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Chemotherapeutic agents used by the ENT surgeons in different clinical situations- A panoptic study

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Abstract: *Background:* Chemotherapeutic agents have become a vital adjunct in otolaryngology, in treating head and neck malignancies, ENT infections, fungal Allergies, Hearing loss and vertigo patients. *Aim of the Study:* This panoptic review aimed to systematically evaluate the chemotherapeutic agents employed by ENT surgeons across various clinical conditions. The review highlights established practices, emerging therapeutic trends, mechanisms of action, and the evolving role of population-based outcomes in optimizing therapeutic strategies. *Methods:* An extensive literature search was performed using PubMed, Scopus, and Web of Science databases for articles published from 2015 to 2024. Keywords included "ENT chemotherapy," "head and neck cancer chemotherapy," "ototoxicity," and "population therapeutics." Studies were selected based on clinical relevance, quality of evidence, and their impact on ENT practice. Preference was given to randomized controlled trials, meta-analyses, and high-quality cohort studies. *Results:* Cisplatin-based regimens remained the backbone of chemo-radiation protocols for squamous cell carcinomas of the head and neck. Taxanes (docetaxel, paclitaxel) and anti-metabolites (5-fluorouracil, gemcitabine) served as adjuncts in aggressive cytoreduction. Targeted therapies, such as cetuximab, and checkpoint inhibitors (e.g., nivolumab, pembrolizumab), proved to be benefiting recurrent and metastatic cases. Invasive fungal infections like mucormycosis, were increasingly treated with chemotherapeutic agents. Chemotherapy-induced ototoxicity, with platinum agents, remained significant concern. *Conclusion:* Modern ENT practice needs a multidisciplinary understanding of chemotherapeutic regimens to improve patient outcomes. The integration of conventional chemotherapy, targeted therapies, and immune-modulators marked a paradigm shift toward precision medicine in otolaryngology. Population-based therapeutic approaches must be prioritized to enhance long-term quality of life for patients.

Keywords: Chemotherapy, Head and Neck Cancer, Immunotherapy, Targeted Therapy, Population Therapeutics.

Introduction

Chemotherapeutic agents have revolutionized the management of head and neck pathologies, offering ENT surgeons' critical adjunctive tools to improve survival outcomes, reduce recurrence rates, and enhance the quality of life in affected patients. While surgery remains the cornerstone in treating many otolaryngological malignancies, the integration of chemotherapy, either as neo-adjuvant, concurrent, or adjuvant therapy, has significantly broadened therapeutic possibilities [1-2]. In India, the burden of head and neck cancers is notably high, accounting for approximately 30% of all cancers, primarily attributed to tobacco, alcohol use, and human papillomavirus (HPV) infections [3].

Platinum-based compounds such as cisplatin, carboplatin, and oxaliplatin continue to form the foundation of chemotherapeutic regimens in squamous cell carcinomas of the head and neck [4]. Newer agents like taxanes (paclitaxel, docetaxel) and antimetabolites (5-fluorouracil) have expanded the

armamentarium, particularly for recurrent or metastatic diseases [5]. Targeted therapies, including monoclonal antibodies like cetuximab, and more recently, immune checkpoint inhibitors such as nivolumab and pembrolizumab, have demonstrated promising survival benefits and are rapidly being incorporated into treatment protocols [6-7].

Beyond malignancies, ENT surgeons increasingly encounter non-neoplastic indications where chemotherapeutic agents have critical roles. Management of invasive fungal infections such as mucormycosis especially following the COVID-19 pandemic has necessitated aggressive use of antifungal chemotherapy like amphotericin B [8]. Moreover, awareness of chemotherapy-induced ototoxicity, notably from platinum agents, has led to a growing emphasis on early detection strategies such as audiological monitoring [9-10] Indian studies have underscored the unique challenges faced in resource-limited settings, where late-stage presentation, poor treatment compliance, and limited access to targeted therapies complicate optimal chemotherapeutic delivery [11].

Population-based therapeutic approaches, integrating evidence-based chemotherapy regimens and precision medicine, are thus vital to enhance outcomes across diverse clinical settings [12]. This panoptic review seeks to consolidate current evidence on chemotherapeutic agents utilized by ENT surgeons across varied clinical scenarios. It highlights mechanisms of action, therapeutic indications, evolving trends, population-level implications, and future directions to support evidence-driven, holistic otolaryngological care.

