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Review Article

# Balancing Efficacy and Tolerability in Nasal Decongestion: A Rationale for the Oxymetazoline and Dexpanthenol Combination

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## ABSTRACT

Nasal congestion, a common and burdensome symptom, significantly impairs quality of life. Topical decongestants like oxymetazoline provide effective and rapid localized relief, making them a primary therapeutic choice. A known consideration with this therapy is the potential for nasal dryness, which can impact the overall patient experience. This review explores the rationale for combining oxymetazoline with dexpanthenol to address this. The role of dexpanthenol is purely supportive. By providing essential mucosal hydration as a humectant, it helps to soothe local irritation and directly counteract the dryness associated with decongestant use. This action helps maintain a healthy mucosal environment conducive to the body's natural repair processes. This integrated approach pairs the primary decongestant efficacy of oxymetazoline with the supportive care of a hydrating agent. The goal is to provide effective symptomatic relief of congestion while simultaneously enhancing the comfort and tolerability of the therapy for the patient.

**Key words:** Nasal congestion; Allergic rhinitis; Rhinosinusitis; Nasal decongestant; Oxymetazoline; Dexpanthenol.

## INTRODUCTION

Nasal congestion is a common, bothersome symptom in Allergic Rhinitis (AR) and rhinosinusitis, characterized by limitation in nasal airflow along with nasal blockage [1,2]. Studies have demonstrated that nasal congestion can lead to impaired Quality of Life (QoL). It causes intermittent hypoxemia, sleep disruption, impaired emotional function, and reduced productivity [3,4]. Over 80% of individuals with nasal congestion due to AR report difficulty falling asleep or increased frequency of waking up at night. Sleep disruptions were increased with increasing severity of nasal congestion [3]. Poor sleep quality leads to fatigue, irritability and reduced daytime function [5]. Social functioning is correlated with the severity of nasal congestion in patients with AR [6]. Individuals with nasal congestion experience difficulties in performing daily activities, including outdoor activities. Furthermore, a decreased ability to concentrate at work and poor productivity are reported by 42% and 36% of adults, respectively [3].

## LITERATURE REVIEW

### Etiology of nasal congestion

Nasal congestion is the result of mucosal inflammation in the presence or absence of increased mucus secretions, and tissue edema without anatomical variations [1,7]. An immune cascade contributes to the development of nasal congestion, wherein antigens in contact with the nasal mucosa are exposed to mast cells, leading to crosslinking of the Immunoglobulin E (IgE) receptors. This is followed by degranulation and release of histamine, proteases, and pro-inflammatory mediators, and subsequently, tissue edema and increased mucus secretion ensue [1,8]. Figure 1 depicts the causes of nasal congestion [1,8-10]

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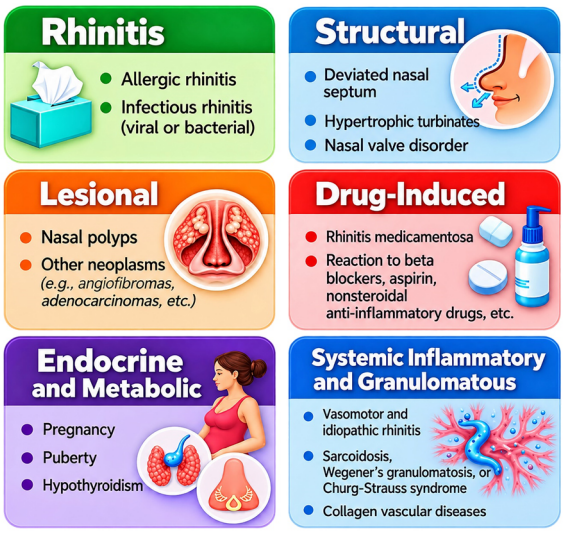



**Figure 1:** Etiology of nasal congestion includes anatomical, pathological and neurological causes.

This literature review aimed to collate the available data on the burden of nasal congestion (with a focus on India) and examine the potential role of topical nasal decongestants in the symptomatic management of nasal congestion. Towards this, databases including PubMed and Science Direct were searched for relevant articles published up to May 2026.

