

Nasal Vestibulitis and Vestibular Furunculosis: a systematic review about two common nasal infections and considerations about correct diagnosis and management

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Abstract

Background. Nasal vestibulitis (NV) and nasal vestibular furunculosis (NVF) are two infectious processes of the nasal vestibule, sharing common etiology, the same risk of complications, and similar treatment while remaining two different pathological entities.

Methods. We performed a comprehensive literature research on NV and NVF in PubMed, Cochrane, and Google Scholar databases, with the aim to review the evidence on these two conditions and discuss the therapeutic approaches.

Results. We identified a total of 248 records; according to our inclusion/exclusion criteria, 27 of them, published over a period of 59 years (1962-2021), were included in this review.

Conclusion. NV and NVF are reported to be common conditions, with well-known etiological agents and risk factors. The diagnosis is clinical and topical antibiotics are the mainstay of treatment. Complications appear to be infrequent. Further studies are necessary to clarify the pathogenetic mechanisms and the exact prevalence of both conditions.

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Key words: Nasal vestibulitis, vestibular furunculosis, nasal infections, nasal vestibule

Introduction

The nasal vestibule is a pear-shaped cavity lying posterior to the nostrils and representing the first contact with the external environment (1); it is bordered laterally by the alar cartilages, and medially by the columella and membranous nasal septum. Posteriorly it is limited by limen nasi, a line that corresponds to the alar cartilage interfacing with lateral cartilage (2). Histologically, the nasal vestibule is lined with stratified squamous epithelium, a continuation of the skin of the face, and has a variable number of vibrissae, which act, together with the sebaceous gland secretions, to entrap large particulate matter (3).

The nasal vestibule could be the site of two infectious processes: nasal vestibulitis (NV), which is a diffuse infection of the epithelium of the nasal vestibule associated with crusts formation, and nasal vestibular furunculosis (NVF), a more localized process (4,5) which manifests as a single or multiple pustular lesion centered at the hairy follicles and surrounded by erythematous skin. NV and NVF share common etiology, pose the same risk of complications, and require similar treatment, and can therefore be included in the same discussion, although they remain two different pathological entities.

Here we present a brief review of the literature regarding NV and NVF and discuss the therapeutic approaches. The purpose of this review is to elucidate the key aspects of these often underestimated clinical entities, in order to help the general practitioner to recognize and adequately treat them. In particular, we aim to answer the following question: what is the most accepted etiological explanation? What are the therapeutic tools at our disposal? When is the ENT consultation paramount?

Methods

This study was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) checklist and statements recommendations.

Search Strategy

A comprehensive search strategy, developed in partnership with a medical librarian, was applied in PubMed, Cochrane, and Google Scholar databases, without time restriction, in September 2021. Search items used include the following keywords: “nasal vestibulitis” OR “nasal furunculosis”, OR “nasal vestibular furunculosis”. The

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search strategy was created in conjunction with these medical librarians using Medical Subject Headings intended for PubMed and then tailored for the other databases. Two independent investigators reviewed the resulting literature written in the English language. Duplicates articles were removed. Any disagreements regarding inclusion were resolved with a discussion between the two reviewers, and a consensus was obtained. The PRISMA guidelines were followed in reporting the steps for inclusion of studies in this review and the full list of references was screened for potentially relevant articles.

Study Selection Criteria

Two authors (P.D.L. and P.M.) independently extracted data from included studies. Discrepancies were resolved by a third author (M.R.). Patient demographics, clinical presentation, pathology characteristics, treatment, and outcomes data were collected.

The following were used as inclusion criteria for this study: all types of studies, English, Spanish or French language, and full-text availability. Commentaries were excluded. The

articles were reviewed in full to assess the study objectives and level of evidence. The nature of this review did not require the Institutional Review Board.

Results

Study Selection

Through PubMed, Cochrane, and Google Scholar databases, we identified 248 records (Fig. 1).

