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REVIEW

Rebound congestion and rhinitis medicamentosa: Nasal decongestants in clinical practice. Critical review of the literature by a medical panel

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KEYWORDS
Nasal decongestant;
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Rebound congestion

Summary
Introduction: Systemic and topical nasal decongestants are widely used in otorhinolaryngology and general practice for the management of acute rhinosinusitis and as an adjuvant in certain forms of chronic rhinosinusitis. These products, very effective to rapidly improve nasal congestion, are sometimes available over the counter and can be the subject of misuse, which is difficult to control. The Société Française d'ORL has recently issued guidelines concerning the use of these decongestants in the doctor's office and the operating room.
Materials and methods: The review of the literature conducted by the task force studied in detail the concepts of ''rebound congestion'' and ''rhinitis medicamentosa'' often reported in a context of misuse, particularly of topical nasal decongestants. The clinical and histopathological consequences of prolonged and repeated use of nasal decongestants have been studied on animal models and healthy subjects.

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Results: Discordant results have been obtained, as some authors reported a harmful effect of nasal decongestants on the nasal mucosa, while others did not identify any significant changes. No study has been able to distinguish between inflammatory lesions induced by chronic rhinosinusitis and lesions possibly related to the use of nasal decongestants.
Discussion: The task force explained the rebound congestion observed after stopping nasal decongestant treatment by return of the nasal congestion induced by rhinosinusitis and rejected the concept of rhinitis medicamentosa in the absence of scientific evidence from patients with rhinosinusitis.
Conclusion: Nasal decongestants are recommended for the management of acute rhinosinusitis to reduce the consequences of often disabling nasal congestion. They are also recommended during rhinoscopic examination and for preparation of the nasal mucosa prior to endonasal surgery.
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Introduction

Nasal congestion is the symptom most commonly reported during acute and chronic rhinosinusitis. The prevalence of nasal congestion in the population is estimated to be 30% [1]. Regardless of its origin, nasal congestion severely affects quality of life by its impact on daily life, especially sleep, work or school and social life [2]. It has been estimated, in the United States, that allergic rhinitis is responsible for about 800,000 days off work and 825,000 days away from school and decreased productivity for 4,250,000 days per year [3].

Systemic and topical nasal decongestants are recommended for the symptomatic treatment of nasal congestion during acute nasopharyngeal diseases in subjects over the age of 15. Many products are available in France (Table 1). Their efficacy has been clearly demonstrated in clinical practice [4]. This remarkable efficacy on nasal congestion is the basis for frequently inappropriate prescription renewals and excessive self-prescribed medication, especially as these products are available over the counter. Misuse of nasal decongestants can be accentuated by the fact that some of them are included in over-the-counter oral fixed combinations with other drug substances (cetirizine, paracetamol, ibuprofen).

Rare but sometimes serious adverse reactions have been described, often related to overdose [5,6]. Central neurological effects essentially consist of headache, seizures and stroke [7]. Cardiovascular adverse reactions include hypertensive crisis, tachycardia or palpitations [8,9]. ''Rebound congestion'' and ''rhinitis medicamentosa'' are terms very frequently used in the literature to describe the consequences of misuse of nasal decongestants, especially topical products. These terms are therefore often used to describe persistent symptoms of nasal congestion in patients who have repeatedly used nasal decongestants. In clinical practice, the diagnostic criteria of these concepts of ''rebound congestion'' and ''rhinitis medicamentosa'' nevertheless remain very vague. Rebound congestion refers to the highly subjective clinical criterion of nasal congestion that can be used to designate blocked nose, stuffiness or inflammation. Rhinitis medicamentosa also raises diagnostic problems, as it can be confused with the rebound effect observed after stopping nasal decongestants.

The Société Française d'ORL issued consensual clinical practice guidelines on the use of nasal decongestants in October 2011. Based on the methodology published by the Haute Autorité de la santé (French National Authority for Health) in 2006, these guidelines were elaborated by a task force and were then validated by a scoring group. A detailed analysis of the literature reviewed the concepts of rebound congestion and rhinitis medicamentosa. The present review is therefore designed to clarify these two entities in order to determine their diagnostic relevance in clinical practice.

