Corticosteroids in Lupus Nephritis and Central Nervous System Lupus

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KEYWORDS

• Systemic lupus erythematosus • Glomerulonephritis • Neuropsychiatric lupus
• Glucocorticoids • Autoimmune disease • Treatment

KEY POINTS

- The current standard of care for active proliferative lupus nephritis and severe central nervous system (CNS) lupus includes corticosteroids in high doses for immunosuppression.
- Despite the potential to be lifesaving in cases of lupus nephritis and CNS lupus, corticosteroids are also associated with long-term damage and early mortality.
- The goal of lupus therapy remains elimination of corticosteroids when possible.

INTRODUCTION

Corticosteroids, often in high doses and typically in combination with other immunosuppressive treatments, are a mainstay of therapy for severe organ-threatening systemic lupus erythematosus (SLE; lupus). The antiinflammatory effects of corticosteroids are pervasive and complex and depend on the timing, dose, and route of administration. Corticosteroids act on multiple immune cell types to inhibit the production of inflammatory mediators and stimulate the production of antiinflammatory proteins through both genomic and nongenomic pathways.

Until recently, the standard design of treatment trials for active lupus allowed, or even mandated, the use of corticosteroids for more immediate control of active disease while awaiting the anticipated benefits of the experimental intervention. It is only recently that interventional trials for active lupus have been designed with minimal use of corticosteroids. Given the known dose-related and duration-related adverse effects of corticosteroids, the potential of treating active lupus with minimal to no

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corticosteroids is appealing. However, the value and lifesaving potential of high doses of corticosteroids for uncontrolled severe lupus is undeniable.

This article reviews the evidence for, and against, the efficacy of corticosteroids in the clinical setting of active lupus nephritis and/or active central nervous system (CNS) lupus. The adverse effects of corticosteroids in patients with lupus nephritis and CNS lupus are also reviewed.

EPIDEMIOLOGY OF LUPUS NEPHRITIS

Lupus nephritis remains one of the most debilitating and potentially life-threatening manifestations of lupus, occurring in 40% to 60% of adults and up to 80% of children with lupus.[1–3] The susceptibility and burden of lupus are substantially higher among black women compared with other groups, with black people having 3 times the incidence rate compared with whites and women having 9 to 10 times the prevalence compared with men.[4,5] Peak age of incidence for both lupus and lupus nephritis is also younger among black women. The disparities in lupus-related risk are most striking when examining renal involvement, with black patients and Hispanic patients having more frequent and more severe lupus nephritis compared with other groups.[2,4–6]

The prognosis of lupus nephritis is related to the degree of active renal inflammation and chronic damage, which is reflected in the renal histologic class on kidney biopsy as well as the associated clinical and laboratory features.[7] Ultimately, 10% to 20% of patients with lupus nephritis require renal-replacement therapy for end-stage renal disease, most commonly with hemodialysis, and early mortality remains unacceptably high.[8]

EVALUATION OF LUPUS NEPHRITIS

Renal biopsy histology helps not only confirm the diagnosis but also helps guide therapy for lupus nephritis. Proliferative lupus nephritis is the most common form, often presenting as proteinuria, microscopic hematuria, urinary casts, hypertension, and potentially including renal insufficiency.[9] Membranous lupus nephritis is also frequently seen histologically either alone or in conjunction with proliferative nephritis, often presenting as nephrotic syndrome with edema, wasting, and hypercoagulability.[9]

TREATMENT GOALS FOR LUPUS NEPHRITIS

Prevention of end-stage renal disease and reducing the risks of chronic kidney disease with associated comorbidities are primary goals of lupus nephritis therapy. Typical immunosuppression for lupus nephritis consists of induction with corticosteroids combined with a cytotoxic medication to achieve a rapid response, followed by a maintenance period of continued but less potent immunosuppression.

In practice, evidence supporting certain treatment regimens for specific clinical and histologic situations is considered in conjunction with other patient-specific variables. These variables influencing therapeutic decisions include patient ethnicity, age, comorbidities, pregnancy plans, fear of certain adverse effects, and any doubts about compliance,[10] which results in a shift away from one-size-fits-all protocols toward more highly individualized treatment regimens.

PROLIFERATIVE LUPUS NEPHRITIS INDUCTION THERAPY

A shift occurred in the 1970s and 1980s from using corticosteroids alone to using them in combination with cytotoxic medications to treat lupus nephritis, based on clinical trial evidence supporting combination therapy.[11] At present, the 3 most widely