprays) for relief of nasal obstruction has been known and demonstrated for almost a century. The powerful sympathomimetic action causes vasoconstriction, and reduces congestion of the mucosa by stimulating the α-adrenergic receptors. Sympathomimetic

Table 1. Causes of nasal obstruction.

Incidence	Children (0 – 10)	Adolescents (11 – 19)	Adults (> 20)
Common	Acute rhinitis Specific and aspecific vasomotor rhinopathy Adenoid hypertrophy	Acute rhinitis Specific and aspecific vasomotor rhinopathy Deviated septum	Acute rhinitis Specific and aspecific vasomotor rhinopathy Deviated septum Rhinitis medicamentosa Metabolic and endocrine causes: • pregnancy • menstrual cycle • hypothyroidism • diabetes
Possible	Deviated septum Chronic rhinosinusitis Foreign bodies Septal haematoma	Rhinitis medicamentosa Chronic rhinosinusitis Foreign bodies Septal haematoma Antro-choanal polyps	Chronic rhinosinusitis Antro-choanal polyps Atropic rhinitis Septal perforations
Rare	Choanal atresia Cystic fibrosis Dysgammaglobulinaemia Neoplasias	Atropic rhinitis Angiofibroma Fibrous dysplasia Tornwaldt's bursitis Rhinolites	Neoplasias Rhinolites Paget's disease Wegener's granulomatoss

Modified from May M, West JW: The 'stuffy' nose. *Otolaryngol. Clin. North. Am.* (1973) **66**:665-674 [27].

nasal decongestants, through the activation of α-adrenergic receptors, which increase noradrenalin release by the adrenergic terminations, lead to rapid relief of obstructive symptoms thanks to their vasoconstrictive action on capacitance blood vessels, particularly abundant in the nasal mucosa [4], and also on the resistance vessels (arterioles, artero-venous anastomoses). In fact, the α-1 and α-2 receptors are located in these vessels, the site of attack of vasoconstrictors, which act by a mechanism of functional antagonism. Sympathomimetic amines are α-1-selective agonists and, therefore, carry on their activity mostly on capacitance vessels. Imidazoline derivatives are α-2-specific agonists and as such, as well as acting on capacitance vessels, also act on resistance vessels due to the presence of α-2 receptors on both vascular structures. Vasoconstriction leads to a reduction of the volume of nasal mucosa in favour of the available volume of nasal cavities for air passage and conditioning. Therefore, vasoconstrictors are widely used in specific and aspecific rhinopathies, where nasal obstruction is prevalent, or in rhinosinusitis and rhino-otitis, as an adjuvant for improving ventilation of sinuses and the middle ear through the Eustachian tube. They also ensure a better diffusion of corticosteroid, antihistamine or mucolytic agents locally administered as nasal sprays.

Sympathomimetic amines and imidazoline derivatives are very different from a pharmacological viewpoint in terms of latency and duration of action (Table 2) [5].

The latency times in the two groups practically overlap, and are on average 10 – 20 min.

On the contrary, the duration of action shows considerable differences: it is short for sympathomimetic amines (20 min – 1.5 h) and much longer for imidazoline derivatives (2 – 12 h).

The vasoconstriction effect of imidozole derivatives (tetryzoline, xylometazoline, naphazoline, oxymetazoline and tramazoline) lasts longer than that of adrenaline derivatives. This more prolonged duration of action may be ascribed to their vasoconstrictive activity on the capacitance vessels, as well as on the resistance vessels, which leads to a considerable reduction of the blood flow, resulting in the delayed elimination of the drug [6].

Several comparative studies reported in literature have shown the efficacy of imidazoline derivatives. Tramazoline and oxymetazoline have proved equally effective, and have an overlapping duration of the decongestant effect, whereas latency is shorter for imidazoline sulphate and nitrate, and tramazoline [6]. The nasal decongestive action has been shown by a number of studies through the application of objective, repeatable and standardised methods, such as active anterior rhinomanometry (AAR) and acoustic rhinometry (AR), before and after administration of a nasal decongestion (nasal decongestion test [NDT]). Such methods are able to demonstrate the true efficacy of decongestants, objectively measure their potency on nasal obstruction, or better identify patients with functional or anatomic nasal respiratory stenosis.