Material and Methods

Study Design: This study was conducted as a comprehensive narrative and thematic panoptic review. The objective was to systematically explore, categorize, and synthesize the pharmaco-therapeutic agents commonly used by ENT surgeons in different clinical scenarios, ranging from malignant and infectious diseases to allergic and functional conditions. Given the vast scope of pharmacological interventions in otolaryngology, a structured thematic synthesis was employed, with findings grouped according to the principal therapeutic domains (oncology, anti-infective therapy, anti-inflammatory agents, symptom control, and biologic therapies).

Literature Search Strategy: An extensive literature search was systematically performed across the following databases: PubMed/ Medline, Scopus, EMBASE, and Web of Science. The search included studies published from January 2010 to March 2025. No geographical restrictions were applied to capture both global and Indian perspectives in ENT pharmacotherapy.

Search Keywords and Terms Used: Relevant MeSH terms and free-text keywords were used, including: "ENT pharmacotherapy," "Otolaryngology drug therapy," "Chemotherapy in head and neck cancer," "Antibiotics in ENT infections," "Antifungals in sinonasal infections," "Antihistamines for allergic rhinitis," "Steroids in ENT disorders," "Antivirals in otolaryngology," "Vestibular suppressants for vertigo," "Gene therapy for hearing loss," "Monoclonal antibodies in chronic rhinosinusitis." Boolean operators ("AND," "OR") were applied to combine search terms appropriately. Filters were applied for human studies, English language, and articles including clinical therapeutic relevance to ENT practice.

Supplementary Searches: Manual cross-referencing from the bibliographies of key articles and standard otolaryngology textbooks (Cummings Otolaryngology: Head and Neck Surgery, Ballenger's Otorhinolaryngology) was performed. Additionally, national and international practice guidelines (e.g., AAO-HNSF, NCCN, Indian guidelines) were consulted.

Inclusion Criteria: Original research articles (Randomized Controlled Trials, Cohort studies, Case-Control studies), High-quality systematic reviews and meta-analyses relevant to pharmacotherapy in ENT. Narrative reviews or consensus papers by expert panels. Practice guidelines issued by professional bodies (e.g., American Academy of Otolaryngology-Head and Neck Surgery, Indian Academy of Otorhinolaryngology). Articles discussing drug mechanisms, indications, adverse effects, and emerging therapies in ENT practice.

Exclusion Criteria: Articles focusing exclusively on surgical techniques without pharmacologic content. Editorials, commentaries, letters to editors without original data in the literature were not included in the study. Case reports and case series with less than 10 patients, Animal studies or preclinical trials not directly relevant to future human applications in ENT practice were excluded.

Non-English articles without English abstracts: Study Selection and Data Extraction: Two independent reviewers screened the titles and abstracts to identify eligible articles. Full texts of selected studies were subsequently reviewed for detailed evaluation. Discrepancies were resolved through consensus or consultation with a third reviewer**.**

Extracted Data Included: Study characteristics: authors, year of publication, country, and study design. Patient population: disease condition (e.g., head and neck cancer, otitis media, allergic rhinitis). Intervention: name of pharmaco-therapeutic agent(s), dosage, and route of administration. Therapeutic outcomes: efficacy, safety, adverse effects, quality of life impacts. Emerging therapies: targeted treatments, gene therapies, monoclonal antibodies in ENT. Special considerations in Indian practice settings (e.g., accessibility, cost issues, antibiotic resistance patterns).

The pharmaco-therapeutic agents were organized thematically based on their clinical indications: Antineoplastic chemotherapeutic agents, Antibiotics (systemic and topical), Antifungal agents, Antiviral therapies, Anti-inflammatory corticosteroids, Antihistamines and nasal decongestants, Ear-specific topical preparations, Vestibular suppressants, Local anesthetics, Miscellaneous and emerging therapies (e.g., biologics, gene therapies).

Quality Assessment: To ensure the reliability and robustness of included evidence: Randomized Controlled Trials (RCTs) were evaluated using the Cochrane Risk of Bias Tool [13]. Observational studies were assessed using the Newcastle–Ottawa Scale (NOS) [14]. Systematic Reviews were appraised using the AMSTAR 2-(A Measurement Tool to Assess Systematic Reviews) tool [15]. Studies were categorized as high, moderate, or low quality. Only moderate- and high-quality studies were included in the final synthesis.

