Original research article

OPEN ACCESS

Inter-societal Delphi Consensus on the topical nasal treatments in Italy

Attilio Varricchio[1], Livio Presutti[2], Ignazio La Mantia[3], Giorgio Ciprandi[4]

[1]Department of Otolaryngology, University of Molise, Campobasso, Italy; [2]ENT Department, University of Bologna, Italy; [3]ENT Department, University of Catania, Catania, Italy; [4]Allergy Clinic, Casa di Cura Villa Montallegro, Genoa, Italy

ABSTRACT

Topical nasal therapy is widely used in clinical practice by different specialists. However, it is multifaceted and still controversial. Namely, there is no consensus about the many aspects, and there needs to be specific guidelines.

Four independent experts involved 14 Italian scientific societies (concerning ENT, allergy, and pediatrics areas) to participate in generating an Intersocietal Delphi Consensus on this matter. Three iterative rounds collected experts (4 in the first round, 20 in the second round, and 45 in the third round) designed by the scientific societies based on their clinical expertise and documented scientific value. Thirty-four statements were discussed and voted on. At the second round, all statements accomplished a very high consensus grade (>95%). At the third round, many statements reached a high or very high grade of consensus (>70%). However, some statements did not obtain sufficient agreement. Consequently, there is a need to implement knowledge about this issue through educational initiatives and new studies conducted with a robust methodology.

In conclusion, topical nasal therapy deserves adequate knowledge as it is widespread and fruitful in managing upper respiratory diseases.

Key words: topical nasal therapy, device, upper respiratory diseases, adults, children

Correspondence: Giorgio Ciprandi, Casa di Cura Villa Montallegro, Via Boselli 5, 16146 Genoa, Italy, Phone 0039 3483200821- E-mail: gio.cip@libero.it

Authors' contributions: All co-authors contributed to the study conception and design. The first draft of the manuscript was written by Giorgio Ciprandi. All the co-authors commented and discussed the draft. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate: Not applicable being the manuscript a Delphi Consensus.

Conflict of interest: The co-authors declare no potential conflicts of interest with respect to research, authorship and/or publication of this article.

Acknowledgement: We would thank the panel of experts who participated to the third round: Eugenia Allegra, Salvatore Barberi, Gianluca Bava, Donatella Bignardi, Luisa Brussino, Carlo Caffarelli, Silvia Caimmi, Elena Cantone, Michele Cassano, Maurizio Catalani, Claudio Cravidi, Giulia Danè, Luca de Campora, Eugenio De Corso, Aurelio D'Ecclesia, Mario Di Gioacchino, Filippo Favuzza, Andrea Gallo, Angelo Ghidini, Cristiana Indolfi, Salvatore Leonardi, Maddalena Leone, Amelia Licari, Nicola Lombardi, Sara Manti, Paola Marchisio, Maurizio Marogna, Alberto Martelli, Antonio Moffa, Francesca Mori, Matteo Naso, Eustachio Nettis, Mario Notargiacomo, Roberta Olcese, Francesca Patria, Guido Pellegrini, Diego Peroni, Stefano Pucci, Erminia Ridolo, Claudia Salmaso, Lucia Semino, Giovanni Traina, Chiara Trincianti, Mona-Rita Yacoub, Anna Maria Zicari.

Introduction

The nose serves as the leading organ for respiration and performs many functions, including i) warming, humidifying, and filtering air; ii) guaranteeing innate and adaptive immune response to antigens; iii) smelling; iv) connecting with paranasal sinuses, Eustachian tuba, and nasopharynx; and v) contributing to speech.

The nose is the front door through which microbes, allergens, pollutants, and noxious agents penetrate the

body. As a result, inflammation and infection can readily occur, starting from the nose and usually spreading to adjacent tissues. The most important diseases affecting the upper airways are rhinitis, rhinosinusitis, otitis, and nasopharyngitis [1].

The nose is a duct characterized by high resistance and turbulence of the inspired airflow. The nasal turbinate structure guarantees an ideal condition to warm and moisten the inspired air. Together, these mechanisms permit nasal physiological health [2]. However, several pathophysiologic mechanisms, including infection, inflammation, trauma, mechanical abnormalities, iatrogenic and physical stimuli, alter nasal physiology.

The most prevalent rhinitis phenotypes are acute viral rhinitis (the common cold) and allergic rhinitis. Although these nasal diseases have different etiopathogenetic mechanisms, both present similar symptoms, including nasal itching, sneezing, rhinorrhea, and nasal congestion.

The term rhinosinusitis replaced the sinusitis definition, as each sinus disease derives from initial rhinitis [3]. Rhinosinusitis may be acute or chronic if it lasts more than one month. Chronic rhinosinusitis (CRS) may present with nasal polyps (CRSwNP) or without (CRSsNP), as stated by the EPOS guidelines [4].

Acute otitis media (AOM) is a common disease mainly affecting children. It usually follows an acute upper airway infection [5]. Allergic rhinitis and turbinate hypertrophy are relevant risk factors for AOM [6].

Acute nasopharyngitis may also include tonsillitis (pharyngotonsillitis) and adenoiditis. This disease is commonly acute, and the cause is infectious, starting from the nose. Namely, the common cold includes nasopharynx involvement [7].

All these upper airway diseases share pathogenic mechanisms. In particular, mucus hypersecretion and defective mucociliary clearance cause mucus accumulation, interfering with airflow passage [8]. Nasal congestion due to vasodilation and turbinate edema also reduces the airflow passage [9]. Also, chronic inflammation causes turbinate hypertrophy, leading to nasal obstruction [10]. As a result, mucus stagnation promotes microbial overgrowth, favoring infection spreading to the sinuses and the middle ear [11]. Posterior rhinorrhea dripping into the pharynx and larynx triggers cough; this phenomenon is called post-nasal drip and defines the rhino-sinus-bronchial syndrome [12].

Namely, impaired nasal function significantly affects lower airways, mainly asthma and sleeping [13].

Consequently, a close and "dirty" nose favors, keeps and magnifies respiratory infections and inflammatory diseases [14]. As a result, an ideal therapy should "open and clean" the nose to ensure the health of the respiratory airways [14]. Thus, opening and cleaning the nose is the most simple and helpful remedy that may be pursued in everyday practice and at all ages.

Physical, medical, and surgical treatments may control upper airway diseases. Intranasal administration of active products represents the safest and most effective way to quickly obtain normal nasal patency, dampen inflammation, contrast pathogens, and consequently relieve symptoms.

Schematically, the types of administration of topical nasal treatments may be classified into three main groups: irrigation, nebulization, and drop instillation. The active compounds topically administrable include saline (hypertonic and isotonic) solutions, nonpharmacological agents (e.g., hyaluronic acid, resveratrol, xylitol, glycerol, glycyrrhetic acid, lactoferrin, oligoelements, vitamins, etc.), and drugs (e.g., antihistamine, corticosteroid, α–adrenergic, antibiotics). All upper respiratory diseases may be treated by topical therapy. Indeed, there is valuable evidence that topical nasal therapy is effective and safe.

However, topical nasal treatments are a debated issue. No *ad hoc* guideline provides general and specific recommendations on this matter, and some doctors are reluctant to prescribe them.

Therefore, an Intersocietal Delphi Consensus faced this theme by proposing a series of statements voted on by a panel of Italian experts on this topic. Namely, the Delphi method was an indirect, anonymous, and iterative way to obtain a consensus [15].

Materials and methods

Delphi method

A modified Delphi method was used to reach a consensus among Italian specialists, including otorhinolaryngologists, pediatricians, and allergologists.

The first round involved a restricted group of independent experts (four) constituting the steering committee that drafted a list of statements to be voted on.

The steering committee requested an interest in participating in a number of Italian scientific societies that are involved in the management of upper airway pathologies, particularly in otorhinolaryngology, pediatrics, and allergology.

The 14 scientific societies that have joined the project are reported in Table 1.

The second round involved a group of 20 experts nominated and delegates by the scientific societies participating in this project (Table 1). These experts participated in a web-based round table discussion that was held in January 2024. During this remote meeting, the statements were discussed, and some changes were made. Subsequently, anonymously, these experts expressed their level of approval.

The third round consisted of administering the statements approved during the second round. For this purpose, a provider agency (Lingomed) set up a web platform that allowed anonymous voting of all statements. The panel of participants included 45 experts selected based on their clinical practice (at least ten years of specialized activity) and scientific value (at least ten publications in peer-reviewed journals on this topic in the last five years).

The participants anonymously voted using the same platform.

After collecting and analyzing the third round's results, the steering committee discussed and approved them.

The Delphi consensus process was conducted between January 2024 and April 2024.

Delphi statements

Table 2 presents the list of the (previously approved) statements proposed to the participants in the third round. The statements are 34 and concerned the most common medical conditions that may benefit

Table 1. List of Scientific Societies participating to the Delphi Consensus and their Delegates who participated to the second round.

