

소아 난치성 신증후군에서 리툭시맙 장기 치료의 치료효과와 안전성

서울대학교 어린이병원 소아청소년과

김지현, 안요한, 박유진, 강희경, 하일수, 정해일

Efficacy and Safety of Prolonged Rituximab Therapy in Children with Refractory Nephrotic Syndrome

Ji Hyun Kim, Yo Han Ahn, Eujin Park, Hee Gyung Kang, Il-Soo Ha, Hae Il Cheong

Department of Pediatrics, Seoul National University Children's Hospital

Objectives: Rituximab (RTX), an anti-CD20 monoclonal antibody, has been proposed as a rescue therapy for steroid-dependent or refractory nephrotic syndrome (NS). While reported efficacy of RTX on steroid-dependent NS is promising, the efficacy and safety of prolonged RTX therapy is not yet known. This study was conducted to assess that of prolonged RTX therapy.

Methods: Clinical characteristics and outcomes of patients who were treated with RTX for more than one year for refractory NS were reviewed. RTX was administered as rescue therapy for steroid and/or CNI dependent NS with significant side effect. RTX of 375 mg/m² were infused intravenously, and only when B lymphocytes were not eradicated with single dose within a week, a repeated dose was given. Decision of administrating next cycle of RTX was made on the basis of clinical course; relapse with reappearance of B cells or patients' preference of RTX as maintenance medication. Steroid and CNI were slowly tapered if remission was achieved.

Results: 23 patients (M:F 15:8, mean age 15.7±6.6 years) with refractory NS, who were treated with prolonged rituximab therapy (more than one year) during 2006 to 2015 at Seoul National University Children's Hospital were included. Duration of NS was 7.0±4.5 years at the time of first treatment of RTX. 18 patients had pathologic diagnosis, which were minimal change disease in 12 and focal segmental glomerulosclerosis in 6. Before RTX treatment, their mean relapse rate was 2.5±2.0 per year. A total of 5.5±2.3 cycles of RTX were administrated during 4.25±2 years, and their relapse rate was decreased to 0.8±0.7 per year. Patients were free of steroid for 7.0±3.5 months per year while on RTX and free of CNI for 4.6±4.6 months per year. Among a total of 156 infusions, 21 were accompanied with infusion reactions (13.5%). Only one patient suffered from severe infection, Swine influenza, requiring hospitalization, and three discontinued RTX treatment due to emergence of anti-RTX antibody. Of yet, no patients suffer from long-term or significant complication.

Conclusions: In this retrospective study to evaluate the efficacy and safety of repetitive dose RTX in children with refractory NS, prolonged RTX therapy was safe and effective. It was effective in reducing immunosuppressant drugs such as steroid or CNI, with reduced relapse rate of NS. Significantly, no long-term or significant complication of prolonged rituximab therapy was observed.

Key Words: 리툭시맙, 난치성 신증후군, 장기 치료

Rituximab, Refractory nephrotic syndrome, Prolonged