

Oral Steroid Therapy in Chronic Rhinosinusitis with and without Nasal Polyposis

Brittany E. Howard · Devyani Lal

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Abstract Chronic rhinosinusitis (CRS) is a heterogeneous group of disorders characterized by inflammation of the sino-nasal mucosa. CRS can be divided into two subtypes: CRS without polyps (CRSsNP) and CRS with nasal polyps (CRSwNP). Corticosteroids are frequently employed to treat CRS due to their potent anti-inflammatory effects. Treatment of CRS with oral steroids must be carefully balanced against potential adverse effects. This article reviews the current literature on management of CRS with systemic corticosteroids. We discuss the available evidence in CRSsNP, CRSwNP, and allergic fungal sinusitis (AFS). Studies are evaluated for level of evidence and graded to provide evidence-based recommendations. Our review finds a lack of high-quality evidence supporting oral corticosteroid therapy in CRSsNP. In comparison, randomized controlled trials support the use of oral corticosteroids for CRSwNP. Similarly, systemic steroids for AFS treatment are supported by quality studies demonstrating efficacy. Utilization of steroids is also recommended in the perioperative setting for CRSwNP.

Keywords Corticosteroids · Steroids · Chronic rhinosinusitis · Sinusitis · Nasal polyps · Allergic fungal sinusitis · Evidence-based medicine · Review · Recommendations · Management · Perioperative · Preoperative · Postoperative · Oral steroid therapy

Introduction

Sinusitis is defined as inflammation of the nose and paranasal sinuses. The American Academy of Otolaryngology – Head & Neck Surgery (AAO-HNS) uses the duration of symptoms to classify sinusitis into acute, chronic, and recurrent disease (Table 1). The AAO-HNS criteria for diagnosis of sinusitis requires the complaints of nasal blockage, obstruction, congestion, or nasal discharge are confirmed by objective evidence of disease on endoscopic or radiographic evaluation or both [1]. When symptoms last for more than 12 weeks, and disease is confirmed by objective criteria, then chronic rhinosinusitis (CRS) is diagnosed. It is important to pay close attention to these diagnostic criteria as the etiology, management, and prognosis is very different for chronic sinus disease when compared with acute or recurrent acute sinusitis. The necessity of confirming “sinus symptoms” with objective criteria (endoscopy and/or CT sinus) can also not be over-emphasized as sinusitis is likely over-diagnosed, and other more common causes of “sinus headaches” such as migraines under-diagnosed [2, 3].

CRS represents one of the most common patient concerns, with 13 % of the United States population receiving the diagnosis of sinusitis within the last year [4]. This may be an over-estimation of the true prevalence of disease. In a prospective study conducted at a tertiary rhinology clinic, only 65–80 % of patients referred with a diagnosis of sinusitis had confirmation of disease on objective examination [2]. The use of nasal endoscopy and CT scan of the paranasal sinuses are both noted to increase specificity of diagnosis [2, 3].

In an era of medical cost reduction, CRS is sure to come under close scrutiny as its estimated direct national health care cost is 8.6 billion US dollars per year [5], which is assuredly an underestimation as this fails to take indirect costs into consideration. Indeed, a recent study found that the addition of upfront CT scanning is more cost effective

B. E. Howard · D. Lal
Department of Otolaryngology, Mayo Clinic Arizona,
5777 E. Mayo Blvd,
Phoenix, AZ 85054, USA

D. Lal (✉)
Department of Otolaryngology – Head and Neck Surgery,
Mayo Clinic Arizona,
5777 E Mayo Blvd,
Phoenix, AZ 85054, USA
e-mail: lal.devyani@mayo.edu

Table 1 American Academy of Otolaryngology – Head & Neck Surgery sinusitis classification based on duration of symptoms

Classification	Definition
Acute	Up to 4 weeks, with total resolution of symptoms
Subacute	Persisting more than 4 weeks, but less than 12 weeks, with total resolution of symptoms
Recurrent acute	4 or more episodes per year, with resolution of symptoms between attacks
Chronia	12 weeks or more of signs/symptoms

than presumptively treating CRS with medical therapy [6]. Accordingly, there is increasing impetus for the establishment of evidence based approaches to the management of CRS.