Berardi Carlo	Associazione Italiana Otorinolaringoiatri Libero Professionisti (AIOLP)
Borrelli Paolo	Associazione Allergologi Immunologi Italiani Territoriali e Ospedalieri (AAIITO)
Brunese Francesco P.	Società Italiana di Allergologia e Immunologia Pediatrica (SIAIP)
Casale Manuele	Società Italiana di Otorinolaringoiatria e Chirurgia Cervico Facciale (SIOeChCF)
Ciprandi Giorgio	Società Italiana di Allergologia e Immunologia Pediatrica (SIAIP)
Cristalli Giovanni	Società Italiana di Otorinolaringologia Pediatrica (SIOP)
Di Maria Domenico	Associazione Ospedaliera Italia Centromeridionale Otorinolaringoiatrica (AOICO)
Gelardi Matteo	Accademia Italiana di Citologia Nasale (AICNA)
La Mantia Ignazio	Società Italiana di Otorinolaringologia Pediatrica (SIOP)
Landi Massimo	Società Italiana per le Malattie Respiratorie Infantili (SIMRI)
Macchi Alberto	Accademia Italiana di Rinologia (IAR)
Marchese Ragona Rosario	Società Italiana di Otorinolaringoiatria e Chirurgia Cervico Facciale (SIOeChCF)
Marseglia Gian Luigi	Società Italiana di Allergologia e Immunologia Pediatrica (SIAIP)
Pagella Fabio	Società Italiana di Otorinolaringoiatria e Chirurgia Cervico Facciale (SIOeChCF)
Passali Giulio	Società Italiana di Rinologia (SIR)
Presutti Livio	Società Italiana di Otorinolaringoiatria e Chirurgia Cervico Facciale (SIOeChCF)
Rossi Oliviero	Società Italiana di Allergologia, Asma ed Immunologia Clinica (SIAAIC)
Tosca Maria Angela	Società Italiana di Allergologia e Immunologia Pediatrica (SIAIP)
Varricchio Attilio	Società Italiana di Pediatria Preventiva e Sociale (SIPPS)
Varricchio Alfonso M.	Associazione Italiana Vie Aeree Superiori (AIVAS)

Table 2. Statements, percentages of agreement grades (4+5), and standard deviations of score 4 + 5 concerning the second round.

Statement	% agreement (scores 4 + 5)	Mean score (SD)
1. The most widely adopted guidelines in Europe are ARIA for rhinitis, EPOS 2020 and EUFOREA for rhinosinusitis.	93%	4.7 (0.4)
2. Rhinitis can be classified into three main phenotypes: allergic, non-allergic (inflammatory and non-inflammatory), and infectious (viral and bacterial).	96%	4.6 (0.5)
3. The nasal spray is the most suitable administration device for treating acute rhinitis and rhinosinusitis.	61%	4.5 (0.5)
4. The nasal spray is the most suitable administration device for treating chronic rhinitis and rhino-sinusitis.	84%	4.5 (0.5)
5. The micronized nasal douche is the most suitable administration device for the treatment of nasopharyngitis.	75%	4.4 (0.5)
6. The operating mechanism of devices dedicated to inhalation therapy consists of the nebulization of a pharmacological solution, with subsequent dispersion of the micronized particles in the various anatomical sites of interest, depending on the mass median aerodynamic diameter (MMAD).	96%	4.7 (0.5)
7. Nasal irrigations are not part of inhalation therapy, as they lack dispersion power and cannot nebulize.	81%	4.5 (0.5)
8. Nasal irrigations, on the other hand, are ideal for mechanically removing secretions and activating mucociliary clearance.	94%	4.7 (0.5)
9. If used beforehand, nasal irrigations increase the therapeutic effectiveness of an inhalation treatment.	87%	4.5 (0.5)
10. Nasal irrigations are divided into three main types: i) gravity-fed (Lavonase-type bag dispenser - Nasir); ii) high-pressure and low-volume (Rinaqua nozzle syringe system – Rinoway; and wave bellows system Atomix, Eukin or Linfovir Iperwash and Isowash); iii) low-pressure and high-volume (Rinoway or XNaso).	89%	4.7 (0.5)
11. Inhaler devices dedicated to nasal cavity medication require a MMAD of more than 15 and less than 100 μm.	84%	4.5 (0.5)
12. The MADD of the atomized particles conditions their deposition at the airway anatomical sites, particularly: i) particles from 100 up to 60 μm stop at the Ostium-Meatal Complex (COM); ii) <60 and up to 30 μm arrive at the Spheno-Ethmoidal Complex (RSE); iii) <30 and up to 15 μm reach the Nasopharynx; iv) <15 μm and up to 10 μm reach the Pharyngeal-Laryngeal District; v) <5 μm reach the Lower Airways.	93%	4.6 (0.5)
13. The indication for topical nasal therapy in diseases of the nasal cavity and Nasopharynx is motivated by three main factors: the immunohistochemical characteristics of inflammation, which is superficial; the high bioavailability of the drugs against a reduced systemic absorption; and the reduction in side effects compared to systemic administration.	94%	4.7 (0.5)
14. Topical nasal therapy does not exclude systemic treatment, which is often synergistic.	98%	4.8 (0.4)
15. The most indicated molecule for treating allergic and non-allergic cell-mediated rhinitis is the topical corticosteroid, administered as a pre-dosed spray.	96%	4.6 (0.5)
16. In allergic and non-allergic rhinitis, topical antihistamines are indicated to reduce 'irritative' (i.e., histamine-dependent) symptoms.	78%	4.6 (0.5)
17. In allergic and non-allergic rhinitis, the fixed combination of topical corticosteroid and antihistamine is indicated to treat both 'irritative' and 'inflammatory' symptoms simultaneously.	83%	4.6 (0,5)
18. In viral infectious rhinitis, the most suitable molecules for treatment are antivirals (e.g., resveratrol and xylitol) during the first 10 days.	66%	4,3 (0.5)
19. The device indicated for viral infectious rhinitis is the pre-dosed spray.	66%	4.3 (0.5)

Statement	% agreement (scores 4 + 5)	Mean score (SD)
20. In bacterial infectious rhinitis, when symptoms persist beyond 10 days, or if they worsen after the first 5 days, topical antibiotics are the most indicated molecules, provided they are dose-dependent (quinolones, aminoglycosides, and macrolides).	57%	4.2 (0.4)
21. The device to be used in bacterial infectious rhinitis is the micronized nasal douche, manual and/or pneumatized.	71%	4.3 (0.4)
22. Ipratropium bromide is indicated in the treatment of 'watery' rhinorrhoea.	64%	4.6 (0.5)
23. Nasal sprays containing α-adrenergic are indicated in the treatment of nasal obstruction only for a few days (within 7 days) and above 12 years of age.	83%	4.5 (0.5)
24. Nasal sprays containing the topical corticosteroid are indicated in acute rhino-sinusitis, as they are capable of decongesting and reducing oedema at the COM and RSE sites, and of promoting mucociliary clearance and ventilation of the anterior and/or posterior rhino-sinus system.	82%	4.5 (0.5)
25. The molecule most indicated as the first therapeutic approach and as maintenance therapy for CRSwNP and CRSsNP is the topical nasal corticosteroid.	94%	4.6 (0.5)
26. The pre-dosed spray is the most suitable device for topical therapy of CRSwNP and CRSsNP.	89%	4.5 (0.5)
27. Nasal drops can be used in the topical therapy of CRSwNP and CRSsNP.	43%	4.4 (0.5)
28. Nasal irrigations with hypertonic saline solution can be used in the topical therapy of CRSwNP and CRSsNP in synergy with pre-dosed sprays containing topical corticosteroid	85%	4.4 (0.5)
29. In viral infectious rhino-pharyngitis, the most suitable molecule for topical treatment is an antiviral during the first 10 days, nebulized with a micronized, manual or pneumatic nasal douche.	57%	4.2 (0.4)
30. In bacterial infectious rhino-pharyngitis, when symptoms persist beyond 10 days, or if they worsen after the first 5 days, topical antibiotics are the most suitable molecules, provided they are dose-dependent (quinolones, aminoglycosides, and macrolides), nebulized with a micronized nasal douche, manual or pneumatic.	56%	4.2 (0.4)
31. In treating chronic adenoiditis, the most indicated molecule is topical corticosteroid for at least 4 weeks, nebulized with the Micronised Nasal Shower.	71%	4.4 (0.5)
32. High molecular weight hyaluronic acid is the molecule indicated in the treatment of remodeling and reparative regeneration of the nasal mucosa, both after surgery and after chronic inflammatory stress.	85%	4.4 (0.5)
33. To optimize the effectiveness of topical nasal therapies, it is essential to explain to the patient the correct way to use and maintain the various devices and the use of the various molecules.	94%	4.7 (0.4)
34. Patient engagement and personalized therapy are based on engaging the patient in decision-making and sharing the most suitable treatment.	94%	4.8 (0.4)

from intranasal therapy and the indications for diseases and compounds.