The nasal decongestion test is used when AR and AAR show altered nasal patency values (respectively, reduced nasal volumes and cross-sectional areas, or increased pressure and resistance values). The test is very simple and consists of spraying two puffs of a short latency decongestant in each nostril, followed by an instrumental evaluation after 5 min. The test is considered positive if the values return to normal, indicating that the nasal stenosis has a functional component. If the nasal resistance and volume remain unchanged after administration of the drug, the

Table 2. Comparison of sympathomimetic amine and imidazoline derivative nasal decongestants.

Substance	Latency	Duration of action	Side effects
Sympathomimetic amines			
Adrenaline	5 – 6 s	20 – 30 min	++++
Ephedrine	10 min	3 – 4 h	+++
Phenylephrine	15 min	1 – 2 h	+++
Tuaminoeptano	15 min	1.5 h	+++
Imidazoline derivatives			
Naphazoline	15 min	2 – 6 h	++
Tetryzoline	15 min	4 – 6 h	++
Xylometazoline	20 min	10 – 11 h	++
Clonazoline	5 min	8 – 12 h	++
Oxymetazoline	20 min	10 – 12 h	++
Tramazoline	5 min	11 – 12 h	+

stenosis is structural and, thus, a surgical approach is the only option.

An interesting study by Bellussi *et al.* [7], conducted on 60 patients (30 with vasomotor rhinopathy, and 30 with septal deviation as main pathological feature), shows the positive decongestive effects of common imidazoline derivatives administered as nasal spray using NDT, AAR and AR as objective methods. Unsurprisingly, the addition of balsamic substances to the compound only gave subjective sensations of greater nasal patency reported by patients, which, however, was not demonstrated by objective nasal functionality data. The efficacy of imidazoline derivatives on the nasal respiratory function is confirmed by an interesting study conducted by Hochban *et al.* [8]. In this study, acoustic rhinometry proved an effective and repeatable objective method in nasal patency determination in that it provides geometric data of nasal fossae as cross-sectional areas, calculated at the head of the inferior and middle turbinates, and the total nasal volume. A total of 108 patients were divided into groups and administered six different imidazole derivatives (oxymetazoline, xylometazoline, indanazoline, naphazoline, tramazoline and tetryzoline). The greatest decongestant effects can be observed after 20 – 40 min for all the substances, but are more prolonged with tramazoline, xylometazoline and oxymetazoline up to 4 h after administration, and a significant decongestant effect is still present after 8 h for oxymetazoline. The authors indicate that the effects of xylo- and oxymetazoline were obtained at the same concentrations.

In a recent study, Caenen *et al.* [9] evaluate the decongestant effect of xylometazoline versus pseudoephedrine by rhinomanometry and NMR. Rhinomanometry was performed after 15 and 30 min and 1, 2, 4, 6 and 8 h of drug administration. NMR was performed after 90 min. Xylometazoline causes an average 37.3% reduction of nasal resistance in all patients over a prolonged 8 h period. Pseudoephedrine exhibits no marked or lasting decongestant effects. Magnetic resonance has highlighted the pre-eminence of xylometazoline compared with pseudoephedrine in nasal mucosa decongestion.

Against their undeniable clinical effectiveness, the widespread and uncontrolled use of theses pharmacological principles has sometimes proven harmful.

Nasal vasoconstrictors reduce the blood flow by acting on the α-2 adrenergic receptors which produce a marked arteriolar constriction, resulting in local ischaemia of the nasal mucosa. This 'ischaemic state', due to the drastic reduction of the blood supply is to be carefully considered as it may be responsible for local side effects which result in serious alterations of mucosal trophism. Aside from minor side effects, such as itching, stinging, irritation, oedema and dryness of the mucosa, sometimes reported by patients administered the topical drug, the rebound effects and tachyphylaxis are far more relevant, and account for mucociliary clearance alterations, and severe damage to the nasal mucosa trophism.

One of the effects that generally occurs a few hours after administration is the 'rebound', or engorgement, due to the stimulation of β-receptors, which lasts longer than α-receptor stimulation. In particular, vasoconstriction induced by topical decongestants may be followed by vasodilation or rebound congestion. The patient, if unaware of this phenomenon, tends to take increasing and frequent doses for relief from the resulting secondary obstruction without knowing that it is induced by the drug itself. In time, the decreased sensitivity of α-adrenergic receptors causes tachyphylaxis. The patient tries to make up for the reduced efficacy of the drug by using larger doses at shorter intervals.

Tachyphylaxis, an effect common to many other medicines, results in a reduced efficacy of a drug dosage after repeated use, probably due to a decreased response of specific receptors. Rebound congestion and tachyphylaxis induce overuse of vasoconstrictors. The persistence of these phenomena and bad habits lead to marked and long-lasting mucosa alterations that result in rhinitis medicamentosa.