Data Synthesis Approach: A narrative thematic synthesis method was utilized due to heterogeneity in study populations, interventions, and outcome measures. Quantitative meta-analysis was not performed due to variability across the included studies. Results were synthesized and presented thematically according to the pharmacologic class and clinical utility in ENT practice, with sub-group emphasis on: Mechanism of action**,** Common indications, Administration protocols, Drug safety and adverse effects (e.g., ototoxicity), Future perspectives in emerging therapies (biologics, targeted agents, gene therapies). Special consideration was given to differences observed in Indian versus international practices concerning drug availability, resistance patterns, and clinical guidelines.

Limitations: Heterogeneity of study designs and outcome reporting limited quantitative aggregation of data. Potential publication bias due to preferential publication of positive therapeutic outcomes was found. Evolving landscape of biologic and gene-based therapies necessitates cautious interpretation of emerging evidence was necessary. Lack of uniformity in drug dosages and protocols across different geographic regions was noted. Despite these limitations, this panoptic review provides a comprehensive, clinically relevant synthesis of pharmaco-therapeutic strategies employed in modern ENT practice.

Results

Following the literature search and selection process, a total of 142 relevant articles were included in this narrative review. These comprised 43 original research studies, 29 systematic reviews and meta-analyses, 24 clinical guidelines or consensus statements, and 46 high-quality narrative reviews, covering the scope of pharmaco-therapeutic interventions in otolaryngology across oncology, infectious diseases, inflammatory conditions, allergic disorders, and functional ENT disorders.

The findings were synthesized into ten major pharmaco-therapeutic domains Table [1]:

1. *Anti-neoplastic Chemotherapeutic Agents:* Head and neck squamous cell carcinomas (HNSCCs) form the primary indication for chemotherapeutic use in ENT. The most commonly used agents are:
    - Cisplatin (standard radio-sensitizing agent in concurrent chemo-radiotherapy)
    - Taxanes (docetaxel, paclitaxel) used in induction regimens (TPF protocol)
    - 5-Fluorouracil (5-FU) as part of combination regimens
    - Cetuximab, an EGFR inhibitor, used in cisplatin-ineligible patients
    - Checkpoint inhibitors like Nivolumab and Pembrolizumab, approved for recurrent/metastatic HNSCC.

Platinum-based regimens remain most effective but are limited by toxicities, including ototoxicity, nephrotoxicity, and myelosuppression.

2. *Antibiotics in ENT Infections:* Systemic antibiotics are widely used in:
    - Acute otitis media (Amoxicillin-clavulanate, Cefuroxime)
    - Chronic sinusitis and mastoiditis (Clindamycin, Levofloxacin, Moxifloxacin)
    - Deep neck infections (Clindamycin + Metronidazole for anaerobic coverage) Macrolides (Azithromycin) are used in penicillin-allergic patients.

    Topical antibiotics include:
    - Ciprofloxacin ear drops – used in otitis externa and tympanostomy-associated infections
    - Neomycin-polymyxin B-hydrocortisone drops for external ear infections

Antimicrobial resistance was noted as an emerging concern, especially in empirical sinusitis treatment.

3. *Antifungal Agents:*
    - Liposomal Amphotericin B remains the drug of choice in rhino-orbito-cerebral mucormycosis, often combined with aggressive surgical debridement.
    - Voriconazole is preferred in aspergillosis, especially in immunocompromised patients.
    - Clotrimazole is commonly used as a topical agent in otomycosis.

Fungal ENT infections, especially post-COVID, saw a major therapeutic reliance on antifungal agents in India.

4. *Antiviral Agents:*
    - Acyclovir/ Valacyclovir are standard treatments in Ramsay Hunt Syndrome and Herpes zoster oticus
    - Oseltamivir is used during seasonal influenza outbreaks with ENT complications
    - Ganciclovir is reserved for CMV-related ENT issues in immunocompromised patients

Although not routinely prescribed, antiviral therapy is crucial in facial nerve palsy and viral labyrinthitis.

5. *Corticosteroids:* Used across multiple ENT conditions:
    - Systemic prednisolone: first-line in Bell's palsy and sudden sensorineural hearing loss
    - Dexamethasone: IV or perioperative use to reduce inflammation
    - Methylprednisolone: intratympanic injection for idiopathic deafness
    - Topical corticosteroids (Fluticasone, Budesonide): standard in allergic rhinitis and CRSwNP (chronic rhinosinusitis with nasal polyps)

Intranasal delivery systems improved local efficacy while minimizing systemic side effects.

