Rituximab treatment for relapsing minimal change disease and focal segmental glomerulosclerosis: a systematic review


CRD summary
This review concluded that rituximab was generally well tolerated and could reduce relapse rates and the use of immunosuppressants for adults with frequently relapsing or steroid-dependent, minimal-change disease or focal segmental glomerulosclerosis. Limitations in the review and the evidence suggest that these conclusions and recommendations for practice may not be reliable; the recommendations for better evidence seem appropriate.

Authors' objectives
To assess the effectiveness of rituximab for adults with steroid-dependent or frequently relapsing, minimal-change disease (of the kidney) or focal segmental glomerulosclerosis.

Searching
PubMed and EMBASE were searched in November 2013, for English-language publications. Search terms were reported, but search dates were not. Reference lists of relevant studies were manually screened.

Study selection
Eligible for inclusion in the review were studies assessing the effectiveness of first-time treatment with rituximab. Patients had to be at least 18 years old, and have steroid-dependent or frequently relapsing, minimal-change disease or focal segmental glomerulosclerosis. Studies of patients with other kidney diseases or with steroid-resistant kidney syndrome were excluded. The outcomes of interest were the reduction in the rate of relapse and the need for concomitant immunosuppressive medication.

In the included studies, most of the patients were male and most had a diagnosis of minimal-change disease, confirmed by kidney biopsy. The median age at the time of disease development was 17.5 years (range one to 73; from table 1). The median age at initial treatment with rituximab was 27.5 years (range 18 to 73). Rituximab regimens varied across the studies, ranging from one to four doses at 375mg/m², or fixed administration between 500mg and 1g. Previous and concomitant immunosuppression treatments were steroids, calcineurin inhibitors, anti-metabolites, and others.

One reviewer screened studies for inclusion.

Assessment of study quality
The authors did not state that they assessed study quality.

Data extraction
One reviewer extracted the number of relapses (as defined in the review) before and after rituximab treatment to calculate the median number per year. The number of patients achieving complete or partial remission at last follow-up was calculated. The same reviewer assessed the intensity of concomitant immunosuppressive therapy (before and after treatment), according to a semi-quantitative scoring system (maximum score 5).

Primary study authors were contacted for any missing data.

Methods of synthesis
The differences in the number of relapses per year and the number of concomitant immunosuppressive treatments, before and after treatment, were assessed for significance using the paired Wilcoxon test. A probability of less than 0.05 was considered significant. Univariate regression analysis was performed to assess the relationship between initial patient characteristics and the treatment response.

Results of the review
Fourteen studies, with 86 patients, were included in the review; two were prospective and the others were retrospective.
Follow-up ranged from 5.1 to 82.2 months.

There was a statistically significant reduction in the relapse rate per year after treatment with rituximab (from 1.3 to zero; 80 patients; p<0.001). Statistically significant reductions were reported at final follow-up for the number of patients receiving immunosuppressive medication in addition to steroids (from 60 to 12; 80 patients; p<0.001) and for proteinuria (from 2.43g/day to zero; 80 patients; p<0.001).

Serum albumin significantly increased after treatment from 2.90g to a median of 4.0g per litre (80 patients; p=0.001).

Of the 81 patients with a follow-up of at least 12 months, 54 were free from clinical relapse. After treatment, two patients were reported to have an estimated glomerular filtration rate of less than 60mL per minute. The results of the regression were reported. There were no serious adverse events. Treatment reactions and long-term complications were fully reported.

**Authors' conclusions**

The evidence suggested that rituximab reduced the number of relapses and the use of immunosuppressants for adults with frequently relapsing or steroid-dependent kidney syndrome, due to minimal-change disease or focal segmental glomerulosclerosis. Rituximab was generally well tolerated.

**CRD commentary**

The review question and supporting inclusion criteria were broadly stated. The search of the literature was limited to two databases, and language and publication restrictions were applied; potentially relevant evidence may have been missed. Study quality was not assessed, but most were retrospective before-and-after studies, which have inherent limitations. Study selection and data extraction do not appear to have been performed by two people, which means that reviewer error and bias cannot be ruled out.

The authors acknowledged the variation between treatment regimens, and the limitations of the small case series, and case reports, included in the review. They acknowledged the limitations of the retrospective studies, including the potential to underestimate serious adverse events.

The authors’ conclusions and recommendations for practice may not be reliable, as data may have been missed, bias was possible, the evidence was limited, and the included studies were retrospective and non-comparative. Their conclusion on the need for more robust evidence was appropriate.

**Implications of the review for practice and research**

**Practice:** The authors stated that due to its acceptable safety profile, rituximab was a promising alternative for patients with minimal-change disease or focal segmental glomerulosclerosis.

**Research:** The authors stated that further controlled prospective trials were needed to confirm these findings.

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