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INVITED REVIEW

Perioperative management of patients receiving glucocorticoids in rheumatology

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ABSTRACT

Glucocorticoids are a cornerstone in the management of rheumatic diseases due to their potent anti-inflammatory and immunomodulatory effects. However, their perioperative use presents distinct challenges, including an elevated risk of infection, impaired wound healing, and the potential for glucocorticoid-induced adrenal insufficiency (GI-AI). This review examines the perioperative implications of glucocorticoid therapy, with a focus on infection risk, adrenal insufficiency, and recommendations from clinical practice guidelines. Evidence indicates a correlation between glucocorticoid use and increased perioperative complications, although the efficacy of dose reduction strategies in mitigating these risks remains uncertain. GI-AI, a common complication of prolonged glucocorticoid use, necessitates careful perioperative management to prevent adrenal crises. Guidelines from British, American, and German societies propose slightly differing approaches, albeit with low levels of evidence, emphasizing the importance of individualized patient care.

Keywords: glucocorticoids, perioperative management, infection risk, adrenal insufficiency.

Introduction

Glucocorticoids play a crucial role in managing various rheumatic diseases due to their potent anti-inflammatory and immunomodulatory effects [1]. However, their use in the surgical setting is associated with an increased risk of significant complications, particularly infection and adrenal insufficiency [2]. Prolonged glucocorticoid therapy may further exacerbate these risks, leading to impaired wound healing, increased skin fragility, hematoma formation, skin ulceration, and a heightened susceptibility to skin tears [1]. These complications can significantly impact patient outcomes, necessitating careful management strategies. Clinicians are thus faced with the complex challenge of balancing the therapeutic benefits of glucocorticoids against their potential perioperative risks.

Infection

Among different factors increasing the risk of infection in a patient with a rheumatic disease undergoing surgery, both historical and current corticosteroid use is an important risk factor [2]. Other factors are also related with corticosteroid use and overall risk of infection, such as disease activity and longer disease duration [3]. They both increase the risk of infection by themselves and by being associated with higher corticosteroid use.

Data regarding the increased risk of infection in the perioperative period are derived from large cohort studies. In a retrospective cohort of fourteen thousand patients undergoing total knee or hip arthroplasty, steroid use was associated with adverse outcomes such as wound dehiscence, surgical site infection, pneumonia, urinary tract infection and readmission, but not

with mortality, venous thromboembolism, post-operative cerebrovascular events, myocardial infarction or sepsis [4]. In a study involving Danish rheumatoid arthritis patients registries, steroid use was associated with about 2.5 to 3 times higher risk of joint infection and death in one year [5]. In two retrospective cohort studies from United States that use post-market surveillance data, among rheumatoid arthritis patients receiving biological therapy, steroid use was found to have dose-dependent risk increase for both non-urinary and urinary hospitalized infection, prosthetic joint infection, 30-day readmission and 90-day mortality [6,7]. Patients using a dose greater than 10 mg/day prednisone equivalent had 1.5 to 2 times higher risk for adverse outcomes than those who did not use steroids.

Various rheumatological societies have published guidelines regarding steroid use in the perioperative period. 2017 British guidelines recommend steroid exposure to be minimized prior to surgical procedures, without going into further detail [8]. American College of Rheumatology and the American Association of Hip and Knee Surgeons guideline published in 2022 make no recommendations regarding pre-operative reduction of steroid dose [9].In the 2017 edition of this guideline, there was a recommendation of tapering to lower than 20 mg/day prednisone equivalent prior to surgery when possible [10], but this was removed in 2022 edition. German guidelines published in 2022 suggest reducing the steroid dose to the lowest possible dose, 10 mg/day prednisone equivalent if possible, in the two to three months preceding surgery [11].However, while higher steroid does are in fact related with adverse outcomes,reducing the dosepreceding the surgery has not been proven to decrease the rate of perioperative complications [6].

Adrenal insufficiency

Glucocorticoid-induced adrenal insufficiency (GI-AI) is a typical side effect associated with exogenous use of corticosteroids [12]. Spectrum of GI-AI ranges from otherwise asymptomatic "biochemical" GI-AI to potentially lethal adrenal crisis [13].However, despite wide-spread use of steroids both for rheumatological and non-rheumatological conditions, data regarding the definition, epidemiology, diagnosis and treatment of this condition come from heterogeneous studies, resulting in a low level of evidence [13].

GI-AI results from suppression of adrenocorticotrophic hormone (ACTH) and corticotropin-releasing hormone (CRH) from pituitary gland and hypothalamus respectively. Chronic suppression of ACTH leads to atrophy of the adrenal cortex, which results in reduced cortisol production during periods of increased requirement [14].

Risk factors

Dose and duration of the steroid therapy are the most important risk factors for the development of GI-AI [15]. When steroids are no longer required to control the underlying condition, various tapering regimens are used to prevent both disease flares and development of GI-AI. A suggested tapering regimen by the 2024 American Endocrine Society (ES) and European Society of Endocrinology (ESE) guideline is given in Table 1 [15].

