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REVIEW

Efficacy and Safety of Corticosteroid Treatments in Chronic Rhinosinusitis Management: A Systematic Review

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Abstract: Chronic rhinosinusitis (CRS) is a prevalent inflammatory disorder of the nasal and paranasal sinus mucosa, affecting 5–15% of the global population. This systematic review evaluated the efficacy and safety of systemic, injectable, and intranasal corticosteroids (CS) for the treatment of CRS and its subtypes. A comprehensive literature search was conducted using PubMed, Scopus, and Web of Science, focusing on studies published between 2010 and 2023. Six studies were finally included in the analysis. Systemic CS, particularly oral CS, significantly improved nasal congestion, reduced nasal polyp size, and enhanced the quality of life in the short term. However, their long-term use is discouraged because of side effects, such as insomnia and gastrointestinal issues. Injectable CS offer longer symptom relief and potentially lower adrenal suppression risk than oral forms, but data are limited. Intranasal CS are preferred because of their safety and efficacy in long-term maintenance therapy, with newer formulations offering increased potency and reduced systemic absorption This review highlights the importance of tailoring CS treatment based on CRS subtype, severity, and patient-specific factors. Future research should focus on optimizing CS delivery methods and exploring novel therapies to enhance the long-term management of CRS, while minimizing adverse effects.

Keywords: Chronic Rhinosinusitis; Corticosteroids; Systemic Corticosteroids; Injectable Corticosteroids; Intranasal Corticosteroids

1. Introduction

Chronic rhinosinusitis (CRS) is a common inflammatory disorder of the nasal and paranasal sinus mucosa that persists for ≥12 weeks [1]. It affects 5–15% of the global population, significantly impacting the quality of life (QoL) and healthcare costs [2].

CRS is characterized by symptoms that persist for 12 weeks or more, including nasal obstruction/congestion, facial pain/pressure, decreased sense of smell (hyposmia), and nasal discharge [3]. Chronic cough, postnasal drip, and headache are common [4]. Purulent rhinorrhea and hyposmia are strong predictors of CRS [5]. However, the correlation between symptoms and CT scan findings is often poor, with minimal association between symptom severity and the extent of sinus involvement on CT scans [6]. This indicates the complexity of CRS and challenges in its diagnosis and management. CRS diagnosis relies on persistent symptoms and objective evidence of mucosal inflammation [7]. Although purulent rhinorrhea and hyposmia are strong predictors, symptom profiles vary among patients. CRS is classified as CRS without nasal polyps (CRSsNP), CRS with nasal polyps (CRSwNP), or allergic fungal RS [8].

In China, the prevalence is approximately 2.2%, which is lower than that in Europe and the United States [9]. CRSsNP involves Th1-type inflammation, whereas CRSwNP involves Th2-type inflammation [9]. The microbiome plays a crucial role in CRS, with bacterial presence and impaired mucociliary clearance contributing significantly to inflammation [10].

CRS is a multifactorial condition with various potential causes involving host susceptibility and environmental factors; however, direct evidence is scarce [11]. Microbial elements, such as bacteria, fungi, and biofilms, significantly contribute to CRS, with bacterial and fungal biofilms on the sinonasal mucosa linked to treatment resistance [12]. Viral infections can trigger CRS, often leading to secondary bacterial infections [13]. An imbalanced microbiome also contributes to CRS [14].

Environmental factors including air pollutants, tobacco smoke, and occupational exposure are associated with CRS [15]. These exposures can cause barrier disruption, microbiome alterations, and immune dysfunctions. Laryngopharyngeal reflux is a possible etiology, although this association is controversial [16].

Genetic factors, immunodeficiencies, and comorbid conditions, such as asthma, allergic rhinitis, and bronchiectasis, are associated with CRS [13, 17]. Defects in innate immunity and dysfunctional inflammatory regulation pathways contribute to the chronic inflammation observed in CRS [11, 18]. CRS arises from diverse and interconnected microbial, environmental, genetic, and immunological factors, making it difficult to identify a single trigger [11]. Further research is needed to clarify the mechanisms of CRS pathogenesis and develop targeted therapies [13, 18].

CRS is a multifactorial disease with incompletely understood etiology. Despite extensive research, the exact cause of CRS remains unclear, with inflammation identified as the primary factor, rather than infection. Various hypotheses explain CRS pathogenesis, including the fungal, superantigen, biofilm, microbiome, eicosanoid, and immune barrier hypotheses, emphasizing environmental and host factors [19]. Genetics, sinonasal microbiomes, infections, and environmental influences are suggested contributors [13].

However, there are contradictions in the classification of CRS subtypes. Some researchers distinguish CRSwNP and CRSsNP as separate clinical entities based on inflammatory mediator profiles [20], whereas others refer to them as subtypes of the same disease [18]. The role of laryngopharyngeal reflux in CRS etiology is contentious, with some studies suggesting a link due to the high prevalence of reflux in patients with CRS [16].

The etiology of CRS is likely multifactorial, involving genetics, immune responses, and environmental factors [18]. Although progress has been made in understanding the CRS pathophysiology, the exact mechanisms remain elusive. Further research is required to develop targeted therapies and reliable biomarkers for this heterogeneous disorder [13].

The first-line treatment for CRSwNP and CRSsNP, primarily includes pharmacological interventions such as corticosteroids (CS). Topical and oral CS (OCS) are key treatments that are often supplemented with nasal saline irrigation, which improves symptoms and QoL [21, 22].

Although endoscopic sinus surgery is recommended when medical treatments fail, studies show that optimal medical treatments can be as effective as surgery after one year [23]. Alternative treatments, such as Ayurvedic medicine, have shown promise without the side effects (SEs) of conventional treatments [24]. In pediatric cases, adenoidectomy and balloon catheter sinuplasty may be considered before traditional ESS [25].