After the removal of duplicates, we screened 165 records, and 138 were excluded since the object was obviously different. For eligibility, we assessed 26 full-test articles for inclusion/exclusion criteria. Twenty-six studies were included in the qualitative synthesis. These studies were published over a period of 59 years, between 1962 and 2021 (Table 1).

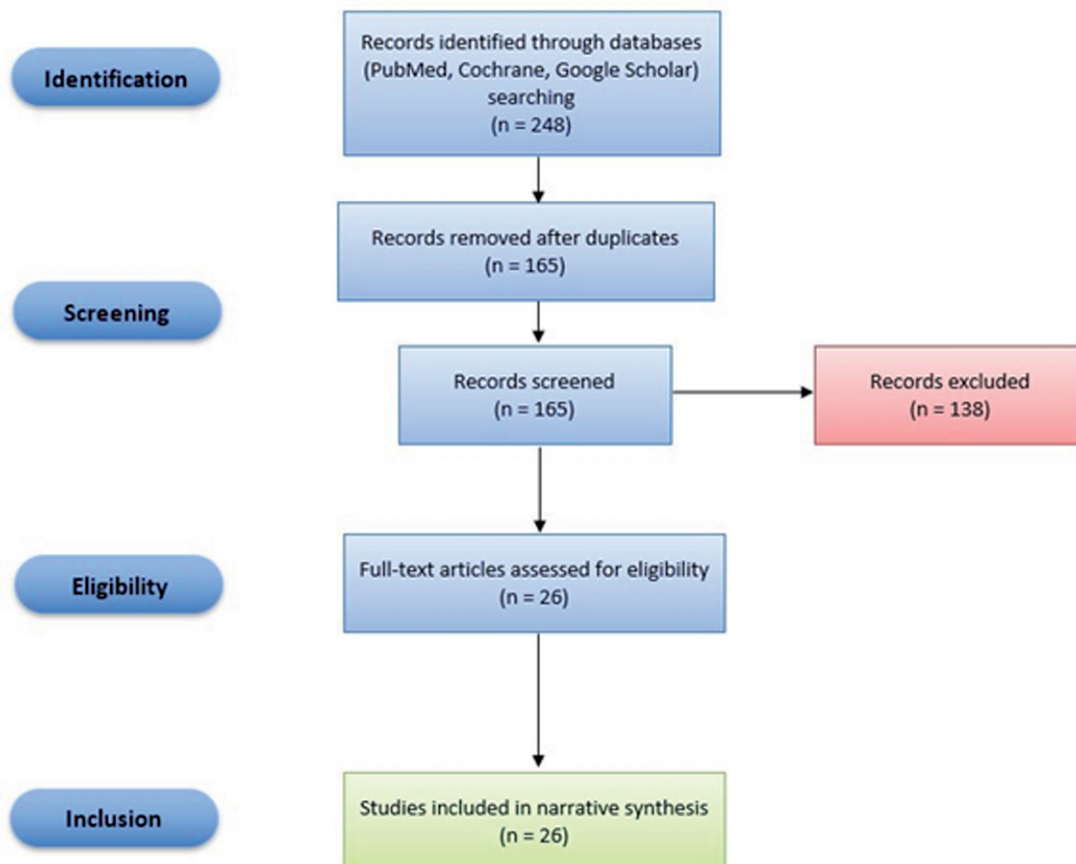


Fig 1. PRISMA flow-chart describing studies selection process

Table 1. Overview on studies included in this review

Author and year	Type of study	Population studied	Results and conclusions
Sheik-Ali, 2021 (4)	Review	Erythema, swelling, tender over the nasal tip most common presentations of nasal vestibular furunculosis. Intranasal topical mupirocin and oral sodium fusidate most frequent successful management of NVF.	
Mohamed-Yassin, 2020 (5)	Case report	36-year-old woman with type-2 diabetes mellitus and dyslipidemia presenting with a four-day history of a red, swollen, and painful nose	Improvement after three days of intravenous antibiotics (ceftriaxone). Discharge with a course of oral cefuroxime.
Alton, 2016 (6)	Case report	6-year-old boy with nasal crusts gradually worsened, bleeding after removal	Antibacterial treatment with mupirocin and complete resolution
Sakat, 2015 (8)	Case report	49-year-old woman with 4-day history of focal red area and tender swelling on the tip of her nose	Intranasal topical mupirocin and oral sodium fusidate, with complete resolution
Lipschitz, 2017 (9)	Retrospective review	118 NV cases admitted to a tertiary medical center between 2008 and 2015; 12 patients (10.17%) diabetic; 3 patients immunosuppressed	Identified NV risk factors: nasal hair plucking (n=15, 14.41%); nose blowing (n=10, 9.32%); nose picking (n=9, 8.47%); nose piercing (n=5, 3.39%). Observed NV symptoms: mid-facial cellulitis (78.81%); abscess of the nasal vestibule (48.30%). MSSA as the most common isolate (81.25%). Risk of major complications extremely low even in complicated cases of NV requiring admission.