Rhinitis medicamentosa [10] is apparently caused by an alteration of the vasomotor tone, resulting in increased parasympathetic activity due to 'fatigue' of the α-adrenergic vasoconstrictor mechanism, which produces an increase in vascular permeability and a tendency towards intravascular oedema formation [11]. Another theory postulates that prolonged vasoconstriction causes tissue hypoxemia, with engorgement and secondary congestion and vasodilatation.

As reported in a study by Graf [12], the risk of developing rhinitis medicamentosa also appears to be associated with antibacterial preservatives dissolved in the spray solution, such as benzalkonium chloride [12,13], a quaternary ammonium compound which has a bactericidal effect because it damages the cell wall of microorganisms. Aside from its well known antiseptic properties, due to the peculiar quaternary ammonium structure, benzalkonium chloride also displays an anticholinergic activity. The presence of this compound is, thus, responsible for the damage caused to the nasal mucosa by the alterations of the ciliated epithelium. Before this happens, there is a reduction of ciliary activity, which the authors have demonstrated to occur only after 10 days of continuous treatment [6], followed by an increased parasympathetic activity and vascular permeability resulting in swelling. The mucosa displays ultrastructural alterations, characterised by a reduced number of vibratile cilia and metaplasia of the coating epithelium which becomes cubic. Recent studies conducted using the electronic microscope have revealed alterations of the mucosa, characterised by a reduced number of ciliated cells, alteration of the vibratile cilia ultrastructure, rupture of the basal layer, and an increased number of endothelial cells resulting in increased risk of interstial oedema [14]. In addition to compromising the nasal and paranasal cavities ventilation, these phenomena produce alterations of the mucociliary clearing capacity which may result in stasis of secretions, or persistence of inflammatory mediators on the nasal mucosa, but mainly in the failure to eliminate viral, bacterial and fungi pathogens that may trigger secondary infections. Rhinitis medicamentosa is an effect associated, in particular, with products containing ephedrine, whereas with modern vasoconstrictors this effect is less relevant and less frequent.

A number of studies have shown that prolonged use of modern short latency and long-acting vasoconstrictors (tramazoline, oxymetazoline, xylometazoline, tetrazoline etc.) does not induce either local or systemic alterations. An interesting study by Yoo [15] has shown, in 10 healthy volunteers, that prolonged use of oxymetazoline, for example taken once daily at night for up to 4 weeks, does not produce any relevant side effect. A similar study by Watanabe [16] demonstrated that rebound and tachyphylaxis effects do not develop with oxymetazoline even when administered three times daily for 4 weeks. The study was conducted on 30 healthy volunteers whereby the peak nasal respiratory flow was evaluated by posterior rhinomanometry and acoustic rhinometry. Petruson [17] administered xylometazoline, (1 mg/ml) 0.15 ml, 3 times daily, to 20 healthy volunteers without finding any functional nasal alteration even after 6 weeks of treatment, by using rhinomanometry. Graf et al. [18] administered oxymetazoline, (0.5 mg/ml) 0.1 ml, 3 times daily, to 8 healthy volunteers, demonstrating that congestion or rebound phenomena do not develop after 10 days of treatment, but only after 30 days. The same study shows that administration of 0.5 mg/ml oxymetazoline hydrochloride 3 times daily for 10 days, does not induce nasal alterations established by acoustic rhinometry, rhinomanometry and subjective symptomatology score, although a potentially damaging action appears to be associated with benzalkonium chloride (0.1 mg/ml), and, therefore, suggests that the vasoconstrictor should not be taken for > 10 days.

According to some 'extreme' studies the use of imidazole derivatives is safe even for prolonged periods. The authors experience suggests that tramazoline chloride, oxymetazoline and xylometazoline should be administered twice daily for 10 days, after which time adaptation phenomena, due to the rebound effect, presumably, reduce their efficacy [5,6].

As long as the alterations remain within certain limits they may be reversible in two weeks after suspension of the treatment. However, in the case of prolonged use (> 30 days) the mucosa alterations are irreversible. In addition to the loss of aspecific defence mechanisms, there is increased nasal resistance and alteration of the circadian nasal cycle [19]. The medical management of rhinitis medicamentosa consists of the progressive reduction of the topical drug, usually starting with the more patent nostril, up to its complete withdrawal. The use of isotonic and hypertonic washes is essential for the cleansing of the nasal fossae (i.e., the elimination of sero-mucous secretions, inflammatory mediators and potentially harmful particles). Nasal congestion may be progressively relieved by using topical corticosteroids, which are capable of containing rebound congestion of the mucosa, and in more severe cases, the use of antihistamines and systemic corticosteroids may be indicated.