CRS management involves a multifaceted approach, with medical treatments forming the cornerstone, including CS, saline irrigation, and, sometimes, long-term antibiotics [21, 22]. When medical management fails, surgical options, such as ESS or Balloon Sinuplasty, are considered [23, 26]. The introduction of biologics has revolutionized the treatment of severe cases of nasal polyps, despite cost concerns [1]. Treatment should be tailored to the patient considering age, comorbidities, and disease severity.

CRS greatly affects patient well-being, with treatments ranging from nasal CS and saline solutions to surgery for resistant cases. Emerging therapies targeting specific inflammatory pathways, such as anti-immunoglobulin E and interleukin inhibitors, have shown promise in managing CRS [27].

Topical and systemic CS (SCS) are crucial for CRS management because of their potent anti-inflammatory effects [28]. Topical nasal CS are the primary treatment, improving symptom scores and mucociliary clearance in both CRSwNP and CRSsNP [29, 30].

Although OCS are frequently prescribed, their efficacy varies among the CRS subtypes. Randomized controlled trials support the use of OCS in CRSwNP, but strong evidence for CRSsNP is limited [28]. Alternative administration methods such as nasal irrigation have been explored to improve drug penetration and absorption [29]. Injected CS (ICS), although not included in international guidelines, have shown longer-lasting effects with potentially fewer SEs than OCS in limited studies [31]. CS remain fundamental in CRS treatment, with topical formulations being preferred first. The use of SCS, particularly OCS, should be cautiously balanced against possible SEs.

CS are essential for managing CRS, and various administration methods have proven to be effective. Topical nasal CS is widely recommended for CRS with and without nasal polyps, as supported by multiple guidelines and meta-analyses [32]. High-volume sinonasal budesonide irrigation has shown efficacy in patients with CRS after endoscopic sinus surgery, although long-term safety requires further evaluation [33]. The exhalation delivery system for fluticasone improves the Sinonasal Outcome Test scores and polyp grades [34]. Topical CS are generally safe, but the literature contains contradictions. Campbell warned against the use of multiple CS types concurrently due to risks such as adrenal and growth suppression in children [35]. Conversely, Friedlander indicated that most studies showed no adrenal or growth suppression in children using low doses with mild SEs [32].

Despite available treatments, the optimal CS regimen remains debated due to CRS presentation variability and differing efficacy and safety of the delivery methods. Advances in formulation and delivery systems are reshaping therapies; however, further comparative evaluations are needed to optimize patient outcomes.

This study evaluated the efficacy and safety of SCS, ICS, and intranasal CS (INCS) for the treatment of CRS and its subtypes. This study compared the therapeutic outcomes of these administration methods, assessed their impact on symptom relief, QoL, and SEs, and explored improvements in the combined treatment strategies for CRS management. By consolidating findings across CS modalities, we aim to provide clinicians with a comprehensive understanding of therapeutic options and guide future research.

2. Methods

This review aimed to evaluate the efficacy and safety of SCS, ICS, and INCS treatments for CRS, while adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines for transparency and replicability [36]. This review analyzed patterns, assessed treatment outcomes, and consolidated evidence to inform clinical practice in CRS management.

To identify studies evaluating the effectiveness and safety of various CS treatments for CRS, a comprehensive literature review was conducted across the PubMed, Scopus, and Web of Science databases, covering publications from January 2010 to August 2023.

In this review, we developed a search strategy to ensure thorough inclusion. The search used a combination of keywords and Medical Subject Headings terms for optimal sensitivity and specificity, including: "Chronic rhinosinusitis," "Corticosteroids," "Systemic corticosteroids," "Injectable corticosteroids," "Intranasal corticosteroids," and "Treatment outcomes." Boolean operators (AND, OR) refined and combined the search terms. Phrases such as "chronic rhinosinusitis AND corticosteroids" and "systemic corticosteroids OR injectable corticosteroids OR intranasal corticosteroids AND treatment outcomes" were used. The search was adapted to each database's indexing terms with filters to limit the results to human studies and English-language articles. Additionally, the reference lists of the retrieved articles were manually reviewed to identify any missed studies. Relevant gray literature, including conference proceedings, theses, and dissertations, was also considered to ensure comprehensive research

inclusion.

The predefined inclusion and exclusion criteria were used to select the most relevant studies.

Inclusion Criteria: Studies involving adult or pediatric patients with CRSsNP and CRSwNP. Studies on CS treatments specifying administration route (systemic, injectable, or intranasal), dosage, frequency, and duration. Studies reporting quantitative outcomes on symptom relief, QoL, reduction in nasal polyp size, imaging findings (e.g., CT scan scores), and SEs or adverse events. Randomized controlled trials (RCTs), cohort studies, case-control studies, and systematic reviews provided high-quality evidence on CS efficacy and safety.

Exclusion Criteria: Studies with fewer than 20 participants were excluded to avoid small sample bias. Non-English publications owing to resource constraints and translation accuracy concerns. Studies lacking sufficient quantitative data on relevant outcomes or providing only qualitative assessments. Studies on rare or atypical CRS presentations, such as fungal CRS or CRS with systemic diseases, cannot be generalized to the broader CRS population.

Two reviewers independently screened the titles and abstracts of the identified articles for eligibility, based on the inclusion and exclusion criteria. Full-text articles were retrieved and reviewed for studies that met the inclusion criteria or had uncertain eligibility. Any disagreements between the reviewers were resolved through discussion, and if consensus was not reached, a third reviewer decided. The selection process was documented with a Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram, detailing the studies identified, screened, excluded, and included, with reasons for exclusion at each stage.

