GLUCOCORTICOIDS IN RHEUMATIC DISEASES. PART II

Glikokortykosteroidy w leczeniu chorób reumatycznych. Część II

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Abstract

Glucocorticoids are an effective and relatively rapid-acting treatment for conditions with a severe, sudden course, which until recently led to significant disability and mortality. Vasculitis, in which the treatment timing and intensity strongly determine its outcomes, as well as chronic diseases, in which the action taken significantly affects the patient's quality of life, are of particular importance. The first part of this review outlined the general principles of glucocorticoid therapy in vasculitis based on detailed expert recommendations and guidelines of recognised rheumatology societies. For very rare diseases, the experience of researchers and generally accepted clinical practice are presented. The second part of the publication discusses the place and role of glucocorticoids in the subsequent lines of therapy for both common and rare conditions of rheumatic origin. This paper summarizes current and structured knowledge of the use of glucocorticoids in the treatment of vasculitis and other rheumatic diseases.

Streszczenie

Glikokortykosteroidy umożliwiają skuteczne i stosunkowo szybkie opanowanie chorób o ciężkim, nagłym przebiegu, które do niedawna prowadziły do znacznej niepełnosprawności lub śmierci. Szczególnie istotne są przypadki zapalenia naczyń, w których czas rozpoczęcia i intensywność terapii silnie determinują jej efektywność, oraz stany przewlekłe, w których podjęte odpowiednie działanie znacznie wpływa na komfort życia pacjenta. W pierwszej części pracy omówiono ogólne zasady wykorzystania glikokortykosteroidów w leczeniu zapalenia naczyń, oparte na szczegółowych rekomendacjach ekspertów oraz wytycznych uznanych organizacji reumatologicznych. W przypadku rzadkich chorób przedstawiono doświadczenia badaczy oraz ogólnie przyjętą praktykę kliniczną. Druga część pracy prezentuje miejsce i rolę glikokortykosteroidów w kolejnych rzutach terapii innych chorób o podłożu reumatycznym, zarówno tych powszechnie występujących, jak i rzadkich. Niniejsze opracowanie podsumowuje aktualną, usystematyzowaną wiedzę na temat wykorzystania glikokortykosteroidów w terapii zapaleń naczyń oraz różnych chorób reumatycznych.

Keywords: rheumatic diseases; pharmacotherapy; glucocorticoids; vasculitis

Słowa kluczowe:choroby reumatyczne; farmakoterapia; glikokortykosteroidy; zapalenia naczyń

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Introduction

Glucocorticoids (GCs) remain one of the most widely used anti-inflammatory therapies. Their use spans several decades, and extensive scientific evidence has confirmed their efficacy in the treatment of many disorders. Due to the complex mechanisms underlying their action, these drugs exert diverse effects across multiple systems and organs. In clinical practice, modulation of immune cells and other components involved in the inflammatory response remains their most extensively utilized action.

Since limiting the effects of inflammation is particularly important in the treatment of rheumatic diseases, GCs have become widely used in rheumatology, providing rapid improvement in conditions previously considered incurable. Unfortunately, during prolonged therapy, the beneficial effects of GCs may be counterbalanced by adverse events that negatively affect the cardiovascular system, glucose and lipid metabolism, the skeletal system, the eyes, and other organs. For this reason, recommended GC dosing regimens are continually revised to incorporate emerging evidence on safety and efficacy.

The previous part of this paper outlined the current guidelines for the use of GCs in arthritis and systemic connective tissue diseases. This part discusses recommendations for GC therapy in vasculitis and other rheumatic disorders. Clinical entities in which inflammation does not constitute the predominant pathological mechanism are also included. The presented management principles are based on recommendations from scientific societies, expert group opinions, and researcher experience in rare diseases.

The role of GCs in the treatment of vasculitis

Current treatment guidelines for anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) include an induction phase, typically lasting 3–4 months, followed by maintenance therapy with low-dose GCs for at least 18–24 months in combination with immunosuppressants. Importantly, it is suggested to include prophylaxis against *Pneumocystis jirovecii* during the period of treatment with high doses of GCs in these clinical entities [1, 2]. GCs are used as induction treatment for granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA). The choice and intensity of the treatment regimen depend on the activity and extent of the disease process; notably, ANCA antibody levels should not serve as the primary determinant of therapy [2]. In severe cases with life-threatening organ involvement, first-line treatment consists of high-dose GCs combined with a potent immunosuppressant, such as rituximab or cyclophosphamide [1]. The recommended initial daily dose of prednisolone is 50–75 mg [1] or 1 mg/kg (up to 80 mg) [2]. In the most severe cases, such as pulmonary alveolar haemorrhage or rapidly progressive renal impairment, intravenous methylprednisolone at 0.5–1.0 g/day for 3–5 days, followed by oral therapy, is an alternative approach. Rapid GC tapering, compared with earlier treatment regimens, can reduce the overall corticosteroid exposure by approximately half, thereby directly improving the safety profile of the therapy. As an example of this approach the PEXIVAS regimen optimizes dosing in patients with severe disease, which is presented in the table. It consists of three-day pulses of methylprednisolone at a cumulative dose of 3 g, followed by intensive, gradually tapered corticosteroid therapy [2]. Low-dose GCs may be used as maintenance therapy in combination with an immunosuppressant; however, there is no clear evidence to establish the optimal duration of such treatment. GC discontinuation appears to be associated with a higher risk of disease exacerbation. According to expert opinion [1], therapeutic decisions should therefore be individualized and based on an assessment of disease activity and relapse tendency. In selected cases, topical GCs may also be employed. Intranasal preparations may be beneficial in patients with active lesions in the paranasal sinuses. However, individuals with long-standing, fibrotic subglottic or endobronchial stenoses unresponsive to standard therapy may require local GC injections administered during endoscopic intervention [2].

