Use of rituximab in treatment of myasthenia gravis

LITERATURE REVIEW

J. Diaz- Manera et al., [23] (2012) carried out a study on long-lasting treatment effect of rituximab in musk myasthenia. In this study, there were 17 patients with generalised myasthenia gravis (6 MuSK+ MG and 11 AChR+ MG) and they compared the response between AChR+ MG and MuSK+ MG patients. They found that 10 of the AChR+ MG improved but six of them needed reinfusion after treatment with Rituximab. But all MuSK+ MG patients achieved a remission (4/6) or minimal manifestations (2/6) status and no reinfusion were needed. Accordingly prednisolone dose reduced significantly and concomitantly Immunosuppressants were withdrawn in the MuSK+ MG group . They concluded that, the long lasting benefit was observed in MuSK+ MG patients and they suggest the use of rituximab as an early therapeutic choice in this group of patients with myasthenia gravis if they do not respond to prednisone.

Roshan Koul et al., [24] (2012) carried out a case study on a child with severe, life-threatening seronegative MG who repeatedly failed extubation but responded dramatically to Rituximab. They found that she achieved complete and sustained remission for more than 9 months, with gradual reduction in steroid dose without any side effects. Finally they concluded that Rituximab appears to be a promising and effective drug with large clinical benefit, and it is well tolerated without major side effects.

Nicolas Collongues et al., [25] (2012) conducted a retrospective study on rituximab in refractory and non refractory myasthenia. In this study, 13 refractory myasthenia and 7 non refractory myasthenia patients treated with

sequential rituximab infusions over 2 years were included. They found that Rituximab induction decreased the annualized relapse rate from 2. 1 to 0. 3 ($p < 0. 001$), and lowered MGFA scores from 5-3b to 4b-0 in refractory MG patients, and from 1. 9 to 0. 1 ($p <0. 001$) and 4b-2b to 3b-0 in non-refractory MG patients. After Rituximab induction, complete corticosteroid withdrawal was obtained in 7 RM and 4 NRM patients. So they concluded that rituximab is efficacious and well tolerated as well as its use allows for dose reduction or removal of corticosteroids.

Richard J. Nowak et al., [26] (2011) conducted a retrospective study on response of patients with refractory myasthenia gravis to rituximab. They found that, rituximab showed sustained clinical improvement in all patients as well as a reduction of conventional immunotherapies. Prednisone dose decreased by a mean of 65. 1%, 85. 7%, and 93. 8% after cycle 1, 2, and 3 of rituximab therapy, respectively. A statistical reduction in plasma exchange phase was seen after first cycle with all patients being off of plasma exchange after third cycle. Acetylcholine receptor antibody titres decreased by a mean of 52. 1% ($p= 0. 0046$) after third cycle. Finally they reported that rituximab is beneficial and well tolerated in the management of refractory myasthenia gravis.

Paul Maddison et al., [27] (2011) conducted a study on the use of riruximab in myasthenia gravis and lambert-eaton myasthenic syndrome. In this study, 10 patients with generalised myasthenia gravis (three of whom were positive for muscle-specific tyrosine kinase (MuSK) antibodies) and two patients with Lambert-Eaton myasthenic syndrome (LEMS) were treated with rituximab.

Using the Myasthenia Gravis Foundation America post intervention status, three patients (25%) achieved remission, and a further five (42%) improved clinically over an 18-month period. They reported that rituximab should be considered as a treatment choice for patients with either myasthenia gravis or lambert-eaton myasthenic syndrome for whom standard immunosuppressive treatment has been failed.

Alexander YL Lau et al., [28] (2011) carried out a case study on response to Cyclophosphamide and Rituximab treatment in a young Chinese woman with seronegative, muscle- specific tyrosine kinase antibody-positive myasthenia gravis. Before treatment with Rituximab she required prolonged intensive care and undergone various treatment with intravenous immunoglobulins, plasmapheresis and cyclophosphamide therapy. But partial response was obtained. So, treated with Rituximab and obtained dramatic and sustained response. Finally they concluded that the use of Rituximab for refractory anti-AChR negative, MuSK- positive myasthenia gravis appears to be a promising treatment choice.

Hans-Peter Tony et al., [29] (2011) conducted a study on safety and clinical outcomes of rituximab therapy in patients with different autoimmune diseases. This study included 370 patients with various autoimmune diseases and they were treated with Rituximab. After treatment with Rituximab they found significant reduction in the dose of corticosteroids and other immunosuppressive agents. So they concluded that Rituximab is a well tolerated therapy with potential beneficial effects in refractory auto- immune diseases.