Two independent reviewers extracted the data using a standardized form tested for consistency in a subset of studies. The information captured included authors, publication year, country, study design, setting, follow-up duration, participant count, age range, sex distribution, CRS subtype (CRSsNP or CRSwNP), initial disease severity, and inclusion/exclusion criteria. CS details recorded included types (systemic, injectable, intranasal), specific agents (e.g., prednisone, methylprednisolone, fluticasone), dosing regimens, administration frequency, delivery routes, and treatment duration. Control interventions such as placebo, no treatment, or alternative medications (e.g., antibiotics and saline irrigation) were also noted. Primary and secondary outcomes included symptom relief (e.g., nasal congestion, rhinorrhea, and facial pain), QoL assessments, objective measures, imaging results, and reported SEs or adverse events. Quantitative data, statistical analyses, effect sizes, confidence intervals, and p values were extracted. Reviewers compared their findings for accuracy and completeness, resolved discrepancies through discussion and consensus, and consulted a third reviewer if necessary.

A thorough risk of bias assessment was performed for studies in a systematic review of CS therapy for CRS, evaluating six areas: selection bias (random sequence generation and allocation concealment), performance bias (blinding of participants and personnel), detection bias (masking outcome assessment), attrition bias (completeness of outcome data), reporting bias (reporting all prespecified outcomes), and other biases (additional risks, such as funding bias or study-specific issues). Each study was rated as Low Risk (1), Some Concerns (2), or High Risk (3), according to the Cochrane Handbook for Systematic Reviews of Interventions. Two reviewers independently assessed each study and resolved disagreements through discussion, and a third reviewer. The quality assessment results were used to interpret the strength and reliability of the evidence.

This review did not involve human participants or confidential patient data, and thus did not require ethical approval. Ethical standards were maintained through accurate representation of findings, proper attribution, and plagiarism avoidance. Constraints included potential publication bias towards positive results and exclusion of non-English studies. Variations in study design, interventions, outcomes, and patient populations limited generalizability. Incomplete reporting in some studies could affect the quality and bias assessment. The focus on short-term outcomes has left a gap in the long-term efficacy and safety data for CS treatment in CRS.

3. Results

Thorough statistical and methodological evaluations were conducted on the six included studies to ensure reliability of the results. The main outcomes examined were symptom alleviation (nasal blockage, runny nose, and facial discomfort), QoL, reduction in nasal polyp size, and adverse effect profiles across various CS types.

Quantitative data, including effect sizes, mean differences, and p values, were extracted. Meta-analysis was considered, but not conducted, because of the diverse study designs and outcomes. Instead, narrative synthesis grouped findings by CS administration route: SCS, ICS, and INCS. The studies included randomized controlled trials and systematic reviews, with participant numbers ranging from 45 to 414, follow-up periods ranging from 2 weeks to 6 months, and different intervention protocols. Each study was evaluated using the Cochrane risk-of-bias tool, revealing "low" to "moderate" risks in selection bias (randomization techniques) and performance bias (blinding), but some studies showed high risks of attrition and reporting biases, which were considered in result interpretation. The included studies employed various intervention protocols, such as tapering regimens for OCS, comparisons of high-dose and low-dose treatments, and innovative delivery systems for intranasal formulations, allowing for a comprehensive evaluation of the effectiveness and safety of different CRS subtypes.

The initial literature search yielded 138 results, with 114 articles excluded because they did not meet the inclusion criteria. After excluding 16 articles due to insufficient data or conclusions, 24 articles were thoroughly examined. Full-text access for two of the remaining eight studies was unattainable despite multiple attempts, leaving six studies for a systematic review [31, 37–41]. **Figure 1** illustrates the selection process and **Table 1** lists the six studies included.

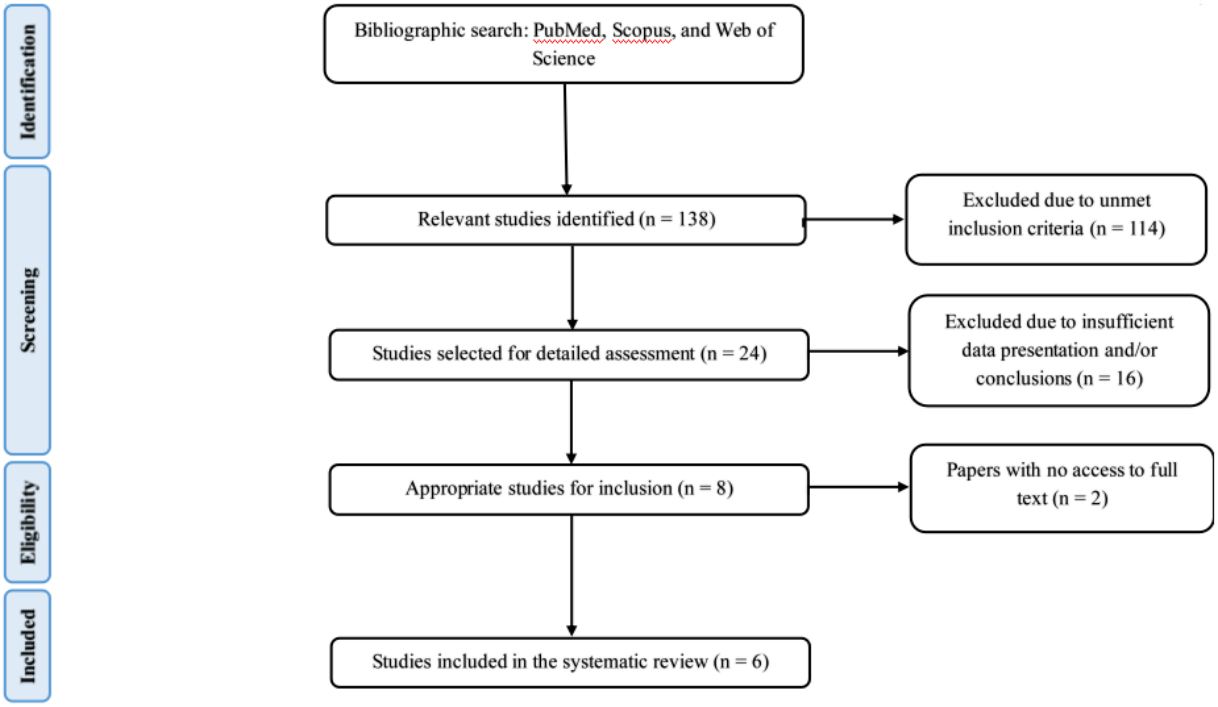

Figure 1. Flow diagram of literature search and study of selection for systematic review (PRISMA flow chart).