There are virtually no systemic side effects at the recommended dose; however, it is important for all otorhinolaryngologists and anaesthesiologists to be aware of the clinical problems associated with topical vasoconstrictors. Recently, guidelines were published on the topical use of phenylephrine in the operating room: the use of α-agonists topically applied can cause an idiosyncratic hypertension that, if treated with selective β-blockers, could result in a rebound refractory bradycardia and vasodilatory pulmonary oedema with several morbid outcomes [20]. In the case of prolonged use or overdose, events that stimulate the cardiovascular system, or the CNS may occur, such as: increase of arterial pressure and heart rate; hyper-reactivity of cerebral activity resulting in insomnia; hallucinations; anxiety and seizures; increase of vesical sphincter tone resulting in inhibition of micturition; increase of thyroid function and glycaemia; and increase of intraocular pressure.

The awareness of these local and systemic side effects suggests a more moderate and rational use of nasal

decongestants, whose efficacy in the rapid resolution of nasal obstruction is undeniable.

There are several other therapies that have gained popularity in relieving nasal obstruction over recent years, such as herbal remedies and homeopathic products. At an experimental level, flavonoids have shown vasoconstricting action through the inhibition of acetylcholine-induced endothelial nitric oxide-dependent relaxation [21]. In clinical practice, the efficacy of xiao qing long tang (a homeopathic decongestant) was tested in the treatment of 45 patients affected by perennial allergic rhinitis in comparison with oral antihistamines (emedastine difumarate and azelastine hydrochloride), as well as fluticasone propionate nasal spray. Acoustic rhinometry and visual analogue scale (VAS) were used for simultaneous objective measurement of nasal cavity, and objective assessment of nasal sensation of airflow. All treatments showed a significant increase in nasal volumes and minimal cross-sectional areas, and these finding were in close agreement with that obtained with VAS [22].

Used principally during nasal surgery, intranasal cocaine is a potent decongestant used as a topical application to decongest the nose and reduce the nasal blood flow to optimise the operative field. Cocaine is methyl benzoyl ecgonine, a benzoic acid ester, and is the only naturally occurring local anaesthetic. In addition to anaesthetic effect, cocaine has vasoconstrictive properties. Cocaine acts by preventing the re-uptake and binding of free catecholamines (mainly noradrenalin) to their receptors at adrenergic terminals, rather than by any direct action on smooth muscle fibres.

The use of a combination of cocaine, sodium bicarbonate and adrenaline, given the eponymous title of 'Moffett's Solution', is standard practice in many rhinological procedures to provide local anaesthesia, vasoconstriction and decongestion [23].

A double-blind study compared the effectiveness of two local anaesthetics with vasoconstrictive activity (10% cocaine and 4% lidocaine with adrenaline 1:1000). Anterior rhinomanometry was used to assess changes in nasal mucosal blood volume from a reduction in congestion of the nasal mucosa to the resulting reduction in nasal resistance. The anaesthetic effects of both agents were comparable, with subjects reporting only a mild discomfort during nasendoscopy. The authors conclude that 4% lidocaine with adrenaline (1:1000) solution is as effective as 10% cocaine [24].

The anaesthetics routinely used, 4% lidocaine with phenylephrine, or 4% cocaine, have been demonstrated to also have varying inhibitory effects on bacterial cultures of *Branhamella catarrhalis*, *Enterobacter* spp., *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Streptococcus pneumoniae* [25].

Due to the argument that one drug could augment the toxicity of the other, in Italy and other countries, possible alternatives to cocaine are commonly preferred and are used in surgical procedures and before nasal fibreoptic endoscopy.