Rebound effect of topical decongestants

Definition

According to the authors who described this effect, rebound congestion is defined by deterioration of the feeling of nasal congestion for which topical nasal decongestants were initially prescribed during repeated use or after stopping this treatment [10,11]. The term ''rebound congestion'' was used for the first time in 1944 by Feinberg and Friedlaender to describe the nasal congestion experienced after the use of naphazoline [12]. However, this concept of rebound congestion remains very controversial. The literature concerning this concept is contradictory, raising a doubt about the real existence of this effect. Published studies that have tried to demonstrate rebound congestion by measuring nasal resistance were conducted in healthy subjects preventing extrapolation of the results to patients with rhinosinusitis.

Evidence in favour of rebound congestion

This potential action of topical nasal decongestants has been observed in several studies, all conducted in healthy subjects using various methods of evaluation. Morris et al. observed an increase of nasal resistance after 3 days of treatment with oxymetazoline in healthy subjects [13]. Several studies by Graf also described rebound congestion. In a study on 18 healthy subjects treated with oxymetazoline 50 μg per day or xylometazoline 280 μg per day for 30 days, the author demonstrated the presence of mucosal oedema on rhinostereometry (optical measurement of the thickness of the mucosa in vivo) after 10 days of treatment,

Table 1 List of products and their indications in France in 2012. Topical nasal decongestants are usually marketed in fixed combinations. Imidazoles are only used in topical nasal decongestants, including some office medicine products containing prednisolone.

Decongestants	French trade name	Drug combination	Route of administration	Associated drug dose	Age of prescription	Type of prescription
Sympathomimetic amines						
Phenolic						
Adrenaline	Adrenaline AGT or REN		IV / IM / SC / nasal			List I
Hydroxyamphetamine	Not marketed					
Phenylephrine	Hexarhume	Biclotymol + Chlorpheniramine	Oral	30 mg / 2 mg	> 15 years	None
	Humoxal SOL nasale	Benzalkonium Chloride	Nasal spray	6 mg	> 15 years	List II
Tuaminoheptane	Rhinofluimucil	Acetylcysteine + Benzalkonium chloride	Nasal spray	100 mg / 1.25 mg	> 15 years	List II
Nonphenolic						
Ephedrine	Rhinamide SOL nasale	Benzoic acid	Nasal spray	0.04 g	> 15 years	List II
Phenylpropanolamine	Not marketed					
Pseudoephedrine	Actifed LP rhin all	Cetirizine	Oral	5 mg	> 15 years	None
	Actifed rhume	Paracetamol + Triprolidine	Oral	500 mg / 2.5 mg	> 15 years	None
	Actifed rhume jour/nuit	Paracetamol / Paracetamol + diphenhydramine	Oral	500 mg / 25 mg	> 15 years	None
	Adviltab rhume	Ibuprofen	Oral	200 mg	> 15 years	None
	Cequinyl	Paracetamol + ascorbic acid	Oral	250 mg / 50 mg	> 15 years	None
	Doli rhume	Paracetamol	Oral	500 mg	> 15 years	None
	Dolirhumepro	Paracetamol / paracetamol + doxylamine	Oral	500 mg / 7.5 mg	> 15 years	None
	Humex rhinite allergique	Cetirizine	Oral	10 mg	> 16 years	None
	Humex rhume	Paracetamol / Chlorpheniramine	Oral	500 mg / 4 mg	> 15 years	None
	Nurofen rhume	Ibuprofen	Oral	200 mg	> 15 years	None
	Rhinadvil	Ibuprofen	Oral	200 mg	> 15 years	None
	Rhinureflex	Ibuprofen	Oral	200 mg	> 15 years	None
	Rhumagrip	Paracetamol	Oral	500 mg	> 15 years	None
	Sudafed		Oral		> 15 years	None
Imidazoline derivatives						
Tetryzoline	Not marketed					
Xylometazoline	Not marketed					
Naphazoline	Derinox	Prednisolone	Nasal Spray	20 mg / 100 mL	> 15 years	List II
	Xylocaïne naphazolinee	Lidocaine hydrochloride	Nasal drops	500 mg / 100 mL	> 6 years	List II
Oxymetazoline	Aturgyl		Nasal Spray		> 15 years	List II
	Deturgylone	Prednisolone	Nasal Spray		> 15 years	List I
	Pernazene		Nasal Spray		> 15 years	List II
Tramazoline	Not marketed					
Clonazoline	Not marketed					