For mild eosinophilic granulomatosis with polyangiitis (EGPA), and in the absence of additional risk factors, GC monotherapy [1] or in combination with a disease-modifying drug [2] is sufficient. When selecting the appropriate therapeutic approach, it is recommended to use the Five-Factor Score, which incorporates predictors of poor prognosis, including age >65 years; cardiac, gastrointestinal, or renal involvement, as well as the absence of nasal, aural, or pharyngeal lesions. The induction phase includes prednisolone at 1 mg/kg/day for 2–3 weeks. As in other AAVs, intravenous methylprednisolone at 7.5–15 mg/kg/day may be considered [3]. However, due to the lack of evidence for the superiority of intravenous (IV) therapy over intensive oral therapy, methylprednisolone pulses should be reserved solely for life-threatening situations [2, 3]. The optimal GC tapering regimen has not yet been established due to limited clinical evidence. Proposed protocols suggest gradual dose reduction to 0.3 mg/kg/day after 3 months and to 0.15 mg/kg/day after 6 months, until discontinuation or achievement of the minimum effective dose [3]. Therapeutic recommendations largely follow the regimens and procedures used in GPA and MPA. Accordingly, topical GCs may be considered in patients

Table. Glucocorticoid dose reduction in ANCA-associated drivers. Based on: Hellmich et al. [1]

Week	Daily prednisone dose (mg)		
	<50 kg	50–75 kg	>75 kg
1	50	60	75
2	25	30	40
3–4	20	25	30
5–6	15	20	25
7–8	12,5	15	20
9–10	10	12,5	15
11–12	7,5	10	12,5
13–14	6	7,5	10
15–18	5	5	7,5
19–52	5	5	5
>52	Dose adjusted to the patient's current health status		

with EGPA and paranasal sinus involvement. The duration of therapy should be individualized based on the patient clinical status. According to some authors, the maintenance dose of prednisolone should not exceed 7.5 mg/day, provided that remission can be sustained at this level [3]. The use of mepolizumab (a monoclonal antibody targeting interleukin-5) as a steroid-sparing agent is recommended in relapsed or refractory EGPA with a non–life-threatening course or with organ involvement, such as persistent GC-related bronchial asthma [1].

GCs are the cornerstone of treatment for giant cell arteritis (GCA), producing significant clinical improvement within a few days (often as early as 2–3 days) after treatment onset. Prompt initiation of therapy markedly reduces the risk of permanent vision loss, which underscores the importance of starting treatment even before the diagnostic workup is fully completed. The induction phase involves prednisone at a daily dose of 40–60 mg [4] or 1 mg/kg (up to a maximum of 80 mg) [5], and, according to some authors, even up to 100 mg. This regimen should be maintained until normalization of clinical and laboratory parameters, typically over 2–4 weeks [6]. In cases of milder GCA, therapy with medium-dose GCs (0.5 mg/kg/day of prednisone) may be considered [5]. Sudden visual deterioration, blindness, or neurological complications are indications for intravenous pulses of methylprednisolone at 0.25–1 g/day for up to 3 days [4]. The use of additional immunosuppressants, such as tocilizumab or methotrexate, may help reduce the cumulative GC exposure, particularly in refractory or relapsing disease. Once disease is controlled, the prednisone dose should be gradually tapered. The target dose is 15–20 mg/day within 2–3 months, followed by ≤5 mg/day after one year [4]. At each stage, the patient's current clinical status should be reassessed, and caution is warranted if relapse risk factors are present, also when considering more rapid tapering protocols. Alternating therapy, in which the drug is dosed every other day, increases the risk of relapse and is therefore not recommended [5]. Expert experience indicates that maintenance therapy in GCA is most often continued for approximately 2 years [4], although it may extend longer (even beyond 5 years) in some patients [6]. Relapses may occur in up to 75% of patients and most commonly arise when prednisone is tapered below 20 mg/day [6]. In cases of severe exacerbation, an increase in GC dose is recommended, following the approach used for newly diagnosed disease. In milder cases, it is possible to resume the last effective dose or to increase the dose by 5–15 mg [4]. In patients with active disease who require vascular surgery, high-dose corticosteroids are recommended during the perioperative period [5].

