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# Rhinitis medicamentosa –mechanism, treatment options and methods of prevention

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## Abstract

## Introduction:

Rhinitis medicamentosa (RM) is a chronic inflammatory condition of the nasal mucosa caused by excessive use of topical nasal decongestants. This leads to tachyphylaxis, increased vascular permeability, chronic inflammation, and structural changes in the nasal mucosa, resulting in medication dependence and persistent nasal congestion.

# **Study Objective:**

This study aims to discuss the mechanisms underlying RM, its clinical consequences, diagnostic methods, and therapeutic strategies. Additionally, it highlights the importance of patient education and healthcare professional awareness in preventing RM and reducing its prevalence.

## **Materials and Methods:**

A comprehensive literature review was conducted, analysing current scientific research on RM, including its pathophysiology, diagnostics and treatment methods. Additionally, the review explored the systemic implications, association with addiction, and the importance of prevention and education in managing the condition.

## **Conclusions:**

There is a need for better education for both patients and healthcare professionals regarding RM. A key element of RM prevention is informing patients about the importance of limiting the use of these medications to a maximum of 5–7 days. Furthermore, further research is necessary to develop more effective therapeutic methods, including the potential use of

alternative substances such as xylitol or hyaluronic acid in the regeneration of the nasal mucosa.

## Keywords

Rhinitis medicamentosa; pharmacology; nasal decongestants;

#### **1. Introduction**

Rhinitis medicamentosa (RM) is a form of non-allergic rhinitis that arises primarily due to the prolonged and excessive use of topical nasal decongestants, including imidazole derivatives (such as xylometazoline, oxymetazoline and naphazoline) and sympathomimetic amines (such as ephedrine, pseudoephedrine, and phenylephrine) [1] [2] [3].

Nasal drops are an essential component in the treatment of various infections accompanied by a runny nose. These preparations contain different active substances, resulting in distinct pharmacological effects. The package inserts of commonly used nasal decongestants typically include a recommendation not to use the medication for more than five days. However, many patients do not adhere to these guidelines. The risk of developing RM significantly increases when the drug is used for more than 7–10 days [2].

Prolonged use of drugs from this class induces tachyphylaxis, characterized by paradoxical mucosal swelling and persistent nasal obstruction [4], which often prompts individuals to increase both the frequency and dosage of decongestant application, ultimately leading to dependence on these medications [5]. The prevalence of RM ranges from 1% to 9%, with the highest incidence observed among young and middle-aged adults with a rising trend in recent years, partly driven by the increasing prevalence of allergic rhinitis and the widespread misuse of  $\alpha$ -adrenergic agonists in its management [6][7].

The aim of this paper is to review the available scientific research on RM, including an analysis of its pathogenesis, risk factors, treatment methods, and therapeutic approaches. Particular attention is given to the role of health education, both in the context of prevention and management of the condition, with the goal of improving patients' quality of life and reducing the misuse of nasal decongestant medications.

## 2. Mechanism of Action of Nasal Decongestant Drops

Nasal congestion is largely a result of multiple physiological processes, including dilation of blood vessels within the nasal submucosa, increased vascular permeability, tissue edema, local inflammation, and excessive mucus secretion [8]. The regulation of vascular tone within the nasal mucosa is predominantly mediated by the sympathetic nervous system, which also interacts with the parasympathetic system to fine-tune the balance between vasodilation and vasoconstriction. Upon stimulation, sympathetic nerve endings release noradrenaline, which subsequently binds to and activates  $\alpha$ 1 and  $\alpha$ 2 adrenergic receptors.

The vascular system of the nasal mucosa is composed of two main types of blood vessels: resistance vessels, which are primarily regulated by alpha-2 adrenoreceptors, and capacitance vessels, which are influenced by both alpha-1 and alpha-2 adrenoreceptors [9]. Topical nasal decongestants are broadly classified into two major categories: beta-phenylethylamine derivatives and imidazoline derivatives. Beta-phenylethylamine derivatives exert their decongestant effects by mimicking the activation of the sympathetic nervous system. These compounds induce vasoconstriction primarily by stimulating alpha-1 adrenoreceptors, leading to a reduction in nasal mucosal swelling. In contrast, imidazoline derivatives predominantly act through alpha-2 adrenoreceptors, modulating vascular tone and contributing to nasal decongestion.