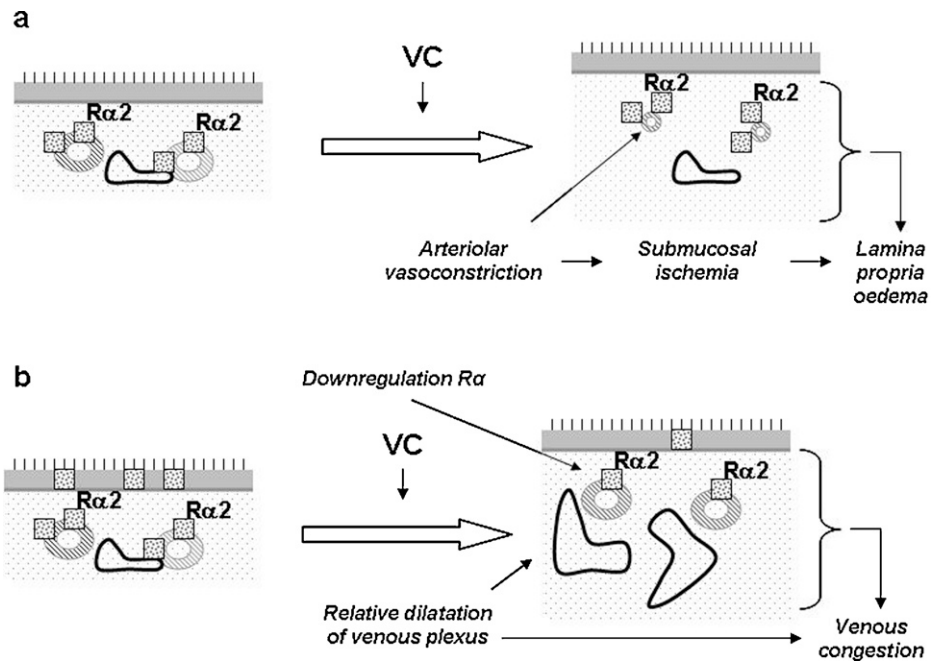

Figure 1 Pathophysiological hypotheses for the rebound effect of nasal decongestants: a: the oedema responsible for the nasal congestion experienced by the patient could be caused by mucosal ischaemia induced by intense stimulation of arteriolar $\alpha 2$ adrenergic receptors (Rα2) by nasal decongestants leading to prolonged vasoconstriction; b: the other hypothesis consists of a feedback effect (downregulation) by repeated stimulation of $\alpha 2$ receptors by nasal decongestants, resulting in a reduction of the number of functional receptors after mucosal, arteriolar and venous internalization, inducing relative congestion of the sinusoid venous plexuses responsible for oedema.

which continued to worsen until the 30th day. This effect was not worsened by increasing the dosage of nasal decongestants, but by the presence of benzalkonium chloride in the preparation [10]. In a study conducted in 19 healthy subjects treated with oxymetazoline 200 μg three times daily for 17 days, Vaidyanathan et al. showed a significant reduction of peak inspiratory flow and a non-significant increase of inspiratory nasal resistance measured by anterior rhinomanometry compared to the measurements performed in these same subjects before treatment [11]. Akerlund and Bende also described rebound congestion, but failed to demonstrate any increase of nasal resistance on rhinomanometry after treatment with xylometazoline in healthy subjects [14].