The management of Takayasu's disease is similar to the approach described above for GCA. Treatment should be initiated as early as possible, as prompt therapy improves efficacy and reduces the risk of vascular complications. According to the recommendations of the European Alliance of Associations for Rheumatology (EULAR) [4], all patients with Takayasu's disease should receive conventional disease-modifying antirheumatic drugs (DMARDs) in addition to corticosteroids. In selected cases, tocilizumab or tumour necrosis factor inhibitors (TNFis) may also be used, as they help stop the progression of arterial lesions and allow for limited corticosteroid use. Monotherapy should be reserved only for mild or diagnostically uncertain cases [5]. The initial phase requires high daily doses of corticosteroids (40–60 mg) [4] or 1 mg/kg (up to a maximum of 80 mg) of prednisone [5]. Disease control is typically achieved after 2–4 weeks, allowing for the initiation of gradual tapering [7]. The goal is to reach a daily prednisone dose of 15–20 mg within 2–3 months and ≤10 mg within one year [4]. Lower doses of prednisone (25–30 mg/day) may be considered in patients with mild, localized disease without organ involvement or limb ischemia [4]. The routine use of intravenous methylprednisolone pulses is not recommended and should be reserved for the most severe cases associated with a high risk of complications [5]. The duration of treatment should be individually tailored. Gradual discontinuation should be attempted in patients who have achieved remission after 6–12 months of GC therapy [5]. Early or rapid tapering may be associated with an increased risk of exacerbation, which, as in GCA, rises at GC doses below 20 mg/day [7]. Management depends on the severity of the relapse: prednisone is increased to the initial dose of 40–60 mg/day in severe cases; the last effective dose is resumed, optionally increased by 5–15 mg, in milder cases [4]. Asymptomatic radiological progression should not prompt treatment modification. Escalation of immunosuppressive therapy is recommended in patients with significant arterial stenoses. If surgery is necessary, high doses of oral corticosteroids should be implemented in the perioperative period [5].

The choice of treatment for leukocytoclastic vasculitis (LCV) depends on its aetiology and stage of progression. Systemic corticosteroids are used relatively infrequently; however, prednisone at 0.5–1 mg/kg/day may be administered in cases presenting with haemorrhagic blisters, necrosis, or refractory or recurrent disease [8]. As the lesions resolve, corticosteroids should be gradually tapered, and the overall duration of therapy is typically short (approximately one week). Nevertheless, some authors recommend a longer treatment period of 3–6 weeks, including gradual tapering [9]. Long-term therapy is generally unnecessary and should be avoided, particularly in limited disease. It is also noteworthy that there is no evidence supporting the efficacy of topical corticosteroids [8]. Management of secondary inflammation should target the underlying cause. Exacerbations occurring in the course of systemic connective tissue diseases or other autoimmune disorders require treatment intensification and, in some cases, management similar to that used in the primary form. Cutaneous cases resistant to corticosteroids, as well as those associated with systemic vasculitis, necessitate the use of additional immunosuppressants. According to Micheletti et al., such therapy should be gradually discontinued after 3–6 months of maintained remission [9].

As with other types of vasculitis, corticosteroids remain the cornerstone of treatment for polyarteritis nodosa (PAN). The use of the Five-Factor Score is recommended to guide therapeutic decision-making. In mild cutaneous forms, management is often symptomatic and includes nonsteroidal anti-inflammatory drugs (NSAIDs) or colchicine in combination with topical corticosteroids. More severe cases may require oral prednisone at 0.5–1 mg/kg/day [10].

According to the recommendations of the American College of Rheumatology (ACR), treatment of active, severe inflammation begins with intravenous pulses of methylprednisolone at 0.5–1 g or 30 mg/kg/day, administered for 3–5 days [11]. Other authors also permit the use of lower doses, typically 7.5–15 mg/kg/day for 1–3 days [10]. Parenteral administration should be reserved for life-threatening situations, such as a high risk of visceral infarction. In all other cases, oral prednisone is preferred at a dose of 1 mg/kg/day, up to a maximum of 80 mg/day [11]. After a short initial period, typically three weeks, gradual tapering should be initiated. French experts recommend tapering to 20 mg/day after 3 months, 10 mg/day after 6 months, and 5 mg/day after one year of therapy [10]. The overall duration of PAN treatment has not been precisely defined; the proposed regimen encompasses a duration of 18–24 months [10]. It is worth noting that the use of an additional immunosuppressant, such as cyclophosphamide, methotrexate, azathioprine, or mycophenolate mofetil, is included in the recommendations [11] and allows for reduced GC exposure. For HBV-associated PAN, GCs should be used only initially, at a dose of 0.5–1 mg/kg/day, for a short period of approximately 15 days [10]. Intravenous pulse therapy (abovementioned regimen) may be considered in severe cases. However, the risk of viral reactivation and increased replication associated with corticosteroid use in patients with chronic hepatitis B should be carefully considered.