Sabine Twork et al., [30] (2010) carried out a study on quality of life and life circumstances in German myasthenia gravis patients. This study included 2, 150 patients with confirmed MG who were asked to respond to a mailed questionnaire. They found that after receiving recommended therapy many patients still suffered from MG related impairments. Finally they concluded that despite extended life expectancy among myasthenia gravis patients, health-related quality of life is low. The outcome arises mainly from impaired mobility and depression. Physical and mental health might be enhancing by additional therapy options. Also, health care resources could be used more efficiently in these patients.

Karl Stieglbauer et al., [31] (2009) conducted a study on rituximab for myasthenia gravis three case reports and review of the literature. In this study two patients had anti-acetylcholine receptor antibodies positive (AChR+) myasthenia gravis and one patient had anti-muscle specific tyrosine kinase antibodies positive (MuSK+) myasthenia gravis. They reported that, in all three patients, treatment with rituximab led to a sustained clinical improvement and discontinuation or reduction of prednisolone and other drugs. Rituximab was well tolerated. Reviewing the anecdotal literature on rituximab for myasthenia gravis, they concluded that initial data on the efficacy and safety of rituximab are hopeful and that further studies in myasthenia gravis should be carried out.

Isabel Illa et al., [32] (2008) carried out a study on sustained response to Rituximab in anti-AChR and anti-MuSK positive myasthenia gravis patients. They reported the results of treatment with Rituximab in six severe, non-

responder myasthenia gravis patients. All patients, one class V and five class IV B, improved significantly with no side effects. Antibody titers declined in all patients (p= 0. 006). The decline was considerably better in MuSK+ MG patients at 9 months (p= 0. 046) and correlated with a more sustained clinical improvement. They concluded that Rituximab produced a radical change in the quality of life of the six patients who all had serious or life-threatening bulbar and respiratory symptoms.

Berit Hain et al., [33] (2006) conducted a study on successful treatment of MuSK antibody positive myasthenia gravis with Rituximab. This study contain a 56 years old woman with MuSK antibody positive MG. She was initially treated with conventional immunosuppression, but they could not maintain the clinical improvement. Hence, treatment with Rituximab was initiated. Finally they concluded that the use of Rituximab in MuSK antibody-positive myasthenia gravis was successful and it leads to stabilization in patients who were weakly responsive to previous immunosuppression.

Y. Nemoto et al., [34] (2005) conducted a study on patterns and severity of neuromuscular transmission failure in seronegative myasthenia gravis. The study contains 57 seropositive and 13 seronegative patients. Finally they concluded that deterioration of neuromuscular synaptic transmission in extensor digitorum communis (EDC) is less marked in seronegative than seropositive myasthenia gravis despite the same clinical seriousness. The difference may partly reflect the distribution of influenced muscles in seronegative patients, but it is possible that other factor, such as impaired

excitation contraction coupling resulting from ryanodine (RyR) antibodies, add to the clinical phenotype.

Luigi Virogolini, Vanda Marzocchi [35] (2004) carried out a study on rituximab in autoimmune diseases. The study contains 287 patients with different autoimmune diseases. Initially, they were treated with different immunosuppressive agents but the response was not good. So they commenced Rituximab therapy and finally concluded that rituximab is effective in most of the patients with autoimmune diseases.

Mark E. Wylam et al., [36] (2003) conducted a study on successful treatment of refractory myasthenia gravis using rituximab. The study contains a 9 year old girl with MG. Initially, she was treated with conventional immunotherapy and no improvement was seen. Finally they concluded that after initiation of anti CD-20 therapy, clinical improvement (muscular strength, pulmonary function) was observed.

N. P. Robertson, J. Deans, and D. A. S. Compston [37] (1998) conducted a population based epidemiological study on myasthenia gravis. The study contains 684000 patients and cases were ascertained from multiple sources. Prevalent patients were visited and assessed by means of standardised questionnaire and examination complemented by review of medical case notes. Finally they concluded that the second highest reported prevalence for myasthenia is likely to be the result of optimum case establishment, increased disease period correspondence of complex diagnostic tests, and the effect of an aging population leading to a relative increase in the prevalence of ocular myasthenia.