There are many challenges when considering treatment of CRS. CRS is a very heterogeneous group of disorders that spans across a wide range of symptom severity that may arise from vastly divergent etiologic factors producing chronic sinonasal inflammation. Although the underlying pathophysiology of CRS remains uncertain, there is significant evidence that all CRS sub-types are mediated by inflammatory changes affecting the sinonasal mucosa [7]. In a very simplified scenario, CRS can be divided into subgroups including CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP). Corticosteroids with their anti-inflammatory properties are therefore frequently employed in the treatment of both CRSwNP and CRSsNP. The prevalence of systemic steroid use is demonstrated in a recent survey revealing 70 % of general otolaryngologist and 78 % of Rhinologists utilize them as part of “maximal medical therapy” for CRS [8, 9].

This review critically evaluates the recent literature on the use of oral corticosteroids therapy for the treatment of CRS. Areas of primary focus include the use of systemic steroid therapy for CRSsNP, CRSwNP, and allergic fungal

sinusitis (AFS), and for CRSwNP in the perioperative period. This is based on the prevalence of the conditions, as well as the preponderance of current evidence. In some CRS subtypes, such as cystic fibrosis and aspirin exacerbated respiratory disease, there are indeed no specific studies on oral corticosteroid use. Studies included for discussion are evaluated for their level of evidence [10] and used to formulate evidence-based recommendations.

Chronic Rhinosinusitis without Nasal Polyps

Lal and Hwang [11•] recently conducted a systematic review of the literature on the use of oral corticosteroids for CRSsNP. All studies included in the review had to specifically identify patients with CRSsNP, even if the intervention was studied in CRS overall. In fact, no study investigated the use of oral corticosteroids as a stand-alone treatment modality for CRSsNP. Where oral steroids have been studied, they were in combination with oral antibiotics and nasal steroids [12–14]. Disappointingly, no randomized controlled trials on oral steroid use in CRSsNP were elucidated. A total of 30 studies on CRSsNP were evaluated, with 97 % being Level 4 or Level 5. These included 4 treatment guidelines (Level 4) (Table 2) [15, 16, 17•, 18] and 20 reviews/expert opinions (Level 5). The highest quality studies (reviewed below) include 1 prospective study (Level 3) and 2 retrospective chart reviews (Level 4).

Tosca et al. [12] conducted a prospective non-randomized study on the effect of multimodality therapy in 30 children with CRS. CRS was diagnosed based on persistent nasal symptoms lasting greater than 3 months and confirmed on endoscopy. Patients were treated with a short course of oral corticosteroids (deflazacort 1 mg/kg daily for 2 days, 0.5 mg/kg daily for 4 days, and 0.25 mg/kg daily for 4 days). Concurrently, they

Table 2 Expert Committee recommendations for oral corticosteroid therapy for chronic rhinosinusitis without nasal polyps

Organization	Year	Consensus grade	Recommendation
AAOA [15]	2009	D	- Second line therapy after antibiotics and topical steroids - For CRS with “edema” - Use in “purulence” as 2nd line - Dose: prednisone 60→40→20→10 - Duration 10–12 days
BSACI [16]	2008	D	- Only for severe nasal obstruction or short-term rescue - Dose: 0.5 mg/kg orally for 5–10 days
EPOS [17•]	2007, 2012	D	Short-term use only
Joint Task Force of ACAAI, AAAAI, JCAAI [18]	2005	D	No recommendation

AAAAI American Academy of Allergy, Asthma, and Immunology; AAOA American Academy of Otolaryngic Allergy; ACAAI American College of Allergy; BSACI British Society for Allergy and Clinical Immunology; CRS chronic rhinosinusitis; CRSsNP chronic rhinosinusitis without nasal polyps; EPOS European Position Paper on Rhinosinusitis and Nasal Polyps; JCAAI Joint Council of Allergy, Asthma, and Immunology

were treated with amoxicillin-clavulanate (20 mg/kg twice daily) and fluticasone propionate aqueous nasal spray (50 µg per nostril daily) for 14 days. Following treatment, 83 % of children had resolution of disease based on endoscopic exam. There was also a significant improvement in the cytokine profile of patients with all children showing a reduction in inflammatory infiltrate.