The proposed treatment approach for Henoch–Schönlein purpura is largely based on studies conducted in the paediatric population, the findings of which have been extrapolated to adults. Most patients require only symptomatic management, particularly in cases confined to the skin or joints. However, corticosteroid therapy may allow for a more rapid resolution of abdominal and joint pain. According to some authors, it may also reduce the risk of persistent kidney disease, recurrence, or the need for surgical intervention [12]. However, it appears that such an approach, particularly when aimed at preventing nephropathy, should not be implemented routinely [12, 13]. According to the European consensus, GC therapy should be reserved for cases that pose a serious threat to health or life, including testicular, pulmonary, gastrointestinal, or neural involvement [13]. In such cases, treatment should be initiated with oral prednisone at 1–2 mg/kg/day continued for 7–14 days, followed by gradual tapering and complete discontinuation within the subsequent 2 weeks. In severe cases, intravenous pulses of methylprednisolone at 10–30 mg/kg/day (up to a maximum of 1 g) for 3 consecutive days should be considered, as this approach improves therapeutic efficacy in this patient group. In patients with nephritis, corticosteroids are the first-line treatment, and the intensity of therapy is determined by biopsy histopathology [13]. In milder cases, oral corticosteroids are preferred, whereas severe cases require intravenous administration and other immunosuppressants. The Pozzi–Locatelli regimen is commonly employed. It consists of two components: the patient receives 1 g of IV methylprednisolone for three consecutive days at the beginning of months 1, 3, and 5, plus oral prednisone 0.5 mg/kg on alternate days. Therapy is typically continued for six months [12].

To date, no formal recommendations have been developed for cryoglobulinemic vasculitis; therefore, the management of this condition is based on clinical experience. Although immunosuppressive therapy is typically not needed in cases of mild localized disease, low-dose corticosteroids may improve symptom control in the presence of concomitant arthritis. Corticosteroids combined with rituximab should be used primarily in patients with moderate to severe vasculitis [14]. Severe cases, particularly those with progressive organ damage, including nephritis, may require intravenous pulses of methylprednisolone followed by continued oral prednisone [14]. As the clinical condition improves, the dose should be gradually reduced over the shortest possible time until discontinuation or the lowest tolerated dose is achieved [15]. Relapse necessitates immediate therapy intensification. In cases of secondary cryoglobulinemia, treatment of the underlying disease is essential; however, patients with severe vasculitis may require prompt initiation of corticosteroids. Intravenous pulses should also be considered in these patient, as described above [15].

The management of Behçet's disease (BD) depends on the severity, location, and duration of lesions, and is based on corticosteroids. Topical agents are used for oral and genital ulcers, promoting faster healing of mucocutaneous lesions and reducing pain. Corticosteroid eye drops may be beneficial in isolated anterior uveitis [16]. Ocular, vascular, gastrointestinal, or CNS involvement necessitates systemic therapy. Treatment typically begins with intravenous pulses of 1 g methylprednisolone for 3 consecutive days in cases of gastrointestinal involvement and for up to 7 days in CNS disease. This is followed by short-term oral prednisolone at 1 mg/kg/day (approximately 1–2 weeks for gastrointestinal and about one month for CNS involvement) [16, 17]. The dose is usually reduced with clinical improvement. A reduction of 5 mg per week is suggested in gastrointestinal involvement, whereas a reduction of 5–10 mg every 10–15 days is recommended in CNS disease [16, 17]. In most cases, another immunosuppressant is added to reduce the risk of relapse. As pointed out by some authors, it should be emphasized that maintenance GC therapy is considered inappropriate and should be avoided [17]. Some specific clinical situations require modification of this regimen. In cases of joint involvement, when symptomatic treatment is insufficient, a low dose of corticosteroids may be considered. If the disease is limited to a single joint, intra-articular corticosteroid injections may be an appropriate option. Local intravitreal administration is recommended as an adjunct to systemic therapy in exacerbations of posterior uveitis [16]. When peripheral arterial aneurysms are diagnosed, combined pharmacotherapy should be initiated prior to any surgical intervention; this approach may be sufficient, particularly in small, low-risk lesions [16].

GC dosing regimens proposed for the treatment of retroperitoneal fibrosis are derived primarily from retrospective studies and small-scale clinical trials, where GCSs are used to limit the extent of retroperitoneal involvement within the first weeks of therapy, ultimately leading to symptom reduction. The clinical decision to implement a given therapeutic model should take into account the nature of the disease process (primary or secondary), as well as its location, stage, and aggressiveness. First-line treatment consists of GCs. The regimen proposed by Vaglio et al. (2011) may serve as a framework for therapeutic man-

agement. It includes the following daily prednisone doses: 1 mg/kg (up to a maximum of 80 mg) during the first month, 0.5 mg/kg during the second month, and 0.25 mg/kg during the third and fourth months. Subsequently, a gradual taper over the following five months should lead to a maintenance dose of 5 mg/day [18]. Detailed treatment protocols developed by individual centers, such as the regimen presented in Figure 1A and based on the experience of Japanese clinicians [19], also offer valuable guidance. It should be emphasized that a weaker-than-expected therapeutic response always warrants the exclusion of secondary lesions. Despite the high overall remission rate (75–95%), low-dose GC maintenance therapy may be needed; however, the optimal duration of such treatment has not yet been clearly established. Similarly, clear recommendations for the management of relapse are lacking. Japanese authors propose GC therapy according to the protocols presented in Figures 1B (for patients experiencing exacerbation after treatment discontinuation) and 1C (for those continuing corticosteroids) [19]. In refractory cases, combined therapy with corticosteroids and an additional immunosuppressant, such as mycophenolate mofetil, appears to be beneficial.