SCS are effective in managing CRS, especially for patients with nasal polyps, significantly reducing symptoms and polyp size, and improving QoL with short-term use [31, 37]. However, their long-term use is discouraged due to SEs. INCS are preferred for their safety and efficacy, with newer formulations offering increased potency and reduced systemic absorption [38, 39]. In children, oral methylprednisolone with antibiotics significantly improved symptoms and computed tomography (CT) results [40]. Although SCS provide short-term benefits, their effects may not last beyond 3–6 months [41]. Research continues to explore new strategies to overcome CS resistance and to enhance the long-term outcomes of CRS.

Table 1. Characteristics of selected studies on the evaluation of treatment using CS in patients with CRS.

Study Details	Study Objectives	Study Design	Intervention	Main Findings
Tamene et al. [31]	To conduct a systematic review of the benefits and possible SEs of ICS or OCS for treating CRS.	Systematic review	Among the 48 trials reviewed, five used ICS or SCS. The number of studies employing OCS varied: three indicated perioperative benefits, four showed no effect, and 19 reported symptom relief.	A systematic review found a scarcity of comparative studies on the efficacy of OCS versus ICS in CRS. The results on OCS were inconsistent, with some studies indicating benefits and others showing no significant impact. Limited data suggest that ICS may provide longer-lasting effects and fewer SEs than OCS do.
Zhang et al. [37]	To assess the efficacy of SCS in patients with CRSwNP and investigat the safety profile of SCS, including SEs, in patients with CRSwNP. Comparison of outcomes between high-dose (≥50 mg per day prednisone) and low-dose (<50 mg per day prednisone) CS treatments.	Meta-analysis evaluated the efficacy and safety of SCS for CRSwNP, focusing on randomized trials comparing CS with placebo and non-steroid controls.	SCS at high (≥50 mg per day prednisone) or low (<50 mg per day prednisone) doses.	In patients with CRSwNP, SCS markedly improved nasal congestion, reduced polyp size, and enhanced the peak nasal inspiratory flow. Both high-dose (≥50 mg per day prednisone) and low-dose (<50 mg per day prednisone) treatments provided similar clinical benefits. However, higher doses led to more SEs, such as insomnia and gastrointestinal issues, than lower doses, which had fewer SEs.
Chong et al. [38]	To evaluate the effects of INCS in patients with CRS.	Systematic review of randomized controlled trials.	INCS, namely beclomethasone dipropionate, triamcinolone acetonide, flunisolide, and budesonide.	The INCS demonstrated a small, statistically significant improvement in the combined European Prediction of Rhinosinusitis symptoms; however, the quality of evidence was insufficient. The effect of INCS on disease-specific health-related quality of life is extremely limited. INCS strongly correlates with an increased likelihood of epistaxis.
Macias-Valle and Psaltis [39]	To evaluate the efficacy of INCS in treating patients with CRS.	A systematic review of the efficacy, safety, and distribution of INCS in the treatment of CRS.	INCS	Patients using INCS experienced notable improvements in both disease-specific and overall quality of life, regardless of United States Food and Drug Administration approval. Thus, the use of INCS formulations appears to be a safe approach to managing CRS.
Ozturk et al. [40]	To assess the efficacy and acceptability of oral methylprednisolone as an anti-inflammatory adjunct in the management of pediatric CRS.	Randomized, double-blind, placebo-controlled trial.	Amoxicillin/clavulanate and methylprednisolone were orally administered for 30 and 15 days, respectively, following a tapering regimen.	Both the methylprednisolone and placebo groups showed significant improvements in symptoms and post-treatment CT scan assessments. However, the methylprednisolone group exhibited greater enhancements in CT scan scores, overall CRS symptoms, and specific symptoms, such as nasal congestion, postnasal drip, and cough. Notably, fewer patients in the methylprednisolone group had abnormal CT scan results at the end of the treatment than those in the placebo group.
Head et al. [41]	To assess the effects of OCS compared to placebo, no treatment, or alternative medications (INCS, antibiotics, and antifungals) for CRS.	Randomized, placebo-controlled trial.	Upto 21 days of OCS.	OCS improved health-related quality of life and decreased symptom severity in patients with CRSwNP after 2–3 weeks compared to placebo or no treatment; however, these effects did not persist at 3–6 months post-treatment. Short OCS courses are associated with an increased risk of insomnia and gastrointestinal problems; however, their impact on mood disorders remains unclear.

Note: CS: Corticosteroids; SEs: Side effects; CRS: Chronic rhinosinusitis; OCS: Oral corticosteroids; ICS: Injected corticosteroids; SCS: Systemic corticosteroids; CRSwNP: Chronic rhinosinusitis with nasal polyps; CT: Computed tomography; INCS: Intranasal corticosteroids.

3.1. SCS

Zhang et al. analyzed seven randomized controlled trials with 414 subjects and found that OCS significantly improved nasal congestion, reduced nasal polyp size, and enhanced peak nasal inspiratory flow [37]. Both high-dose (≥50 mg per day prednisone) and low-dose (<50 mg per day) treatments were effective; however, higher doses caused more insomnia and gastrointestinal issues. Other SEs were minimal and similar across dosages. Head et al. confirmed the initial benefits, but noted that improvements in QoL and symptom relief diminished after 10 weeks, suggesting that OCS provide rapid yet short-lived relief from CRS symptoms [41]. SEs such as gastrointestinal problems and insomnia were more frequent, although mood changes did not differ significantly from those in the placebo group. These findings indicate that SCS may not be ideal for the long-term management of CRS because of their temporary effects and potential SEs.