## Burden of nasal congestion in India

Various etiologies contribute to the development of symptoms of nasal congestion. The International Study of Asthma and Allergies in Childhood (ISAAC) Phase 3 study reported that the prevalence of nasal symptoms among children aged 6-7 and 13-14 years was 12.9% and 23.6%, respectively [11]. An observational study at a tertiary-care hospital reported that blocked nose affected 62.4% of children aged 3-15 years, and was the second most frequent nasal symptom in the study [12]. Table 1 describes the reported burden of nasal congestion in Indian studies based on etiology [13-22].

**Table 1.** Reported burden of nasal congestion in Indian studies based on etiology.

| Study details | Etiology | Patient group | Burden of nasal congestion |
|---|---|---|---|
| Kochar, et al. (2025) [17] | Allergic rhinitis | Children (N=9,039) aged 2-14 years attending a tertiary-care OPD; of whom, 486 children had allergic rhinitis | Moderate: 52%<br>Severe: 22% (of patients with allergic rhinitis) |
| Pereira, et al. (2025) [19] | Allergic rhinitis | 40,001 patients aged ≥ 11 years, of whom 21,480 had allergic rhinitis | 71% (of patients with allergic rhinitis) |
| Kumar, et al. (2024) [18] | Allergic rhinitis | 33 children aged 6-16 years (rural and urban) | Rural area: 84.6%<br>Urban area: 80% |
| Chauhan, et al. (2022) [14] | Allergic rhinitis | College students (N=1,337; of which 257 had allergic rhinitis) | 71.21% |
| Sharma, et al. (2021) [21] | Allergic rhinitis | 148 patients aged ≥ 10 years | 74.40% |
| Sushma, et al. (2024) [22] | Rhinosinusitis | 88 patients aged 15-70 years | Symptomatic nasal obstruction: 54.5%<br>Congestion on rhinoscopy: 61.4% |
| Rekhade, et al. (2021) [20] | Chronic rhinosinusitis | 100 patients aged ≥ 11 years | CRSwNP: 100%<br>CRSsNP: 93.65% |
| Garg, et al. (2019) [16] | Chronic rhinosinusitis | 94 patients aged>18 years with a history of runny nose for>12 weeks | 87.20% |

| | | | |
|---|---|---|---|
| Dewan, et al. (2024) [15] | Common cold | 200 patients aged 18-60 years with symptoms of common cold of recent onset | Mild: 40.5%<br>Moderate: 34.7%<br>Severe: 15.6%<br>Very severe: 9.3% |
| Ashwinirani, et al. (2023) [13] | Deviated nasal septum | 124 symptomatic patients aged 18-60 years | 72.50% |

**Note:** CRSsNP: Chronic Rhinosinusitis Without Nasal Polyposis; CRSwNP: Chronic Rhinosinusitis with Nasal Polyposis; OPD: Outpatient Department.

## Nasal congestion: The current approach to assessment and topical treatment

While nasal congestion can stem from complex pathologies requiring specialist evaluation, the vast majority of cases are due to common conditions like allergic rhinitis and the common cold, which are typically self-diagnosed by the patient. In this real-world context, the primary driver for seeking treatment is the patient's own subjective experience of their symptoms. Reflecting this patient-centric approach, the clinical evaluation also prioritizes subjective assessment. The patient's description of their symptoms (nasal blockage, facial pressure and impact on quality of life) is the basis of assessing severity and the need for intervention. The Visual Analog Scale (VAS) is a validated tool used to formally quantify this subjective experience and monitor treatment response. An objective confirmation is then achieved through physical examination and if required, nasal endoscopy, and functional testing such as nasal peak inspiratory flow and rhinomanometry [23,24].

## Nasal decongestants for symptomatic relief

Topical nasal decongestants are the most effective treatment for nasal congestion due to allergic rhinitis [25]. The topical route of administration delivers decongestants directly to the site of action, the nasal mucosa, which has increased permeability and vascularity. Additionally, the large surface area (~150 $cm^2$) permits greater absorption of intranasal formulations, which in turn can allow the use of lower doses compared to systemic drugs. Topical nasal decongestants also avoid first pass hepatic metabolism, have a rapid onset of action, are non-invasive, convenient, safe and patient-friendly. This may contribute to increased patient compliance [8,26,27].

Imidazolines are sympathomimetic drugs which are commonly used for the symptomatic management of nasal congestion, having proven efficacy and tolerability. Their lipophilic nature permits rapid absorption at the nasal mucosa. The first imidazoline derivative used in nasal sprays was naphazoline, while tymazoline has been specifically used for rhinitis. However, both are no longer widely used. The management of nasal congestion commonly involves xylometazoline and oxymetazoline. These imidazoline derivatives were formulated to have a rapid onset of action, and recent derivatives have longer duration of action [25].