 $\alpha$ 1 adrenergic receptors, primarily located in postcapillary venules, initiate intracellular signalling cascades that increase calcium levels, leading to the contraction of blood vessels and subsequent vasoconstriction [8]. Similarly,  $\alpha$ 2 adrenergic receptors, predominantly found in precapillary arterioles, enhance calcium influx, further stimulating the contraction of vascular smooth muscle cells. As a result, reduced blood flow to the nasal mucosa, along with diminished extracellular fluid accumulation, effectively alleviates congestion. The activation

of adrenergic receptors, therefore, plays a key role in minimizing mucosal blood volume and swelling, ultimately improving nasal airflow.

In RM, chronic and pathological changes in the nasal mucosa occur as a consequence of prolonged vasoconstrictor use [10]. These pathological alterations include structural damage and abnormalities in the cilia, squamous cell metaplasia, and excessive mucus secretion. Additionally, increased intercellular permeability, vascular proliferation, and fibrosis contribute to the progressive deterioration of nasal function. Edema of the epithelial layer, goblet cell hyperplasia, and upregulation of epidermal growth factor receptors further exacerbate mucosal dysfunction. Histological analyses have also revealed an increased presence of lymphocytes, fibroblasts, and plasma cells, which suggest a persistent chronic inflammatory response.

## 3. Pathophysiology of Rhinitis Medicamentosa

According to Wahid and Shermetaro [9], although the exact pathophysiology of RM is not fully understood, several hypotheses have been proposed to explain its mechanisms.

First theory suggests that prolonged vasoconstriction induced by nasal decongestants leads to ischemia of the nasal mucosa, which in turn predisposes individuals to interstitial edema as a compensatory response.

Another hypothesis posits that the continuous activation of vasoconstrictive pathways over time leads to their eventual fatigue, resulting in reactive hyperemia and worsening nasal congestion. This process is believed to be associated with a decreased sensitivity of adrenoreceptors to endogenous catecholamines, ultimately leading to tachyphylaxis—a phenomenon in which progressively higher doses of nasal decongestants are required to achieve the same therapeutic effect.

Additionally, researchers have proposed that alterations in vasomotor tone play a role in RM by contributing to increased vascular permeability, which subsequently leads to mucosal edema and congestion.

Another possible mechanism involves an imbalance between beta- and alpha-adrenoreceptor activity. In this model, the prolonged stimulation of beta-adrenoreceptors may override the vasoconstrictive effects mediated by alpha-adrenoreceptors, leading to rebound vasodilation and persistent nasal congestion.

Collectively, these hypotheses suggest that RM is a complex condition involving multiple overlapping mechanisms rather than a single isolated pathway.

Histopathological studies further support the idea that prolonged use of nasal decongestants induces microscopic alterations in the nasal mucosa, which may contribute to long-term structural damage and dysfunction [11]. These changes include goblet cell hyperplasia, leading to excessive mucus production, squamous cell metaplasia, which alters the normal epithelial structure, and ciliary destruction, which impairs mucociliary clearance. Furthermore, chronic exposure to vasoconstrictive agents has been associated with persistent inflammation and fibrosis, both of which may exacerbate nasal obstruction and mucosal dysfunction over time [12].

## 4. Systemic Implications of Rhinitis Medicamentosa

Chronic misuse of topical adrenergic decongestants leads to rebound congestion, a condition characterized by nasal obstruction upon discontinuation [13]. This phenomenon occurs due to excessive blood flow and swelling of the nasal mucosa, triggered by the dilation of cavernous sinuses following initial vasoconstriction. As a result, patients increasingly rely on higher and more frequent doses of nasal drops, further exacerbating their symptoms. Additionally, mucosal dryness and paradoxical excessive serous secretion may develop.

Over time, the nasal mucosa undergoes progressive pathological changes. In the early stages, it appears pale, edematous, and congested, while later stages are marked by atrophy, crusting, and a decline in glandular and secretory cells. Histopathological findings reveal ciliary loss, epithelial metaplasia, and fibrosis. These mucosal alterations are not solely caused by the active drug but also by preservatives and excipients present in nasal drop formulations.