3.2. ICS

Tamene et al.'s review of 48 studies revealed that ICS offer significant benefits in treating CRS, providing longer symptom relief and lower adrenal suppression risk compared to OCS [31]. Although the data are limited, the findings suggest that ICS could effectively provide extended symptom control while minimizing the systemic SEs associated with prolonged OCS use.

3.3. INCS

Macias-Valle and Psaltis assessed INCS for CRS, emphasizing their importance [39]. Both FDA-approved and non-approved INCS formulations significantly improved the disease-specific QoL and symptoms. INCS was found to be safe for long-term use due to its minimal systemic absorption, making it suitable for maintenance therapy. The study suggested that new IN delivery methods could improve outcomes by better targeting the sinuses, which is crucial for long-term symptom management.

Chong et al.'s analysis of 18 randomized controlled trials with 2,738 participants confirmed that INCS effectively alleviates nasal congestion, runny nose, and loss of smell [38]. However, the results for facial pain and pressure have been inconsistent. INCS use is associated with increased nosebleeds, emphasizing the need for patient supervision. INCS is an effective maintenance treatment option for long-term symptom control, with minimal systemic risk.

3.4. Combination Therapy

Ozturk et al. examined the effects of combining methylprednisolone (a CS) with antibiotics (amoxicillin/clavulanate) versus antibiotics alone in 45 patients [40]. Both groups showed significant improvement in symptoms and sinus CT score. However, the methylprednisolone group experienced better outcomes for nasal obstruction, postnasal discharge, cough, and CT abnormalities. By the end of treatment, this group had fewer abnormal CT scans and lower clinical relapse rates, suggesting that CS and antibiotic combination therapy offers better short-term relief and sinus health improvement than antibiotics alone. Adverse event rates were similar in both groups, supporting the safety and efficacy of the combination therapy for acute CRS treatment.

3.5. Risk of Bias Assessment

The selected studies were systematically evaluated for bias risk in six key areas: selection, performance, detection, attrition, reporting, and others.

Selection Bias: Most studies implemented random sequence generation effectively, ensuring an equitable distribution between the intervention and control groups. However, some lacked clarity in allocation concealment, potentially introducing selection bias and affecting outcomes due to imbalanced group composition.

Performance Bias: Inconsistent blinding of participants and personnel was noted, particularly in studies with subjective outcomes, such as symptom relief or quality of life, potentially exaggerating treatment effectiveness due to enhanced placebo effects.

Detection Bias: Inadequate masking of outcome assessors was common, especially in studies relying on self-reported measures or clinician-graded scores, increasing the risk of observer bias and potentially inflating the perceived benefits of CS treatment.

Attrition Bias: The dropout rates varied, with some studies inadequately addressing the incomplete outcome data. High attrition rates or a lack of intention-to-treat analyses undermined the reliability of the results, particularly in studies with extended follow-up periods.

Reporting Bias: Most studies adhered to predefined outcome measures; however, some exhibited selective reporting, focusing primarily on positive findings, which reduced transparency and may have obscured the balance between benefits and adverse effects.

Other Biases: Potential funding biases were identified in studies supported by pharmaceutical companies, where conflicts of interest, although disclosed, might have influenced the study design, data interpretation, and reporting. Variations in CS dosages, delivery methods, and patient demographics further complicated the comparative analyses.

The biased risk assessment results underscore the need for stringent methodological practices in future research. The observed methodological inconsistencies challenge the robust conclusions. Although the included

studies provided valuable insights into CS efficacy and safety in CRS management, their varying risk profiles necessitated cautious interpretation. Future research should prioritize comprehensive blinding, standardized outcome measures, and transparent reporting to enhance the reliability of evidence in this field.

Figure 2 categorizes each study and bias type by risk level, highlighting limitations in the design or reporting that may affect the interpretation of CS efficacy and safety in CRS.