## Oxymetazoline

Oxymetazoline is an imidazoline derivative which has lower toxicity and improved efficacy compared with xylometazoline. Oxymetazoline has other beneficial actions including anti-inflammatory, anti-rhinoviral and antioxidant properties. In contrast, xylometazoline only has antioxidant properties. Oxymetazoline exhibits significantly higher affinity for α 1A-receptors than xylometazoline and is a more potent α 2B-receptor agonist. This allows its use at lower concentrations compared with xylometazoline. Furthermore, oxymetazoline exhibits slower dissociation kinetics and has a duration of action of 10-12 hours (*vs.* 6-10 hours for xylometazoline) [25,28]. A comparison of the key parameters of oxymetazoline and xylometazoline is presented in Figure 2.

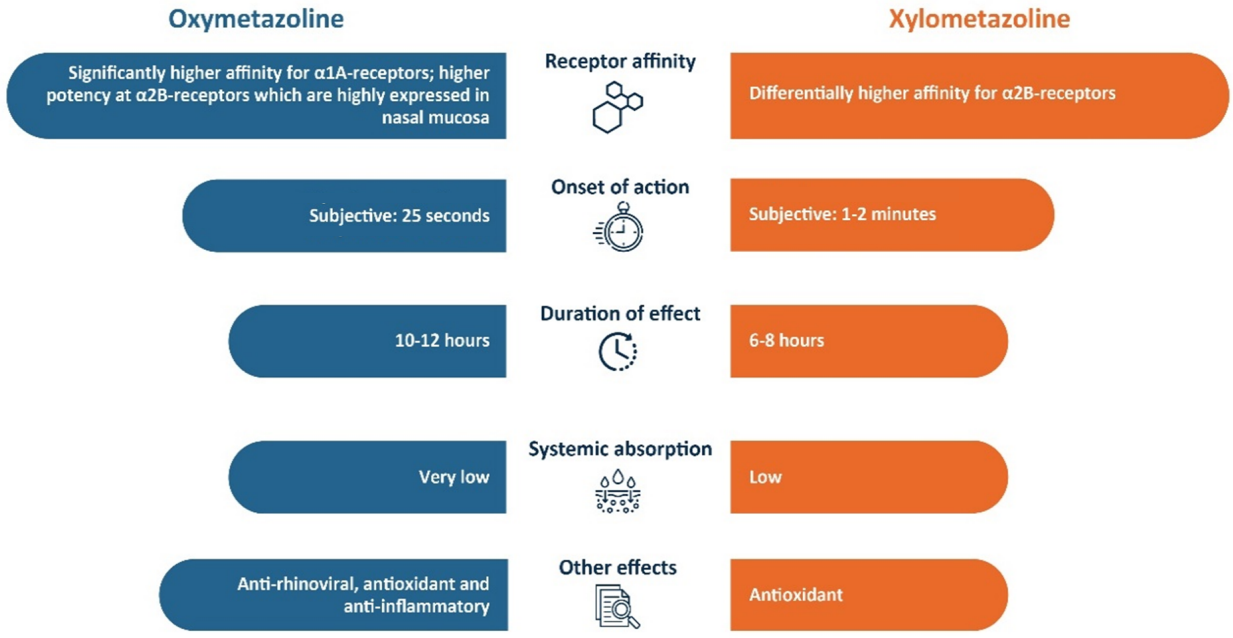



**Figure 2:** Difference between Oxymetazoline and Xylometazoline [28].

Oxymetazoline acts directly on α-1 and α-2 adrenergic receptors in the arterioles of the nasal mucosa. It causes vasoconstriction which reduces the swelling of inferior and middle turbinates and improves nasal airway patency. Magnetic Resonance Imaging (MRI) studies on patients with nasal congestion due to Upper Respiratory Tract Infection (URTI) displayed a 54% difference (oxymetazoline *vs.* placebo) in inferior turbinate volume at 1 hour and 42% difference at 12 hours. The corresponding values for middle turbinate volume were 20% at 1 hour and at 12 hours. Symptom scales and rhinomanometric measurement of nasal airway resistance supported these findings, demonstrating the efficacy of oxymetazoline as a nasal decongestant [29].