The impact of RM extends beyond nasal symptoms. According to Pham et al. [14], excessive use of nasal decongestants—especially when combined with vasoactive substances such as serotonergic antidepressants, cannabis, or alcohol (particularly in cases of binge drinking) -

may increase the risk of reversible cerebral vasoconstriction syndrome. A case report by Daniel Leupold and Katja E. Wartenberg [15], concluded that the misuse of nasal decongestants containing imidazole derivatives represents a significant risk factor for ischemic strokes in young adults.

Additionally, RM can impair the senses of smell and taste, reduce physical activity, and contribute to snoring, sleep apnea, and insomnia [16]. It may also elevate the risk of chronic sinusitis, otitis media, nasal polyps, and atrophic rhinitis.

# 5. Rhinitis Medicamentosa and Its Association with Addiction

Rhinitis medicamentosa, as described by Lakatos et al. [17], exhibits key components of addiction, as defined by Griffiths. It significantly impairs patient's quality of life, contributing to sleep disturbances, a sensation of suffocation, and psychological distress related to nasal congestion. These factors create a cycle of dependence, making it increasingly difficult for patients to discontinue decongestant use.

Furthermore, psychological dependence and withdrawal symptoms—including headaches, restlessness, and anxiety—are commonly reported upon discontinuation of nasal decongestants [18]. These withdrawal effects, combined with persistent nasal obstruction, further reinforce the cycle of dependency, making RM a challenging condition to manage.

The potential relationship between RM and opioid use disorder has also been investigated. Patel et al. [19] identified a higher prevalence of opioid dependence among patients with RM compared to those with chronic rhinitis in general. Their findings suggest that individuals suffering from RM may be at an increased risk of developing opioid addiction, emphasizing the need for cautious opioid prescribing practices in this patient population. Given this potential link, healthcare providers should be particularly vigilant when managing RM patients who may require pain management therapies involving opioids. Conversely, Birinci et al. [20] proposed that the association between RM and other addictive substances remains unclear. Their findings indicate that RM patients do not exhibit a higher tendency toward substance use disorders compared to the general population. As a result, they argue that there is no justification for adopting a distinct approach when prescribing medications with addictive potential in RM patients. This perspective challenges the assumption that RM inherently predisposes individuals to substance dependence and highlights the need for further research to clarify this relationship.

## 6. Diagnosis

In the case of RM, a thorough medical interview is essential. Particular attention should be given to obtaining detailed information from the patient regarding their previous treatment for rhinitis, including the specific medications used, dosages, and duration of treatment. The classical rhinoscopic examination reveals erythematous and hyperemic nasal mucosa, often described as intensely red. It is characterized by congestion, a granular texture, and the presence of punctate bleeding due to increased tissue friability [21]. There are also regions of reddened, thickened mucosa along with dull areas [22].

In the differential diagnosis, allergic rhinitis and drug-induced rhinitis should be considered. Rhinitis medicamentosa is classified as a subset of drug-induced rhinitis [23]. However, various other medications have also been implicated in causing nasal mucosal swelling as an adverse effect [10] [2] [24] [25]. These include antihypertensive agents such as  $\beta$ -blockers, reserpine, guanethidine, phentolamine, methyldopa, and angiotensin-converting enzyme inhibitors. Additionally, hormonal therapies, including oral contraceptives and exogenous estrogens, may contribute to drug-induced rhinitis. Phosphodiesterase type 5 inhibitors (e.g., sildenafil, tadalafil, vardenafil), commonly used for the treatment of erectile dysfunction, have also been associated with rebound nasal congestion. Furthermore, pain relievers such as aspirin, acetaminophen, and nonsteroidal anti-inflammatory drugs (NSAIDs) can provoke similar symptoms. Certain psychotropic medications, including chlorpromazine, risperidone, and thioridazine, have also been linked to drug-induced nasal congestion. Finally, cocaine use has been recognized as a significant cause of chronic nasal congestion due to its vasoconstrictive and rebound effects [26].

A well-conducted patient history, including details on medication use, dosage, and treatment duration, is typically sufficient for differential diagnosis. Notable differences can also be observed during nasal examination: RM is characterized by a distinctive erythematous and swollen mucosa, whereas drug-induced rhinitis generally lacks specific physical findings in the nasal cavity [23].