6. *Antihistamines and Decongestants:*
    - Second-generation antihistamines (Loratadine, Fexofenadine, Bilastine) are preferred due to minimal sedation.
    - Nasal decongestants (Oxymetazoline) are effective but limited to <5 days due to rebound rhinitis risk.
    - Pseudoephedrine used systemically but contraindicated in hypertensives

Combination therapy is often employed in seasonal allergic rhinitis.

7. *Ear Preparations:*
    - Cerumenolytics (carbamide peroxide, sodium bicarbonate) effectively manage impacted cerumen.
    - Antibiotic-steroid combinations (e.g., Ciprofloxacin-dexamethasone) are effective in otorrhea and otitis externa.
    - Patient adherence to topical regimens was generally high due to localized relief.

8. *Vestibular Suppressants:*
    - Betahistine is the most widely prescribed drug in Meniere's disease, improving vertigo and tinnitus symptoms.
    - Prochlorperazine, Promethazineare useful in acute vestibular crises, although sedative effects limit long-term use.

Vestibular suppressants are also used in motion sickness and central vertigo syndromes.

9. *Local Anesthetics:*
    - Lidocaine sprays are routinely used for diagnostic procedures like nasoendoscopy, laryngoscopy.
    - Lidocaine injections are used in nerve blocks for minor ENT surgeries.

These agents offer rapid action and excellent mucosal absorption with low systemic toxicity.

10. *Miscellaneous and Emerging Therapies*
    - Montelukast is used as an adjunct in allergic rhinitis and asthma–rhinitis overlap syndromes.
    - Allergen-specific immunotherapy (SCIT/SLIT) is emerging in India for refractory allergic rhinitis.
    - Dupilumab, an anti-IL-4 receptor monoclonal antibody, is approved for CRSwNP and has shown dramatic results in polyp reduction and symptom control.
    - Gene therapy and anti-VEGF agents are under investigation for hereditary hearing loss and vascular anomalies, respectively.

Table-1: Showing the summary of Drug Class Findings (Brief Table Overview)

Drug Class	Common Indications in ENT	Representative Agents
Antineoplastic agents	HNSCC, salivary gland tumors	Cisplatin, Docetaxel, Cetuximab, Nivolumab
Antibiotics	Otitis media, sinusitis, neck infections	Amoxicillin-Clavulanate, Clindamycin, Ciprofloxacin
Antifungals	Mucormycosis, otomycosis	Amphotericin B, Voriconazole, Clotrimazole
Antivirals	Herpes oticus, CMV	Acyclovir, Valacyclovir, Ganciclovir
Corticosteroids	SSNHL, Bell's palsy, CRSwNP	Prednisolone, Budesonide
Antihistamines/ Decongestants	Allergic rhinitis	Loratadine, Fexofenadine, Oxymetazoline
Ear preparations	Otorrhea, ear wax	Ciprofloxacin-dexamethasone, Cerumenolytics
Vestibular suppressants	Meniere's, Vertigo	Betahistine, Promethazine
Local anesthetics	ENT procedures	Lidocaine spray/injection
Biologics & Emerging agents	CRSwNP, hearing loss research	Dupilumab, Anti-VEGF, Gene therapy

Total number of pharmacological agents discussed across all categories: Over 50 distinct drugs, mapped to specific ENT clinical contexts.

Discussion

This panoptic review comprehensively synthesized the wide spectrum of pharmaco-

therapeutic agents employed in ENT clinical practice. The findings reaffirm that ENT pharmacotherapy encompasses not only oncologic chemotherapy but also antimicrobials, anti-inflammatory agents, biologics, and specialized drugs for symptom control, making it a dynamic and multidisciplinary therapeutic domain.

Chemotherapeutic Applications in Head and Neck Oncology: The pivotal role of cisplatin-based chemoradiotherapy in head and neck squamous cell carcinoma (HNSCC) remains undisputed, with several randomized controlled trials confirming its superiority in locoregional control and survival outcomes [5, 16] Indian studies, such as by Sinha et al, [17] have further optimized weekly cisplatin dosing schedules for enhanced tolerability in resource-limited settings. The addition of taxanes in induction protocols (e.g., TPF regimens) further improves response rates but carries a higher toxicity burden [3]. Cetuximab, though less toxic, remains cost-prohibitive for many Indian patients [18]. The incorporation of immune checkpoint inhibitors such as nivolumab and pembrolizumab has revolutionized the management of recurrent/metastatic disease. The KEYNOTE-048 trial confirmed pembrolizumab's survival benefit in PD-L1 positive patients [19], though access to these biologics in low- and middle-income countries remains a challenge.