## Dexpanthenol

A known consideration of nasal decongestant therapy is the potential for local nasal dryness and irritation, which can impact the patient experience and may be more pronounced with certain formulations [30,31]. Dexpanthenol is a humectant that is well-suited to address these local tolerability concerns. Its primary supportive action is to provide essential hydration to the nasal mucosa. As a hygroscopic agent, it attracts and retains moisture, directly counteracting dryness. This creates a protective, hydrating environment that soothes irritation and supports the natural regenerative capacity and barrier function of the nasal epithelium [32-35].

The local environment plays a crucial role in the process of mucosal repair. An *in vitro* study reported that complete re-epithelialization of epithelial cell layers occurred within 24 hours in the presence of dexpanthenol, whereas healing was incomplete with vaseline. The hygroscopic nature of dexpanthenol could provide the optimal epithelial hydration necessary for effective functioning of natural repair mechanisms (Table 2) [32,34,36,37]. In the presence of dexpanthenol, cells maintained their integrity, in contrast to the cytotoxic effects and cellular stress observed with Vaseline. This demonstrates that dexpanthenol not only facilitates a supportive environment for natural regeneration but also has excellent local tolerability [35,36].

*In vitro* studies have shown that dexpanthenol can help mitigate the negative effects of decongestants on cell growth [34]. When dexpanthenol is added to a nasal decongestant, patients often report a better overall symptomatic experience, likely due to the soothing and moisturizing effect of dexpanthenol on the nasal mucosa, rather than an enhancement of the decongestant action [35]. Verse, et al., evaluated the tolerability of a preservative-free dexpanthenol 5% nasal spray against an ointment. The study measured mucociliary clearance via the saccharin test, and found no statistical difference between the two, indicating that the convenient spray formulation is a viable delivery method for providing these supportive benefits (Table 2) [37].

**Table 2.** Evidence-based data for the mucosal benefits of dexpanthenol.

| Study | Study model/design | Key findings (Supportive Action) |
|---|---|---|
| Develioglu, et al. [32] | *Ex vivo* study comparing dexpanthenol and Vaseline on healing cells | Dexpanthenol was non-toxic. In its presence, scratch wounds were entirely re-epithelialized within 24 hours, demonstrating its ability to support the natural healing process by maintaining a moist environment, in contrast to incomplete healing with Vaseline. |
| Klocker, et al. [34] | *In vitro* study of the action of dexpanthenol after xylometazoline (with or without benzalkonium chloride) treatment of human amniotic cell line | Pre-treating cells with dexpanthenol mitigated the local irritant effects of xylometazoline on cell growth. Dexpanthenol demonstrated a protective effect, supporting mucosal integrity and function. This suggests its potential in preventing local mucosal irritation. |
| Verse, et al. [37] | *In vivo* mucociliary clearance in human volunteers under dexpanthenol spray or ointment | Dexpanthenol nasal spray is at least as effective as the ointment formulation in supporting healthy mucociliary clearance, as measured by saccharin migration time. |

## Improving the tolerability of oxymetazoline therapy with the supportive action of dexpanthenol

Topical nasal decongestant treatment is commonly prescribed for the symptomatic management of nasal congestion, and α-sympathomimetics have demonstrated efficacy [25]. However, local irritation and rebound congestion are shortcomings of this approach, and can impact patient compliance and, in turn, treatment outcomes [36]. Topical nasal decongestants such as oxymetazoline represent a cornerstone of therapy for patients seeking rapid, effective relief from nasal congestion [25]. The ability to act directly on the nasal vasculature provides a fast onset of action and makes topical decongestants a suitable choice for short-term symptomatic management.

A known consideration with this effective class of therapy is the potential for local nasal dryness, which can impact the overall patient experience and treatment outcomes [36]. Early studies have demonstrated that prolonged use (beyond the recommended dose and duration) of xylometazoline and oxymetazoline leads to rebound congestion [38,39]. This creates a clear therapeutic rationale for combining the primary decongestant with a supportive agent designed specifically to enhance local comfort and tolerability.

