#2001 - Rituximab in Pediatric Nephrology

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Body

Rituximab (RTX), a chimeric monoclonal antibody specific for human CD20 leads to rapid and sustained depletion of B cells. RTX causes B cell death by antibody dependent cell-mediated cytotoxicity, complement mediated cytotoxicity and apoptosis. This drug has been used for the treatment of different kind of disorders like autoimmune diseases, malignancies, solid organ transplantations, some hematologic disorders and opsoclonus-myoclonus syndrome. RTX has been successfully used as a rescue therapy in some children with nephrologic problems like nephrotic syndrome.

Idiopathic nephrotic syndrome is the most frequent glomerular disease during childhood. Although immunosuppressive agents are usually effective, some severe cases remain difficult to treat. RTX has a significant steroid-sparing effect in children with steroid-dependent nephrotic syndrome (SDNS). Based on previous studies B-cell depletion with RTX might have altered the course of SDNS.

Safety and pharmacokinetics of a single dose of RTX for the treatment of refractory SDNS were evaluated in children and usually all patients were able to discontinue steroids at a median of 74 days after treatment. The frequency of relapses was significantly reduced and the steroid-free period per 6 months was significantly increased after treatment compared with those before treatment. It seems that treatment with a single dose of RTX may be effective for refractory SDNS, but its efficacy to prevent relapses was transient in most of the patients. In addition, a single RTX infusion may improve response to CsA in patients with persistent SDNS due to the phenomenon of secondary resistance to CsA. Therefore, RTX could be an effective treatment for severe steroid-dependent or resistant nephrotic syndrome.

Rituximab may be an effective treatment for recurrence of nephrotic syndrome after transplantation. After renal transplantation, activated B cells may play a pivotal role in the recurrence of heavy proteinuria and clinical signs of nephrosis.

RTX has been proposed for use in the treatment of systemic lupus erythematosus (SLE). The results of several studies in lupus nephritis supported the efficacy of rituximab as adjunctive treatment in children and they hypothesized that rituximab was well tolerated by the majority of patients.

RTX complications include acute infusion reactions, susceptibility to bacterial infections, and reactivation of viral infections. Adverse effects to RTX can be classified as immediate, acute and delayed. Immediate reactions are infusion reactions. Their incidence is about 25%, and they could be mild to moderate associated with fever, chills, nausea, pruritus, angioedema, hypotension, headache, bronchospasm, urticaria, rash, myalgia, and hypertension. Rarely, severe reactions may occur with hypoxia, pulmonary infiltrates, acute respiratory distress syndrome, cardiogenic shock, or anaphylaxis leading to death. The other side effects are serious cardiovascular reactions after the first administration of the medication, kidney failure, tumor lysis syndrome, severe mucocutaneous reactions, and progressive multifocal leukoencephalopathy.

In conclusion RTX appears to be beneficial for treatment of pediatric patients with refractory autoimmune diseases or nephrologic problems and may reduce corticosteroid exposure.

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