Antibiotic Use and Resistance in ENT: Antibiotic therapy remains the most frequent pharmacological intervention in ENT practice. Indian ENT surgeons favour amoxicillin-clavulanate for acute otitis media and rhinosinusitis, consistent with international guidelines [20-21]. However, antimicrobial resistance has emerged as a significant concern, particularly with fluoroquinolones and macrolides, due to widespread empirical use [22]. Rational antibiotic prescribing, guided by culture sensitivity and local antibiograms, must be emphasized.Topical antibiotics, such as ciprofloxacin ear drops, demonstrate high local efficacy with minimal systemic effects, making them invaluable in postoperative and otitis externa settings [23].

Fungal ENT Infections: The Mucormycosis Surge: The surge of rhino-orbito-cerebral mucormycosis (ROCM) in India post-COVID-19 pandemic presented a therapeutic challenge. High-dose liposomal amphotericin B, in conjunction with surgical debridement, formed the treatment backbone [24]. However, renal toxicity, cost, and supply shortages hindered optimal treatment. Second-line azoles such as posaconazole and isavuconazole provided alternatives with good oral bioavailability [25].

Antiviral and Steroid Therapies in Facial Nerve and Inner Ear Disorders: Acyclovir and steroids remain the standard treatment in Ramsay Hunt Syndrome and Bell's palsy, respectively. Early initiation of prednisolone significantly improves facial nerve recovery, as validated by Sullivan et al. [26]. In sudden sensorineural hearing loss, both systemic and intratympanic methyl-prednisolone provide comparable efficacy [27].

Anti-inflammatory and Symptom-Based Therapies: Intranasal corticosteroids (budesonide, fluticasone) and second-generation antihistamines (loratadine, fexofenadine, bilastine) are mainstays in allergic rhinitis and chronic rhinosinusitis with nasal polyposis (CRSwNP) [28]. Indian studies report good clinical improvement, although patient compliance with nasal sprays remains suboptimal due to poor technique and misconception of side effects [29]. Oxymetazoline and pseudoephedrine provide rapid decongestion but carry risks of rebound congestion and cardiovascular side effects, particularly with prolonged use.

Vertigo Management and Vestibular Suppressants: Vertigo disorders such as Meniere's disease are managed pharmacologically with betahistine, which improves microcirculation in the inner ear [30]. Acute vestibular crises benefit from prochlorperazine or promethazine, though long-term use may suppress central compensation. Compliance with vestibular rehabilitation exercises remains critical for long-term recovery.

Biologics and Emerging Therapies: The advent of biologic agents, particularly dupilumab, has significantly improved

outcomes in patients with recalcitrant CRSwNP. Studies from India and abroad have reported drastic reductions in polyp burden and systemic steroid dependence [31-32]. Despite its promise, high cost, limited insurance coverage, and lack of local clinical experience pose barriers to widespread adoption. Gene therapy and anti-VEGF therapies are in preclinical and early clinical trial phases for treating hereditary hearing loss and vascular anomalies, respectively. These represent promising avenues but require further validation before routine ENT application [33].

Need for Indian Guidelines and Pharmacovigilance: Despite the availability of international guidelines (e.g., NCCN, AAO-HNSF), India lacks comprehensive ENT-specific pharmacotherapy protocols. Variability in prescribing patterns, over-the-counter medication use, and self-medication practices highlight the need for national consensus guidelines. Furthermore, there is inadequate reporting of adverse drug reactions (ADRs) in ENT practice, underscoring the importance of integrating pharmacovigilance into clinical workflows.

Conclusions

Pharmaco-therapeutic interventions in ENT practice are extensive and evolving. From curative chemotherapy in oncology to supportive care in allergy, vertigo, and infections, ENT surgeons are increasingly reliant on multidisciplinary pharmacologic knowledge. While evidence-based drug use is well-established in global literature, India-specific challenges in cost, access, resistance, and awareness must be addressed. National policy frameworks, CME programs, and practice audits are vital to standardize rational pharmacotherapy in otolaryngology.

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