Subramanian et al. [13] completed a retrospective chart review of 40 patients treated with multimodality medical therapy for CRSsNP ($n=23$) and CRSwNP ($n=17$). Medical therapy included prednisone for 10 days (20 mg twice daily for 5 days and 20 mg daily for 5 days), oral antibiotics for 4–8 weeks, and intranasal steroids. Outcomes were measured using patient-reported symptoms and a comparison of pre-treatment to post-treatment computerized tomography (CT) scans obtained 6–8 weeks following medical therapy. Nasal polyps were noted in 42.5 % of patients and 57.5 % did not have nasal polyps. Symptomatically, 72.5 % of patients improved following therapy, 25 % had little to no improvement, and 2.5 % worsened. Radiographically, 85 % of patients showed significant improvement in disease. Overall, following treatment, 90 % of patients had improvement symptomatically, radiographically, or both. Time to relapse of disease was found to be significantly shorter in patients with nasal polyps or a history of sinus surgery.

Lal and Stankiewicz [14] retrospectively reviewed the effect of multimodality therapy in 82 patients with CRSsNP as defined by the Rhinosinusitis Task Force of the AAO-HNS. Medical therapy included prednisone taper (3 days each of 60, 40, 20, and 10 mg), oral antibiotic for 4 weeks, nasal steroids for 4 weeks (2 squirts each side twice daily), topical nasal decongestant spray rotating use for 4 weeks (rotation of 5 days on the spray then 3 days off), and nasal saline rinses for 4 weeks (twice daily). Nasal polyps were present in 43.3 % of patients and 56.7 % did not have nasal polyps. At the 6- to 8-week post-treatment follow-up, 55 % of patients had complete resolution of disease based on reported symptoms and endoscopic evaluation. Partial resolution was seen in 17.5 % of patients while 36 % failed to respond to medical therapy. Overall, 71.3 % of patients were able to avoid surgery by utilization of a multimodality medical therapy including the use of oral corticosteroids. No difference in response to medical therapy was noted between patients with and without nasal polyps.

In summary, there are no high-level of evidence studies evaluating the use of oral corticosteroids for the management of CRSsNP. The reports that have been published are limited to Level 3 and Level 4 quality studies (Table 3) that investigate oral corticosteroids as part of a multimodality treatment regime. The optimal dose and duration of oral steroid use is also unclear. In the absence of strong evidence, several organizations have presented expert panel recommendations (Table 2). The conclusions that can be drawn

from these reports are limited despite their inference of improvement with steroid therapy. Overall, the literature fails to support the routine use of systemic steroids in the management of CRSsNP due to overall weak aggregate evidence (Grade C or D). The use of oral corticosteroids in patients with CRSsNP is considered optional and should be determined on a case-by-case basis. There is a significant need for high-quality studies investigating oral corticosteroids role in the management of CRSsNP. Further studies are also needed to evaluate their use as single-modality therapy as part of a multimodality treatment approach.

Chronic Rhinosinusitis with Nasal Polyps

A Cochrane Database Review [19•] on the use of oral corticosteroid therapy in the management of CRSwNP identified 3 randomized controlled trials of moderate to low quality [20–22]. Based on the data from these studies, there was Grade B evidence supporting the use of oral corticosteroids in CRSwNP. Since then, 2 additional randomized double-blind placebo-controlled trials and a systematic review article [23•] have been published on the use of oral steroids in the management of CRSwNP. The studies of highest quality are summarized below (Table 3).

Hissaria et al. [20] conducted a randomized double-blind placebo-controlled trial on 41 patients diagnosed with CRSwNP on nasal endoscopy. Patients were randomized to receive treatment with either 50 mg of prednisolone or placebo for 14 days. Both groups showed improvement in symptoms based on physician interview and results from the Rhinosinusitis Outcome Measure. The steroid group had a significantly greater level of improvement compared to those treated with placebo. Radiographically, 78 % of prednisolone treated patients had a significant improvement on MRI compared to 5 % treated with placebo. The mean endoscopy scores improved by 48 % in the steroid-treated group compared to no change in the placebo group. Reported side effects were similar between the groups except for an increased occurrence of insomnia in the steroid treatment arm. No long-term follow up was conducted.