From a pathophysiological point of view, the vascular network of the nasal mucosa can be divided into resistance vessels (arterioles) and capacitance vessels (venous plexus) surrounded by sympathetic nerve fibres innervating $\alpha-$ and β-adrenergic receptors. α-adrenergic receptors are predominant in the nasal mucosa and stimulation of these receptors induces vasoconstriction. The vasomotor activity of capacitance vessels is regulated by both $\alpha 1$ and $\alpha 2$ receptors, while that of resistance vessels is regulated by $\alpha 2$ receptors. Nasal decongestants mimic the action of noradrenaline on $\alpha 1$ and $\alpha 2$ receptors, either directly by stimulating the receptor or indirectly by inducing the release of noradrenaline from storage vesicles [15].

Two pharmacobiological hypotheses (Fig. 1) have been formulated on the basis of these studies in healthy subjects to explain rebound congestion:

- hypothesis 1: this effect may be due to ischaemia of the nasal mucosa; stimulation of $\alpha 2$ receptors induces intense vasoconstriction of submucosal arterioles [16]. This ischaemia would predispose to the development of interstitial oedema [17,18] (Fig. 1a);
- hypothesis 2: the number of membrane α adrenergic receptors would be decreased by downregulation and endogenous noradrenaline production would be decreased by presynaptic negative feedback. These effects would induce relative dilatation of the submucosal sinusoid venous plexuses due to loss of dynamic venous vasoconstriction [17,19,20] (Fig. 1b). Adrenergic receptors could also become refractory to nasal decongestants, causing the patient to increase the doses of nasal decongestants (tachyphylaxis) [16,21]. This phenomenon would be associated with decreased sensitivity to endogenous catecholamines [19], especially affecting $\alpha 1$ receptors [22].

The results of these studies in favour of the rebound effect of decongestants cannot be directly extrapolated to clinical practice, as they were conducted in healthy subjects in whom the nasal mucosa is not subjected to the cytokine environment associated with inflammation.

Evidence against rebound congestion

It is difficult to extrapolate the results of the above studies to clinical practice, as inflamed nasal mucosa treated with a topical decongestant does not present the same

absorption properties as healthy nasal mucosa. Evaluation of the congestion possibly induced by a topical nasal decongestant is consequently biased by the underlying disease.

A review of the literature also reveals a similar number of studies, also conducted in healthy subjects that failed to demonstrate any rebound effect of decongestants. For example, Yoo et al. did not observe this phenomenon after 4 weeks of treatment with oxymetazoline 200 μg in the evening in 10 healthy subjects [23]. Watanabe et al. also did not observe any modification of inspiratory nasal flow after 4 weeks of treatment with oxymetazoline 200 μg 3 times daily in 30 healthy subjects [24]. Petruson and Hansson reached similar conclusions based on rhinomanometric analysis of 20 healthy subjects treated with oxymetazoline 150 μg three times daily for 6 weeks [25].

Finally, clinical experience shows that rebound congestion is not observed in most patients despite prolonged self-prescribed use of topical nasal decongestants without dose escalation. However, these clinical observations do not eliminate the need for nasal decongestant prescribing rules, as their possible harmful effects cannot be formally excluded.

The task force's conclusions after evaluation by the scoring group

The rebound effect of topical decongestants, i.e. increased nasal resistance after stopping treatment, has only been described experimentally in healthy subjects. The ''rebound congestion'' classically described in patients, i.e. recurrence or deterioration of nasal congestion after stopping treatment, could actually correspond to persistence of the disease initially justifying prescription of the decongestant.

The rebound effect of topical nasal decongestants described in the literature in healthy subjects has not been studied in patients with rhinosinusitis.

Rhinitis medicamentosa

Definition

The term ''rhinitis medicamentosa'' is used in the English language literature to describe persistent rhinitis induced by prolonged use of topical nasal decongestants (sympathomimetic amines and imidazoles) [21]. Rhinitis medicamentosa usually occurs following an episode of acute viral rhinitis and is characterized by persistent nasal congestion, usually isolated, and occurring increasingly rapidly after application of nasal decongestants [20]. This congestion causes the patient to increase the frequency of application and the quantity applied, resulting in dependence on topical nasal decongestants [17]. Clinical rhinoscopic examination is non-specific, showing areas of red, thickened mucosa and dull zones [21].

