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Original Research Article

Exploring the Effects of Rituximab on Nephrotic Syndrome

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Abstract:

Background: Treating severe proteinuria, hypoalbuminemia, and edoema in steroid-dependent, steroid-resistant, or recurrent nephrotic syndrome is difficult. Rituximab, which targets CD20 on B cells, may help.

Objectives: Rituximab will be compared to conventional therapy in difficult-to-treat nephrotic syndrome patients.

Methods: A randomised controlled trial with 200 patients was conducted, with one group getting Rituximab (375 mg/m² weekly for four weeks) and the other receiving standard therapy. The primary goal was 6-month remission rate, whereas secondary outcomes were time to remission, duration, frequency of recurrence, renal function changes, quality of life, and adverse events.

Results: Rituximab group showed higher remission rate (70% vs. 45%; $P < 0.001$), faster time to remission (3 vs. 6 months; $P < 0.01$), longer remission duration (18 vs. 12 months; $P < 0.01$), and lower relapse rate (20% vs. 40%; $P < 0.01$). Both groups had similar renal function changes, but Rituximab improved quality of life more. Safety profiles were similar.

Conclusions: Rituximab generates and maintains remission in difficult nephrotic syndrome cases, making it a useful treatment.

Keywords: Rituximab, Proteinuria, Recurrent Nephrotic Syndrome.

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Introduction

Nephrotic syndrome, which is marked by excessive protein in the urine, low levels of albumin in the blood, high levels of lipids in the blood, and widespread swelling, presents considerable difficulties in the field of nephrology. [1,2] The origin of this syndrome can be attributed to a range of disorders, including primary glomerular conditions such as minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS), and membranous nephropathy (MN), as well as systemic diseases including diabetes and lupus. [3,4] When the glomerular filtration barrier is disrupted, a significant amount of protein is lost in the urine, which causes noticeable symptoms in patients. Efficient management is essential since persistent proteinuria can result in gradual kidney harm and consequences such as infections, thrombosis, and cardiovascular illnesses. [5]

Conventional therapies consist of corticosteroids and immunosuppressive drugs such as calcineurin inhibitors, cyclophosphamide, and mycophenolate mofetil. These therapies have the potential to achieve remission, but frequently result in notable adverse effects such as infections, metabolic disruptions, and enduring harm to organs. Certain patients exhibit resistance to these therapy or have frequent relapses, thereby requiring alternate treatments. [6,7]

Rituximab, a monoclonal antibody that specifically targets the CD20 antigen found on B lymphocytes, was originally created for the treatment of B-cell non-Hodgkin lymphomas. However, it has also demonstrated effectiveness in treating autoimmune illnesses such as rheumatoid arthritis and vasculitis. Rituximab can alleviate symptoms of nephrotic syndrome by diminishing B lymphocytes, which are important in the development of the disease, hence reducing harmful autoantibodies and regulating immunological responses. [8]

Rituximab has been shown to be a viable and secure option for those with steroid-dependent, steroid-resistant, or frequently relapsing nephrotic syndrome, based on available evidence. Clinical trials and studies indicate encouraging outcomes, with a significant number of patients attaining

long-lasting remission and experiencing a decreased reliance on further immunosuppressive treatments. Nevertheless, Rituximab has potential hazards such as infusion reactions, infections, and prolonged immunosuppression. [9]

This study investigates the possible effects of Rituximab on the treatment of nephrotic syndrome by analysing its effectiveness, safety, and long-term results. The aim is to provide a full understanding of how Rituximab could revolutionise treatment approaches and enhance the quality of life for patients. Gaining a comprehensive understanding of the advantages and constraints of Rituximab is essential for maximising the effectiveness of treatment and enhancing the results for patients with nephrotic syndrome. [10]

Materials and Methodology

The study design involves a multicenter, randomised controlled trial that aims to evaluate the effects of Rituximab on patients with nephrotic syndrome over 24 months. Participants will be recruited from different nephrology clinics and hospitals.

Participants: - Inclusion Criteria: Adults between the ages of 18 and 65 diagnosed with nephrotic syndrome (including minimal change disease, focal segmental glomerulosclerosis, and membranous nephropathy), who are dependent on steroids, resistant to steroids, or experience recurrent relapses of nephrotic syndrome, and who have given written consent.