The addition of a moisturizing agent like dexpanthenol to a decongestant formulation can help address the local tolerability issues associated with decongestant use. By providing essential hydration, dexpanthenol can soothe the nasal mucosa, which may reduce the patient's compulsion to overuse the product and thus mitigate the factors that contribute to rebound congestion [40]. The benefit of this combination stems from pairing the decongestant efficacy of oxymetazoline with the supportive care provided by dexpanthenol. Dexpanthenol helps mitigate the local irritation, likely by forming a protective, moisturizing film on the nasal mucosa [34]. Furthermore, by maintaining a hydrated environment, it supports the natural processes of epithelial recovery and helps ensure the efficient functioning of mucociliary clearance [32,41].

An *ex vivo* study supports the role of dexpanthenol as a supportive agent. Data showed that dexpanthenol did not alter the permeated amount of xylometazoline, indicating that it does not interfere with the primary action of the decongestant [42]. Instead, dexpanthenol's benefits stem from its ability to improve local hydration. This moisturization provides a protective film on the nasal mucosa, which helps soothe irritation and creates a favorable environment for the natural recovery processes. A well-hydrated mucosa is essential for efficient ciliary function and maintaining epithelial integrity. Therefore, by reducing nasal dryness and improving the condition of the mucosal environment, this combination can contribute to a more comfortable patient recovery [25,36,43].

This formulation offers a comprehensive approach to managing the patient experience associated with nasal congestion. It leverages the vasoconstrictive efficacy of oxymetazoline to provide rapid relief from the primary symptom of congestion. Concurrently, it incorporates the mucosal-soothing and hydrating benefits of dexpanthenol to address the local irritation and dryness that can accompany decongestant therapy. This aims to provide effective decongestion, while ensuring a favorable tolerability profile.

### A rationale for combining oxymetazoline with dexpanthenol

An adjunctive formulation like oxymetazoline plus dexpanthenol offers a promising strategy. This combination is designed to leverage the vasoconstrictive efficacy of oxymetazoline for rapid relief from nasal congestion, while simultaneously utilizing the supportive properties of dexpanthenol to maintain a healthy mucosal environment. By improving local hydration and supporting mucosal health, the dexpanthenol component serves to enhance the overall tolerability and comfort of decongestant therapy [36].

## GUIDELINE RECOMMENDATIONS

Various guidelines highlight the role of nasal decongestants in the symptomatic management of allergic rhinitis and sinusitis, as outlined in Table 3 [44-51].

**Table 3.** Guideline recommendations for the use of nasal decongestants.

| Guideline | Indication | Treatment recommendation |
|---|---|---|
| Indian expert consensus on allergic rhinitis in women, 2026 [42] | Women with allergic rhinitis-severe or refractory cases or difficult-to-treat allergic rhinitis | Nasal/oral decongestant ( ≤ 7 days, for sudden nasal blockage<br>Use of nasal decongestants for longer than three days is cautioned because of risk of rebound congestion |
| Expert forum consensus group-India, 2025 [43] | Allergic rhinitis in patients with asthma | Nasal decongestants can be helpful for short-term relief from nasal congestion, and are useful during an acute flare<br>Chronic use is not recommended due to the risk of RM |
| International Consensus Statement on Allergy and Rhinology: Allergic rhinitis (ICAR-Allergic Rhinitis) 2023 [44] | Allergic rhinitis | Nasal decongestants can provide effective short-term relief of nasal congestion during an acute flare<br>Chronic use is not recommended due to the risk of RM |
| Indian guidelines on allergic rhinitis -Association of Otolaryngologists of India (AOI), 2021 [45] | Allergic rhinitis | Nasal decongestants should be used as short-term therapy for 5-10 days as prolonged use can lead to RM<br>Contraindicated in patients with uncontrolled hypertension, severe coronary artery disease, and pregnant women |
| European Forum for Research and Education in Allergy and Airway Diseases (EUFOREA) 2020 [46] | Severe allergic rhinitis or failure of previous treatment | Nasal decongestants can be used as add-on therapy for 7 days or less for sudden nasal blockage |
| American academy of otolaryngology-head and neck surgery foundation [47] | Acute bacterial sinusitis | Decongestant nasal sprays can be taken for no more than 3 days to avoid worsening congestion |
| National Health Systems Resource Centre (NHSRC)-India, 2017 [48] | Sinusitis with severe nasal congestion | Recommends the use of topical decongestants for a maximum of 5 days<br>Use with precautions in patients with hypertension |
| Ministry of health, Singapore (2010) [49] | Adolescents and adults with common cold | Topical nasal decongestants can be used for up to 3 days to avoid toxicity and RM |
| | Adults with acute infective rhinosinusitis | Topical nasal decongestants can be used for less than 10 days |
| | Children with infective rhinosinusitis | Topical nasal decongestants can be used for no longer than 4-5 days to avoid toxicity and RM |
| | Adults with allergic rhinitis | Can be used for severe nasal obstruction |
| | Children with allergic rhinitis | Can be considered in pediatric patients before eating and sleeping for a short period of time |