Delphi assessment

The Delphi Consensus Panel was requested to rate their agreement with each questionnaire statement using a 5-point Likert scale, ranging from 1 (strongly disagree) to 5 (strongly agree). Each expert provided individual and anonymous feedback on the statements, considering routine RRIs practice and clinical evidence. The number and percentage of participants scoring each item as 1–2 (disagreement) or 4–5 (agreement) was calculated.

The scientific committee then discussed the results in a virtual meeting. For each questionnaire statement, the consensus was considered to have been achieved based on the agreement (score 4-5) of at least 70% of the Consensus Panel and the successive acceptance of the steering committee.

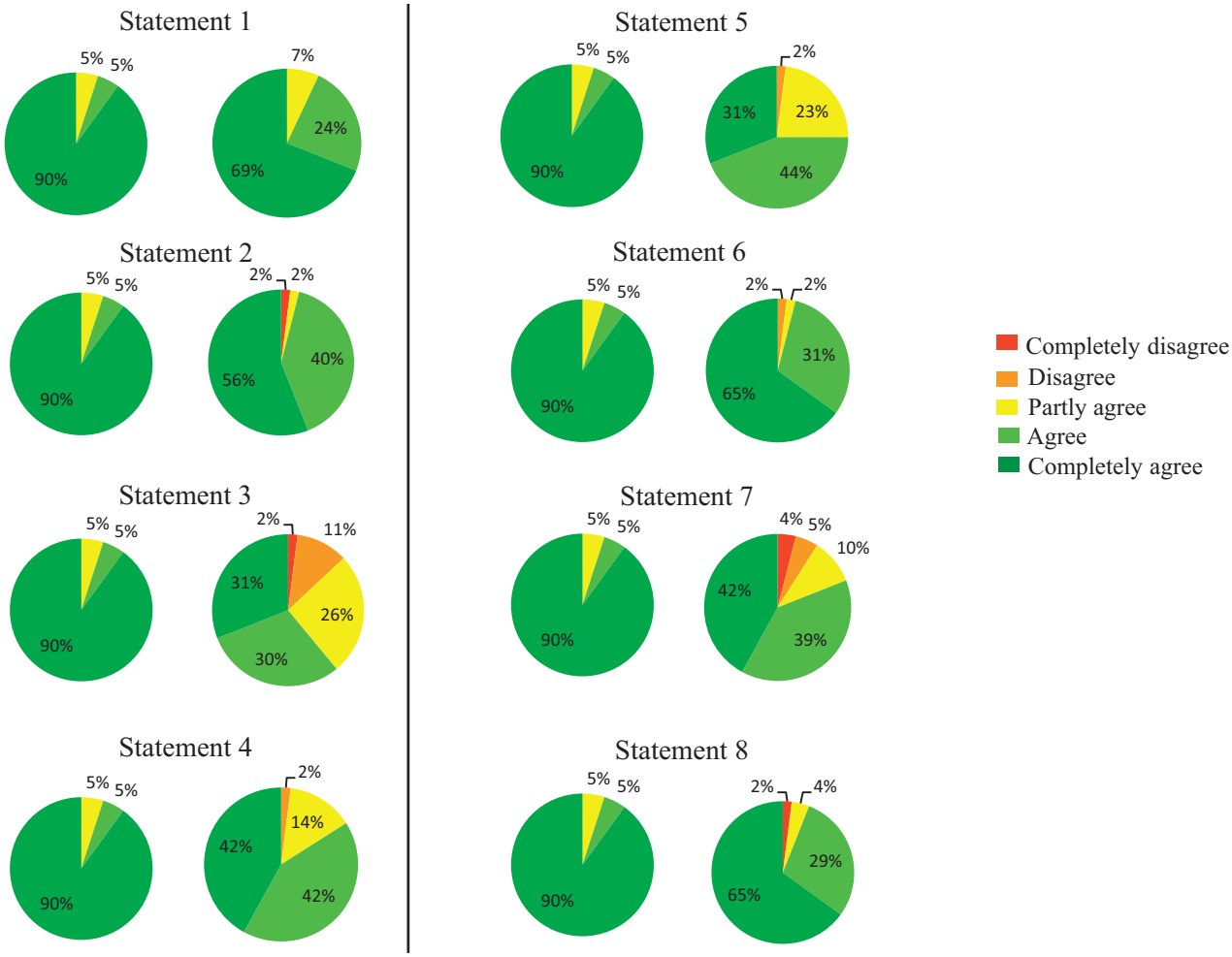

Figure 1. Distribution of agreement grades for the statements 1-8.

The statistical analysis was descriptive and a mean score of the sum of 4+5 scores was calculated also considering the standard deviation.

Results

The first round served to draft a list of statements to administer to the panel of experts designed by the 14 Italian scientific societies involved in the management of upper respiratory disorders. This round included five independent experts who constituted the steering committee. The agreement among these steering committee members was entire, i.e., a 100 percent complete agreement (score 5) was reached for all 34 statements.

The second round included 16 other experts, designed by the scientific societies, who discussed and voted on the 34 statements. The agreement among these experts was very high: 90% complete agreement (score 5) for all statements and 95% considering also score 4, the results are reported in Table 2 and Figures 1-5.

The third round considered a panel of experts selected by the steering committee. The voting results are reported in Figures 1-5.

Ten statements (1, 2, 6, 8, 13, 14, 15, 25, 33, and 34) obtained an agreement level >90%.

Nine statements (4, 9, 10, 17, 23, 24, 26, 28, and 32) obtained an agreement level between 80% and 89%.

Five statements (7, 11, 12, 16, 21, and 31) obtained an agreement level between 70% and 79%.

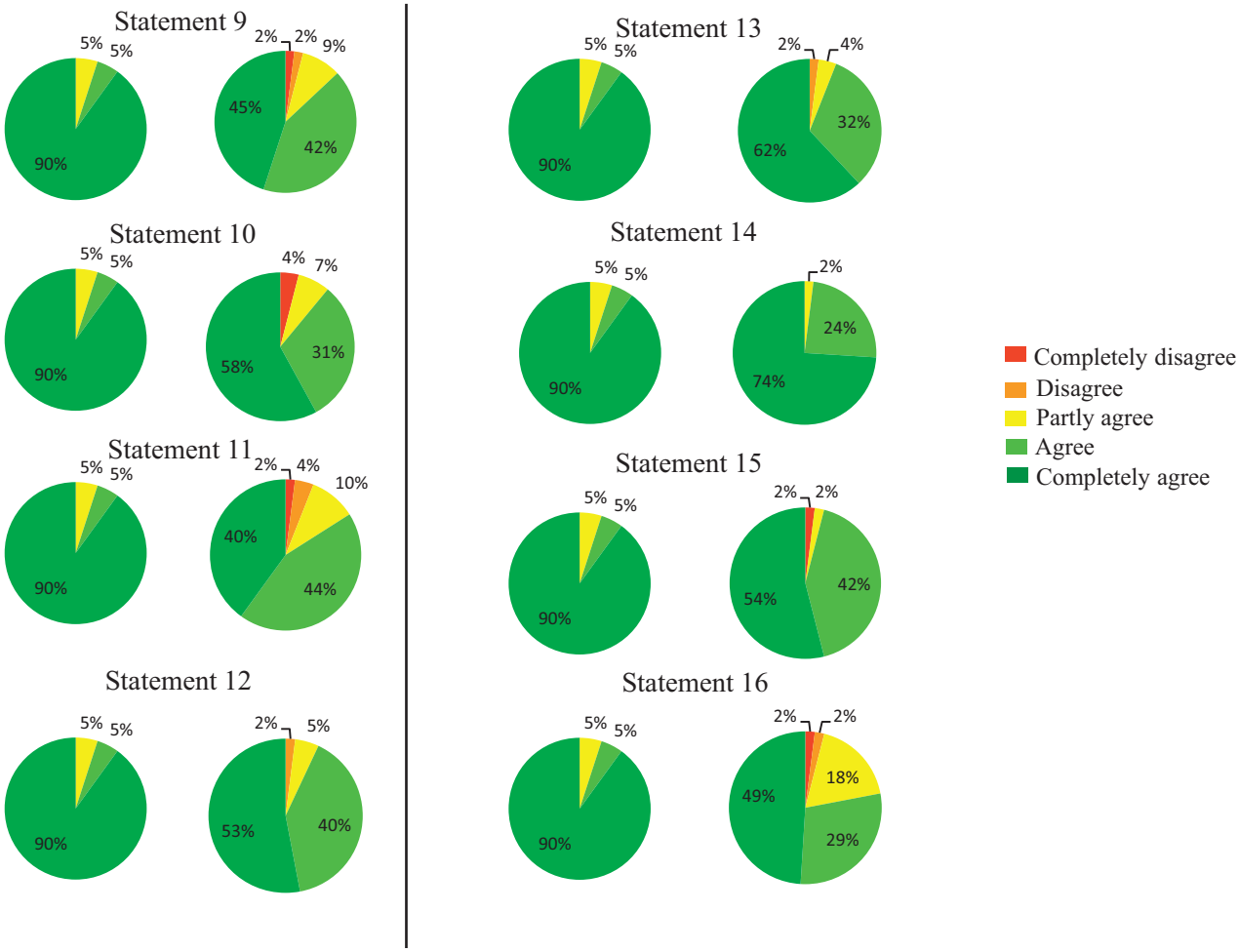

Figure 2. Distribution of agreement grades for the statements 9-16.