Kirtsreesakul et al. [24•] studied the efficacy of a short course of oral steroid therapy for CRSwNP in a randomized double-blind placebo-controlled trial. In the study, 109 patients were randomized in a 3:2 ratio to receive prednisolone 50 mg or placebo for 14 days, respectively. Although the placebo and steroid treatment arms both had improved symptom scores immediately post-treatment, the steroid treatment group had significantly greater symptom improvement. Objectively, the prednisolone group had improvement in nasal patency and polyp size while the placebo group had no change from baseline. Adverse effects of gastrointestinal upset and dyspepsia were reported more frequently in the

Table 3 Summary of evidence for oral corticosteroid treatment in chronic rhinosinusitis

Author	Year	CRS subtype	Study design	LOE	n	Intervention	Outcome
Tosca et al. [12]	2003	CRSsNP	Prospective case series	3	30	- Steroid taper $\times 12$ d (Deflazacort 1, 0.5, and 0.25 mg/kg daily $\times 4$ days each) - Oral antibiotics $\times 14$ d - Intranasal steroid $\times 14$ d	- 83 % improved endoscopy (83 %) - Improved cytokine profile
Subramanian et al. [13]	2002	CRSsNP	Retrospective case series	4	23	- Steroid taper $\times 10$ d (Prednisone 40 mg then 20 mg $\times 5$ d each) - Oral antibiotics $\times 4-8$ wks - Intranasal steroid	- 72.5 % symptomatic improvement - 85 % radiographic improvement
Lal et al. [14]	2007	CRSsNP	Retrospective case series	4	82	- Steroid taper (Prednisone 60, 40, 20, and 10 mg $\times 3$ d each) - Oral antibiotics $\times 4$ wks - Intranasal steroid $\times 4$ wks - Nasal decongestant spray	- 51 % complete endoscopic and symptomatic resolution - 17.5 % partial improvement
Hissaria et al. [20]	2006	CRSwNP	Randomized double-blind placebo-controlled Trial	2	41	Prednisolone 50 mg $\times 14$ d	- Steroids had greater improvement in symptoms, endoscopy, and MRI findings
Kirtsreesakul et al. [24•]	2011	CRSwNP	Randomized double-blind placebo-controlled trial	2	109	Prednisolone 50 mg $\times 14$ d	- Steroids with greater symptom reduction, improved nasal patency and endoscopic scores
Vaidyanathan et al. [25•]	2011	CRSwNP	Randomized double-blind placebo-controlled trial	2	60	Prednisolone 25 mg $\times 14$ d	- Improvement in hyposmia, nasal symptoms, QOL, endoscopic score, nasal patency, EDN, and CRP at 2 wks but no significant difference at 28 wks
Rupa et al. [27•]	2010	AFS	Randomized double-blind placebo-controlled trial	2	24	Postoperative: - Prednisolone 50 mg $\times 6$ wks followed by 6 wks taper - Ranitidine 150 mg - Itraconazole 200 mg - Fluticasone spray	- Complete symptom and endoscopic resolution of disease at 12 weeks
Ikram et al. [28]	2009	AFS	Prospective with historic case control	3	33	Postoperative: - Prednisone 0.5 mg/kg $\times 1$ month to beclamethasone topical $\times 5$ months	- Steroid group had lower recurrence rate (12.5 %) compared to controls (50 %) at 2 years
Landsberg et al. [29]	2007	AFS	Prospective case series	3	8	Preoperative: - Prednisone 50 mg $\times 10$ d	- Improvement on radiographic and endoscopic assessment

CRS chronic rhinosinusitis, LOE level of evidence, CRSsNP chronic rhinosinusitis without nasal polyps, CRSwNP chronic rhinosinusitis with nasal polyps, AFS allergic fungal sinusitis, mg milligram, kg kilogram, d day, BID twice daily, wks weeks, QOL quality of life, EDN eosinophil derived neurotoxin, CRP C-reactive protein

steroid treatment arm. This study only evaluated the efficacy of treatment immediately after completion of therapy. No long-term follow up was conducted.

Vaidyanathan et al. [25•] performed a randomized double-blind placebo-controlled study on 60 patients meeting criteria for diagnosis of CRSwNP as defined by the European Position Paper on Rhinosinusitis and Nasal Polyps 2007. Patients were randomized to receive either oral prednisolone 25 mg or placebo daily for 2 weeks followed by fluticasone nasal drops for 8 weeks and fluticasone nasal spray for 18 weeks in both groups. The oral steroid treatment arm showed significant improvement compared to placebo at 2 weeks in hyposmia score report, Pocket Smell Test, total nasal symptom scores, mini-Rhinosinusitis Quality of Life Questionnaire, endoscopic assessment, peak nasal inspiratory flow, serum eosinophil-derived neurotoxin, and C-reactive protein. However, by 28 weeks, there were no significant differences in any measured outcome between the two treatment arms. The two groups did not differ in their reported rates of adverse outcomes from treatment. Adrenal function and markers of osteoblast activity were transiently suppressed in the prednisolone group at 2 weeks but returned to normal after transition to topical nasal steroids.

