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INVITED REVIEW

Glucocorticoid doses according to tissue/organ involvement in ANCA-associated vasculitis

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ABSTRACT

Antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitides (AAV) are a group of disorders that include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), renal-limited vasculitis, and eosinophilic granulomatosis with polyangiitis (EGPA). Infections and cardiovascular diseases are the main causes of death in patients with AAV. New treatment regimens with low-dose glucocorticoidsare proposed to reduce the frequency of side effects. Studies related to the use of glucocorticoids in AAV patients were searched in the literature and results were summarized. Low-dose steroid protocols are not inferior to standard dose treatment and have fewer side effects. Although their effectiveness appears to be similar and their side effects appear to be less, the long-term results of low-dose regimens should also be evaluated.New studies are needed for alternative treatment regimens.

Keywords: ANCA-associated vasculitis, treatment, glucocorticoid, low-dose regimen.

Introduction

Antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitides (AAV) are a group of disorders that include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), renal-limited vasculitis, and eosinophilic granulomatosis with polyangiitis (EGPA) [1,2].

AAV is a life-threatening disease, especially in untreated patients [3]. The main causes of death in patients with AAV are infections and cardiovascular diseases rather than the disease itself [3]. New treatment regimens with lowertoxicity is proposed for reduced frequency of side effects.

Treatment of AAV consists of remission induction and maintenance therapies. The affected organ and severity determine induction therapy. Kidney involvement in AAV has a great impact on survival and long-term prognosis. High doses of glucocorticoids are the cornerstone of the treatment but low-dose regimens are being considered due to long-term side effects.

Organ-life-threatening manifestations of AAV are glomerulonephritis, pulmonary hemorrhage, cerebral vasculitis, progressive peripheral or cranial neuropathy, orbital pseudotumor, scleritis, gastrointestinal hemorrhage, and cardiac involvement [4]. Episcleritis,non-cavitating pulmonary nodules, skin involvement without ulceration, myositis, and nasal and paranasal disease without bony involvement or cartilage collapse or olfactory dysfunction or deafness are identified as non-organ-life-threatening manifestations of AAV [4].

In patients with non-organ-life-threatening manifestations, methotrexate combined with 0.5 mg/kg/day prednisolone equivalent is the treatment of choice. Maintenance treatment is planned according to a low-dose regimen [5].

In organ-life-threatening disease 1 mg/kg/day prednisolone equivalent is the preferred

regimen. In the presence of rapidly progressive glomerulonephritis, alveolar hemorrhage, mononeuritis multiplex, or optic neuritis pulse steroid (1 g/day) is recommended. A low-dose regimen is used in combination with immunosuppressives. In refractory disease or relapse, it is recommended to use glucocorticoids for 4-6 months, tapering off more slowly [6].

Current literature contains studies comparing low-dose and standard-dose glucocorticoid regimens. Of these, the PEXIVAS trial is an important study conducted in patients with severe ANCA-associated vasculitis to compare the efficacy of plasma exchange with no plasma exchange with respect to death or end-stage kidney disease (ESKD).The PEXIVAS trial also compared the reduced-dose regimen of glucocorticoids with a standard-dose regimenover the first 6 months of the treatment period to determine whether the reduced dose was non-inferiorto the standard dose concerningdeath or ESKD [6]. Table 1 shows the glucocorticoid doses of patients in both groups.

It has been observed that the low-dose glucocorticoid regimen is not inferior to the standard dose regimen on mortality and end-stage CRF and has fewer side effects.

In the LoVAS study [3], patients were randomized to receive reduced-dose prednisolone(0.5mg/kg/d) plus rituximab (RTX) (375mg/m2/wk, 4 doses) (n = 70) or high-dose prednisolone (1mg/kg/d) plus RTX (n = 70). In newly diagnosed GPA patients (without severe GN or alveolar hemorrhage), combined therapy of low-dose glucocorticoid and RTX is non-inferior to the combination of high-dose glucocorticoid and RTX.Infections and other GC-related side effects were less common in patients receiving a low-dose treatment regimen.

EULAR recommendations for the management of AAV were published in 2022. As part of regimens for induction of remission in GPA orMPA, treatment with oral GCs at a starting doseof 50–75 mg prednisolone equivalent/day, depending on body weight is recommended. stepwise reduction in GCs according toPEXIVAS protocoland achieving a dose of 5 mg prednisolone equivalent perday for 4–5 months [7].

In patients with new-onset or relapsed EGPA, a combination of high-dose glucocorticoids and cyclophosphamide is recommended if there is a life/organ-threatening situation. Unlike MPA and GPA, EGPA does not have a different glucocorticoid protocol. A similar protocol can be used, but asthma and ear-nose-throat (ENT) exacerbations may increase steroid requirements, and tapering may take longer. Glucocorticoid treatment is recommended for remission induction in patients with new-onset or relapsed EGPA, even if there is no life/organ-threatening condition. In the absence of poor prognostic factors, remission is achieved in >90% of patients treated with GC alone.

Table 1. Glucocorticoid doses in standard and reduced-dose groups in the PEXIVAS trial

Week	Standard			Reduced-dose		
	<50 kg	50-75 kg	>75 kg	<50 kg	50-75 kg	>75 kg
	Pulse	Pulse	Pulse	Pulse	Pulse	Pulse
1	50	60	75	50	60	75
2	50	60	75	25	30	40
3-4	40	50	60	20	25	30
5-6	30	40	50	15	20	25
7-8	25	30	40	12.5	15	20
9-10	20	25	30	10	12.5	15
11-12	15	20	25	7.5	10	12.5
13-14	12.5	15	20	6	7.5	10
15-16	10	10	15	5	5	7.5
17-18	10	10	15	5	5	7.5
19-20	7.5	7.5	10	5	5	5
21-22	7.5	7.5	7.5	5	5	5
23-52	5	5	5	5	5	5
>52	Investigator's local practice			Investigator's local practice		

Relapse is common when the dose is reduced, but studies with immunosuppressives have shown that they do not affect recurrence. In this case, there is no recommended reduction scheme, it is recommended to make an individual decision by evaluating the risks of recurrence and infection [7].

Avacopan is a complement 5a receptor inhibitor and according to EULAR and ACR recommendations, avacopan reduces exposure to glucocorticoids. But long-term results are not known yet.

It seems that low-dose steroid protocols are not inferior to standard dose treatment and have fewer side effects. New studies are needed for alternative treatment regimens.

Author contribution

Study conception and design: NŞYB; draft manuscript preparation: NŞYB. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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