Consequently, 24 statements reached a positive consensus, such as >70%. Contrarily, ten statements did not achieve a sufficient agreement.

Discussion

Topical nasal therapy is ideal for administering solutions and active compounds in managing patients with upper airway diseases. In this regard, the prototypical model is the nasal lavage. The nasal lavage removes mucus, inflammatory cells, mediators, cytokines, pathogens, and harmful substances by washing the nasal cavity away. In addition, nasal lavage includes different administration methods, such as pre-dosed spray, nasal shower, irrigation, insufflation, fumigation, and nebulization [16]. Therefore, nasal lavage is an umbrella definition that encompasses many methods and active compounds' use. However, nasal lavage does not medicate nasal diseases, but simply washes. To medicate, other tools should be used, but there is congeries of devices and substances that are used in clinical practice, seldom inappropriately.

Consequently, this matter is complex and discussed. For these reasons, an Intersocietal Delphi Consensus may help define and clarify controversial aspects and suggest a pragmatic approach in clinical practice.

This document may be relevant as it was shared by a group of particularly qualified experts representing as many as 14 Italian Scientific Societies. Therefore, the results obtained can be applied at a national

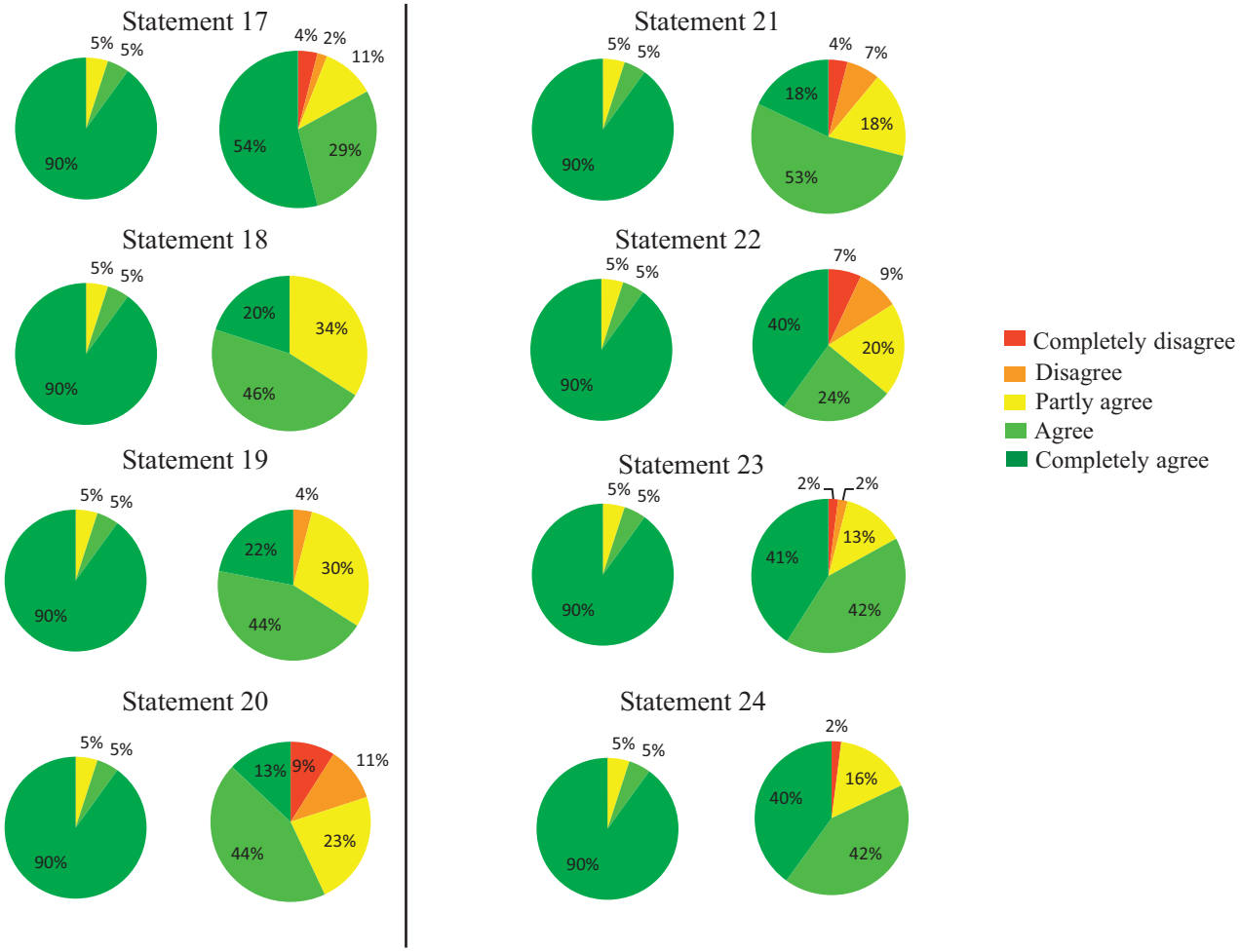

Figure 3. Distribution of agreement grades for the statements 17-24.

and interdisciplinary level. This opportunity also represented a virtuous, integrated, and multidisciplinary management model of prevalent diseases.

In particular, most statements achieved a good level of agreement, but as expected, some statements had a low consensus level. This fact is not surprising, as some aspects are controversial and require adequate attention.

The results of the vote at the third round of each statement is presently discussed in this document.

Statement 1 declared that the most widely adopted guidelines in Europe are ARIA for rhinitis, EPOS 2020, and EUFOREA for rhinosinusitis [3,4,17,18]. This statement had a 93% consensus, attesting that these guidelines are widely accepted and shared.

Statement 2 stated that rhinitis can be classified into three main phenotypes: allergic, non-allergic (inflammatory and non-inflammatory), and infectious (viral and bacterial), as reported in the literature [4,17]. This statement reached 96% agreement, confirming the high grade of consensus.

Statement 3 proposed that nasal spray is the most suitable administration device for treating acute rhinitis and rhinosinusitis [4,19,20]. However, this statement obtained only 61% of the consensus. This low agreement level conflicts with guidelines and the results of the second round. This discrepancy could depend on the belief that acute rhinitis is substantially the common cold most people retain and is self-resolving without treatment.