Note: Rhinitis Medicamentosa

## CLINICAL EVIDENCE

### Evaluation of the effect of oxymetazoline on the duration of rhinitis

Reinecke, et al., evaluated the efficacy of oxymetazoline for the symptomatic management of nasal congestion in a double-blind, placebo-controlled clinical trial including 247 patients with acute rhinitis. Patients received oxymetazoline hydrochloride nasal spray or normal saline nasal spray three times daily. Complete resolution of symptoms (symptom score of 0) was noted for 75% of patients using oxymetazoline compared with 25% of patients using normal saline. There was a significant reduction in the duration of rhinitis in the oxymetazoline group (4 days *vs.* 6 days). Oxymetazoline displayed a rapid onset of action compared with normal saline (25 s *vs.* 90 s; $p<0.001$). Physicians' assessment of global efficacy was excellent or good for more patients in the oxymetazoline group (85% *vs.* 38%; $p<0.001$). Patients' efficacy assessment reflected similar results, with a good or excellent rating in 84% of patients using oxymetazoline compared with 44% of patients using normal saline ($p<0.001$). A low rate of withdrawal was reported (0.37%), and the tolerability of oxymetazoline was 98% (*vs.* 95% for normal saline). This study demonstrated the superior clinical efficacy of oxymetazoline nasal spray compared with normal saline for the management of rhinitis (Table 4) [52].

**Table 4.** Summary of key clinical findings for oxymetazoline and dexpanthenol.

| Study | Patients | Treatment | Outcomes |
|---|---|---|---|
| Reinecke, et al. [52] | 247 patients with acute rhinitis | Oxymetazoline 0.05% nasal spray three times daily *vs.* normal saline nasal spray for 10 days | Reduced duration of rhinitis (4 days *vs.* 6 days), rapid onset of action (25 s *vs.* 90 s) and higher rating by physicians (85% *vs.* 38%) and patients (84% *vs.* 44%) |
| Druce, et al. [53] | 128 patients with acute coryzal rhinitis | Oxymetazoline 0.05% nasal spray (single dose study) *vs.* normal saline nasal spray | Significant improvement in nasal congestion and nasal airflow starting from 1 hour and continuing until 12 hours |
| Parikh, et al. [55] | 160 patients with nasal congestion due to allergic rhinitis | Oxymetazoline 0.05% plus menthol, eucalyptol and xylitol drops (OM) *vs.* oxymetazoline 0.05% plus dexpanthenol 5% (OD) drops, xylometazoline 0.1% plus sorbitol 2% (XS) drops, and xylometazoline 0.1% (XL) drops (all three times daily for 5 days) | OM provided statistically significantly lower nasal congestion compared with xylometazoline-based formulations and OD from early as Day 3 |
| Jagade, et al. [36] | 100 patients with nasal congestion due to allergic rhinitis and following nasal surgery | Oxymetazoline 0.05 % plus dexpanthenol 5% *vs.* xylometazoline 0.1 % nasal drops (administered four times a day for 6 days) | Oxymetazoline and dexpanthenol combination provided better efficacy, shorter recovery time, lesser rebound congestion along with better tolerability than xylometazoline alone. |
| Tantalipikorn, et al. [41] | Patients with Chronic Rhinosinusitis (CRS) who had undergone endoscopic sinus surgery | Dexpanthenol 5% nasal spray *vs.* normal saline nasal spray for 6 weeks | Supported efficient mucociliary function, reflected by a faster mucociliary transit time (8.4 min *vs.* 1.7 min). This is attributed to improved mucosal hydration. Also led to more effective clearance of nasal discharge (74% *vs.* 50% of patients with a symptom score of 0 at 6 weeks). |
| Thieme, et al. [54] | Patients suffering from dry nose symptoms | Hyaluronic acid *vs.* hyaluronic acid plus dexpanthenol *vs.* isotonic saline nasal spray for 4 weeks | The role of dexpanthenol as a supportive moisturizing agent was highlighted where its addition to hyaluronic acid led to a significantly higher patient perception of nasal moisturization compared to hyaluronic acid alone. This superior moisturizing effect translated into greater reductions in patient-reported symptoms of nasal dryness and crusting, as captured by the Rhinitis Sicca Symptom Score (RSSS). |