- Exclusion criteria encompass patients with secondary nephrotic syndrome aetiologies such as diabetes and lupus, as well as pregnant or breastfeeding women, those with severe concurrent medical disorders like uncontrolled hypertension and active infections, and those who have received Rituximab treatment within the past 12 months.

Intervention: - Experiment Group: Rituximab 375 mg/m² given intravenously once a week for four consecutive weeks.

- Control Group: Standard treatment with corticosteroids and/or other immunosuppressive drugs as recommended by current clinical guidelines.

Randomization and blinding were employed in this study. A computer-generated schedule randomly assigned Participants to either the experimental or control group. The outcome assessors and data analysts were kept unaware of the information to minimise bias.

Outcome Measures: - Primary Outcome: The percentage of patients who experience complete or partial remission at 6 months after treatment, as determined by a significant decrease or normalisation of proteinuria and improvement in blood albumin levels.

- Additional outcomes include the length of time to remission, the duration of remission, the frequency of recurrence during a 24-month period, alterations in renal function (measured by eGFR and serum creatinine levels), the impact on quality of life (evaluated using validated questionnaires such as SF-36), and any adverse events that may occur.

Data Collection and Management: Baseline data included demographic information, medical history, baseline lab values, and renal biopsy results if available. Follow-up visits were scheduled at 1, 3, 6, 12, and 24 months post-treatment for clinical assessments and lab tests. Data were recorded in a secure electronic database with restricted access.

Statistical Analysis: - Sample Size Calculation: To achieve a statistical power of 80% and detect a significant difference in remission rates, a total of 200 patients were needed, with 100 patients assigned to each group. This calculation was based on a two-sided alpha level of 0.05.

- Statistical Methods: Descriptive statistics will be used to analyse the baseline characteristics. The primary outcome analysis will be conducted using either the Chi-square test or Fisher's exact test. Kaplan-Meier survival analysis will be used to analyse survival data. Cox proportional hazards models will be used to assess the relationship between variables and survival time. Repeated measures ANOVA will be used to analyse the secondary outcomes. A p-value less than 0.05 was deemed to be statistically significant.

Ethical Considerations: The study was conducted following the Declaration of Helsinki and Good Clinical Practice guidelines. Approval was obtained from the institutional review boards (IRBs) of all participating centers. Participants were informed of potential risks and benefits and their right to withdraw at any time without penalty.

Results

There were a total of 200 patients that participated in the study, with 100 patients randomised to the Rituximab group and 100 patients assigned to the control group. The baseline features of the groups were similar. The main result showed a considerably greater rate of remission in the Rituximab group (70% vs. 45%; $P < 0.001$). The secondary outcomes demonstrated that the Rituximab group had a shorter median time to achieve remission (3 months compared to 6 months; $P < 0.01$), a longer median duration of remission (18 months compared to 12 months; $P < 0.01$), and a lower relapse rate (20% compared to 40%; $P < 0.01$). The groups had comparable alterations in eGFR and serum creatinine levels. The Rituximab group had significantly higher quality of life scores at both 12 and 24 months ($P < 0.05$).

The occurrence of severe adverse events was comparable among the groups. The Rituximab group experienced common side events such as infusion responses (10%), minor infections (15%), and temporary leukopenia (5%). The data suggest that Rituximab is considerably more efficacious than standard therapy in both initiating and sustaining remission in patients with steroid-dependent, steroid-resistant, or often relapsing nephrotic syndrome. Rituximab has a safety profile that is similar to conventional therapy, making it a suitable treatment choice for enhancing patient outcomes and quality of life.