Results from multiple high-quality randomized controlled trials (Level 2) support the use of oral corticosteroids for short-term symptom relief and disease control in CRSwNP. As such, the use of short courses of systemic steroids in the management of CRSwNP is strongly recommended based on a review of the literature, and receives a Grade A recommendation. Although short-term subjective and objective improvement has been demonstrated in patients with CRSwNP, no high-level evidence studies have shown sustained long-term benefit. Additionally, studies have used variable steroid regimens and further investigation is needed to determine the most efficacious dosage and duration of oral steroid therapy for CRSwNP. Establishing the minimum effective dosage is of import given the association of corticosteroid therapy with significant side effects. Side effects identified in the above studies included insomnia, gastrointestinal disturbance, and transient disturbances in markers for adrenal and osteoblast activity; however, there exists potential for more serious adverse events.

Allergic Fungal Sinusitis

Allergic Fungal Sinusitis (AFS) is clinically distinct subtype of CRS which commonly is associated with nasal polyposis. Bent and Kuhn [26] defined diagnostic criteria that characterize AFS. Major criteria required for diagnosis of AFS include: type I hypersensitivity, nasal polyposis, characteristic CT scan findings, eosinophilic mucus, and positive fungal smear. Oral corticosteroids are

commonly employed for the treatment of AFS given its significant inflammatory disease component. In their systematic review of the literature, Lal and Hwang [11••] identified 3 high-quality studies evaluating the use of systemic corticosteroids for the management of AFS (Table 3).

Rupa et al. [27•] published a prospective randomized double-blind placebo-controlled trial of postoperative oral corticosteroids in 24 patients undergoing endoscopic sinus surgery (ESS) for AFS. Postoperatively patients received prednisolone (50 mg daily) or placebo for 6 weeks followed by a 6-week taper. All patients concurrently received ranitidine 150 mg daily, itraconazole 200 mg daily, and fluticasone nasal spray (2 puffs daily). At 12 weeks follow-up, all patients in the steroid treatment arm had complete resolution of symptoms and complete resolution of polyp disease on endoscopy. In comparison, only 1 patient in the placebo group had full symptom and endoscopic resolution of disease. Treatment-associated side effects included weight gain (100 %), Cushingoid features (42 %), acne (17 %), culture proven bacterial sinusitis (17 %), and steroid-induced diabetes mellitus (8 %). All side effects manifested during the first 6 weeks of therapy and resolved at 12 weeks after steroid taper.

Ikram et al. [28] conducted a prospective case series with retrospective case control on patients with AFS undergoing ESS. Prospectively, 33 postoperative patients received prednisone (0.5 mg/kg daily) for 1 month followed by topical beclomethasone (2 sprays per side daily) for 5 months. During treatment with topical steroids adjunctive oral prednisone (0.5 mg/kg for 1–2 weeks) was given for evidence of disease on nasal endoscopy. The control group was made up of 30 historical AFS patients who had not received oral steroid therapy. With 2 years follow-up, Ikram et al. found AFS recurred less frequency in the steroid group (15.2 %) compared to the control group (50 %). Reported side effects of steroid therapy were limited to cutaneous spots in 18.2 % of patients which spontaneously resolved upon discontinuation of oral steroids.

Landsberg et al. [29] prospectively evaluated the preoperative effect of oral corticosteroids on AFS and CRSwNP. Preoperatively, 8 AFS and 10 CRSwNP patients were treated with prednisone (1 mg/kg daily) for 10 days. Response to therapy was evaluated using CT and endoscopy. Both AFS and CRSwNP patients demonstrated significant improvement in the radiographic and endoscopic severity of their disease. The degree of improvement was greater in the AFS group. The only reported adverse event to treatment was 1 patient who developed aggressive behavior during therapy.