Druce, et al., reported the findings of two randomized, double-blind, single-dose trials which studied the effects of oxymetazoline 0.05% nasal spray (*vs.* normal saline nasal spray) in patients with acute coryzal rhinitis. The oxymetazoline group demonstrated a significant change in nasal congestion from the first hour after administration and continuing until 12 hours (except at 11 hours). There was significant improvement in nasal airflow over the entire 12-hour dosing interval at each hourly time-point. These improvements were noted regardless of the history of allergic rhinitis. Only mild adverse effects were reported in the study (Table 4) [53].

## Dexpanthenol is a useful add-on to decongestant formulations

Tantalipikorn, et al., studied the effect of dexpanthenol nasal spray compared with normal saline in patients with Chronic Rhinosinusitis (CRS) who had undergone endoscopic sinus surgery. Nasal spray was dosed four to six times a day for 6 weeks. Findings demonstrated that the dexpanthenol group maintained efficient mucociliary function, with significantly faster Mucociliary Transit Time (MTT) compared to saline (difference in MTT: 8.4 min for dexpanthenol *vs.* 1.7 min for normal saline; p=0.016). This effect was attributed to its ability to keep the nasal mucosa hydrated, ensuring effective mucosal clearance. The supportive environment created by dexpanthenol may have contributed to a more effective clearance of nasal discharge, with significantly more patients in the dexpanthenol group reporting a symptom score of 0 after 6 weeks (p=0.031) [41].

This primary role as a moisturizer is further supported by studies showing that dexpanthenol, when combined with hyaluronic acid, leads to a significantly improved patient perception of nasal moisturization compared to hyaluronic acid alone in patients with symptoms of dry nose [54].

## Oxymetazoline and Dexpanthenol Combination for Nasal Congestion

Parikh, et al., compared the efficacy and tolerability of oxymetazoline 0.05% plus menthol, eucalyptol and xylitol drops (OM) *versus* oxymetazoline 0.05% plus dexpanthenol 5% (OD) drops, xylometazoline 0.1% plus sorbitol 2% (XS) drops, and xylometazoline 0.1% (XL) drops (all three times daily for 5 days) in patients aged 18-60 years with acute allergic rhinitis. This prospective, open-label, randomized study reported that OM provided statistically significant lower nasal congestion score compared with all other groups (OM: 1.16; OD: 1.43; XL: 1.55; XS: 1.52). The findings indicated a shorter recovery time for oxymetazoline-based formulations as compared with xylometazoline-based formulations. Additionally, the rate of rebound congestion was higher for xylometazoline-based formulations on day 3 (XL: 20%; XS: 26.67%) and on day 5 (XL: 17.5%; XS:23.33%) compared with oxymetazoline-based formulations (OD: 18.18% on day 3 as well as on day 5; OM: 0%). Oxymetazoline-containing treatments showed better compliance compared with xylometazoline-containing treatments (XL and XS). Non-compliance was seen in 2 patients of XL 0.1% and 2 patients in XS groups [55].

Jagade, et al., evaluated the efficacy of oxymetazoline 0.05% plus dexpanthenol 5% (OD) *vs.* xylometazoline 0.1% (XO) in a phase IV clinical study in India. Patients with nasal congestion due to allergic rhinitis or following nasal surgery received either oxymetazoline 0.05% plus dexpanthenol 5% or xylometazoline 0.1% as nasal drops (both administered four times daily for 6 days). Compared with the xylometazoline group, the combination group showed significantly greater improvement in nasal congestion, nasal discharge, and nasal irritation, with higher rate of recovery (OD: 93.75%; XO: 59.57%) and lower rate of rebound congestion (OD: 6.25%; XO: 82.98%). In addition, the recovery time was significantly shorter for the combination group (OD:1.08 h; XO: 1.54 h). Good-to-excellent response for Physicians Global Assessment of Response to Therapy (PGART) favored the combination therapy (93.75% *vs.* 51.28%; p<0.05), as did good-to-excellent response for the Patients Global Assessment of Tolerability to Therapy (PGATT; 95.83% *vs.* 52.91%; p<0.05). The high recovery rate for the combination group by day 4 of treatment further supports its use as this recovery is achieved within the maximum treatment duration recommended by various guidelines (Table 3) [36].