GCs in the treatment of other rheumatic diseases

In osteoarthritis, GCs are used when symptoms are severe and when NSAIDs are either contraindicated or fail to provide adequate relief. Intra-articular injection is the recommended route of administration. Scientific societies, including the ACR (2019) [20] and EULAR (2018) [21], strongly support this approach in cases involving knee or hip joints. However, injections into the hand joints are not recommended unless severe pain in the interphalangeal joints is present. At least 3–4 weeks should elapse between subsequent injections, and the total number of injections should not exceed four per year [22]. In this context, the potential destructive effect of GC injections on joint cartilage remains an important consideration. The reported phenomenon of cartilage thinning is of uncertain clinical significance, as it has not been associated with functional deterioration or increased pain in the affected joint [23].

After the onset of erythema nodosum, NSAIDs should be used as first-line therapy; however, if they prove ineffective or symptoms are severe, corticosteroids may also be included. To date, no clear recommendations for treatment duration or intensity have been established. In clinical practice, the dose ranges from a few milligrams to up to 40–60 mg of oral prednisone daily [24]. Systemic effects may be minimized with triamcinolone injections at 5 mg/mL [24] or by applying potent topical corticosteroids under wet wraps around particularly painful nodules. Panniculitis may develop in the course of pancreatic disorders, infections, dermatomyositis (DM), systemic lupus erythematosus, and other conditions; in such cases, prompt diagnosis of the underlying disease and initiation of causal therapy are essential. If severe panniculitis occurs in a patient with DM, systemic corticosteroids are used; however, it is important to first exclude an underlying malignancy. Local corticosteroid injections into the affected areas may also be considered [25]. Notably, corticosteroid injections themselves may induce panniculitis, a reaction thought to be triggered by carrier substances contained in pre-mixed formulations [25].

GCs play a key therapeutic role in acute gout attacks, particularly in patients intolerant to NSAIDs or colchicine. In such cases, oral therapy is preferred, typically for 3–5 days, using a daily dose equivalent to 30–35 mg of prednisone [26]. When the inflammatory process is limited to only a few joints, intra-articular corticosteroid injections may be used as an alternative to systemic treatment. It should be emphasized that the 2016 EULAR recommendations advise considering combined first-line therapy with colchicine and GCs [26]. The choice of a specific regimen should always be individualized, taking into account contraindications, disease duration, the anatomical location of the affected joints, as well as the severity of symptoms. A similar therapeutic approach, based primarily on intra-articular GC injections, and, in more challenging cases, also incorporating systemic therapy, is used in disorders associated with the deposition of calcium pyrophosphate crystals in soft tissues and joint cartilage, commonly referred to as pseudogout.

GCs are the cornerstone of IgG4-RD therapy. Contemporary therapeutic regimens rely on administering an initial dose sufficient to induce remission, followed by a gradual taper. These protocols vary primarily in the recommended intervals and dosing ranges. According to

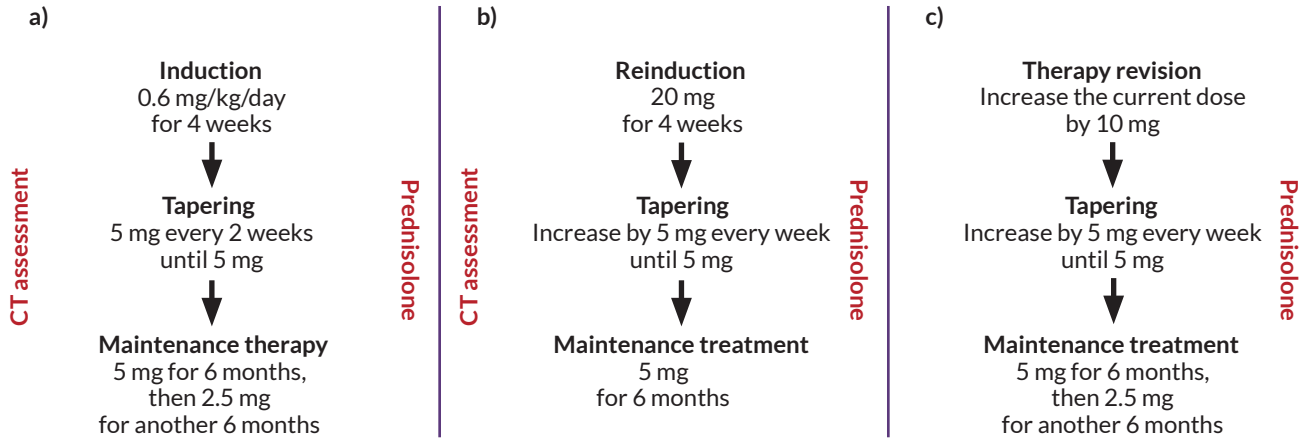

Figure 1. The use of GCs in retroperitoneal fibrosis. Based on Tanaka and Masumori [19]

a 2015 statement by an international panel of experts, initiating therapy with prednisone at 40 mg/day offers no clear benefit over a starting dose of 30 mg/day [27]. The initial dose should be maintained for the first 2–4 weeks of therapy and subsequently tapered by 10 mg every two weeks until a dose of 20 mg is reached. After maintaining this dose for two weeks, further reductions of 5 mg every two weeks are recommended. The therapeutic goal is GC discontinuation, if feasible, within 3–6 months. However, some authors advocate continuing low-dose GC therapy for up to 3 years [27]. Valuable guidance may be drawn from the experience of Japanese investigators, as illustrated in Figure 2 [28]. After treatment initiation, the patient's condition should be closely monitored and the therapeutic response carefully assessed. Delayed or unsatisfactory improvement should prompt another diagnostic evaluation to confirm the initial diagnosis. The literature also indicates that more rapid tapering and early treatment discontinuation are associated with an increased risk of disease exacerbation.

