

Steroids in Otolaryngology

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Steroids are increasingly being used to treat a wide spectrum of otolaryngological disorders. It is important for ear-nose-throat surgeons to understand the short- and long-term complications associated with steroid use. The aim of this study was to review the role of steroids in common ear-nose-throat disorders. Corticosteroid therapy has been shown to be effective in the management of idiopathic facial nerve palsy, allergic rhinitis, acute sinusitis, sinonasal inflammatory polyposis, and croup. The therapeutic efficacy of steroids in the management of Meniere's disease, sudden idiopathic sensorineural HL, chronic otitis media, and vestibular neuronitis remain controversial.

Key Words: Steroid, corticosteroids, idiopathic facial nerve palsy, allergic rhinitis, acute sinusitis, sinonasal inflammatory polyposis, croup, Meniere's disease, sudden idiopathic sensorineural hearing loss, chronic otitis media, vestibular neuronitis.

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INTRODUCTION

Corticosteroids are frequently used in a wide range of ear-nose-throat (ENT) conditions due to their anti-inflammatory properties. It is important to understand the basic pharmacology of commonly used steroid preparations in addition to their potential side effects. The aim of this study was to review steroid use in common ENT conditions to develop evidence-based guidelines on which appropriate safe steroid use can be made.

STEROID PHARMACOLOGY

Pharmacodynamics

At a subcellular level, corticosteroids have an anti-inflammatory effect by activating glucocorticoid receptors, which interact with inflammatory transcription factors resulting in suppression of proinflammatory molecules.¹ At a cellular level, corticosteroids reduce the quantity of inflammatory cells (eosinophils, T lymphocytes, mast cells, and dendritic cells), the degree of

inflammatory suppression correlates with the tissue concentration of steroid.

Pharmacokinetics

Corticosteroids can be administered orally, intravenously, topically, or by intralesional injection. They are metabolized by the liver and excreted by the kidneys. Intranasal topical corticosteroids have short half-lives and rapid first-pass hepatic metabolism, with minimal hypothalamic-pituitary suppression.²

Table I shows the relative potencies of oral and intravenous corticosteroids.

Table II shows the relative potencies of topical intranasal corticosteroids. Oral bioavailability indicates the risk of producing systemic side effects.

Complications Associated with Short-term Use of Steroids

Absolute contraindications for steroid use include uncontrolled systemic sepsis and steroid allergy.

Hypothalamic-pituitary-adrenal axis suppression. Prednisone doses of less than 5 mg/day (administered in the morning), do not suppress the Hypothalamic-Pituitary-Adrenal axis. Doses of 5 mg/day or higher have considerable variability in Hypothalamic-Pituitary-Adrenal axis suppression.⁴ Abrupt withdrawal of steroid therapy can result in an acute adrenal crisis that can be life threatening, thus doses of greater than 5 mg of prednisone (or equivalent) for more than 5 days should be tapered on withdrawal. Steroid withdrawal syndrome, which consists of malaise, fatigue, diffuse myalgias, and arthralgia, can be experienced after as little as 2 weeks of steroid therapy.

Hyperglycemia. Glucocorticoids have a variety of actions that lead to hyperglycemia. Patients with diabetes mellitus or glucose intolerance exhibit increased difficulty with glycemic control. New-onset hyperglycemia (or rarely, a nonketotic hyperosmolar state) can develop.⁵

Gastrointestinal effects. Glucocorticoids increase the risk of gastritis, peptic ulcer formation, and gastrointestinal bleeding. The risk of developing peptic ulcer disease during corticosteroid therapy is 1.1 to 1.5 times normal.⁶ The combination of systemic steroids and nonsteroidal anti-inflammatory drugs results in a 15 times increased risk of gastrointestinal complications.^{7,8}

Psychiatric effects. Steroids commonly result in an improved sense of well-being that is independent of any improvement in the underlying disease process. About 6% of patients may develop psychiatric side effects, but 90% of

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TABLE I.
Commonly Used Corticosteroids.