3. Conclusions

Over 30 years clinical experience in the field of rhinology suggests that there is a rationale for the use of nasal decongestants in all rhinopathies and rhinosinusitis where nasal flow is reduced. Recent recommendations restrict the use of topical decongestants to a maximum of two weeks [26]. In the authors' experience, the risk of developing rhinitis medicamentosa and tolerance phenomena is virtually nonexistent if the treatment period is limited (10 – 15 days) and followed by wash-out periods of 10 – 15 days between cycles. For prevention of local side effects, the use of substances with short latency (a few minutes), long duration of action (10 – 12 h) and sufficient, but not excessive, strength is recommended. Although short latency has little direct influence on rebound and tachyphylaxis, it avoids repeated administration at short intervals, which would be necessary in the case of slow-acting decongestants. The duration of action, instead, is directly related to local side effects, as it allows to reduce the number of daily doses. As already mentioned, the ideal duration of treatment, in light of the authors' review and experience, should include a drug discontinuation period of at least 10 days, during which time the normal mucociliary transport is restored. The rhinological conditions in which the use of nasal decongestants is recommended require, in any case, careful evaluation by an otolaryngologist, nasal functionality tests such as AAR and AR and, above all, assessment of the mucociliary transport to document ciliary activity and thus the trophism of the mucosa. In the authors' opinion, the therapeutic purpose should not simply be to relieve the nasal obstruction symptom, which is so troublesome for the patient, but the prevention and treatment of possible complications for which nasal congestion is often responsible. The blockage of the sinus ostia as a result of inflammation, infection, allergy, or irritation causes the onset of a pathological sinusal cycle which predisposes to rhinosinusitis. A similar condition affects the Eustachian tube where the nasal problem manifests itself as otitis media and other complications. It follows that the use of nasal decongestants should be alternated with wash-out periods to allow trophism and cleaning of the mucosa, and discriminated from use of topical corticosteroids, antihistamines and mucolytics, depending on the problems highlighted in clinical history and instrumental tests.

If the directions of the physician are accurate, and they are strictly followed by the patients, the chances that phenomena associated with the indiscriminate use of these drugs may occur, and result in rhinitis medicamentosa or local side effects are unlikely.

4. Expert opinion

In recent history, several studies regarding the effects of nasal decongestants have been conducted. Most focused on patient symptom relief, and only few studies underline the positive effects of nasal decongestants on the basis of objective data, such as AAR and AR and mucociliary transport time.

21. HUANG Y, YAO XQ, TSANG SY,
     LAU CW, CHEN ZY: Role of
     endothelium/nitric oxide in vascular
     response to flavonoids and epicatechin.
     Acta Pharmacol. Sin. (2000)
     21(12):1119-1124.

22. YAMAGIWA M: Acoustic evaluation of the
     efficacy of medical therapy for allergic nasal
     obstruction. *Eur. Arch. Otorhinolaryngol.*
     (1997) 254(Suppl. 1):S82-S84.

23. BENJAMIN E, WONG DK, CHOA D:
     'Moffett's' solution: a review of the evidence
     and scientific basis for the topical
     preparation of the nose. *Clin. Otolaryngol.
     Allied Sci.* (2004) 29(6):582-587.

24. KASEMSUWAN L, GRIFFITHS MW:
     Lignocaine with adrenaline: is it effective
     as cocaine in rhinological practice?
     Clin. Otolaryngol. Allied. Sci. (1996)
     21(2):127-129.

25. ALDOUS WK, JENSEN R, SIECK BM:
     Cocaine and lidocaine with phenylephrine
     as topical anesthetic: antimicrobial activity
     against common nasal pathogens.
     Ear Nose Throat J. (1998) 77(7):554-557.

26. LUND VL, AARONSON D,
     BOUSQUET J, DAHAL R, DAVIES RJ:
     International consensus report on the
     diagnosis and management of rhinitis.
     Eur. J. Allergy Clin. Immunol. (1994)
     49:1-34.

27. MAY M, WEST JW: The 'stuffy' nose.
     Otolaryngol. Clin. North. Am. (1973)
     66:665-674.

Affiliation
Desiderio Passàli[†1] MD, PhD,
Lorenzo Salerni[2] MD, PhD,
Giulio Cesare Passàli[2] MD, PhD,
Francesco Maria Passàli[3] MD
& Luisa Bellussi[2] MD, ChD
[†]Author for correspondence
[1]Chief Professor, ENT Clinic University of
Siena Medical School, Policlinico 'Le Scotte'
viale Bracci, 53100 Siena, Italy
Tel: +39 577585470;
E-mail: passali@unisi.it
[2]Assistant Professor, Assistant Professor,
Associate Professor, ENT Clinic University of
Siena Medical School, Policlinico 'Le Scotte' viale
Bracci, 53100 Siena, Italy
[3]PhD Student, ENT Clinic University of Siena
Medical School, Policlinico 'Le Scotte' viale
Bracci, 53100 Siena, Italy