OBSERVATIONAL STUDY COMPARING RITUXIMAB AND TACROLIMUS IN TREATMENT OF IDIOPATHIC MEMBRANOUS NEPHROPATHY

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ABSTRACT:

BACKGROUND: Primary membranous nephropathy is one of the commonest causes of adult-onset nephrotic syndrome and also a common glomerular cause of End-Stage Renal Disease (ESRD). It is a B-cell mediated disease and rituximab, an anti CD_{20} monoclonal Ab has emerged as a promising treatment option. Current treatment options include corticosteroids, alkylating agents and calcineurin inhibitors(CNIs). CNIs are an effective and preferred treatment for membranous nephropathy in the United States and Canada. However, these agents are associated with a high incidence of relapse after discontinuation. So the study was designed to compare the efficacy of rituximab with tacrolimus.

AIM: The study was conducted to compare the safety and efficacy of intravenous rituximab with tacrolimus in the management of idiopathic membranous nephropathy.

METHODS: Since February 2021, 18 patients with biopsy-proven primary MN were given 4 weekly doses of rituximab (375 mg/m^2). Administration of 100 mg i.e. methylprednisolone before the first dose was done. A different baseline test was performed like 24-hour urine protein, serum creatinine, albumin and lipid profile after the 6th and 12th months. Patients who completed 12 months of follow-up were compared to 18 patients with primary MN treated with tacrolimus. The primary outcome of this study was a cumulative number of patients who experienced both partial or complete remission(PR/CR). The secondary outcome was a change in 24-hour urine protein, serum albumin, eGFR and adverse effects. The definition of PR/CR, relapse, treatment failure and inclusion criteria was followed according to KDIGO guidelines. Exclusion criteria were: patients with active infection/TB, DM, HBV/HCV/HIV, neoplasia, pregnancy, membranous lupus nephritis, previous therapy with prednisolone, MMF, CNIs within 4 months and alkylating agents within 6 months.

RESULTS: At 12th month 9 of 18 patients (50 %) achieved primary endpoint (complete remission 2 and partial remission 7) in rituximab group and 12 of 18 patients (66.6 %) (complete remission 4 and partial remission 8) in tacrolimus group (p=0.31). In the 12th month, 24-hour urine protein was reduced from 6.96 to 1.37(p=0.14) in the rituximab group and 6.8 to 1.1 (p=0.1) in the tacrolimus group. In the end, when comparing both groups, there was no significant difference in change in 24-hour urine protein, serum albumin or eGFR. In the tacrolimus group, a serious adverse event occurred in 3 patients, whereas it was 2 in the rituximab group.

CONCLUSIONS: In conclusion, tacrolimus appears to be effective in achieving CR/PR of proteinuria in 66.6%, but there was no significant change in GFR. When we compared it with rituximab, there was no significant difference in remission rate, proteinuria reduction or GFR changes.

BIOGRAPHY:

Dr Aneesh Nanda is the consultant nephrologist working in Accord superspeciality hospital. I graduated from the Institute of Post Graduate Medical Education & Research (S.S.K.M. Hospital) in Kolkata West Bengal, India. I have presented papers/posters at various conferences.

ABOUT RESEARCH TOPIC:

Membranous glomerulonephritis (MGN) is one of the commonest causes of adult-onset nephrotic syndrome and a common glomerular cause of end-stage renal disease. It is B cell-mediated disease and IgG4 antibodies are found against podocyte antigens.

In our membranous registry, a large proportion of patients are of the younger age group. So we need a newer treatment regimen with a better side effect profile. Of the newer agents being explored for IMN, rituximab has emerged as the most likely candidate to be incorporated into treatment guidelines. Most of the reported experiences with rituximab are from uncontrolled pilot trials or case series. Till now RCT comparing rituximab and tacrolimus is not available. So we have designed this open-label RCT to compare the safety and efficacy of intravenous rituximab with tacrolimus in the management of primary membranous nephropathy.