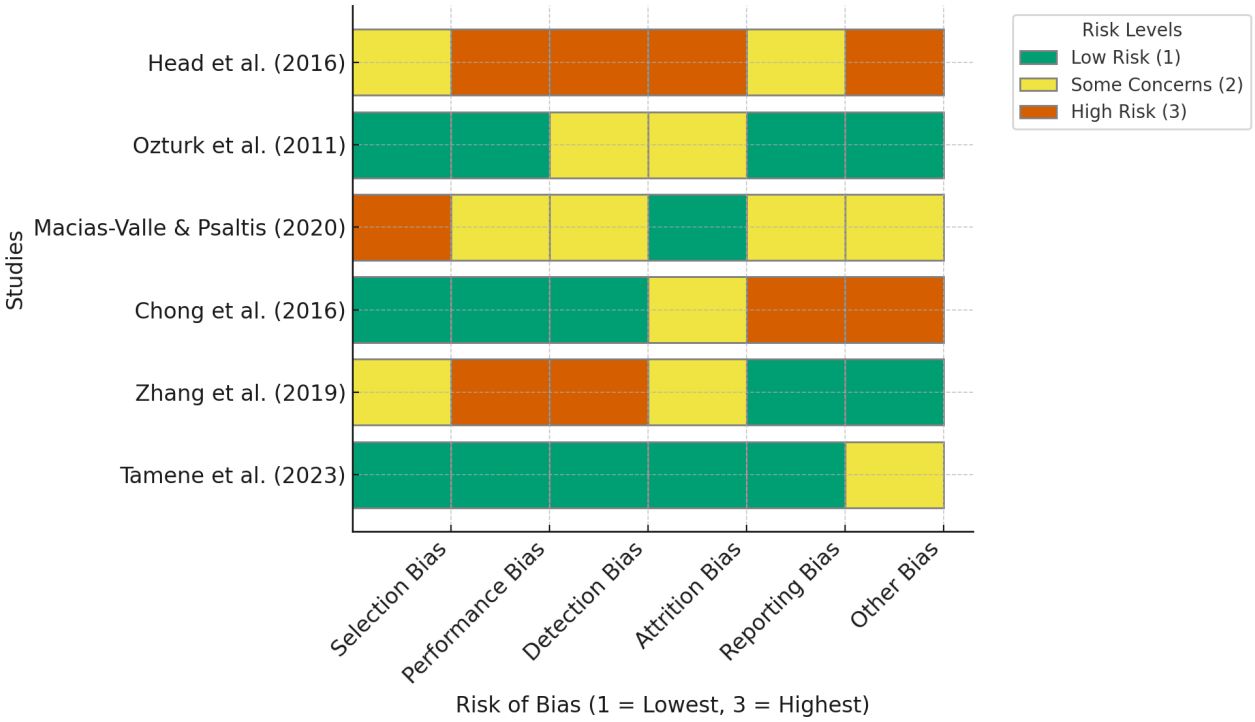

Figure 2. Risk of bias assessment in systematic review of CS treatments in patients with CRS.

4. Discussion

Topical and SCS significantly relieve CRS symptoms, such as nasal congestion, discharge, and anosmia, owing to their potent anti-inflammatory properties that reduce mucosal edema and polyp growth [42, 43]. Patients using CS show improved QoL and experience fewer and less severe CRS exacerbations, which enhance daily functioning and overall well-being [44, 45]. CS polyp size, relieve nasal obstruction, and improve airflow in patients with CRSwNP, which is crucial for CRS management [46, 47]. Prolonged SCS use can cause adverse effects, such as osteoporosis, adrenal suppression, weight gain, and increased infection risk. Thus, careful evaluation of the therapy duration and dosage is necessary.

Topical CS are generally safer, offering effective localized action with minimal systemic absorption and reduced adverse effects, although local issues such as nasal irritation or epistaxis require monitoring [48, 49]. Long-term studies show the safety of topical CS, but continuous monitoring is essential to manage potential local adverse effects [47, 48]. CS are crucial for CRS treatment, while new medications like biologics offer alternative options with different safety profiles, beneficial for those with CS contraindications or significant SEs [50, 51].

Treatment should be individualized based on the patient's CRS subtype, severity, and treatment response, ensuring effective management tailored to their needs [42, 45]. Regular assessment of the therapeutic effectiveness and SEs is vital. Adjustments, such as dose reduction or switching to biologics, should be made based on patient response and tolerance.

This systematic review evaluated the effectiveness and safety of different CS delivery methods in treating CRS, offering insights into their usefulness across various CRS subtypes. SCS, especially OCS, are commonly used because of their strong anti-inflammatory properties, particularly in CRSwNP. However, the short-lived nature of symptom

relief, typically lasting no more than 10 weeks, highlights the challenges of long-term management [37, 41]. Although high OCS doses improve nasal congestion and reduce polyp size, they also increase the likelihood of sleep disturbances and digestive issues [37].

ICS present an interesting option by offering prolonged symptom alleviation and potentially lowering the risk of adrenal suppression. This makes them suitable for patients requiring ongoing intervention, but unsuitable for long-term oral therapy due to SEs [31]. Despite promising results, research on ICS remains scarce, indicating the need for additional studies to optimize dosing regimens and verify their long-term safety.28

INCS have become crucial for maintenance therapy because of their localized effects and minimal systemic absorption, making them ideal for ongoing symptom control in mild-to-moderate CRS cases [38, 39]. Extended INCS use effectively reduces nasal congestion and improves QoL without significant systemic SEs, which is essential for managing persistent symptoms [30]. Recent innovations in IN delivery techniques have shown promise for improved outcomes by more effectively targeting sinonasal pathways, thus enhancing drug efficacy in CRS treatment [29].

The three CS administration methods improved symptom relief and QoL, with varying effectiveness and duration. Nasal sprays significantly reduce symptoms, such as congestion and rhinorrhea, enhancing daily function and patient satisfaction [52]. OCS provide the greatest short-term benefits but are frequently associated with systemic SEs [53]. Injections notably improve the QoL of patients with persistent symptoms, especially when other treatments failed [54].

Combined therapies, particularly CS and antibiotics, show greater efficacy in decreasing clinical relapse rates and improving symptom resolution in acute CRS presentations. These combinations capitalize on the anti-inflammatory benefits of CS and the antimicrobial effects of antibiotics, providing a balanced approach for managing infection-related CRS flare-ups. Clinical trials suggest that CS and antibiotic combination therapy yields better results for nasal obstruction, postnasal discharge, and cough than antibiotics alone with similar adverse event rates, making it appropriate for specific patient groups [14, 16].

Analysis of the risk of bias reveals insights into the reliability of evidence supporting CS treatment for CRS. Significant performance and detection bias risks suggest difficulties in achieving proper blinding, potentially inflating treatment effects, particularly for subjective outcomes. Low selection bias in most studies indicates confidence in randomization; however, concerns about attrition and reporting bias in some studies emphasize the need for transparency, as high dropout rates or insufficient data reporting may introduce biases affecting outcomes. Additional biases such as funding sources or conflicts of interest underscore the importance of considering external influences in future research. These findings highlight the necessity of improving the study design and adhering to bias-reduction strategies in CRS research, particularly in randomized controlled trials evaluating CS therapies.