Figuereido, 2006 (13)	Randomized prospective trial	420 cases of nasal foreign bodies removed in the ENT service between December 1992 and December 1998	Vestibulitis and epistaxis commonest complications of nasal foreign bodies (9.05% of the cases)
von Schoenberg, 1992 (14)	Randomized prospective trial	105 patients with intranasal splints	Intranasal splints associated with significantly greater post-operative pain and a higher incidence of septal perforation and vestibulitis
Zambetti, 1994 (15)	Randomized prospective trial	60 HIV patients undergoing to a complete ENT examination	NV in stage 1 of HIV disease
Cathcart-Rake, 2018 (16)		100 patients undergoing systemic antineoplastic therapy, interviewed regarding the presence of nasal symptoms	Nasal symptoms (dryness, pain, bleeding, and scabbing) in 41% of surveyed patients. NV common among patients receiving taxane (71%) and VEGF-related therapies (78%).
Saracino, 2018 (17)	Case report	Diabetic 75-year-old woman with NV, worsened in the preceding 20 months despite multiple antibiotic cycles	Diagnosis of M. tuberculosis (fully susceptible to all antitubercular drugs), with following complete resolution
Shivaprakash, 2012 (18)	Case report	An adult diabetic patient	Identification of a nasal vestibular abscess due to Nocardiosis dasonvillei, successfully treated with clarithromycin and levofloxacin
Hemmaoui, 2014 (19)	Case report	26-year-old man with bilateral nasal obstruction associated with rhinitis, mild epistaxis and ulcerated lesion in the nasal vestibule, progressively invading the upper lip, present for almost 2 years	No response to ampicillin after positive biopsy for S. aureus. Identification of Leishmania in a second biopsy, with a favorable course in response to treatment with meglumine antimoniate (20 mg/kg/day for 30 days).
Maan, 2020 (20)	Case report	11-year-old child with a complicated nasal septal abscess, progressed from vestibulitis to septal abscess and further leading to sinusitis, orbital, and intracranial complications	Good response to aspiration of pus and medical treatment

