Corticosteroids in Antineutrophil Cytoplasmic Antibody–Associated Vasculitis

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KEYWORDS

• Glucocorticoids • ANCA-associated vasculitis • Granulomatosis with polyangiitis
• Microscopic polyangiitis

KEY POINTS

- Glucocorticoids (GCs) are an important component of antineutrophil cytoplasmic antibody–associated vasculitis (AAV) treatment, in part because of their rapid onset of action.
- Intravenous GCs are important to consider in severe AAV, although the evidence base for their use is limited.
- There is considerable variation in the duration of GC therapy, ranging from less than 6 months to more than 24 months.
- Local GCs can be an important adjunctive treatment of sinonasal, ocular, and subglottic disease, but are generally not sufficient as monotherapy.
- Studies are currently underway examining the dose and duration of GC therapy in AAV as well as the effectiveness of GC-sparing therapies.

INTRODUCTION

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) are a group of conditions associated with inflammation of small and medium-sized blood vessels. This article focuses on the 2 major categories of AAV, granulomatosis with polyangiitis (GPA; formerly Wegener's granulomatosis) and microscopic polyangiitis.

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Glucocorticoids (GCs) have been the cornerstone of AAV management therapy since the 1950s.[1–4] Long before cytotoxic agents became the mainstay of management, GCs were relied on as the primary treatment modality in AAV. Several case reports and patient series highlight the early role of GCs in AAV and their ability to reduce disease activity.[5,6] Historical studies showed that untreated systemic vasculitis is typically fatal. However 5-year survival rates increased from less than 15% to 48% when GC therapy was used.[4]

In 1971, Fauci and colleagues[7] published the first experience with the use of cyclophosphamide in GPA. Subsequent studies showed that the addition of cyclophosphamide to prednisone leads to remission in more than 90% of cases.[6,8,9] Most patients are now able to achieve clinical remission with cyclophosphamide-based, rituximab-based, or methotrexate-based regimens. However, GCs remain a mainstay of therapy, in part because of their rapid onset of action.[10] It is notable that despite major advances in the treatment of AAV, mortality still exceeds that of the general population, with most deaths having causes other than active vasculitis.[8] Therefore, in order to achieve successful outcomes, a careful balance between GC treatment efficacy and toxicity must be achieved.

Herein we discuss the current role of GCs in various phases of AAV treatment, including remission induction, maintenance therapy, treatment of relapses, and the local use of GCs. We also review current controversies relating to GC use as well as research efforts that seek to reduce GC toxicity in AAV.

REMISSION INDUCTION THERAPY

A critical goal in the treatment of AAV is achieving rapid and durable remission with minimal toxicity. According to the European League Against Rheumatism (EULAR), remission is defined as "the complete absence of disease activity attributable to active vasculitis."[11,12] When choosing the initial treatment regimen for remission induction of active disease (whether caused by new-onset vasculitis or disease relapse), clinicians must decide whether to administer GCs as an intravenous (IV) pulse (typically 500–1000 mg daily for 3 days), what starting dose of GCs to use, and how to reduce oral GCs, maintaining a balance between efficacy and toxicity. Despite extensive experience with GCs in AAV, there is no published consensus on induction dosing or tapering schedules.

Intravenous Glucocorticoids

The question of whether GCs should be initially administered as an IV or oral formulation in AAV is most relevant when treating severe disease. Definitions of severe disease have differed in the literature and may be defined as a Five-Factor Score of 1 or more,[13] a Birmingham Vasculitis Activity Score for Wegener Granulomatosis with 1 major item or greater than 3 points,[14] or as "disease that poses an immediate threat to either the patient's life or vital organ function."[15,16] Although definitions of severe AAV vary, generally pulse GCs are considered in patients who have glomerulonephritis, diffuse alveolar hemorrhage, mesenteric ischemia, and central or peripheral nervous system involvement, such as mononeuritis multiplex.[2,17] In addition, pulse GCs should be considered if there is insufficient response or progression of disease despite high-dose oral GCs.

Little is known about the comparative efficacy of IV GCs. Support for pulse GCs arose from a study by Bolton and Sturgill[18] that retrospectively analyzed 63 patients with acute crescentic rapidly progressive glomerulonephritis. Forty-six patients received pulse GCs (at a dose of 30 mg/kg, maximum daily dose of 3 g, every other