In distinguishing drug-induced and RM from allergic rhinitis, it is useful to inquire about typical symptoms include nasal congestion, watery rhinorrhea, sneezing, and itching, along with a family history of atopy, early onset (<20 years), and coexisting conditions such as allergic conjunctivitis, atopic dermatitis, asthma, or food allergies [27]. Physical examination may reveal watery nasal discharge, nasal obstruction, infraorbital dark circles, lower eyelid folds, postnasal drip, and a transverse nasal crease in the lower third of the nose, resulting from frequent itching and rubbing.

# 7. Treatment Strategies for Rhinitis Medicamentosa

The primary treatment for RM is discontinuing topical decongestants to reduce rebound congestion symptoms [9][28]. Patients should be informed that nasal congestion may initially worsen following discontinuation to prevent misinterpretation as treatment failure.

To alleviate discomfort during this process, moisturizing agents such as intranasal saline or seawater solutions may be recommended as an initial therapy [7]. According to aptekarzpolski.pl [29] nasal rinses with saline or seawater solutions help cleanse the nasal

passages, improve mucociliary function, and maintain hydration. Additional formulations containing dexpanthenol, sesame oil, or hyaluronic acid may further promote mucosal healing.

Steam inhalation is not recommended unless a controlled steam inhaler is used, as it may lead to mucosal dryness [30]. Patients undergoing treatment for RM should be advised to avoid even short-term use of decongestant medications containing sympathomimetics.

If necessary, topical glucocorticosteroids (e.g., beclomethasone, flunisolide, budesonide, fluticasone, mometasone) can be introduced, with treatment duration tailored to the patient's response, typically lasting between 2 to 6 weeks [7]. In cases requiring additional nasal decongestion, a combination of oral sympathomimetics and antihistamines may be considered under appropriate medical supervision.

Several experimental studies have investigated novel treatment approaches for RM. A study by Abdullah Tas et al. [31] assessed the effects of Mometasone furoate nasal spray on nasal mucosal damage caused by prolonged oxymetazoline use in guinea pigs over an eight-week period. The results demonstrated significant therapeutic benefits, as Mometasone furoate reduced edema, congestion, and fibrosis compared to groups receiving either medicated saline or no treatment.

Similarly, research by Cam B. et al. [12] on 30 Wistar rats suggested that xylitol may be as effective as nasal steroids in treating RM, as its molecular properties support mucosal healing. Given its affordability and excellent safety profile, xylitol represents a promising alternative therapy. Xylitol exhibits promise as a topical treatment that reduces mucus viscosity and viscoelasticity, facilitates the dissolution of existing mucus crusts, and enhances the body's innate antibacterial defence mechanisms [32][33][34].

Findings by Casale et al. [35] indicate that nebulized topical sodium hyaluronate could play a key role in RM treatment, further expanding potential therapeutic options. Research by Gelardi M. et al. [36] showed that incorporation of sodium hyaluronate into a treatment regimen comprising intranasal corticosteroids and systemic antihistamines led to a reduction in neutrophil presence in nasal cytology among individuals with allergic and nonallergic rhinitis. Additionally, this combination therapy was associated with significant improvements in both clinical symptoms and endoscopic findings, while demonstrating good tolerability.

#### **Surgical Interventions**

Beyond conservative management, surgical interventions have been considered for refractory RM cases. Given that structural abnormalities, such as a deviated nasal septum, often contribute to prolonged decongestant use, surgical correction may be a necessary intervention in select cases [29]. Margulis et al. [6] analysed 47 patients and found that those who underwent endoscopic medial flap inferior turbinoplasty had significantly reduced nasal decongestant use and improved quality of life compared to those receiving conservative treatment. However, the role of surgery in RM remains controversial. According to Doshi [28], surgical procedures such as turbinate reduction are generally not recommended, as they may further damage the nasal mucosa. To minimize risks, patients undergoing elective nasal surgery for unrelated conditions (e.g., nasal polyposis) should first complete at least three months of successful RM treatment before considering surgical intervention. These conflicting perspectives highlight the need for further research to clarify the indications and long-term outcomes of surgical treatment in RM management.