Author and year	Type of study	Population studied	Results and conclusions
Ruiz, 2015 (21)	Retrospective chart review	115 cancer patients (68% treated with an EGFRi-based regimen)	13% of patients with multiple NV episodes. Nasal cultures obtained in 60% of episodes (94% positive for one or more organisms). Staphylococcus aureus as the most isolated organism (MSSA 43%; MRSA 3%).
Rohana, 2008 (25)	Case report	Teenage female with superior ophthalmic vein thrombosis and cavernous sinus thrombophlebitis after a 1-week history of a single acne-like lesion or furuncle at the anterior tip of the nose	Aggressive management with heparin and intravenous antibiotic, with improvement of signs and symptoms after 2 weeks of treatment and discharge with an anticoagulant.
Rambur, 1994 (27)	Letter to the editor	Description of etiology, sign and symptoms, management and treatment of nasal vestibulitis	
Anzai, 2020 (29)	Case series	4 cryosurgical ablation procedures treating common warts on the nasal vestibule	Absence of adverse event. Successful treatment.
Manole, 2021 (30)	Case report	2 cases of nasal NKTL: - a 73-year-old man with recurrent NV despite antibiotic treatment; - a 79-year-old woman with a large mass on the hard palate, invading into the floor of the nose	Definitive diagnosis with biopsy and histopathological and immunohistochemistry analysis. Multidisciplinary treatment, involving radiotherapy and medical oncologists.
Badran, 2004 (31)	Case report	62-year-old male smoker with a 6-year history of intermittent soreness and scabbing of the right nostril, treated with topical antibiotics (diagnosis of psoriasis and recurrent nasal furunculosis)	Area of ulceration on the lateral aspect of the right nasal vestibule, referring for an invasive squamous cell carcinoma arising in an area of carcinoma in situ. Surgical treatment (excision biopsy).
Mahasin. 2001 (33)	Case report	2-year-old boy developing multiple bilateral orbital abscesses secondary to nasal furunculosis	
Deweese, 1962 (34)	Letter to the editor		Treatment of NV with 5% ammoniated mercury into the skin of the vestibule 2 to 3 times daily, continuing for a week to 10 days
Sakr, 2015 (35)	Review		Mupirocin nasal ointment used for the nasal decolonization and prevention of staphylococcal infections in various settings like surgeries. Rising rates of resistance to mupirocin.
Williams, 1992 (36)	Clinical trial	30 patients commencing isotretinoin for acne, entering a double-blind, randomized, placebo-controlled trial to investigate the effect of pulsed intra-nasal mupirocin ointment on Staphylococcus aureus colonization	Increase in isolation of S. aureus throughout the period of treatment with isotretinoin in both mupirocin and placebo groups (increase significantly less in the mupirocin-treated group)
Williamson, 2017 (37)	Review		Use of topical antimicrobials (mupirocin and fusidic acid) in nasal decolonization of S. aureus, in the prevention and treatment of chronic wound infections
Okano, 2000 (38)	Clinical trial	0.5% gentian violet used in 28 cases of skin lesions once a day; a 0.3% solution applied on the nasal vestibules of 9 cases twice a day.	Period for eradication: 28 skin cases, 9.1 ± 6.0 days; 9 nasal lesions, 15.3 ± 9.0 days. No adverse reactions. Gentian violet potentially effective against MRSA.
Cathcart-Rake, 2020 (39)	Randomized controlled trial	40 patients with nasal vestibulitis associated with breast cancer-directed therapy (58% taxanes), treated with rose geranium nasal spray	Symptomatic benefit in all patients using the rose geranium nasal spray: little benefit in one, moderate in 11 (55%) and dramatic or complete resolution in 8 (40%).

NVF: nasal vestibular furunculosis; NV: nasal vestibulitis; MSSA: methicillin-sensitive Staphylococcus aureus; MRSA: methicillin-resistant Staphylococcus aureus; NKTL: nasal-type natural killer/T-cell lymphoma

Discussion

Epidemiological data about NV are uncertain due to the unavailability of studies that analyze prevalence and incidence in the general population. It is probably a common condition in both adults and children (6) with some reports even suggesting that it is the most common external nasal infection (7). The incidence and prevalence of NVF are also unknown (8).

Staphylococcus aureus is commonly isolated in the vestibule of patients suffering from NV and is thought to be the main cause of NV and NVF (9). Studies have shown that *S. aureus* can be found in the nose of 30% percent of the healthy human population (10); nasal vestibule could represent an ecological niche for the bacteria and its clinical importance is not limited to local infection, but also involves a risk of systemic spreading, particularly in frail patients (11); several studies highlighted the implication of its eradication for systemic infection prevention (12). Risk factors frequently reported for the development of NV are nose picking, excessive nose blowing, nasal hair plucking (9), nose piercing, nasal trauma, and foreign body retention (13). The right nostril appears to be more frequently affected, probably because of the right-hand predominance (7). Colder temperature, low humidity, air irritants, and smoking could play a role. Iatrogenic factors, such as nasal surgery and nasal splint placement, have also been implicated (14). All the above-mentioned factors probably create epithelium damage, which can be exploited by *S. aureus* for invasion and replication. As expected, diabetes and immunological disease, like HIV (15), predispose to nasal vestibule infections and could increase the odds of complications.