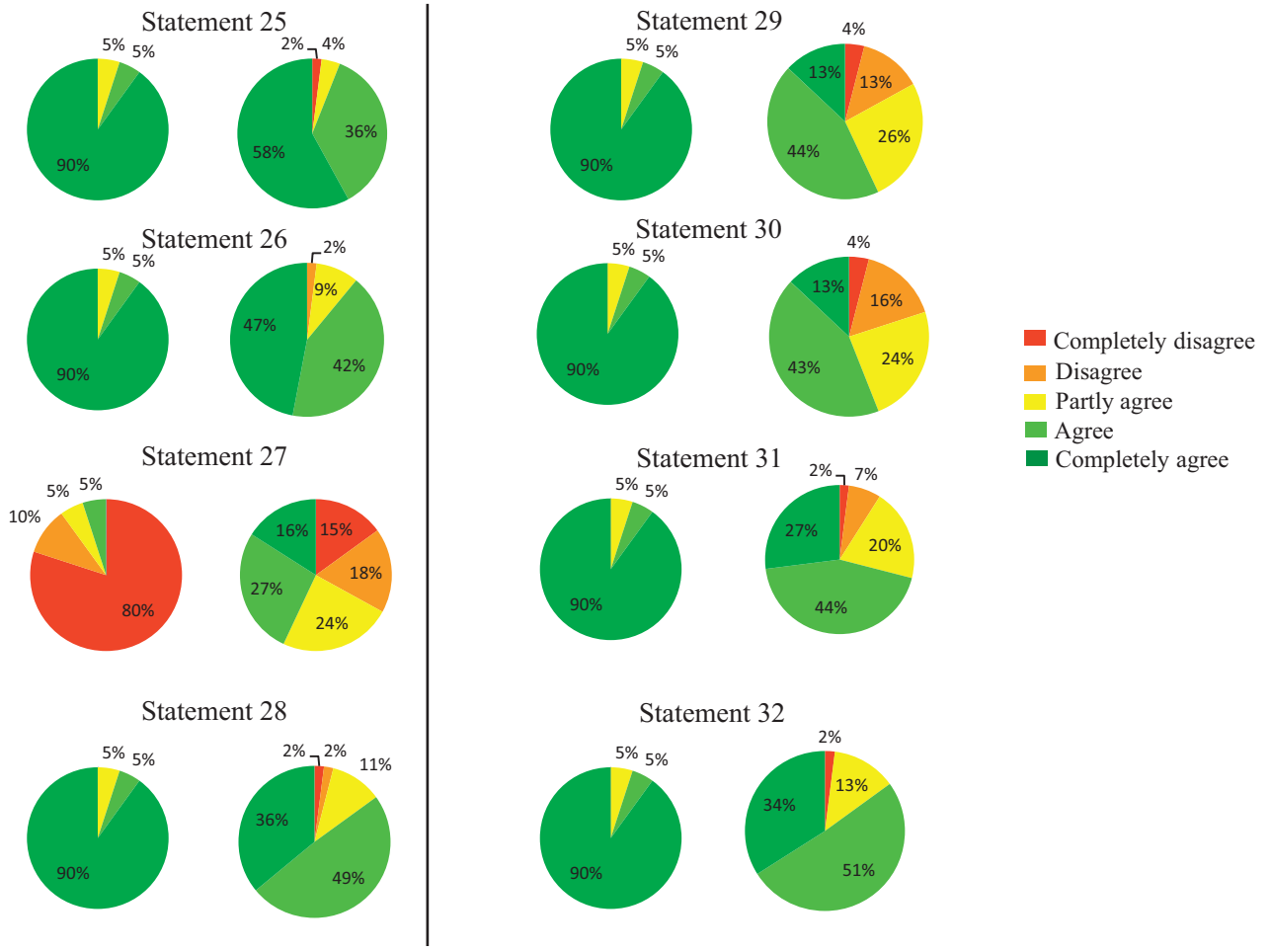

Figure 4. Distribution of agreement grades for the statements 25-32.

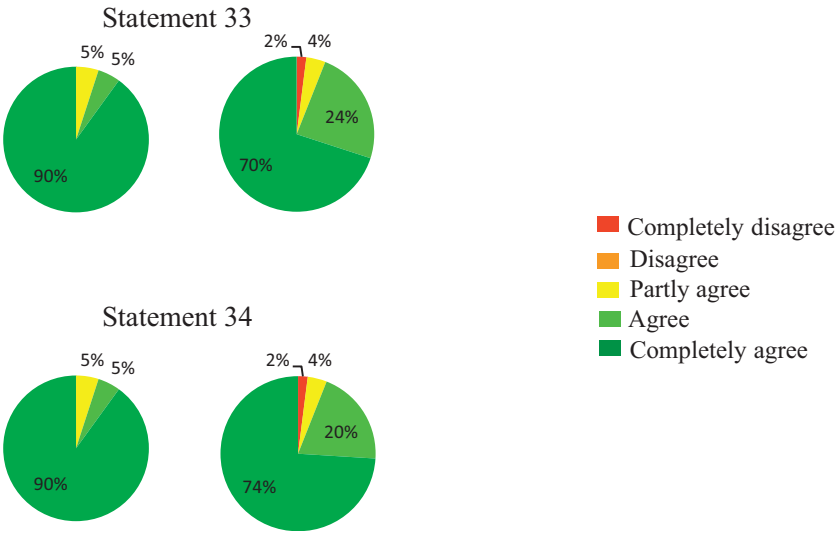

Figure 5. Distribution of agreement grades for the statements 33-34.

Statement 4 defined nasal spray as the most suitable administration device for treating chronic rhinitis and rhinosinusitis [4]. This statement obtained 84% agreement. This outcome might mean there is confidence in the need for a nasal spray for chronic conditions but not acute ones.

Statement 5 concerned the micronized nasal douche is the most suitable administration device for the treatment of nasopharyngitis [21-24]. The agreement was 75%. Probably, this low consensus depends on the fact that there is poor knowledge concerning the actual value of micronized douche in topically treating nasopharyngitis despite published studies [21-24].

Statement 6 proposed that the operating mechanism of devices dedicated to inhalation therapy consists of the nebulization of a pharmacological solution, with subsequent dispersion of the micronized particles in the various anatomical sites of interest, depending on the mass median aerodynamic diameter (MMAD). This statement was 95% agreed upon. The literature on this topic is well-known and accepted [25-27].

Statement 7 reported that nasal irrigations are not part of inhalation therapy, as they lack dispersion power and cannot nebulize. The agreement was 81%; inhalation therapy implies that a liquid should be transformed so that it can be dispersed and thus inhaled. This modality, therefore, requires the nebulization of a compound, which usually takes place using special instruments: nebulizers. Nasal irrigation consists of administering a given volume of liquid that is not changed in its state, i.e., always remains liquid [28]. Thus, irrigation does not belong to inhalation therapy. Some participants may not know this information.

Statement 8 declared that nasal irrigations, on the other hand, are ideal for mechanically removing secretions and activating mucociliary clearance. The consensus was 93%, which confirmed widespread belief about the benefit of nasal irrigation [29-31].

Statement 9 declared that nasal irrigations increase the therapeutic effectiveness of an inhalation treatment if used beforehand. This statement achieved 86% agreement, confirming the widely documented benefit of this method [32-34].

Statement 10 stated that nasal irrigations are divided into three main types: i) gravity-fed (Lavonase-type bag dispenser - Nasir); ii) high-pressure and low-volume (Rinaqua nozzle syringe system – Rinoway; and wave bellows system Atomix, Eukin or Linfovir Iperwash and Isowash); iii) low-pressure and high-volume (Rinoway or XNaso). The consensus was 89%. There was good knowledge concerning the types of irrigation, as also evidenced by several studies [4,35-37].

Statement 11 declared that inhaler devices dedicated to nasal cavity medication require an MMAD of over 15 and less than 100 μm. The agreement was 83%. There was probably incomplete knowledge about the physics of mass median aerodynamic diameters despite the topic being investigated adequately [25-27,38,39].

Statement 12 defined that the MADD of the atomized particles conditions their deposition at the airway anatomical sites, particularly: i) particles from 100 up to 60 μm stop at the Ostium-Meatal Complex (COM); ii) <60 and up to 30 μm arrive at the Spheno-Ethmoidal Complex (RSE); iii) <30 and up to 15 μm reach the nasopharynx; iv) <15 μm and up to 10 μm reach the Pharyngeal-Laryngeal District; v) <5 μm reach the Lower Airways. This statement had 83% of consensus. Although there is evidence about the relevance of the mass diameters, this matter still requires adequate information for some specialists [25-27,38,39].

Statement 13 stated that the indication for topical nasal therapy in diseases of the nasal cavity and nasopharynx is motivated by three main factors: the superficial immunohistochemical characteristics of inflammation, the high bioavailability of the drugs against a reduced systemic absorption, and the reduction in side effects compared to systemic administration. The agreement was 93%, attesting that these concepts are well-documented in the literature [40-43].

Statement 14 reported that topical nasal therapy does not exclude systemic treatment, which is often synergistic. The agreement was almost full (97%). This statement effectively proposed a concept that is rather obvious and shared [4,17].

Statement 15 asserted that the most indicated molecule for treating allergic and non-allergic cell-mediated rhinitis is the topical corticosteroid, administered as a pre-dosed spray. Consistent with the previous statement, this statement also had a high agreement (95%) and is well recognized by guidelines [4,17,18].

Statement 16 expressed that in allergic and non-allergic rhinitis, topical antihistamines are indicated to reduce 'irritative' (i.e., histamine-dependent) symptoms. The consensus was 78%. Some participants believe symptom occurrence depends on several mediators that exceed the mere histamine effects. However, there is a consideration of the relevance of antihistamines as a valuable option in managing "histamine-dependent" symptoms [44,45].

Statement 17 stated that in allergic and non-allergic rhinitis, the fixed combination of topical corticosteroid and antihistamine is indicated to simultaneously treat both 'irritative' and 'inflammatory' symptoms. The agreement was 82%. There is consolidated evidence that this association is effective, but some experts are not very convinced about its complete effectiveness despite several studies [17,47,48].

Statement 18 expressed that in viral infectious rhinitis, the most suitable molecules for treatment are antivirals (e.g., resveratrol and xylitol) during the first ten days. The consensus was 66% A considerable number of experts considered that the use of topical antivirals is not indicated in this clinical condition. The robustness of the evidence is likely not particularly high in studies that have explored this aspect because they were all conducted in Italy, and the methodology was not particularly robust [49-52].