This review included six studies on SCS, ICS, and INCS for CRS. OCS provide short-term benefits for CRSwNP by reducing congestion and polyp size and improving nasal flow. Both high-dose (≥50 mg per day prednisone) and low-dose (<50 mg per day prednisone) regimens were effective, although higher doses caused more SEs such as insomnia and gastrointestinal issues. The benefits were diminished after 10 weeks. ICS offer prolonged relief with fewer SEs than OCS, although the data are limited.

The long-term safety and efficacy of ICS in CRS raise concerns. Prolonged use can lead to various side effects, such as suppression of the hypothalamic-pituitary-adrenal axis, potentially causing adrenal insufficiency [55, 56], reduced bone mineral density, weight gain, glucose intolerance, and increased cardiovascular disease risk [57]. Topical CS may thin the nasal mucosa, increase susceptibility to infection and nosebleeds [58], and mask the symptoms of underlying diseases, delaying accurate diagnosis and treatment [59]. Long-term studies are necessary to evaluate the sustained effectiveness and safety profile of ICS in managing CRS symptoms [57, 59], including comparisons with newer medications such as biologics, which offer an alternative, especially in cases with nasal polyps [60–62]. Longitudinal studies should focus on patient-centered outcomes [62, 63], and understanding individual variations in responses could inform personalized treatment strategies and improve efficacy while minimizing risks [64, 65].

INCS are effective and safe for long-term use in mild to moderate CRS, reducing congestion, rhinorrhea, loss of smell, and improving QoL. Minimal systemic absorption made INCS suitable for continuous use, although SEs, such as epistaxis, occurred. Innovative delivery methods, such as exhalation systems and enhanced drug targeting. In pediatric CRS, combining oral methylprednisolone with antibiotics was better than antibiotics alone, supporting combination therapies for acute CRS.

CS therapy is crucial in CRS management but requires careful consideration of patient-specific factors, disease severity, and CRS subtype. SCS provided rapid relief but had higher risks of systemic SEs, limiting its long-term use. INCS is preferred for ongoing therapy owing to its safety and effectiveness. ICS have the potential for extended symptom control, with a lower systemic risk. Combination therapy with CS and antibiotics improved short-term outcomes.

The use of CS for CRS necessitates balancing efficacy with potential adverse effects. SCS are associated with numerous SEs due to their systemic absorption.

CS therapies show immediate benefits for CRS, but their long-term safety and effectiveness remain underresearched. Current studies have focused on short-term symptom relief and quality of life improvements, with limited data on extended outcomes [37–39]. Although INCS are safer for long-term use, their effects on nasal tissues, such as thinning or irritation, require further investigation [35, 38]. Similarly, data on the long-term safety of ICS are lacking [31]. Additionally, the comparative long-term efficacy of different CS formulations and administration methods has been understudied. Addressing these gaps is crucial for developing treatments that minimize risks while ensuring long-term effectiveness.

SCS can cause increased appetite and weight gain, elevated blood glucose levels, posing risks for diabetics or those prone to metabolic syndrome, decrease bone density, and heighten fracture risk, particularly in the elderly and postmenopausal women [66, 67]. Prolonged use may suppress the hypothalamic-pituitary-adrenal axis, necessitating careful tapering to prevent withdrawal symptoms and adrenal insufficiency [66]. Their immunosuppressive properties increase the risk of infection with their extended use [67]. Patients may also experience mood swings, anxiety, and severe psychological effects such as depression or psychosis. Additionally, CS can cause gastritis or peptic ulcers due to stomach mucosal irritation [66, 67].

Topical CS are generally safer due to lower systemic absorption, but can still cause local SEs such as nasal mucosal irritation, dryness, burning sensations, or epistaxis if improperly dosed [44, 48]. Prolonged use may lead to nasal mucosa atrophy, underscoring the need for patient education regarding proper dosing [48]. Limiting the duration and using minimal effective doses of systemic CS are crucial to minimize adverse effects. Topical CS should be prioritized when possible due to their safer profile [48, 66]. Regular follow-up and monitoring are vital, particularly for long-term use. Educating patients on correct nasal spray techniques can reduce local SEs and enhance the therapeutic effectiveness.

Biologics, such as Dupilumab (IL-4 receptor antagonist), Omalizumab (anti-IgE monoclonal antibody), Mepolizumab, and Benralizumab (IL-5 targets), are crucial for managing CRSwNP and asthma by targeting specific inflammatory pathways [51, 60–62, 64]. Innovative therapies complementing biologics include advanced Endoscopic Sinus Surgery techniques, drug-eluting implants, topical antimicrobial and antifungal agents, immune modulators like low-dose macrolides, probiotics, and microbiome modulation [62, 63, 65]. These treatments represent significant progress in CRS management, especially for refractory cases or comorbidities, potentially improving outcomes and reducing the need for surgery [64, 65]. Medical professionals should tailor therapies according to individual patient needs and disease characteristics.

To address potential biases, future research should employ advanced blinding methods such as double-blind designs for subjective outcomes (e.g., symptom relief). Standardized protocols incorporating validated tools should be developed for data collection and outcome assessment to reduce detection bias. Transparency in data handling, including detailed reporting of randomization procedures, allocation concealment, and dropout rates, is crucial for minimizing attrition and selection bias. Adhering to established methodologies, documenting all findings (including adverse events), and fully disclosing funding sources and potential conflicts of interest can mitigate selective reporting and publication biases. Utilizing standardized outcome measures across studies enhances comparability and reliability, leading to more robust and unbiased results.

This review emphasizes that while SCS remains important in CRS treatment, it may be most effective when limited to short-term use or specific indications, such as CRSwNP. ICS and INCS offer valuable options for long-term management, with fewer SEs, and combination therapies enhance outcomes in patients with concurrent infections.