#### **Consideration of Excipients**

In addition to active substances, excipients should also be considered, particularly benzalkonium chloride (BKC) [37]. This antimicrobial agent is included in some nasal solutions to prevent bacterial growth. Findings from Bernstein [37] suggest that BKC may have harmful biological effects, such as ciliostasis and impaired mucociliary transport. Consequently, the use of products containing benzalkonium chloride is generally discouraged [38]. However, the author highlights that data from in vitro and in vivo studies remain somewhat inconsistent.

On the other hand, research by Marple et al. [39] suggests that there is insufficient evidence to justify the categorical avoidance of BKC. Based on their findings, BKC appears to be a safe and well-tolerated excipient for both short-term and long-term use.

#### 8. Preventive Measures and Patient Education

Rhinitis medicamentosa is a condition that can be prevented; therefore, educating both healthcare professionals and patients about the risks associated with excessive use of nasal decongestants is crucial [40]. When dispensing  $\alpha$ -sympathomimetics for rhinitis, a pharmacist should ensure that patients with acute symptoms, use these medications strictly according to the recommended dosage and for a duration not exceeding 10 days [41].

According to data collected by Fowler et al. [11] on public and primary care awareness regarding the proper use of nasal decongestants, the majority of participants felt that current warning labels were insufficiently visible and inadequate in conveying safety information. Among those expressing dissatisfaction, proposed improvements predominantly concerned label modifications, such as increasing font size, enhancing contrast between text and background, enlarging the label, including explicit warnings about short-term use (maximum of three days), and highlighting the product's addictive potential. Additional suggestions focused on pharmacy-based measures, including restricting decongestants to behind-the-counter sales or requiring a prescription. Additionally, more than half of respondents reported having encountered patients who were inappropriately advised by other healthcare professionals to misuse nasal decongestants. Despite this, a majority of participants perceived primary care physicians as adequately informed about the risks associated with prolonged decongestant use.

A Belgian cross-sectional study conducted by Els Mehuys et al. [42], revealed a high prevalence of intranasal decongestant overuse, affecting nearly half of the studied population. This occurred despite the fact that the majority of patients had been informed about the recommended duration of use. The likelihood of overuse was significantly lower among individuals using intranasal glucocorticosteroids, as well as those who utilized other medications such as oral H1 antihistamines, oral decongestants, or nasal saline solutions. Additionally, the presence of symptoms like itchy or watery eyes and colored nasal discharge was associated with a reduced risk. Conversely, factors that increased the likelihood of overuse included more severe nasal congestion, prolonged symptom duration, sleep disturbances, higher body mass index, and previous medical advice regarding the restricted

duration of intranasal decongestant use. Further research is needed to establish a standardized treatment protocol for RM and improve educational efforts across healthcare settings [43].

# 9. Conclusion

Rhinitis medicamentosa (RM) is a form of non-allergic rhinitis resulting from the chronic use of topical nasal decongestants. The pathophysiology of this condition involves tachyphylaxis, increased vascular permeability, and a chronic inflammatory state leading to structural changes in the nasal mucosa. The long-term consequences of using these medications include psychological and physical dependence, recurrent nasal congestion, histopathological alterations, and potential systemic complications, such as an increased risk of stroke.

The diagnosis of RM is based on a thorough medical history and rhinoscopic examination. The primary treatment approach involves the immediate discontinuation of nasal decongestants and the implementation of supportive therapy, such as nasal mucosa hydration and the use of intranasal corticosteroids. Surgical treatment should only be considered in selected cases.

Findings from recent studies highlight the need for better education of both patients and healthcare professionals regarding the appropriate use of nasal decongestants. A key element of RM prevention is informing patients about the importance of limiting the use of these medications to a maximum of 5–7 days. Furthermore, further research is necessary to develop more effective therapeutic methods, including the potential use of alternative substances such as xylitol or hyaluronic acid in nasal mucosa regeneration.

Both physicians and pharmacists should actively monitor patients' use of nasal decongestants and recommend safer alternatives, especially in cases of chronic rhinitis. The establishment of stricter regulations regarding the availability of these medications and the implementation of effective educational programs could contribute to reducing the incidence of RM in the population. **Conceptualization:** Martyna Byrska, Hanna Barska-Kobylińska, Marta Janura, Maja Weimann, Emilia Biczak, Oliwia Biegańska

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