Statement 19 declared that the device indicated for viral infectious rhinitis is the pre-dosed spray. The agreement was 66%. Also, in this case, some panelists believed that this statement had no sufficient evidence and, consequently, expressed their perplexity on this issue, as recently outlined [53].

Statement 20 affirmed that in bacterial infectious rhinitis, when symptoms persist beyond ten days or if they worsen after the first five days, topical antibiotics are the most indicated molecules, provided they are dose-dependent (quinolones, aminoglycosides, and macrolides). The agreement was low: 56%. Many participants may have misunderstood the meaning of the statement, believing that topical therapy should substitute systemic treatment. Severe infections require adequate systemic antibiotics, but there is evidence that topical antibiotics could also effectively treat this condition [54,57].

Statement 21 stated that the device to be used in bacterial infectious rhinitis is the micronized nasal douche, manual and/or pneumatized. The consensus was 71%. This matter is strictly the domain of the ENT specialist; in fact, studies have been conducted in that field [54,55,58]. As a result, the other specialists need to familiarize themselves with this subject.

Statement 22 stated that ipratropium bromide is indicated in the treatment of 'watery' rhinorrhoea. The consensus was 64%. For some participants, little is known about this molecule, and few studies have been conducted on it. However, a recent meta-analysis has again reconsidered this molecule [59].

Statement 23 proposed that nasal sprays containing a-adrenergic are indicated for treating nasal obstruction only for a few days (within seven days) and for children above 12 years of age. The agreement was 82%. There is awareness that decongestants are effective, but they are burdened with significant side effects, and the Italian regulatory agency (AIFA) has proscribed them for children under the age of 12. However, use must be limited in time to avoid even irreversible damage [60,61].

Statement 24 declared that nasal sprays containing the topical corticosteroid are indicated in acute rhinosinusitis, as they can decongest and reduce edema at the COM and RSE sites and promote mucociliary clearance and ventilation of the anterior and/or posterior rhinosinus system. The consensus was 82%. This point has been underlined in the EPOS guidelines [4]. However, some participants (not ENT) may not know this recommendation.

Statement 25 stated that the topical nasal corticosteroid is the molecule most indicated as the first therapeutic approach and as maintenance therapy for CRSwNP and CRSsNP. The agreement was 94%. This high consensus endorsed the widespread dissemination of EPOS guidelines and literature [4,62].

Statement 26 reported that the pre-dosed spray is the most suitable device for topical therapy of CRSwNP and CRSsNP. The agreement was 89%. Also, for this statement, the EPOS recommendations are well-known and adopted [4].

Statement 27 affirmed that nasal drops can be used in the topical therapy of CRSwNP and CRSsNP. The agreement was 43%. However, this statement had to be considered adversely. Namely, there is evidence that nasal drops quickly slide out of the nasal cavity

after instillation, so they cannot exert a local therapeutic effect [21]. However, nasal drops are still popular, as many doctors continue to prescribe them without knowing this drawback.

Statement 28 expressed that nasal irrigations with hypertonic saline solution can be used in the topical therapy of CRSwNP and CRSsNP in synergy with pre-dosed sprays containing topical corticosteroid. The consensus was 85%. Indeed, the EPOS guidelines recommend nasal irrigations for treating both CRS phenotypes [4].

Statement 29 stated that in viral infectious rhino-pharyngitis, the most suitable molecule for topical treatment is an antiviral during the first ten days, nebulized with a micronized, manual or pneumatic nasal douche. The agreement was 56%. This result consisted of other outcomes concerning the use of topical antivirals. There is widespread belief that viral infections do not require specific treatments, and antivirals, such as xylitol or resveratrol, are not indicated despite positive literature [49-52,63].

Statement 30 expressed that in bacterial infectious rhino-pharyngitis when symptoms persist beyond ten days or if they worsen after the first five days, topical antibiotics are the most suitable molecules, provided they are dose-dependent (quinolones, aminoglycosides, and macrolides), nebulized with a micronized nasal douche, manual or pneumatic. The consensus was 56%. Likewise, statements 20 and 21 need to be revised for a better agreement. This statement might generate a misunderstanding about the use of antibiotics, as systemic antibiotics use is settled in clinical practice. A recent review pointed out that solid evidence was lacking for nebulized antibiotics for treating upper respiratory infections [64]. However, there is conflicting evidence for systemic antibiotics, as recently considered by a meta-analysis [65].

Statement 31 declared that in treating chronic adenoiditis, the most indicated molecule is topical corticosteroid for at least 4 weeks, nebulized with the Micronized Nasal Shower. The agreement was 71%. The degree of consensus was not particularly high despite the fact that many studies and documents support this recommendation [66-69].

Statement 32 declared that high molecular weight hyaluronic acid is the molecule indicated in the treatment of remodeling and reparative regeneration of the nasal mucosa, both after surgery and after chronic inflammatory stress. The agreement was 84%. Evidence shows that hyaluronic acid at high volume effectively restores mucosal structure and function [4,70-73].

Statement 33 stated that to optimize the effectiveness of topical nasal therapies, it is essential to explain to the patient the correct way to use and maintain the various devices and the use of the various molecules. The agreement was 93%. Indeed, there is convinced belief that correct use and adequate compounds are fundamental requirements for treatment efficacy and safety [74-76].

Statement 34 expressed that patient engagement and personalized therapy are based on engaging the patient in decision-making and sharing the most suitable treatment. The consensus was 93%. Patient engagement is of paramount relevance in managing every disease, so this aspect is critical for nasal conditions [78,79].

The comparison of the results obtained during the second round and the third allows to draw some relevant considerations. The second round achieved a very high consensus probably as it derived from a face-to-face interaction and the possibility to discuss and modify the initial proposal (first round). An in depth evaluation of the statement and the possibility to reflect on the contents probably was determinant for obtaining very high agreement. Contrarily, the third round reflected an immediate evaluation of the statement that was based on clinical practice. Moreover, it has to be underlined that this initiative involved specialists belonging to different areas so it is likely that some specialists are unfamiliar with some practical aspects or do not adequately know the peculiar literature on some topics. As a result, it is not particularly surprising to note this discrepancy between second and third round outcomes. Surely, these findings obligate to think that there is the need to implement the knowledge grade on specific issues, such as topical antibiotics, antiviral agents, and devices. Indeed, these results underscored a relevant gap between participants. However, there is the need to increase the level of evidence on these topics by performing new studies conducted with robust methodology. Effectively, some

topics were investigated by a few studies performed only in Italy and usually monocentric.

This Delphi Consensus did not, furthermore, consider specific issues, including bacteriotherapy (administration of "good" bacteria), halotherapy (dry salt inhalation), thermal therapy, dilators, intranasal filters, and other topical remedies. Further studies should address these topics.

The present Delphi Consensus had strength because 14 scientific societies endorsed this project and cover three main specialized areas: ENT, allergy, and pediatrics. In addition, the participants' documented clinical expertise and scientific value were considered when selecting them. As a result, the outcomes represented valuable experts' opinions. In addition, the Delphi method consisted of three iterative rounds, guaranteeing a more careful evaluation of the statements.

However, this Delphi Consensus had limitations, including the results reflecting participants' personal knowledge and clinical expertise, the need for a systematic review of the literature concerning this issue, and the limited number of participants to the third round. On the other hand, the present statements may be fruitful in clinical practice as there are no specific guidelines on this topic. In this regard, further detailed studies on administration devices, molecules, and schedules should follow the present initiative. This new information should serve to implement Intersocietal guidelines and promote educational initiatives. In addition, another aspect deserving adequate attention is the role of topical nasal therapy in the self-management. This aspect is relevant as there is growing interest in this approach [79]. Also, telemedicine could implement a medical supervision of self-administered topical remedies [80].

Conclusion

In conclusion, topical nasal therapy is a complex and debated matter, but it is widespread and applied to various medical conditions managed by different specialists. There is also the need to implement the knowledge of this topic and provide new and robust evidence about this therapy. There is a shared belief that topical nasal therapy is a meaningful option in managing upper respiratory diseases as it may significantly improve other therapeutical strategies.