5. Clinical Implications

This review highlights the therapeutic implications of CS in CRS treatment. SCS, especially OCS, provides rapid but short-term relief from CRS symptoms, particularly in CRSwNP, but its SEs limit long-term use. ICS offers pro-

longed symptom relief with fewer systemic SEs, making it suitable for repeated treatments and minimizing oral therapy complications. For long-term management, INCS is preferred because of its minimal systemic absorption and sustained efficacy in both CRSwNP and CRSsNP. Combining CS with antibiotics in acute CRS exacerbations leverages their anti-inflammatory and antimicrobial properties, thereby offering comprehensive management. Tailoring CS therapy based on CRS subtype, severity, comorbidities, and treatment goals is crucial for improving outcomes while minimizing adverse effects. Advances in CS delivery and research on biologics and targeted therapies have shown promise for enhanced efficacy and reduced SEs. Healthcare providers must balance the anti-inflammatory benefits of CS with potential risks, especially with systemic formulations, through proper dosing, duration, and patient monitoring. These insights emphasize the vital role of CS in CRS treatment, while highlighting the need for further research to optimize their use, explore alternatives, and address evidence gaps.

6. Recommendations

CS therapy for CRS should be personalized based on subtype, severity, and patient factors. SCS provides rapid relief, especially in CRSwNP, but their long-term use has potential adverse effects. CS injections offer long-term relief for patients intolerant to SCS; however, further research is needed. Nasal CS sprays are preferred for maintenance because of their localized action, safety, and effectiveness. CS-antibiotic combinations are recommended for acute or severe cases. Innovative INCS delivery methods enhance drug targeting and therapeutic outcomes.

Research priorities include long-term studies on ICS and new intranasal formulations; comparative analyses of CS types; exploration of biological therapies for CS-resistant CRS; CS efficacy and safety in children; and QoL, adherence, and satisfaction research.

Practical review considerations include addressing study biases; evaluating dose, efficacy, and SEs of SCS; and informing healthcare professionals about nuanced CS use and strategies to mitigate SEs.

7. Limitations

Only six studies met the inclusion criteria, potentially limiting the applicability of our results across different populations and CRS types. The studies varied in design, patient characteristics, CRS subtypes, and CS intervention details, such as dosage, duration, and administration method, complicating data comparison and integration. Most research has focused on immediate CS treatment efficacy and safety, with underexplored long-term effects and adverse reactions. Bias assessment indicated potential performance, detection, reporting, and attrition biases, undermining outcome reliability. Scarce research on ICS limits conclusions about its efficacy and safety compared to other administration routes. Insufficient evidence precludes thorough subgroup analyses based on CRS subtype, patient age, or coexisting conditions. The study focused on CS, excluding newer medications, such as biologics or other anti-inflammatory drugs, which could offer a more comprehensive view of CRS management. Language bias may have been introduced by excluding non-English studies, and publication bias may have been exacerbated by omitting unpublished research or studies with negative results. Limited research on pediatric populations hinders extrapolation to younger patients with CRS. Variability in outcome measurements such as symptom scores, QoL, and SEs may have affected data synthesis.

These limitations underscore the need for well-designed multicenter randomized controlled trials to produce more robust and generalizable data on the efficacy and safety of various CS treatments for CRS.

8. Future Prospects

Innovative CS formulations, including nanotechnology-based delivery systems, can enhance targeted drug delivery to the sinonasal mucosa, increasing efficacy, while reducing systemic absorption and SEs. Optimizing combination therapies, such as CS with biologics that target specific inflammatory pathways, could offer tailored treatments for refractory CRS. Monoclonal antibodies, such as anti-IL-5 or anti-IgE, may revolutionize CRSwNP. Future research should focus on identifying biomarkers to predict individual responses to CS therapies, thereby enabling personalized medicine for CRS management. Investigating the long-term effects of SCS and ICS, including adverse effects such as adrenal suppression and osteoporosis, is crucial. Developing advanced intranasal delivery systems for deep sinus penetration could significantly improve the effectiveness of INCS, especially in cases of complex sinus anatomy. Innovations may include wearable or minimally invasive devices for the real-time monitoring of treat-

ment responses, providing physicians with actionable data. Artificial intelligence and machine learning can aid in the predictive modeling of treatment outcomes, enabling the selection of the most effective CS regimen based on patient-specific factors.

9. Conclusions

CS is essential for the management of CRS because of its potent anti-inflammatory effects. SCS provides rapid relief, especially for CRSwNP, but is limited to short-term use owing to serious side effects. INCS is preferred for long-term management, offering consistent efficacy with minimal systemic absorption, and is suitable for mild-to-moderate CRS. Although less researched, ICS provides an alternative for patients intolerant of systemic formulations, offering prolonged symptom control with potentially reduced systemic risks.

Combined treatments, such as CS and antibiotics, enhance the efficacy of acute CRS exacerbations with infectious components. Advances in intranasal delivery systems show promise for improving drug distribution and targeting within the sinuses.

Variations in research methodologies, patient populations, and treatment protocols necessitate standardized guidelines tailored to CRS subtypes, severity, and patient-specific factors. Future research should focus on the long-term safety and efficacy of CS, particularly its injectable and intranasal forms, while exploring emerging biologics and personalized medicine approaches to address CS resistance and refractory cases.

CS remain crucial in CRS management, with effectiveness enhanced through personalized treatments, careful monitoring of side effects, integration of innovative delivery methods and adjunct therapies, refining current clinical practices, and paving the way for more comprehensive, patient-centered CRS treatment strategies.

Author Contributions

Conception: W.A. (Wajan Alqathanin), M.K., W.A. (Wajin Alruwili), L.A.; Design of the work: B.A. (Bader Almutairi), B.A. (Bayan Alghamdi), M.H., F.O.; Data acquisition: S.A., F.H., M.R., M.S.; Data synthesis: F.H., M.R., M.S., H.N., F.K.; Manuscript drafting: W.A. (Wajan Alqathanin), M.K., W.A. (Wajin Alruwili), L.A.; Manuscript review: F.H., M.R., M.S., H.N., F.K.

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