In Cogan syndrome, the primary therapeutic goal is to prevent hearing loss, vestibular dysfunction, and ocular or systemic complications associated with active vasculitis. Unfortunately, GCs have only limited efficacy in treating inner ear involvement. Nevertheless, when initiated within the first two weeks after the onset of auditory symptoms, they can reduce the risk of permanent hearing impairment [29]. Treatment includes subconjunctival and systemic corticosteroids. In severe cases, prompt initiation of systemic prednisolone at a dose of 1–2 mg/kg/day is essential. If clinical improvement occurs, the corticosteroid dose should be gradually tapered over 2–6 months, depending on the patient's condition [30].

Susac syndrome can lead to irreversible complications, including hearing and vision loss. Early initiation of immunosuppressive therapy is therefore crucial and significantly improves prognosis. The recommended regimen includes intravenous methylprednisolone at 1 g/day for 3–7 days, followed by oral prednisone at 60–80 mg/day for 2–4 weeks. After this period, the dose should be reduced by 10% every two weeks until a maintenance dose of 20 mg/day is reached. Subsequently, tapering cycles are extended to 4 weeks until a maintenance dose of 5 mg/day is achieved [31]. More rapid tapering may be used in patients with mild disease. In the event of relapse, IV methylprednisolone for 3 days or oral prednisone 60 mg/day should be administered, followed by the previously described tapering regimen as clinical improvement occurs [31]. Intratympanic corticosteroid injections may also be considered; however, evidence supporting their efficacy in Susac syndrome remains limited.

For relapsing polychondritis, corticosteroids are indicated in patients with rapid symptom onset, severe disease, organ or systemic involvement, and vasculitis. They may also be used in mild cases when first-line therapies, such as NSAIDs, are not tolerated. The dose of prednisone depends on the severity of symptoms and typically ranges from 0.25–1 mg/kg/day, followed by a gradual taper as clinical improvement occurs. In severe cases, a several-day course of IV methylprednisolone at 0.5–1 g/day, followed by continued prednisone therapy, may be considered [32]. Local administration of infiltrative corticosteroids may also be used in cases of laryngeal, tracheal, or bronchial involvement. Once the acute phase of the disease is controlled, GCs should be gradually tapered. The duration and rate of tapering depend on the severity of the disease and the response to treatment. In some cases, complete discontinuation of corticosteroids is achievable. However, long-term maintenance therapy is often required to sustain remission. In such cases, the addition of other immunosuppressants should be considered.

Soft tissue rheumatism is a collective term for disorders affecting the soft tissues around joints, including conditions like tendinopathies, enthesopathies, periarthropathies, tenosynovitis, bursitis, and fibromyalgia. With the exception of fibromyalgia, these conditions share similar therapeutic strategies. GCs are most commonly used when physiotherapy and NSAIDs fail to provide adequate symptom control. In such cases, they are administered as local injections directly into the most affected areas, often combined with lidocaine [33]. Bursal injections should be preceded by evacuation of the inflammatory fluid. In patients with active autoimmune disease, such as rheumatoid arthritis (RA), episodes of superficial bursitis require not only aspiration and possible corticosteroid injection, but also intensification of therapy for the underlying condition. According to some reports, pain reduction and functional improvement following corticosteroid injections for tendinopathy are only temporary [34]. In the long run, such therapy may impair tissue healing and contribute to further progression of the disease.

The lack of evidence supporting the efficacy of GCs in fibromyalgia, together with their substantial risk of adverse effects, is reflected in the 2016 EULAR recommendations, which do not endorse their use in this group of patients [35]. Although the potential utility of GCs and

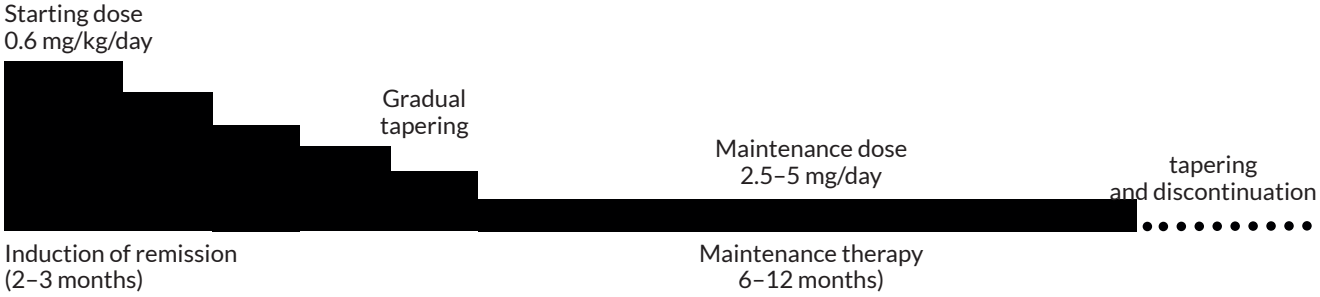

Figure 2. GC tapering in IgG4-related disease. Based on Kamisawa, et al. [28]

lidocaine injections into trigger points was suggested in the past, no evidence has confirmed the efficacy of this approach.