References

1. Wise SK, Damask C, Greenhawt M, Oppenheimer J, Roland LT, Shaker MS, et al. A Synopsis of Guidance for Allergic Rhinitis Diagnosis and Management From ICAR 2023. J Allergy Clin Immunol Pract 2023;11(3): 773-96.
2. Xavier R. Overview of Nasal Airway and Nasal Breathing Evaluation. Facial Plast Surg 2024;40(3):268-74.
3. Hellings PW, Lau S, Scadding GK, Bjermer L, Backer V, Chaker AM, et al. EUFOREA summit in Brussels 2023: inspiring the future of allergy & respiratory care. Front Allergy 2023;4:1236977.
4. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. Rhinology 2020;Suppl. 29: 1-464.
5. El Feghaly RE, Nedved A, Katz SE, Frost HM. New insights into the treatment of acute otitis media. Expert Rev Anti Infect Ther 2023;21(5):523-34.
6. Ciprandi G, Tosca MA. Turbinate Hypertrophy, Allergic Rhinitis, and Otitis Media. Curr Allergy Asthma Rep 2021; 21(9):44.
7. Eccles R. Common cold. Front Allergy 2023;4:1224988.
8. Bansil R, Turner BS. The biology of mucus: composition, synthesis and organization. Adv Drug Deliv Rev 2018; 124:3-15.
9. Harvey RJ, Roland LT, Schlosser RJ, Pfaar O. Chief Complaint: Nasal Congestion. J Allergy Clin Immunol Pract 2024;12(6):1462-71.
10. Karkouli G, Douros K, Moriki D, Moutsatsou P, Giannopoulou I, Maratou E, et al. Dysfunctional Breathing in Children: A Literature Review. Children (Basel) 2024;11(5):556.
11. Taherali F, Varum F, Basit AW. A slippery slope: On the origine, role and physiology of mucus. Adv Drug Deliv Rev 2018;124:16-33.
12. Keicho N, Hijikata M, Miyabayashi A, Wakabayashi K, Yamada H, Ito M, et al. Impact of primary ciliary dyskinesia: Beyond sinobronchial syndrome in Japan. Respir Investig 2024;62(1):179-86.
13. Ciprandi G, Cirillo I The lower airway pathology of Rhinitis. Update Review J Allergy Clin Immunol 2006; 118:1105-9.
14. Ciprandi G, Gelardi M. Open and clean: the healthy nose. Acta Biomed 2019;90(2-S):4-6.
15. Jones J, Hunter D. Consensus methods for medical and health services research. BMJ 1995;311(7001):376–80.

16. Martínez-Serrano A, Martínez-Campos P, Seijoso-González L, Ruiz-Rojo H. Literature review of nasal lavage technique in paediatrics. Enferm Clin (Engl Ed) 2021; 31(3):189-94.
17. Brożek JL, Bousquet J, Agache I, Agarwal A, Bachert C, Bosnic-Anticevich S, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines-2016 revision. J Allergy Clin Immunol 2017;140(4):950-8.
18. Bousquet J, Schünemann HJ, Togias A, Bachert C, Erhola M, Hellings PW, et al. Next-generation Allergic Rhinitis and Its Impact on Asthma (ARIA) guidelines for allergic rhinitis based on Grading of Recommendations Assessment, Development and Evaluation (GRADE) and real-world evidence. J Allergy Clin Immunol 2020;145(1):70-80.e3.
19. Dykewicz MS, Wallace DV, Amrol DJ, Baroody FM, Bernstein JA, CraigTJ, et al. Rhinitis 2020: A practice parameter update. J Allergy Clin Immunol 2020;146(4): 721-67.
20. Meltzer EO, Bachert C, Staudinger H. Treating acute rhinosinusitis: comparing efficacy and safety of mometasone furoate nasal spray, amoxicillin, and placebo. J Allergy Clin Immunol 2005;116(6):1289-95.
21. Varricchio A, Brunese FP, La Mantia I, Ascione E, Ciprandi G. Choosing nasal devices: a dilemma in clinical practice. Acta Biomed 2023;94(1):e2023034.
22. Varricchio A, De Lucia A, Varricchio AM, Della Volpe A, Mansi N, Pastore V, et al. Sinuclean Nebules treatment in children suffering from otitis media with effusion. Int J Pediatr Otorhinolaryngol 2017:94:30-5.
23. Varricchio A, Capasso M, Di Gioacchino M, Ciprandi G. Inhaled thiamphenicol and acetylcysteine in children with acute bacterial rhinopharyngitis. Int J Immunopathol Pharmacol 2008;21(3):625-9.
24. Varricchio A, Capasso M, Avvisati F, Varricchio AM, De Lucia A, Brunese FP, et al. Inhaled hyaluronic acid as ancillary treatment in children with bacterial acute rhinopharyngitis. J Biol Regul Homeost Agents 2014;28(3): 537-43.
25. Djupesland PG. Nasal drug delivery devices: characteristics and performance in a clinical perspective. Drug Deliv Trans Res 2013;3(1):42-62.
26. Xi J, Si X, Kim JW, BerlinskiA. Simulation of airflow and aerosol deposition in the nasal cavity of a 5-year-old child. J Aerosol Sci 2011;42(3):156-73.
27. Kimbell JS, Segal RA, Asgharian B, Wong BA, Schroeter JD, Southall JD, et al. Characterization of deposition from nasal spray devices using a computational fluid dynamics model of the human nasal passages. J Aerosol Med 2007;20(1):59-74.
28. Berlinski A. Pediatric Aerosol Therapy. Respir Care. 2017; 62(6):662-677.
29. Ocak E, Mulazimoglu S, Kocaoz D, Mirici E, Dagli E, Acar A. Effect of adjunctive sodium hyaluronate versus surfactant nasal irrigation on mucociliary clearance in allergic rhinitis: a single-blind, randomised, controlled study. J Laryngol Otol 2021;135(6):529-32.
30. Ural A, Oktemer TK, Kizil Y, Ileri F, Uslu S. Impact of isotonic and hypertonic saline solutions on mucociliary activity in various nasal pathologies: clinical study. J Laryngol Otol 2009;123(5):517-21.
31. Donaldson SH, Bennett WD, Zeman KL, Knowles MR, Tarran R, Boucher RC. Mucus clearance and lung function in cystic fibrosis with hypertonic saline. N Engl J Med 2006;354(3):241-50.
32. Hermelingmeier KE, Weber RK, Hellmich M, Heubach CP. Nasal irrigation as an adjunctive treatment in allergic rhinitis: a systematic review and meta-analysis. Am J Rhinol Allergy 2012;26(5):e119-25.
33. Jung M, Lee JY, Ryu G, Lee KE, Hong SD, Choi J, et al. Beneficial effect of nasal saline irrigation in children with allergic rhinitis and asthma: A randomized clinical trial. Asian Pac J Allergy Immunol 2020;38(4):251-57.
34. Nguyen SA, Psaltis AJ, Schlosser RJ. Isotonic saline nasal irrigation is an effective adjunctive therapy to intranasal corticosteroid spray in allergic rhinitis. Am J Rhinol Allergy 2014;28(4):308-11.
35. Salib RJ, Talpallikar S, Uppal S, Nair SB. A prospective randomised single-blinded clinical trial comparing the efficacy and tolerability of the nasal douching products Sterimar™ and Sinus Rinse™ following functional endoscopic sinus surgery. Clin Otolaryngol 2013;38(4):297-305.
36. Gelardi M, Mezzoli A, Fiorella ML, Carbonara M, Di Gioacchino M, Ciprandi G. Nasal irrigation with Lavonase as ancillary treatment of acute rhinosinusitis: a pilot study. J Biol Reg 2009;23:79-84.
37. Gelardi M, Taliente S, Piccininni K, Silvestre G, Quaranta N, Ciprandi G. Nasal irrigation with Nasir® in children: a preliminary experience on nasal cytology. J Biol Reg 2016;30:1125-30.
38. Frank DO, Kimbell JS, Pawar S, Rhee JS. Effects of anatomy and particle size on nasal sprays and nebulizers. Otolaryngol Head Neck Surg 2012;146(2):313-9.
39. Keeler JA, Patki A, Woodard CR, Do F-I. A Computational Study of Nasal Spray Deposition Pattern in Four Ethnic Groups. J Aerosol Med Pulm Drug Deliv 2016;29(2):153-66.
40. Stjärne P, Blomgren K, Cayé-Thomasen P, Salo S, Søderstrøm T. The efficacy and safety of once-daily mometasone furoate nasal spray in nasal polyposis: a randomized, double-blind, placebo-controlled study. Acta Otolaryngol 2006;126(6):606-12.
41. Campbell RG. Risks and management of long-term corticosteroid use in chronic rhinosinusitis. Curr Opin Otolaryngol Head Neck Surg 2018;26(1):1-7.
42. Antunes MB, Feldman MD, Cohen NA, Chiu Dose-dependent effects of topical tobramycin in an animal model of Pseudomonas sinusitis. Am J Rhinol 2007;21(4):423-7.
43. Lim M, Citardi MJ, Leong J-L. Topical antimicrobials in the management of chronic rhinosinusitis: a systematic review. Am J Rhinol 2008;22(4):381-9.

