

A Randomized Controlled Trial on Corticosteroid Efficacy in IRGN—A Commentary

By Natarajan Gopalakrishnan and Tanuj Moses Lamech

Infection-related glomerulonephritis (IRGN) is typically considered an immune-complex glomerulonephritis. Previously known only as “post-streptococcal” glomerulonephritis, it is now recognized that any infection can trigger immunologically mediated glomerular injury, which can even occur concurrently with the infection that precipitated it.

Observational data suggest that a significant number of patients with IRGN experience incomplete or even non-recovery of kidney function (1–3). Consequently, the possibility that the natural history of the disease might be amenable to manipulation with broad immunosuppression using corticosteroids was entertained by many authors (4–7). In fact, steroid administration became standard clinical practice in many clinical settings, despite the absence of clear evidence of its benefit (8, 9).

The trial

The single-center, open-label, parallel-arm, 1:1 randomized controlled trial, reported in *Kidney International Reports* (10), included adults with IRGN and a serum creatinine of >1.5 mg/dL. Patients who met trial inclusion and exclusion criteria were randomly assigned to receive either corticosteroids plus supportive care (intervention arm) or supportive care alone (control arm). Steroids were administered in the form of intravenous methylprednisolone, 1 g daily for 3 days, followed by oral prednisolone, 1 mg/kg/day for 1 month, and then a slow taper of 5 mg per week.

The disruptions to routine clinical care that ensued during the COVID-19 pandemic necessitated the premature termination of the trial in May 2020, at which time, 52 patients had undergone randomization. At 6 months post-randomization, the primary end point of complete renal recovery (defined as an estimated glomerular filtration rate >60 mL/min/1.73 m²) was achieved in 65.4% of patients in the intervention arm and in 53.8% of patients in the control arm—a difference that did not reach statistical significance. Adverse events, however, were significantly higher in the steroid arm, with infectious complications being the most frequent, followed by other signs of steroid toxicity.

Discussion

Although the trial's primary outcome was not met, it should be kept in mind that the study was underpowered, as it did not reach its target sample size. A potential benefit of steroids in specific patient subsets, such as those with crescentic IRGN and dialysis-requiring IRGN, cannot therefore be ruled out. The significant adverse effects of steroids, particularly infection risks, should give us pause, particularly when treating patients with long-standing diabetes. Furthermore, the steroid doses used in the trial are, by today's standards, exceptionally high, although they were in keeping with standard practice at the time of the trial design.

Our interpretation of the data is that the efficacy of steroids remains unclear, whereas the potential harms are evident. Nevertheless, because of the otherwise poor prognosis in certain specific subgroups of patients, such as those with crescentic IRGN or rapidly progressive glomerulonephritis, we suggest that, in the absence of better data, a short, closely supervised trial of steroids could still be attempted at the discretion of the treating clinician. However, we suggest that the doses used be much lower than those used in the previous trial.

Potential avenues for further research

The lack of a specific diagnostic biomarker and the heterogeneity of the histopathology in patients with IRGN

necessitate continued reliance on the Nasr et al. diagnostic criteria (9). This results in a non-homogeneous study population that complicates the interpretation of trial data. Recent literature suggests that anti-factor B antibodies may help to specifically identify cases of acute post-streptococcal glomerulonephritis (11). Identification of a similar biomarker for other forms of IRGN would simplify enrollment in future clinical trials.

Given the increasing recognition of the primary role of the complement system in driving the pathogenesis of at least some forms of IRGN, it follows that perhaps therapies specifically targeting the complement cascade may be more appropriate than broad immunosuppression with corticosteroids. However, this currently remains within the realm of speculation. ■

Natarajan Gopalakrishnan, MD, DM, FRCP, is director and Tanuj Moses Lamech, MD, DM, DrNB, is an assistant professor of the Institute of Nephrology, Madras Medical College, Chennai, India.

The authors report no conflicts of interest.

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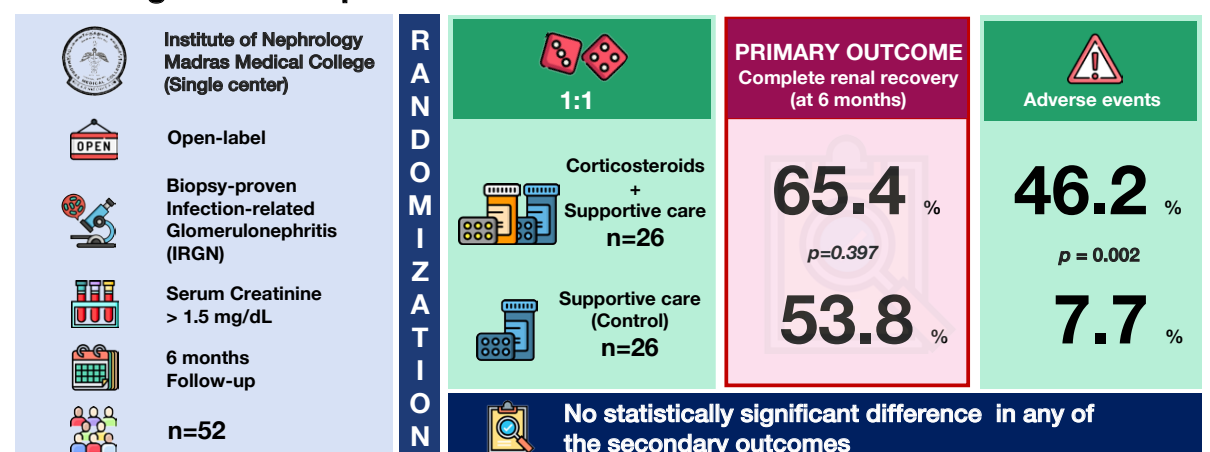
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Safety and efficacy of corticosteroids in infection-related glomerulonephritis

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Conclusion In this single-center trial, corticosteroids did not result in a statistically significant increase in rates of complete renal recovery at 6 months. There was a significantly increased risk of adverse events associated with the use of corticosteroids..

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Visual Graphic by Edgar Lerma, MD, FASN