GCs are used in the treatment of the vast majority of rheumatic diseases. Their efficacy is well established; however, emerging research prompts further improvements in therapeutic regimens. As with any therapy, the primary goal is to achieve optimal clinical outcomes while minimizing the risk of adverse effects.

The efficacy of GCs strongly depends on the appropriate selection of the initial dose, the rate of dose tapering, and the overall duration of therapy. Similarly, the risk of complications is largely determined by treatment length and cumulative exposure. Adequate monitoring should substantially reduce the risk of adverse effects. This issue is frequently emphasized in clinical recommendations, particularly for conditions requiring long-term GC use. The use of appropriate preventive strategies, together with adequate patient education, has become an essential component of GC therapy and should be considered whenever treatment is initiated. For preventing complications, the concurrent use of immunosuppressants is particularly important as it helps sustain the therapeutic effect of GCs while enabling their more rapid discontinuation.

Despite their broad spectrum of adverse effects, the widespread use of GCs remains justified by the absence of alternative therapies with comparable properties. Their key benefits include a rapid onset of therapeutic action and the ability to titrate the dose across a wide range tailored to disease activity and the patient's clinical status. For these reasons, glucocorticoids still play a pivotal role in the management of acute and life-threatening conditions, both within and beyond rheumatology.

It seems that the importance of GC therapy in rheumatic diseases will not diminish in the near future. Ensuring treatment safety and preventing adverse effects therefore remain key priorities. These objectives can be achieved through the use of GCs in accordance with current medical evidence and published recommendations.

References

1. Hellmich B, Sanchez-Alamo B, Schirmer JH, et al. EULAR recommendations for the management of ANCA-associated vasculitis: 2022 update. Ann Rheum Dis, 2024; 83: 30–47. doi: 10.1136/ard-2022-223764
2. Chung SA, Langford CA, Maz M, et al. 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Antineutrophil Cytoplasmic Antibody-Associated Vasculitis. Arthritis Rheumatol, 2021; 73: 1366–1383. doi: 10.1002/art.41773
3. White J, Dubey S. Eosinophilic granulomatosis with polyangiitis: A review. Autoimmun Rev, 2023; 22: 103219. doi: 10.1016/j.autrev.2022.103219
4. Hellmich B, Agueda A, Monti S, et al. 2018 Update of the EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis, 2020; 79: 19–30. doi: 10.1136/annrheumdis-2019-215672
5. Maz M, Chung SA, Abril A, et al. 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Giant Cell Arteritis and Takayasu Arteritis. Arthritis Rheumatol, 2021; 73: 1349–1365. doi: 10.1002/art.41774
6. Ling ML, Yosar J, Lee BW, et al. The diagnosis and management of temporal arteritis. Clin Exp Optom, 2020; 103: 572–582. doi: 10.1111/cxo.12975
7. Pugh D, Karabayas M, Basu N, et al. Large-vessel vasculitis. Nat Rev Dis Primers, 2022; 7: 93. doi: 10.1038/s41572-021-00327-5
8. Sunderkötter C, Bonsmann G, Sindrilaru A, Luger T. Management of leukocytoclastic vasculitis. J Dermatolog Treat, 2005; 16: 193–206. doi: 10.1080/09546630500277971
9. Micheletti RG, Pagnoux C. Management of cutaneous vasculitis. Presse Med, 2020; 49: 104033. doi:10.1016/j.lpm.2020.104033
10. Terrier B, Darbon R, Durel CA, et al.; Collaborators. French recommendations for the management of systemic necrotizing vasculitides (polyarteritis nodosa and ANCA-associated vasculitides). Orphanet J Rare Dis, 2020; 15(Suppl 2): 351. doi: 10.1186/s13023-020-01621-3. Erratum in: Orphanet J Rare Dis, 2021; 16: 155. doi: 10.1186/s13023-021-01787-4
11. Chung SA, Gorelik M, Langford CA, et al. 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Polyarteritis Nodosa. Arthritis Care Res (Hoboken), 2021; 73: 1061–1070. doi: 10.1002/acr.24633
12. Maritati F, Canzian A, Fenaroli P, Vaglio A. Adult-onset IgA vasculitis (Henoch-Schönlein): Update on therapy. Presse Med, 2020; 49: 104035. doi: 10.1016/j.lpm.2020.104035
13. Ozen S, Marks SD, Brogan P, et al. European consensus-based recommendations for diagnosis and treatment of immunoglobulin A vasculitis-the SHARE initiative. Rheumatology (Oxford), 2019; 58: 1607–1616. doi: 10.1093/rheumatology/kez041
14. Nelveg-Kristensen KE, Paterson A, Willcocks LC. Cryoglobulinaemic vasculitis diagnostic and treatment recommendations. Rheumatology (Oxford), 2021; 60(Suppl 3): iii39–iii42. doi: 10.1093/rheumatology/keab121
15. Roccatello D, Saadoun D, Ramos-Casals M, et al. Cryoglobulinaemia. Nat Rev Dis Primers, 2018; 4: 11. doi: 10.1038/s41572-018-0009-4
16. Hatemi G, Christensen R, Bang D, et al. 2018 update of the EULAR recommendations for the management of Behçet's syndrome. Ann Rheum Dis, 2018; 77: 808–818. doi: 10.1136/annrheumdis-2018-213225
17. Skef W, Hamilton MJ, Arayssi T. Gastrointestinal Behçet's disease: a review. World J Gastroenterol, 2015; 21: 3801–3812. doi: 10.3748/wjg.v21.i13.3801
18. Vaglio A, Palmisano A, Alberici F, et al. Prednisone versus tamoxifen in patients with idiopathic retroperitoneal fibrosis: an open-label randomised controlled trial. Lancet, 2011; 378: 338–346. doi: 10.1016/S0140-6736(11)60934-3
19. Tanaka T, Masumori N. Current approach to diagnosis and management of retroperitoneal fibrosis. Int J Urol, 2020; 27: 387–394. doi: 10.1111/iju.14218
20. Kolasinski SL, Neogi T, Hochberg MC, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. Arthritis Care Res (Hoboken), 2020; 72: 149–162. doi: 10.1002/acr.24131. Erratum in: Arthritis Care Res (Hoboken), 2021; 73: 764. doi: 10.1002/acr.24615