Oral/IV Corticosteroids	Relative Anti-inflammatory Potency	Equivalent Dose (mg)
Short acting (8–12 H)		
Cortisol (hydrocortisone)	1	20
Intermediate acting (18–36 H)		
Prednisone (inactive precursor of prednisolone)	4	5
Long acting (36–72 H)		
Dexamethasone	25	0.75
Methylprednisolone	5	4

Adapted from Haynes RCJ, Murad F. *The Pharmacological Basis of Therapeutics*.³

these are reversible on termination of therapy. Manifestations range from mild mood alteration to frank psychosis. Dosages of prednisone greater than 40 mg/D greatly increase the risk. The onset of psychiatric symptoms is highly variable (1 to 210 days after continuous treatment), with a median duration of treatment of 11 days.⁹

Complications Associated with Long-term Use of Corticosteroids

Avascular necrosis (AVN) of the femoral head is a serious, well-known complication of chronic corticosteroid therapy and has an incidence of 5% and 3% in renal and cardiac transplantation patients, respectively.^{10,11} It is also common in patients taking long-term steroids for autoimmune disorders and it has been estimated that 10% of systemic lupus erythematosus patients will develop AVN.¹² It is difficult to quantify the risk of developing AVN after a short-term course of steroid; however, a retrospective study of 1,352 neurosurgical patients given between 60 and 150 mg (cumulative dose) of dexamethasone for between 15 and 27 days concluded that the incidence of AVN was 0.3%.¹³ To our knowledge, there are no studies that address the risk of AVN developing in immunocompetent patients taking a 1 to 2 week course of low-moderate dose prednisone, but the risk must be extremely small. A review found that there is no increased risk with single dose steroid therapy.¹⁴

Other long-term adverse effects associated with chronic corticosteroid use such as osteoporosis, cushingoid appearance, accelerated atherosclerosis, early cata-

TABLE II.
Relative Potencies of Topical Intranasal Corticosteroids.

Topical Nasal Steroids	Binding Affinity to Glucocorticoid Receptor	Oral Bioavailability (%)
Beconase (beclomathasone monopropionate)	2.0	26
Rhinocort (budesonide)	1	6–11
Nasonex (mometasone furoate)	2.8	<1

acts, and skin thinning and pupura are unlikely to occur at dosage regimens used in otolaryngology.

Otological Conditions

It is well established that 80% of patients with Bell's palsy recover normal or near normal facial nerve function without treatment.¹⁵ Corticosteroids are widely used to treat Bell's palsy, based on either their possible immune modulating effect on the presumed viral etiological agent and/or their anti-inflammatory effect in reducing neural edema within the facial canal. Austin¹⁶ originally reported improved facial nerve recovery in Bell's palsy patients receiving corticosteroids compared with placebo; however, 29% of patients in this study were lost to follow-up. Ramsey et al. performed a meta-analysis of 27 prospective trials evaluating steroid therapy for Bell's palsy in 2000. Only two studies were included in the final analysis, which concluded that steroid therapy improves complete facial recovery by 17%, which was clinically and statistically significant.¹⁷ A Cochrane review of four RCTs in 2007 concluded that corticosteroids did not confer benefit in patients with Bell's palsy.¹⁸ Subsequent to this Cochrane review, a recent double-blind, placebo-controlled, randomized trial involving approximately 500 patients with Bell's palsy concluded that early treatment with prednisolone alone significantly improves the chance of complete facial nerve recovery at 3 and 9 months, thus extending the evidence to support steroid use in Bell's palsy.¹⁹

Despite their widespread empirical use, there is paucity of data to support the use of systemic steroids in the management of Meniere's disease. There are no published prospective clinical trials evaluating the role of prednisone alone for treating acute vertigo in Meniere's disease.