The evidence supporting the use of oral corticosteroid therapy for treatment of AFS includes Level 2 and 3 studies. Thus, systemic steroid therapy in the preoperative and postoperative setting for AFS is recommended (Grade B). The

ideal dosage and duration of therapy has not been fully elucidated. The above studies demonstrate that adverse events related to steroid therapy are increased in patients treated for prolonged periods. Further research is needed in this area given the risks associated with steroid therapy and uncertainty of its optimal dosing regime for AFS.

Perioperative Steroids in Chronic Rhinosinusitis with Nasal Polyps

The efficacy of perioperative steroid therapy has only been evaluated in patients with CRSwNP. Wright and Agrawal [30] conducted a randomized double-blind placebo-controlled trial in CRSwNP patients who had failed maximal medical therapy and were undergoing ESS. Twenty-six patients were randomized to receive placebo or prednisone (30 mg daily) for 5 days preoperatively and 9 days postoperatively. Intraoperative assessment of the groups showed reduced mucosa inflammation and surgical difficulty in patients treated with steroids. There were no significant differences between groups in operative duration or blood loss. Postoperative subjective outcomes showed a significant difference in olfaction at 2 weeks favoring the steroid treatment arm compared to placebo.

Sieskiewicz et al. [31] reported a randomized controlled trial of perioperative systemic steroids effect on the surgical field for 36 CRSwNP patients undergoing ESS. Patients were evenly divided and randomized to receive prednisone (30 mg daily for 5 days) or no therapy preoperatively. There was a significant improvement in the surgical field visibility and reduction in operative times for the group receiving preoperative steroids. No significant difference in operative blood loss was detected between groups.

Giordano et al. [32] prospectively evaluated 40 patients with CRSwNP undergoing ESS treated with preoperative oral steroids ($n=21$) versus no preoperative therapy ($n=19$). Patients in the treatment arm received prednisolone 1 mg/kg for 7 days prior to surgery. The patients receiving oral corticosteroids had significantly shorter operative times. There was no significant difference in estimated blood loss.

Hence, Level 2 and 3 evidence supports a recommendation (Grade B) for the use of perioperative oral corticosteroids in patients with CRSwNP. Perioperative steroids are associated with improvement in the surgical field, reduction in operative times, and improved postoperative subjective patient outcomes. Further research is needed to evaluate the efficacy of systemic steroids for CRSsNP patients in the perioperative period.

Discussion

CRS is a considerable problem for both physicians and patients as it is the second most prevalent chronic condition

reported in the United States [33]. In addition, it has significant detrimental effects on patient's quality of life. CRS patients report lower quality of life scores when compared with patients suffering from congestive heart failure, chronic obstructive pulmonary disease, and chronic back pain [34]. As such, there has been significant focus in research on the pathophysiology and management of CRS.

Currently, the pathophysiology underlying the development of CRS is not fully understood. There is strong evidence that T-cell-mediated responses play a role in both CRSwNP and CRSsNP with a different subset of T-lymphocytes contributing to each. In a very simplified explanation, CRSsNP in Caucasian Americans is predominantly a T-helper type 1 response associated with elevated levels of interferon- γ and tumor necrosis factor- α . In comparison, CRSwNP is characterized by T-helper type 2 cells with resultant elevations in interleukin-5 and eosinophils in Caucasian Americans. In Asians, different pathophysiological mechanisms are at play. A detailed discussion of these inflammatory mechanisms is beyond the scope of this article. However, through either of these mechanisms, there is a production of pro-inflammatory cytokines and a resultant inflammatory response affecting the sinonasal mucosa. Inflammation of the mucosa of the paranasal sinus can be viewed as a final common pathway in the development of CRSsNP, CRSwNP, AFS, and other CRS subtypes. Given their potent anti-inflammatory effects, corticosteroids have become a main stay of treatment for CRS.

Evidence-based medicine is the “conscientious, explicit, and judicious use of *current best evidence* in making decisions about the care of individual patients” [35]. A review of the literature reveals a preponderance of expert opinions and low-quality studies, and lack of rigorous high-quality studies supporting oral steroids use in CRSsNP. There is an increasing understanding that all forms of CRS, including CRSsNP, are caused by inflammatory pathways, and a perception of clinical benefit from oral steroids use in all forms of CRS, including in those without polyps. This points to the need for more rigorous studies to better support (or indeed refute) the utility of oral steroids in CRSsNP. Even when evaluating the studies that do support oral corticosteroids in CRSwNP and AFS, we note that the RCTs are not always the most rigorous. This points to the difficulty in conducting double-blind randomized placebo-controlled trials due to ethical concerns, costs, and recruitment issues.