Combining a primary decongestant such as oxymetazoline with a supportive agent like dexpanthenol represents a rational therapeutic strategy. Theoretically, by pairing the vasoconstrictive efficacy of oxymetazoline with the hydrating and mucosal-soothing properties of dexpanthenol, this combination has the potential to offer improved clinical outcomes over xylometazoline monotherapy. However, this specific hypothesis has not been confirmed, as it has yet to be tested in a direct, head-to-head clinical trial.

The existing clinical evidence, while not providing a direct comparison to oxymetazoline monotherapy, does suggest favorable outcomes for the combination when compared to xylometazoline-based formulations [36,55]. The study by Jagade, et al., for instance, demonstrated that the oxymetazoline-dexpanthenol combination provided a shorter recovery time and enhanced tolerability *versus* xylometazoline monotherapy [36]. Similarly, the study by Parikh, et al., study reported that the oxymetazoline-dexpanthenol arm had lower nasal congestion scores compared to the xylometazoline arms [55].

A key consideration in interpreting these findings is the choice of xylometazoline as the comparator in both studies. As neither trial included an oxymetazoline-only arm, a future study would be required to precisely quantify the additive contribution of dexpanthenol. Further methodological considerations include the single-center design of these studies and their reliance on patient-reported outcomes for key endpoints.

Therefore, while definitive data against oxymetazoline monotherapy is awaited, the collective findings from the studies by Jagade, et al., and Parikh, et al., suggest that the combination of oxymetazoline and dexpanthenol may be considered a more effective and better-tolerated option than traditional xylometazoline-based formulations for the symptomatic management of nasal congestion.

## Treatment approach for the symptomatic management of nasal congestion

Topical nasal decongestants represent a primary therapeutic option for the symptomatic relief of nasal congestion. Oxymetazoline has a rapid onset of action (within 25 seconds) and a prolonged duration of action (up to 12 hours), making it a suitable treatment option for nasal congestion. The mucosal support provided by dexpanthenol can improve nasal moisturization and reduce nasal dryness and crusting. While the literature is limited, there is some favorable evidence suggesting the combination of these agents help reduce symptoms and severity of nasal congestion while also improving tolerability of the formulations.

## Safety considerations for topical decongestant therapy

Imidazoline nasal formulations have undergone various changes to improve safety. Since nasal sprays are less likely to flow compared with nasal drops, there is a lower risk of swallowing. Nasal sprays permit the use of the lowest effective dose which leads to improved tolerability and fewer adverse effects. In terms of efficacy, the improvement in symptoms of rhinitis leads to a reduction in difficulties associated with feeding [25]. Specifically, Metered-Dose Nasal Sprays (MDNS) provide precise control of spray velocity and plume geometry, reproducible drug delivery, lower variance of particle size, and optimized distribution for better nasal absorption.

The droplet size produced with MDNS has high deposition rates in the turbinates. The regulated dispensing of these devices helps avoid post-nasal drip and improves patient comfort and therefore, compliance. Nasal drops have a variable clearance half-time while MDNS have a predictable clearance half-time. This allows MDNS to achieve predictable activity [56]. Rebound congestion can be prevented by using nasal decongestants for limited periods of time and at the appropriate dose [57].

## CONCLUSION

The combination of oxymetazoline and dexpanthenol offers a rational therapeutic strategy that pairs the vasoconstrictive efficacy of oxymetazoline with the supportive, hydrating properties of dexpanthenol. This integrated approach allows for rapid relief from the primary symptom of congestion while actively maintaining mucosal health. The available clinical evidence suggests that this integrated approach results in a more favorable overall therapeutic outcomes, characterized by better efficacy, shorter patient recovery times and enhanced tolerability than xylometazoline. This approach may in turn, help mitigate the factors that contribute to the risk of rebound congestion. In conclusion, this integrated formulation represents an effective strategy for the short-term symptomatic management of nasal congestion, successfully balancing the primary efficacy of a decongestant with the supportive care required to ensure an enhanced and favorable tolerability profile.

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Not applicable.

## AUTHOR CONTRIBUTIONS

All authors contributed equally to concept, literature search, drafting and editing of the manuscript.

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## AI DECLARATION

Artificial intelligence-assisted technologies were not used for the development of this manuscript.

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