The use of intratympanic steroids (ITS) in Meniere's disease also remains controversial. Study comparison is difficult because of variations in steroid dose, duration, method of application, and patient selection and follow-up periods. Sennaroglu et al. applied daily transtympanic dexamethasone after grommet insertion for 3 months and reported a 72% vertigo control rate in patients with intractable vertigo refractory to standard medical therapy; however, long-term follow-up results were not reported. In a retrospective review, Barrs reported a 24% rate of vertigo control with no significant hearing improvement, after 2 years using intratympanic dexamethasone injections weekly for 4 weeks in 34 patients with intractable Meniere's disease. A prospective randomized double blind study using five consecutive daily intratympanic dexamethasone injections for 22 patients with unilateral intractable Meniere's disease reported 80% vertigo control after 2 years compared with 60% with placebo. They also reported subjective improvement in tinnitus (48% vs. 20% placebo) and HL (35% vs. 10% placebo).²⁰ A prospective study evaluated combined intratympanic and systemic dexamethasone treatment in 17 patients with Meniere's disease and reported vertigo control in 76% but no significant improvement in hearing or tinnitus.²¹

Idiopathic sudden sensorineural HL (SSHL) is a relatively common otologic disorder of uncertain etiology with spontaneous recovery of hearing occurring in up to 65% patients.²² Steroids alone or in combination with

other therapeutic modalities have been used for decades to treat this frustrating disorder with conflicting results. An RCT performed by Wilson demonstrated significant hearing recovery in patients receiving oral steroids while a subsequent RCT failed to demonstrate the efficacy of systemic steroids in SSHL.^{23,24} More recently, ITS therapy has been used to treat SSHL in an effort to achieve higher inner-ear steroid concentration while avoiding potential systemic side effects. Once again, the heterogeneity of study variables makes interpretation of published studies difficult. The addition of ITS to systemic steroid therapy did not confer any hearing recovery benefit in two recent studies.^{25,26} Multiple retrospective studies of salvage ITS therapy after failure of systemic steroids have reported improved hearing outcomes; however, the variability of study parameters makes comparison difficult and a well-designed prospective randomized trial is warranted to further clarify the role of ITS.

In summary, a Cochrane review of all RCTs in which steroids were used to treat SSHL and compared with either observation or placebo concluded that the value of steroid therapy in the treatment of SSHL remains unproven.²⁷ A similar systematic review and meta-analysis of 20 prospective RCTs on the treatment of patients with SSHL also concluded that no evidence exists to support any specific treatment modality in SSHL.²⁸

Vestibular neuritis, like Bell's palsy, is presumed to have a viral etiology and has a high rate of spontaneous recovery. Ohbayashi et al.²⁹ retrospectively reviewed the role of steroids in the recovery of vestibular function in patients with vestibular neuritis and found no correlation between steroid use and improvement in subjective symptoms, despite improved canal paresis recovery in the steroid group.

A prospective, double blind, RCT demonstrated daily administration of systemic methylprednisolone for 3 weeks significantly improved recovery of peripheral vestibular function as measured by ENG in patients with vestibular neuritis, however, clinical symptom outcomes were not measured.³⁰ Thus, the issue of whether steroid-induced improvement in vestibular paresis confers clinical benefit requires more definitive clinical trials.

A recent Cochrane review evaluated the efficacy of systemic and intranasal corticosteroids in the management of otitis media with effusion (OME). Oral steroids alone or in combination with an antibiotic seem to improve resolution of OME in the short term. Similarly, topical intranasal steroids combined with oral antibiotic also demonstrated an effect in clearing effusions in the short term. There is very little evidence to support oral or topical intranasal steroids for the long-term control of effusions or for HL associated with OME.³¹

Rhinologic Conditions

Nasal topical steroids are well established as first-line therapy in allergic rhinitis, which affects up to 25% of the general population.¹ There is clear benefit in using intranasal corticosteroids over antihistamines in allergic rhinitis while short courses of oral steroids may be indicated in severe cases.³² There is no consensus regarding the optimal

duration of treatment with published studies reporting efficacy using 4 to 26 weeks of intranasal steroid therapy.