Pharmacokinetically, dexamethasone has the highest potency and the longest duration of action compared to other steroid formulations [16]. However, when equivalent doses are used, type of steroid used does not have an effect in adrenal suppression [14]. Pulse steroid therapy, alternative single day dosing and shorter duration (less than 14 days) are unlikely to cause GI-AI [14]. Concomitant use of other CYP3A4 inhibitors, such as clarithromycin and azole type of antifungals increase the level of active metabolites of steroid and thus the risk of GI-AI [14]. Other risk factors for developing GI-AI include age and obesity [15].

Clinical findings

Clinical findings of GI-AI are non-specific can overlap with a myriad of other conditions [17].

Table 1. Suggested tapering regimen by 2024 ESE/ES guideline

Current daily dose	Suggested dose decrement
>40 mg	5-10 mg every week
20–40 mg	5 mg every week
10–20 mg	2.5 mg every 1–4 weeks
5–10 mg	1 mg every 1–4 weeks
5 mg	1 mg every 4 weeks

* Doses are given as prednisone equivalent. ES: Endocrine Society, ESE: European Society of Endocrinology

Onset of the symptoms can be insidious, and the level of symptoms depend on the level of stress. Many findings such as fatigue, arthralgia and myalgia can also be associated with underlying rheumatological condition. If the body is unable to secrete an appropriate amount of endogenous cortisol for the stress faced, the condition may progress to an adrenal crisis, which is characterized by severe fatigue, nausea and vomiting, hypotension, hypoglycemia, shock and death [15].

Diagnosis

Measurement of basal morning cortisol can be used as a screening test [14]. Diagnosis if adrenal insufficiency is based on the measurement of the hypothalamus-pituitary-adrenal axis by a stress test. ACTH stimulation test (also known as Synacthen test) is the most common one used in clinical practice [14]. However, guidelines used in rheumatology currently do not recommend routine screening for GI-AI using screeningtests [8,9,11].

Treatment

Cornerstone of the treatment for GI-AI is steroid replacement to mimic normal physiology as closely as possible [17]. Hydrocortisone is the preferred steroid formulation given its pharmacokinetic properties, however other preparations such as prednisone can also be used. Based on the physiological requirements of the body, approximately 15–25 mg hydrocortisone per day is used, usually one or two divided doses [14]. In a patient with suspected adrenal crisis, prompt steroid administration is essential. An initial 100 mg bolus of parenteral hydrocortisone, followed by 200 mg hydrocortisone over 24 hours. Additional measures such as fluid resuscitation, electrolyte and glucose requirement, and treatment of possible triggers of adrenal crisis are other components of the treatment [15].

Peri-operative care for prevention

Patients at risk of developing GI-AI should receive priority when scheduling for procedures, to minimize potential triggers such as fasting and dehydration [18]. 2017 British, 2022 American and 2023 German guidelines by rheumatology societies do not recommend routine increase in steroid doses in the perioperative period [8,9,11]. Summary of recommendations by American Endocrine Society and European Society of Endocrinology are given in Table 2 [15].

Conclusion

List of recommendation by various societies are given in Table 3.

Author contribution

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Conflict of interest

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Table 2. Summary of perioperative recommendations from 2024 ESE/ES guideline [15]

Type of procedure	Level of stress	Recommendation
• Minor surgery and procedures requiring local anesthesia	Minor stress	• Patients taking ≥10 mg/day prednisone equivalent: No extra dose needed • Patients taking <10 mg/day predisone equivalent: Increase to 10 mg total daily dose, to be given one hour prior to the procedure. Continue increased dose in patient who remain unwell after the procedure until clinically stable.
• Surgery and procedures requiring general or regional anesthesia • Labor, including vaginal delivery and cesarean section	Moderate to major stress	• Intra-operative: IV hydrocortisone 100 mg at induction, followed by 200 mg of hydrocortisone over 24 hours • Post-operative: Resume oral steroid at increased dose for 48 hours (prednisone 10 mg/day). After 48 hours, resume pre-surgical dose. In case of post-operative complications, maintain an increased oral dose or give stress-dose steroid IV as clinically appropriate

Table 3. Recommendations regarding peri-operative steroid use

	2017 BSR/BHPR	2022 ACR/AAHKS	2023 GSR
Infection	Steroid exposure should be minimized prior to surgical procedures	No recommendation	Must be reduced to the lowest possible dose, 10 mg/day if possible in the last 2–3 months before surgery.
Adrenal insufficiency	Increase in dose to prevent adrenal insufficiency is not recommended.	Continuation of the current daily dose, rather than supraphysiological doses, is recommended	Peri-operative steroid dose is recommended to remain constant.

AAHKS: American Association of Hip and Knee Surgeons, ACR: American College of Rheumatology, BHPR: British Health Professionals in Rheumatology, BSR: British Society of Rheumatology, GSR: German Society for Rheumatology.

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