A recent study highlighted the importance of NV awareness in oncology practice, showing that patients receiving chemotherapeutic agents, particularly taxanes, often report nasal vestibule symptoms, such as dryness and epistaxis, probably due to the negative effects of these drugs on immune response and epithelial proliferation (16). Finally, it is worth noting that unusual infectious agents are rarely but notably implicated in NV, such as *Mycobacterium*, *Actinomyces*, or *Leishmania* (17-19). A major concern in NV and NVF is the possible spread of the infectious process in contiguous soft tissues, leading to nasal cellulitis, facial cellulitis, and septal abscess (20). Vascular dissemination, and subsequent intracranial involvement, must also be considered. This possibility is often attributed to the peculiar venous conformation of the so-called “danger area” of the face (or danger triangle zone), the area from the corners of the mouth to the bridge of the nose, including the nasal vestibule, where the risk of spread to contiguous facial areas and to the cavernous sinuses is thought to be higher. It is commonly assumed that this is due to the valveless nature of this vascular tract (21), but an anatomic study demonstrated the presence of venous valves in the facial vein and superior ophthalmic vein, inquiring that it is not the absence of venous valves, but rather the consistent communication between the facial vein and cavernous sinus that is important in the spread of infection (22).

Vascular dissemination may lead to troublesome and potentially life-threatening conditions such as ophthalmic vein thrombosis (23), preseptal cellulitis, and orbital cellulitis.

Intracranial dissemination can lead to brain abscess, meningitis, and thrombosis of the cavernous sinus. In this case, even with appropriate management, the prognosis is poor, and mortality remains up to 35% (24). The incidence of septic cavernous sinus thrombosis has been considerably reduced in developed countries with the introduction of antibiotics (25). In an Israeli retrospective study of 118 cases, no intracranial complications were encountered, suggesting that these complications can be avoided with appropriate treatment or being merely rare (9).

Primary care is usually the first presentation setting (5). A wide variety of nasal signs and symptoms are reported, such as pain (localized or radiating to nearby areas) (26), local erythema, dryness, yellow crusting, bleeding, nasal liquid discharge, congestion, nasal sores, and, infrequently, epistaxis (27). NVF causes erythema, swelling, and localized tenderness (8). A septal abscess can manifest as nasal obstruction and painful swelling of the anterior septum. Fever, headache, eye pain, and findings such as eye swelling, proptosis, reduction in visual acuity, and impaired eye motility are associated with serious complications such as orbital cellulitis and cavernous sinus thrombosis (24,28).

Diagnosis can be made clinically via anterior rhinoscopy, using a headlamp and nasal speculum. Differentials include nasal warts (29), eczema, lupus vulgaris tuberculosis, impetigo, nasal septum abscess, and neoplasms. A high index of suspicion is necessary in case of chronic or recurrent vestibulitis refractory to local therapy, which can be a sign of underlying malignancy (30,31). Cranial nerve examination is also important to rule out the possibility of a spread of the infection.

The opportunity for a nasal swab and bacterial culture for organisms identification, antibiotic susceptibility, and MIC profile (26) is not discussed in the relevant literature. Swabbing each and every patient suspected of having NVF could be impractical in an outpatient setting, where a “destroy-only” strategy is probably adequate and cost-effective compared to a “search-and-destroy” approach; moreover, obtaining a culture can be difficult because of crusting (6).

In case of suspected complications, a quick referral to an ENT specialist is warranted, and the threshold for admission should be low, especially in patients with advanced age and suffering from other comorbidities (immunosuppression, diabetes). The subsequent diagnostic flow includes neuroimaging with either contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) (24,32). A plain and contrast-enhanced CT scan is usually the first line, as it allows to evaluate cavernous sinus and other intracranial structures and assess the need for a surgical approach (33).