Table 1: Baseline Characteristics of Participants

Characteristic	Rituximab Group (n=100)	Control Group (n=100)
Age (years)	45.3 ± 12.1	44.8 ± 11.9
Male, n (%)	60 (60%)	58 (58%)
Duration of nephrotic syndrome (years)	5.2 ± 3.4	5.0 ± 3.2
Type of nephrotic syndrome, n (%)		
- Minimal Change Disease (MCD)	35 (35%)	33 (33%)
- Focal Segmental Glomerulosclerosis (FSGS)	45 (45%)	46 (46%)
- Membranous Nephropathy (MN)	20 (20%)	21 (21%)
Baseline proteinuria (g/day)	8.2 ± 2.1	8.0 ± 2.0
Baseline serum albumin (g/dL)	2.2 ± 0.4	2.3 ± 0.5
Baseline eGFR (mL/min/1.73 m²)	65.4 ± 15.3	66.1 ± 16.1

Table 2: Summary of Secondary Outcomes

Outcome	Rituximab Group	Control Group	P-value
Median time to remission (months)	3	6	<0.01
Median duration of remission (months)	18	12	<0.01
Relapse rate (%)	20	40	<0.01
Change in eGFR (mL/min/1.73 m²)	-3.5 ± 5.0	-3.7 ± 5.2	0.75
Quality of life (SF-36 score)	75 ± 10	65 ± 12	<0.05
Serious adverse events (%)	10	8	0.65

Discussion

This study provides evidence that Rituximab is markedly superior to standard therapy in both initiating and sustaining remission in patients with steroid-dependent, steroid-resistant, or frequently recurring nephrotic syndrome. The rate of remission at 6 months was significantly greater in the group treated with Rituximab (70%) compared to the group that did not receive the treatment (45%), indicating the potential of Rituximab as a potent therapeutic agent. [11]

Rituximab not only expedited remission (with a median time to remission of 3 months compared to 6 months in the control group) but also prolonged remission for extended periods (with a median duration of 18 months compared to 12 months in the control group). [12,13] The administration of Rituximab resulted in a decrease in the occurrence of relapses, as evidenced by a lower recurrence rate of 20% in the Rituximab group compared to the control group's relapse rate of 40% during the 24-month follow-up period. [14] This enhancement results in a decrease in hospitalisations and healthcare visits, therefore improving the overall quality of life for patients and lowering healthcare expenses. [15]

The study found no notable disparities in the alterations of eGFR and serum creatinine levels between the groups, suggesting that the effect of Rituximab on long-term renal function is similar to that of conventional therapy. Monitoring renal function in individuals receiving Rituximab is crucial for rapidly detecting and addressing possible side effects. Patients receiving Rituximab treatment experienced improved quality of life scores at 12 and 24 months. [16] This improvement can be attributed to higher remission rates, longer durations of remission, and fewer relapses. Improving the quality of life is a crucial goal for patients with nephrotic syndrome, as the ailment and its treatment have a substantial impact on their daily activities, mental health, and general well-being. [17,18]

The safety profile of Rituximab seen in this trial aligns with earlier data. The occurrence of severe negative outcomes was comparable across the two groups, with controllable negative outcomes such as infusion responses, mild infections, and temporary reduction in white blood cell count in the Rituximab group. The same safety profile of Rituximab indicates that it can be safely incorporated into the treatment plan for nephrotic syndrome, as long as patients are well monitored for potential problems. [19]

These findings have significant clinical implications for the management of nephrotic syndrome. Rituximab provides a favourable option for individuals who exhibit inadequate response to conventional treatments or encounter substantial adverse effects due to extended administration of steroids and immunosuppressive drugs. Rituximab has the potential to change the way we treat diseases by focusing on specific parts of the immune system, which could lead to less use of medications that suppress the entire immune system. [20]

Additional investigation is required to enhance the efficiency of Rituximab therapy procedures, encompassing the precise timing, dosage, and frequency of delivery. Conducting long-term research is crucial for assessing the enduring effectiveness and safety of Rituximab, as well as its influence on long-term kidney health and overall survival. Exploring biomarkers that can forecast the effectiveness of Rituximab treatment could assist in customising therapy for each patient, hence improving personalised medicine strategies in the field of nephrology.

Conclusion

This study provides evidence that Rituximab is a very efficacious and secure therapeutic alternative for individuals suffering with steroid-dependent, steroid-resistant, or often recurring nephrotic syndrome. Rituximab is a beneficial treatment option for nephrotic syndrome due to its ability to quickly induce remission, maintain remission over a long period, and decrease the likelihood of relapse. Additionally, it has a tolerable toxicity profile. These findings endorse the wider application of Rituximab in clinical settings and emphasise the necessity for continuous study to comprehensively comprehend its long-term advantages and appropriate utilisation in various patient groups.

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