The harmful effects of prolonged treatment by topical nasal decongestants on the nasal mucosa have also been described in animal models and in healthy subjects. As for rebound congestion, it is difficult to extrapolate these results to patients in whom the nasal mucosa is already inflamed.

Evaluation on animal models

Published studies on the mucosal effects of nasal decongestants are relatively old and were conducted in animal models [26]. A first report, published in 1947, on rabbits treated four times daily with intranasal 1% ephedrine or naphazoline, showed loss of ciliated cells on D5, epithelial lesions at 1 week, oedema at 2 weeks, epithelial hypertrophy with fibrosis at 3 weeks, complete disorganization of the mucosal architecture at 5 weeks and squamous cell metaplasia of the respiratory mucosa with vascular sclerosis at 8 weeks [20,27]. Using a rabbit model, Talaat el al compared the normal nasal mucosa and the nasal mucosa treated with 1% ephedrine after 2 weeks and 3 weeks. Architectural disorganization of the ciliary axoneme, loss of intercellular junctions and submucosal oedema with collagen infiltration were observed on electron microscopy after 2 weeks of treatment. Reduction of the number of ciliated cells and thickening of the basement membrane were observed after 3 weeks [28]. An analysis of the effects of 0.05% naphazoline administered three times daily to guinea-pigs sacrificed at regular intervals revealed similar abnormalities after 2 weeks of treatment with an initial increase of mucosal cells followed by loss of these cells starting at 6 weeks. Immunohistochemical analysis showed increased cholinesterase activity on periglandular nerve fibres, suggesting a reduction of the parasympathetic response to nasal decongestants [29]. More recently, Suh et al. evaluated the effects of nasal decongestants by comparing three groups of 30 rabbits treated with phenylephrine, oxymetazoline or saline for 1, 2 or 4 weeks. Sub-mucosal oedema and loss of cilia on ulcerated respiratory epithelium were observed after 2 weeks of treatment in the two groups treated with nasal decongestants. These lesions were more severe at 4 weeks. In the phenylephrine group, features of purulent acute sinusitis were observed in four rabbits and six rabbits after 2 and 4 weeks, respectively. The authors attributed this infectious complication to alteration of the mucosa barrier due to destruction of ciliated cells [30].

Evaluation in humans

The results observed in man are less convincing, preventing any valid conclusions concerning the possible harmful effects of topical nasal decongestants on the nasal mucosa. Furthermore, when oedema was described in patients treated with topical nasal decongestants, it is often unclear whether rhinoscopy had been performed in these patients before inclusion in the study to eliminate preexisting sinonasal disease.

A study in 20 healthy adults treated with xylometazoline three times daily (0.75 mg) for 6 weeks did not reveal any morphological changes of the mucosa, basement membrane or lamina propria [25,31,32]. Five of these 20 patients developed acute viral rhinosinusitis during the study without any epithelial abnormalities attributable to treatment [25,31,32]. In 2004, Lin et al. compared the nasal mucosa of eight adult patients with non-allergic chronic rhinitis, eight patients with symptoms suggestive of nasal decongestant misuse and five healthy subjects. The authors did not define

the clinical criteria used to include these eight patients with rhinitis medicamentosa. Microscopic examination demonstrated epithelial metaplasia with epithelial hyperplasia, loss of ciliated cells and an increase of mucus-secreting cells and submucosal glands in the nasal decongestant group [31]. Another study in eight healthy adults did not reveal any significant mucosal oedema after 10 days of treatment with oxymetazoline 0.05 mg three times daily with poor reactivity on the histamine provocation test [17]. In contrast, oedema measured by rhinostereometry was described after 30 days of use of this nasal decongestant with deterioration of oedema after application of histamine [33—36]. Histological abnormalities (destruction of ciliated cells, arteriolar dilatation, mucus-secreting cell hyperplasia) were described by Wang and Bu in 30 adults treated with naphazoline and presenting symptoms suggestive of rhinitis medicamentosa [37]. Knipping et al. reported similar findings in 22 patients with a history of topical nasal decongestant use for more than 6 months compared to 10 non-treated control subjects. Light microscopy revealed loss of ciliated cells, thickening of the epithelial basement membrane, and submucosal perivascular oedema [38].