Some authors suggest adopting a clinical severity grading scale, with mild, moderate, and severe cases, requiring different therapeutic approaches (21). The management is mostly carried out on an outpatient basis (9).

For mild cases, boric acid, sulfathiazole, 5% ammoniated mercury, and many other agents have been used in the past (34). Nowadays topical antibiotics are the mainstay of treatment. Mupirocin is considered the gold standard for *Staphylococcus aureus* eradication (35) (regimen: twice a day for five days) (36), and it's indicated for nasal furunculosis as well (8). Mupirocin has the advantage of also acting

against MRSA, and this could have important implications since a higher prevalence of Methicillin-resistant strains is expected in the future (9); however, mupirocin resistance has been well described and while its prevalence varies between different countries, it has probably increased over the last decade (35).

Alternative topical antibiotic regimens include fusidic acid, which has been considered not justifiable as a monotherapy in cutaneous infections given the likelihood of resistance; neomycin, which probably performs less well than other topical antibiotics in this kind of infection; and bacitracin, which could be associated with contact allergy. Combinations of neomycin, bacitracin, and polymyxin (the so-called TAO, triple antibiotic ointment) are available and generally associated with low rates of *S. aureus* resistance (37).

Other topical agents, such as chlorhexidine, povidone-iodine, or alcohol are rarely reported in the relevant literature, although they could prove useful in dealing with antibiotic resistance. Topical gentian violet could have a potential effect on MRSA (38)

Prior to antibiotic ointment, saline irrigation or half-strength peroxide applied with a cotton swab is recommended by some (27); since the crusts appeared to represent an ideal medium for bacterial growth, it is reasonable to assume that the lavage of the nostrils is useful for the bacterial eradication (12). A recent study highlighted the efficacy of rose geranium in sesame oil nasal spray in treating nasal symptoms associated with chemotherapy (39). In case of considerable swelling and inflammation, some authors (6, 27) recommend applying hot packs and warm compresses several times a day, in order to promote circulation to the affected area. Incision and drainage may be useful in presence of fluctuance (6).

Severe cases and immunocompromised patients may require more aggressive approaches. Oral antibiotics are appropriate in case of infections refractory to topical antibiotics (21); some report the successful utilization of cephalexin (12). Nasal cellulitis is often treated with amoxicillin (40). If oral antibiotics fail, unusual infectious agents should be suspected (e.g. tuberculosis or actinomyces, leishmaniasis) (17-19), and adequate therapy should be established.

Finally, if complications occur, prompt hospitalization and head and neck referral are warranted, in order to administer intravenous antibiotics and supportive care and evaluate for surgical treatment.

Limits of the study

Our study presents a series of limits. Firstly, there are few studies on NV and NVF, almost all case report, with a lack of prospective randomized studies: consequentially, evidence is quite limited. Secondly, much literature is relatively outdated in time: the 27 studies included in this review were published over a period of 59 years, with the first article dating back to 1962.

Considering the widespread of both diseases in the general population, further studies are necessary, to better clarify their pathogenesis and prevention strategies, topics on which the literature is severely lacking.

Conclusions

Nasal vestibulitis and nasal vestibular furunculosis are reported to be common diseases mainly caused by *Staphylococcus aureus*. Risk factors include all conditions causing damage to the nasal epithelium, but also colder temperature, low humidity, air irritants, and smoking. Both NV and NVF are diagnosed clinically via anterior rhinoscopy, reserving neuroimaging to cases with intracranial involvement, and topical antibiotics remain the mainstay of treatment. A high index of suspicion is necessary in refractory cases and a quick referral to a head and neck specialist is warranted in case of complications. Further studies are required in order to clarify the pathogenetic mechanisms and the exact prevalence of these two conditions.

Statements and declarations

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript. No funds, grants, or other support was received.

Declarations

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