ABOUT INSTITUTION:

Accord Superspeciality Hospital, (A Unit of SCL Healthcare Pvt. Ltd.) situated at Sector-86, Greater Faridabad, Haryana spread over 5 Acre of land is India's first hospital owned by prominent and qualified superspecialist medical professionals having more than 15 years' experience of various corporate hospitals in Delhi/NCR. Our visionaries believe in the old saying that the best doctor is the one who not only heals his patients but also cares for them. We are 380 Bedded Hospital with 100 critical care beds, 30 specialities, 9 Modular OTs, AI-based equipment & technology, offering world-class infrastructure in the heart of the city. The kidney transplant unit offers a 4-bed facility.

REFERENCES:

1. Beck LH Jr, Bonegio RG, Lambeau G, Beck DM, Powell DW, Cummins TD, Klein JB, Salant DJ: M-type phospholipase A2 receptor as target antigen in idiopathic membranous nephropathy. N Engl J Med 361:11–21, 2009.

2. Heymann W, Hackel DB, Harwood S, Wilson SG, Hunter JL: Production of nephrotic syndrome in rats by Freund's adjuvants and rat kidney suspensions. Proc Soc Exp Biol Med 100:660–664, 1959.

3. Hofstra JM, Beck LH Jr, Beck DM, Wetzels JF, Salant DJ: Anti-phospholipase A_2 receptor antibodies correlate with clinical status in idiopathic membranous nephropathy. Clin J Am Soc Nephrol 6: 1286–1291, 2011.

4. Beck LH Jr, Fervenza FC, Beck DM, Bonegio RG, Malik FA, Erickson SB, Cosio FG, Cattran DC, Salant DJ: Rituximab-induced depletion of anti-PLA2R autoantibodies predicts response in membranous nephropathy. J Am Soc Nephrol 22: 1543–1550, 2011.

5. Stanescu HC, Arcos-Burgos M, Medlar A, Bockenhauer D, Kottgen A, Dragomirescu L, Voinescu C, Patel N, Pearce K, Hubank M, Stephens HA, Laundy V, Padmanabhan S, Zawadzka A, Hofstra JM, Coenen MJ, den Heijer M, Kiemeney LA, Bacq-Daian D, Stengel B, Powis SH, Brenchley P, Feehally J, Rees AJ, Debiec H, Wetzels JF, Ronco P,

Mathieson PW, Kleta R: Risk HLA-DQA1 and PLA(2)R1 alleles in idiopathic membranous nephropathy. N Engl J Med 364: 616–626, 2011.

6. Karine Dahan, Hanna Debiec, Emmanuelle Plaisier, Marine Cachanado, Alexandra Rousseau, Laura Wakselman, Pierre-Antoine Michel, Fabrice Mihout, Bertrand Dussol, Marie Matignon, Christiane Mousson, Tabassome Simon and Pierre Ronco, on behalf of the GEMRITUX Study Group: Rituximab for Severe Membranous Nephropathy:A 6-Month Trial with Extended Follow-Up. J Am Soc Nephrol 28: 2016.

7. Fervenza FC, Canetta PA, Barbour SJ, Lafayette RA, Rovin BH, Aslam N, Hladunewich MA, Irazabal MV, Sethi S, Gipson DS, Reich HN, Brenchley P, Kretzler M, Radhakrishnan J, Hebert LA, Gipson PE, Thomas LF, McCarthy ET, Appel GB, Jefferson JA, Eirin A, Lieske JC, Hogan MC, Greene EL, Dillon JJ, Leung N, Sedor JR, Rizk DV, Blumenthal SS, Lasic LB, Juncos LA, Green DF, Simon J, Sussman AN, Philibert D, Cattran DC; Mentor Consortium group: A Multicenter Randomized Controlled Trial of Rituximab versus Cyclosporine in the Treatment of Idiopathic Membranous Nephropathy (MENTOR).Nephron 130: 159–168, 2015.

8. Francis JM, Beck LH Jr, Salant DJ. Membranous nephropathy: a journey from bench to bedside. Am J Kidney Dis. 2016;68(1):138–147.

9. Ronco P, Debiec H. Pathophysiological advances in membranous nephropathy: time for a shift in patient’s care. Lancet. 2015;385(9981):1983–1992.

10. Ayalon R, Beck LH Jr. Membranous nephropathy: not just a disease for adults. Pediatr Nephrol. 2015;30(1):31–39.