Are the histological lesions allegedly induced by topical nasal decongestants reversible?

No published clinical study has described the natural history of the epithelial lesions observed after stopping prolonged use of topical nasal decongestants. Various authors have also emphasized the difficulty of describing lesions specifically induced by topical nasal decongestants when these lesions occur in a context of preexisting rhinosinusitis, as the underlying disease prevents reliable baseline assessment of the nasal mucosa [20].

Studies on the prolonged use of topical nasal decongestants have essentially focussed on the reversibility of clinical signs and the treatment modalities useful for nasal decongestant withdrawal. These studies also did not define rigorous diagnostic criteria (clinical or histological) for the diagnosis of rhinitis medicamentosa. The nasal congestion described in these studies could therefore be attributed to nasal decongestants or to the presence of concomitant rhinitis. Several studies have highlighted the efficacy of topical corticosteroids to relieve the congestion experienced by these patients. A randomized, double-blind, placebo-controlled study in 19 healthy subjects treated with oxymetazoline 200 μg three times daily for 14 days showed that nasal congestion resolved after administration of fluticonasone 200 μg twice daily for 3 days, despite continued use of the nasal decongestant [11]. The authors suggested that this effect was due to increased expression of α-adrenergic receptors induced by corticosteroids, thereby eliminating the tachyphylaxis effect of nasal decongestants (rapid internalization of α-adrenergic receptors by repeated stimulation by adrenergic agonists) [11]. In a study conducted in 10 subjects with rhinitis medicamentosa after 30 days of oxymetazoline, Graf showed a reduction of mucosal oedema 14 days after stopping the nasal decongestants. However, resolution of mucosal oedema could not be attributed to withdrawal of the nasal decongestant, as these patients were treated with budesonide 200 μg twice daily after stopping oxymetazoline [10]. Another randomized double-blind study in 20 patients with rhinitis medicamentosa present for at least 2 years evaluated the effect of fluticasone propionate 200 μg daily versus placebo for 14 days on nasal congestion, nasal resistance, peak inspiratory flow and nasal areas (acoustic rhinomanometry) after stopping nasal decongestants. An improvement of the symptoms was observed on D4 with corticosteroids and on D7 with placebo. The reduction of nasal oedema, as measured by nasal resistance, was observed on D7 in both groups, but was significantly greater in the 10 subjects treated with topical corticosteroids [39].

The action of topical corticosteroids on nasal mucosa submitted to nasal decongestants has been evaluated in an animal model. In a study on 20 guinea-pigs with rhinitis medicamentosa, Elwany and Abdel-Salaam described a reduction of interstitial oedema by treating the nasal mucosa with fluticasone propionate 50 μg per day for 2 weeks after stopping nasal decongestants [29]. Tas et al. reported similar results after stopping nasal decongestants by comparing six guinea-pigs treated with mometasone furoate 50 μg per day for 14 days, six treated animals with isotonic saline and six non-treated animals. A reduction of oedema and inflammatory infiltrate was observed only in the rhinitis medicamentosa group treated with topical corticosteroids [40]. Studies on human tissues have also demonstrated the value of topical corticosteroids to improve the epithelial lesions observed in rhinitis, but no specific study has been conducted on rhinitis medicamentosa. A microscopic study in 46 patients with chronic rhinitis treated with mometasone furoate 200 μg/day for 12 months described an increase of ciliated epithelium zones and a reduction of metaplastic zones [41].

These various studies emphasize the efficacy of topical corticosteroids in the treatment of nasal congestion induced by mucosal oedema. Topical corticosteroids appear to constitute an alternative to nasal decongestants for the treatment of nasal congestion rather than an antidote for the treatment of hypothetical rhinitis medicamentosa.

