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Original article

IGA nephropathy – Are intravenous steroid pulses more effective than oral steroids in relapse prevention?

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ABSTRACT

Introduction: It is recommended that IgA nephropathy (IgAN) is treated with steroids when the glomerular filtration rate (GFR) is >50 ml/min and proteinuria >1 g/day. Few studies have been performed comparing the two accepted steroid regimens (1 g/day methylprednisolone pulses for 3 consecutive days at the beginning of months 1, 3 and 5, followed by 0.5 mg/kg prednisolone on alternate days vs. 1 mg/kg/day oral prednisolone). The aim of this study was to compare these two steroid regimens in IgAN treatment.

Methods: We selected 39 patients with biopsy-proven IgAN treated with steroids. Mean age at diagnosis was 37.5 years, 23 males (59%), baseline proteinuria (Uprot) was 2.1 g/day and median serum creatinine (SCr) was 1.5 mg/dl. The mean follow-up period was 56 months. Twenty-five patients (64%) were treated with methylprednisolone pulses and 14 (36%) with oral steroids.

Results: Patients treated with steroid pulses presented lower relapse risk, defined as the reappearance of Uprot >1 g/day and an Uprot increase of more than 50% (incidence rate ratio of 0.18, 95% CI 0.02–0.5). The Kaplan–Meier analysis showed longer relapse-free period ($p = 0.019$). This result was confirmed in a multivariate analysis ($p = 0.026$). However, we did not find other differences between the two steroid regimens.

Conclusions: In comparison to oral steroids, the intravenous pulse regimen was associated with a lower risk of relapse in IgAN, a known independent negative predictor of renal survival. No differences were found regarding the other renal outcomes.

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Nefropatía por IgA. ¿Son los esteroides intravenosos más eficaces que los esteroides orales en la prevención de recaídas?

Palabras clave:
Nefropatía por IgA
Esquemas de esteroides
Supervivencia renal

RESUMEN

Introducción: Se recomienda el tratamiento de la nefropatía por IgA (NIgA) con esteroides cuando el índice de filtración glomerular (IFG) > 50 ml/min y proteinuria > 1 g/día. Pocos han sido los estudios realizados comparando los 2 esquemas de esteroides aceptados (1 g/día de metilprednisolona en pulsos durante 3 días consecutivos en el principio de los meses 1, 3 y 5 seguido de 0,5 mg/kg en días alternos de prednisolona vs. 1 mg/kg/día de prednisolona oral). El objetivo de este estudio fue comparar estos 2 esquemas de esteroides en el tratamiento de la NIgA.

Métodos: Fueron seleccionados 39 pacientes con NIgA demostrada por biopsia y tratados con esteroides. La edad media al diagnóstico fue de 37,5 años, 23 varones (59%), proteinuria basal (Uprot) 2,1 g/día y la creatinina sérica mediana (SCR) 1,5 mg/dl. El periodo medio de seguimiento fue de 56 meses. Veinticinco de los pacientes (64%) fueron tratados con pulsos de metilprednisolona y 14 (36%) con esteroides orales.

Resultados: Los pacientes tratados con pulsos de esteroides presentan menor riesgo de recaída, definido como la reaparición de una Uprot > 1 g/día y aumento de más del 50% de la Uprot (razón de tasa de incidencia: 0,18; IC 95%: 0,02-0,5) y el Kaplan-Meier mostró período más largo libre de recaída (p = 0,019). Este resultado se confirmó en un análisis multivariante (p = 0,026). Sin embargo, no se encontraron otras diferencias entre los esquemas de esteroides.

Conclusiones: En comparación con los esteroides orales, el esquema en pulsos intravenosos se relacionó con un menor riesgo de recaída en la NIgA, un conocido predictor negativo independiente de la supervivencia renal. No se encontraron diferencias en cuanto a los otros *outcomes* renales.

Introduction

IgA nephropathy (IgAN) is the most frequent primary glomerulonephritis in the developed countries. Regardless of the treatment used, more than 50% of the patients with IgAN have a progressive disease.[1] The VALIGA cohort estimated a rate of glomerular filtration ratio (GFR) decline of 1.8 ± 7.5 ml/min/year.[2] Therefore, it is predictable that 20–40% of these patients develop end-stage renal disease (ESRD) within 20 years.[3]

Currently there is not a specific treatment for the pathogenic process beyond IgAN. The KDIGO guidelines[4] recommend blood pressure control with the use of one renin–angiotensin system inhibitor/blocker in all patients. This approach has the stronger evidence in slowing the disease progression and reducing the proteinuria and the slope of GFR.[4,5]

Besides these measures, with a significantly lower evidence, this guidelines also suggest the use of corticosteroids for 6 months in those that have proteinuria higher than 1 g/day and preserved GFR (GFR > 50 ml/min) after supportive therapy.[4] The treatment with steroids was associated with lower risk of progression to ESRD and lower urinary protein excretion.[6]

There are two steroid regimens accepted to treat IgAN: the steroid pulse regimen (also known as "Pozzi scheme", i.e. 1 g/day methylprednisolone pulses for 3 consecutive days at the beginning of months 1, 3 and 5 followed by 0.5 mg/kg of oral prednisolone in alternate days) and the oral steroid regimen (oral prednisolone 1 mg/kg/day for 2 months and then a reduced dose for the next 4 months).[4] According to the available studies any of these therapeutic schemes can be used, because both showed to be better than supportive therapy alone.[7–9]

Currently, we do not have any reason to choose one steroid scheme to treat IgAN instead of the other, as no RCT compared both regimens, so this choice is only based on the beliefs of the physicians and it is not an evidence-based decision. Since the use of pulses scheme is more laborious and expensive it is important to clarify whether its use is associated with better renal outcomes relatively to the simpler and cheaper oral scheme.

The aim of this study was to investigate if there is any advantage of a steroid pulse regimen relatively to oral steroid scheme in the outcomes of the IgAN treatment.

Study design

This is a single center, 9-year retrospective cohort study of patients with biopsy-proven IgAN treated with steroids.