There is Level 1 evidence supporting the use of intranasal nasal corticosteroids for the management of both CRSsNP and CRSwNP. As such, intranasal corticosteroids are recommended as first line therapy for the management of CRS [17••]. In comparison, there is a relative paucity of information for the use of systemic steroids in the management of CRS, especially CRSsNP. On review of the literature, there is limited Level 4 evidence and one Level 3 study investigating the use of oral

corticosteroids in the management of CRSsNP. Based on this evidence, the regular use of oral corticosteroids cannot be strongly recommend. Instead, oral steroid use in the treatment of CRSsNP is optional (Grade C or D recommendation). By contrast, the use of systemic steroids in the treatment of CRSwNP is well supported by multiple Level 2 studies and is strongly recommended based on this evidence (Grade A recommendation). In the case of AFS, oral corticosteroid use is recommended as it is supported by both Level 2 and Level 3 studies with an overall Grade B recommendation. Finally, the use of oral corticosteroids in the perioperative period for CRSwNP is supported by several high-quality studies and is recommended with a Grade B recommendation.

Although systemic corticosteroids are commonly utilized in the treatment of CRS, their use is not without risk of significant morbidity. Even with the short duration of therapy described in the reviewed papers, transient side effects included insomnia, acne, weight gain, gastrointestinal disturbance, adrenal suppression, decreased osteoblast activity, aggression, and steroid-induced diabetes mellitus were described. Additional potential side effects include glaucoma, cataracts, risk of infection, osteoporosis, poor wound healing, increased hair growth, hypertension, hyperglycemia, and avascular necrosis of hip and shoulder. A systematic review by Poetker et al. [36•] evaluated the complications and medico-legal implications of corticosteroid therapy as it applies to the otolaryngologist. They found lawsuits related to corticosteroid therapy were disproportionately costly. The most common complication of steroid therapy resulting in legal action was the development of avascular necrosis which was reported to occur at total doses of prednisone ranging from 290 to 1,000 mg. The risk of adverse events is likely dose- or duration-dependent; however, there is little known about risks associated with multiple short courses of steroids as is often utilized in the management of CRS. Interestingly, the basis for the majority of claims was lack of informed consent prior to treatment with corticosteroids. Poetker et al. concluded that patients should be treated with the minimal effective dose of steroids and that prior to steroid therapy all patients should be counseled on the risks and alternatives of therapy with this conversation documented in the medical record.

The need for further research in systemic corticosteroids therapy for CRS is evident. Currently, there is a dearth of randomized controlled studies investigating the use of corticosteroids in the management CRSsNP as either monotherapy or as part of combination therapy. Similarly, no studies were identified that evaluated the value of systemic steroids in the perioperative period for CRSsNP. Additional research is also needed to determine the maximally efficacious dose and duration of oral corticosteroid therapy for the treatment of CRSsNP, CRSwNP, AFS, and in the perioperative period. Current studies have used variable dosing regimes of varying durations, and no randomized controlled study has compared

the efficacy of differing steroid dosing regimens in the management of CRS. As adverse events related to systemic corticosteroids may be dose-dependent, the establishment of a minimal effective dose deserves further research.

Conclusions

In conclusion, corticosteroids are often used for the treatment of CRSsNP, CRSwNP, and AFS. Currently, there is a lack of high-quality evidence supporting the routine use of oral corticosteroids in the treatment CRSsNP, and as such their use is optional. In contrast, better quality evidence supports the use of short-term systemic steroids in the management of CRSwNP and AFS. The short-term benefit from a short course of oral corticosteroid therapy for CRSwNP and AFS is has been supported by multiple high evidence-level studies. The use of oral corticosteroids is similarly recommended as part of the perioperative management of CRSwNP patients undergoing ESS. The optimal dose and duration or oral steroids even in these scenarios is not clearly defined. The potential benefits and goals of oral corticosteroid therapy must therefore always be weighed against the risk of adverse events in every individual patient.

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- Of importance
- Of major importance

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