The use of intranasal corticosteroids in conjunction with oral antibiotics has been demonstrated to be more effective than antibiotics alone for achieving symptomatic improvement in patients with acute rhino sinusitis.^{33–35} A recent multi-institutional, double blind, RCT demonstrated that twice daily intranasal mometasone spray alone for 14 days was more effective than amoxicillin in treating uncomplicated rhinosinusitis suggesting that monotherapy with intranasal steroids may be an effective treatment option for community-acquired uncomplicated acute sinusitis.³⁵ A meta-analysis of four randomized, controlled studies supported the use of intranasal corticosteroids as monotherapy or as an adjuvant therapy to antibiotics.³⁶

There are no randomized controlled trials evaluating the efficacy of systemic corticosteroids in chronic rhinosinusitis without nasal polyposis. An *in vitro* study using cultured nasal mucosa cells from patients with chronic rhinosinusitis supports the use of oral prednisolone by showing significant reductions in inflammatory cytokines.³⁷ Similar *in vivo* studies also support steroid use.³⁸ Several randomized controlled trials have evaluated the role of intranasal steroids in chronic rhinosinusitis with the majority demonstrating a beneficial effect.^{39–43}

The clinical efficacy of corticosteroids in the management of chronic rhinosinusitis with nasal polyposis is well established. A recent double-blind randomized controlled trial clearly established the clinical utility of a short course of oral prednisone in patients with nasal polyps.⁴⁴ Two recent clinical trials similarly established the safety and efficacy of topical nasal steroids in polyposis.^{45,46} A retrospective study evaluating a short course oral prednisolone (1 mg/kg for 5 days) followed by daily intranasal beclomethasone showed this treatment to be effective in 85% of patients with only 15% of patients requiring endoscopic sinus surgery.⁴⁷ This treatment paradigm was supported by a recent RCT comparing oral prednisone and intranasal budesonide with oral placebo and intranasal budesonide in patients with severe nasal polyps.⁴⁸

Oral steroids used preoperatively in patients undergoing endoscopic sinus surgery for nasal polyposis have been shown to reduce vascularity and improve surgical nasal field conditions resulting in shorter operating time.⁴⁹ Postoperative administration of intranasal corticosteroids has also been demonstrated to reduce nasal polyp recurrence after endoscopic sinus surgery.¹

Head and Neck Conditions

Steroids are regularly used to reduce upper aerodigestive tract edema resulting from trauma, surgery, infections, and anaphylaxis. Treatment of croup or laryngotracheobronchitis with steroids is well documented.⁵⁰ Corticosteroid use as adjunctive therapy for other upper aerodigestive tract infections such as pharyngitis, epiglottitis, and tonsillitis is common despite the paucity of evidence to support their use.

A recent prospective RCT evaluated the use of a single intravenous steroid dose (2–3 mg/kg methylprednisolone) in addition to antibiotic therapy and needle aspiration, compared with needle aspiration and antibiotics

alone for the treatment of peritonsillar abscess. The steroid group had a statistically improved clinical outcome with no complications reported.⁵¹

Steroid use in Infectious Mononucleosis has been associated with concern about the potential for steroid-induced peritonsillar abscess formation; however, a review concluded that there is no reliable evidence to support this association.⁵²

The use of perioperative steroids to reduce tonsillectomy morbidity has been extensively investigated. Steroids certainly appear to reduce post operative nausea and vomiting however their effect in reducing post operative pain is only minimal.⁵³ A recent meta-analysis reviewed eight RCTs to establish the association between steroid use and posttonsillectomy pain and concluded that steroid use had a minimal effect on postoperative pain levels, with pain being reduced by one point on a 10-point scale for the first 24 hours.⁵⁴

SUMMARY

Corticosteroids clearly have an important role in the management of a diverse array of ENT conditions faced by clinicians in daily practice. Although evidence-based recommendations are important to provide appropriate guidelines for physicians, randomized-controlled trials are often logistically difficult to construct and hence steroid use is often based on anecdotal evidence or physician preference. It is important to balance steroid treatment benefits with the potential for side effects especially when using high-dose systemic therapy.

Well-constructed clinical trials are required to further clarify the role of steroids in ear, nose, and throat conditions. This will assist clinicians in constructing appropriate evidence-based treatment paradigms.

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