Conclusions of the task force after evaluation by the scoring group

Rhinitis medicamentosa is an entity with no precise clinical or histopathological criteria in a pathological context of rhinosinusitis. This entity could be more appropriately considered to reflect the patient's dependence on topical decongestants to relieve nasal congestion. In this setting, the practitioner must review the aetiological work-up (allergy, irritant and environmental factors) in order to more clearly define this poorly identified functional nasal sinus disease and propose possible alternative treatments.

Management of persistent nasal congestion despite decongestants

According to their marketing authorisations, topical or systemic nasal decongestants cannot be used for more than 3 to 5 days. When the patient reports prolonged use of nasal decongestants, particularly topical nasal decongestants, to treat persistent nasal congestion, the clinician

must propose alternative treatments. First of all, the clinical assessment must be repeated to avoid missing a local or systemic aetiology amenable to specific treatment. The clinical interview (triggering factors, associated systemic and local signs), endoscopic examination of the nasal mucosa and architecture, complementary examinations (allergy assessment, computed tomography with dental evaluation, MRI when necessary, functional investigations, nasal cytology according to the context) should allow identification of the various forms of rhinitis and rhinosinusitis.

Alternative treatment options to nasal decongestants can be proposed. Hypertonic saline has a weak anti-oedema action, but its clinical value was nevertheless demonstrated by Garavello et al. in a series of 20 patients treated with 3.0% hypertonic saline three times daily during the pollen season (6 weeks) [42] and by Rabago et al. in a series of 40 patients treated by hypertonic saline as required for 12 months versus 14 control subjects using isotonic saline [43]. Few studies are available in the literature allowing comparison of saline versus decongestants, especially in acute rhinitis. In the context of bacterial rhinosinusitis, Inanli et al. demonstrated no difference in the degree of improvement of mucociliary clearance between oxymetazoline, 3.0% or 0.9% saline nasal irrigation and an untreated control group [44].

Topical corticosteroids have a recognized efficacy in the treatment of nasal congestion. In a randomized double-blind study in 967 patients with acute rhinosinusitis, Nayak et al. showed that topical corticosteroids in combination with amoxicillin + clavulanic acid were more effective in terms of improvement of nasal congestion scores than antibiotics alone by the 4th day [45]. However, no published studies are available to compare the efficacy of topical corticosteroids versus decongestants in the management of nasal congestion.

Other nasal medications (antihistamines, cromoglycate sodium, anticholinergics) have no or only a moderate action on nasal congestion and do not constitute per se an alternative to nasal decongestants.

Turbinate surgery has a major place in the management of nasal congestion induced by mucosal oedema. Various technical modalities (turbinoplasties, radiofrequency, laser, microresection) can be proposed as a complement to the alternative treatments described above.

Conclusion

Very few studies have been published on rebound congestion and rhinitis medicamentosa and some of them report contradictory results. Studies precisely analysing the consequences of prolonged use of nasal decongestants were conducted on animal models or healthy subjects. Various pathophysiological hypotheses have been proposed to explain the accentuation of congestion induced by nasal decongestants, but they cannot be extrapolated to the clinical setting. Other studies are therefore necessary to specifically compare patients with rhinitis or rhinosinusitis treated by various modalities.

The analysis conducted by the task force tends to refute the concepts of rebound congestion and rhinitis medicamentosa. Nasal decongestants must nevertheless be used in a controlled medical setting, in compliance with prescription guidelines in view of the potentially serious systemic effects. In patients with persistent nasal congestion despite the use of nasal decongestants or accentuation of nasal congestion after stopping nasal decongestants, the physician must review the aetiological work-up of an often poorly defined nasal sinus disease. Alternative medical and/or surgical treatments must then be proposed.

Disclosure of interest

Dr M. François reports a conflict of interest: participation in a study on the value of tuaminoheptane present in Rhinofluimicil® (Zambon).

The other authors report no conflict of interest in relation to this article.

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