21. Kloppenburg M, Kroon FP, Blanco FJ, et al. 2018 update of the EULAR recommendations for the management of hand osteoarthritis. Ann Rheum Dis, 2019; 78: 16–24. doi: 10.1136/annrheumdis-2018-213826
22. Guermazi A, Hunter DJ, Kloppenburg M. Debate: Intra-articular steroid injections for osteoarthritis – harmful or helpful? Osteoarthr Imaging, 2023; 3: 100163. doi: 10.1016/j.ostima.2023.100163
23. McAlindon TE, LaValley MP, Harvey WF, et al. Effect of intra-articular triamcinolone vs saline on knee cartilage volume and pain in patients with knee osteoarthritis: a randomized clinical trial. JAMA, 2017; 317: 1967–1975. doi: 10.1001/jama.2017.5283
24. Pérez-Garza DM, Chavez-Alvarez S, Ocampo-Candiani J, Gomez-Flores M. Erythema nodosum: a practical approach and diagnostic algorithm. Am J Clin Dermatol, 2021; 22: 367–378. doi: 10.1007/s40257-021-00592-w
25. Wick MR. Panniculitis: A summary. Semin Diagn Pathol, 2017; 34: 261–272. doi: 10.1053/j.semdp.2016.12.004
26. Richette P, Doherty M, Pascual E, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. Ann Rheum Dis, 2017; 76: 29–42. doi: 10.1136/annrheumdis-2016-209707
27. Khosroshahi A, Wallace ZS, Crowe JL, et al. International Consensus Guidance Statement on the Management and Treatment of IgG4-Related Disease. Arthritis Rheumatol, 2015; 67: 1688–1699. doi: 10.1002/art.39132
28. Kamisawa T, Okazaki K, Kawa S, et al. Amendment of the Japanese Consensus Guidelines for Autoimmune Pancreatitis, 2013 III. Treatment and prognosis of autoimmune pancreatitis. J Gastroenterol, 2014; 49: 961–970. doi: 10.1007/s00535-014-0945-z
29. Espinoza GM, Wheeler J, Temprano KK, Keller AP. Cogan's syndrome: clinical presentations and update on treatment. Curr Allergy Asthma Rep, 2020; 20: 46. doi: 10.1007/s11882-020-00945-1
30. Iliescu DA, Timaru CM, Batras M, et al. Cogan's syndrome. Rom J Ophthalmol, 2015; 59: 6–13
31. Marrodan M, Fiol MP, Correale J. Susac syndrome: challenges in the diagnosis and treatment. Brain, 2022; 145: 858–871. doi: 10.1093/brain/awab476
32. Mathian A, Miyara M, Cohen-Aubart F, et al. Relapsing polychondritis: A 2016 update on clinical features, diagnostic tools, treatment and biological drug use. Best Pract Res Clin Rheumatol, 2016; 30: 316–333. doi: 10.1016/j.berh.2016.08.001
33. Jeka S, Dura M. Soft tissue rheumatism. Reumatologia/Rheumatology Supplements, 2016: 114–123. doi: 10.5114/reum.2016.60013
34. Millar NL, Silbernagel KG, Thorborg K, et al. Tendinopathy. Nat Rev Dis Primers, 2021; 7: 1. doi: 10.1038/s41572-020-00234-1. Erratum in: Nat Rev Dis Primers, 2021; 7: 10. doi: 10.1038/s41572-021-00251-8
35. Macfarlane GJ, Kronisch C, Dean LE, et al. EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis, 2017; 76: 318–328. doi: 10.1136/annrheumdis-2016-209724