44. Liebermann P. Management of allergic rhinitis with a combination antihistamine/anti-inflammatory agent. J Allergy Clin Immunol 1999;103(3 Pt 2):S400-4.
45. Klimek L, Mullol J, Ellis AK, Izquierdo-Dominguez A, Hagemann J, Casper I, et al. Current management of allergic rhinitis. J Allergy Clin Immunol Pract 2024;12:1399-412.
46. Feng S, Fan Y, Liang Z, Ma R, Cao W. Concomitant corticosteroid nasal spray plus antihistamine (oral or local spray) for the symptomatic management of allergic rhinitis. Eur Arch Otorhinolaryngol 2016;273(11):3477-86.
47. Golden S, Teets SJ, Lehman EB, Mauger EA, Chinchilli V, Berlin JM, et al. Effect of topical nasal azelastine on the symptoms of rhinitis, sleep, and daytime somnolence in perennial allergic rhinitis. Ann Allergy Asthma Immunol 2000;85(1):53-7.
48. Berger W, Meltzer EO, Amar N, Fox AT, Just J, Muraro A, et al. Efficacy of MP-AzeFlu in children with seasonal allergic rhinitis: Importance of paediatric symptom assessment. Pediatr Allergy Immunol 2016;27(2):126-33.
49. Baldassarre ME, Di Mauro A, Labellarte G, Pignatelli M, Fanelli M, Schiavi E, et al. Resveratrol plus carboxymethyl-β-glucan in infants with common cold: A randomized double-blind trial. Heliyon 2020;6(4):e03814.
50. Ciprandi G, La Mantia I, Brunese FP, Varricchio A, Varricchio AM. Hypertonic saline with xylitol and hyaluronate may shorten the viral shedding duration in asymptomatic COVID-19 positive subjects: a pilot study. J Biol Regul Homeost Agents 2021;35(3):1151-4.
51. Mastromarino P, Capobianco D, Cannata F, Nardis C, Mattia E, De Leo A, et al. Resveratrol inhibits rhinovirus replication and expression of inflammatory mediators in nasal epithelia. Antiviral Res 2015:123:15-21.
52. Rossi GA, Sacco O, Capizzi A, Mastromarino P. Can Resveratrol-Inhaled Formulations Be Considered Potential Adjunct Treatments for COVID-19?. Front Immunol 2021:12:670955.
53. Drago L, Daglia M, Brindisi G, Brunese FP, Dinardo G, Gori A, et al. Certainty and uncertainty in the biological activities of resveratrol. Food Front (in press).
54. Varricchio A, Tricarico D, De Lucia A, Utili R, Tripodi MF, Miraglia Del Giudice M, et al. Inhaled tobramycin in children with acute bacterial rhinopharyngitis. Int J Immunopathol Pharmacol 2006;19(1):131-40.
55. Varricchio A, Capasso M, Di Gioacchino M, Ciprandi G. Inhaled thiamphenicol and acetylcysteine in children with acute bacterial rhinopharyngitis. Int J Immunopathol Pharmacol 2008;21(3):625-9.
56. Solares CA, Batra PS, Hall GS, Citardi MJ. Treatment of chronic rhinosinusitis exacerbations due to methicillin-resistant Staphylococcus aureus with mupirocin irrigations. Am J Otolaryngol 2006;27(3):161-5.
57. El-Hennawi DM, Ahmed MR, Farid AM, Al Murtadah AM. Comparative study of the efficacy of topical steroid and antibiotic combination therapy versus oral antibiotic alone when treating acute rhinosinusitis. J Laryngol Otol 2015;129(5):462-7.
58. Passàli D, Damiani V, Passàli FM, Passàli GC, Bellussi L. Atomized nasal douche vs nasal lavage in acute viral rhinitis. Arch Otolaryngol Head Neck Surg 2005;131(9):788-90.
59. El Khoury P, Hamad WA, Khalaf, MG El Hadi C, Assily R, Rassi S, et al. Ipratropium Bromide Nasal Spray in Non-Allergic Rhinitis: A Systematic Review and Meta-Analysis. Laryngoscope 2023;133(12):3247-55.
60. Deckx L, De Sutter AI, Guo L, Mir NA, van Driel ML. Nasal decongestants in monotherapy for the common cold. Cochrane Database Syst Rev 2016;10(10):CD009612.
61. Yoo JK, Seikaly H, Calhoum KH. Extended use of topical nasal decongestants. Laryngosope 1997;107(1):40-3.
62. Snidvongs K, Kalish L, Sacks R, Sivasubramaniam R, Cope D, Harvey RJ. Sinus surgery and delivery method influence the effectiveness of topical corticosteroids for chronic rhinosinusitis: systematic review and meta-analysis. Am J Rhinology Allergy 2013;27(3):221-33.
63. Liao X, Guan Y, Asakawa T, Lin Z, Tang Q, Ma Z, et al. Benefit of Nasal Douche in COVID-19 Patients with Recurrence of Positive SARS-CoV-2 Viral RNA. Infect Drug Resist 2023:16:6269-76.
64. Esposito S, Rosazza C, Sciarrabba CS, Principi N. Inhaled Antibiotic Therapy for the Treatment of Upper Respiratory Tract Infections. J Aerosol Med Pulm Drug Deliv 2017;30(1):14-9.
65. Head K, Chong LY, Piromchai P, Hopkins C, Philpott C, Schilder AG, et al. Systemic and topical antibiotics for chronic rhinosinusitis. Cochrane Database Syst Rev 2016; 4(4):CD011994.
66. Chadha NK, ZhangL , Mendoza-Sassi RA, César JA. Using nasal steroids to treat nasal obstruction caused by adenoid hypertrophy: does it work? Otolaryngol Head Neck Surg 2009;140(2):139-147.
67. Ciprandi G, Varricchio A, Capasso M, Varricchio AM, De Lucia A, Ascione E, et al. Intranasal flunisolide treatment in children with adenoidal hypertrophy. Int J Immunopathol Pharmacol 2007;20(4):833-6.
68. Duse M, Santamaria F, Verga MC, Bergamini M , Simeone G, Leonardi L, et al. Inter-society consensus for the use of inhaled corticosteroids in infants, children and adolescents with airway diseases. Ital J Pediatr 2021;47(1):97.
69. Zeroli C, Gorica A, Monti G, Castelnuovo P, Bignami M, Macchi A. A systematic review of randomized controlled trials on topical nasal steroids. Acta ORL Ital 2024;44:71-5.
70. Montella S, Cantone E, Maglione M, Iengo M, Santamaria F. Sodium hyaluronate improves quality of life and nasal endoscopy features in preschool children with upper respiratory tract infections. J Biol Regul Homest Agents 2016;30(1):303-8.
71. Mozzanica F, Preti A, Gera R, Bulgheroni C, Cardella A, Albera A, et al. Double-blind, randomised controlled trial on the efficacy of saline nasal irrigation with sodium hyaluronate after endoscopic sinus surgery. J Laryngol Otol 2019;133(4):300-8.
72. Macchi A, Castelnuovo P, Terranova P, Digilio E. Effects of sodium hyaluronate in children with recurrent

upper respiratory tract infections: results of a randomised controlled study. Int J Immunopathol Pharmacol 2013; 26(1):127-315.
73. Liu H, Chen Y, Wang H, Luo X, Xie D, ji Q, et al. Efficacy of hyaluronic acid in the treatment of nasal inflammatory diseases: a systematic review and meta-analysis. Front Pharmacol 2024;15:1350063.
74. Rollema C, van Roon EN, van Boven JFM, Hagedoorn P, Klemmeier T, Kocks JH, et al. Pharmacology, particle deposition and drug administration techniques of intranasal corticosteroids for treating allergic rhinitis. Clin Exp Allergy 2022,52:1247-63.
75. Rudmik L, Xu Y, Liu M, Bird C, Kukec E, QuanH. Utilization Patterns of Topical Intranasal Steroid Therapy for Chronic Rhinosinusitis: A Canadian Population-Based Analysis. JAMA Otolaryngol Head Neck Surg 2016;142(11):1056-62.
76. Yoo F, Ference EH, Kuan EC, Lee JT, Wang MB, Suh JD. Evaluation of patient nasal saline irrigation practices following endoscopic sinus surgery. Int Forum Allergy Rhinol 2018;8(1):32-40.
77. Hellings PW. Paving the future of rhinosinusitis care. Rhinology 2017;55(3):193-4.
78. McCarronTL, Moffat K, Wilkinson G, Zelinsky S, Boyd JM, White D, et al. Understanding patient engagement in health system decision-making: a co-designed scoping review. Syst Rev 2019;8(1):97.
79. Ciprandi G. Self-Management in Allergic Rhinitis: Strategies, Outcomes and Integration into Clinical Care. J Asthma Allergy 2023;16:1087-95.
80. Ciprandi G. Recent advances in the practical management of allergic rhinitis. Recenti Prog Med. 2024;115(4):1-10.

Received for publication: 27 June 2024 - Accepted for publication: 26 July 2024

Licensee Mattioli 1885, Italy
Multidisciplinary Respiratory Medicine 2024; 19: 991
doi: 10.5826/mrm.2024.991