The Libyan International Medical University

Faculty of Basic Medical Science

Rituximab in Refractory Myasthenia Gravis

Malak Tajouri

Supervised by: Dr. Esam

Assisted by: Lujien Shakmak

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Abstract:

Myasthenia gravis (MG) is an autoimmune disease caused by complement-fixing antibodies against acetylcholine receptors (AChR). Cholinesterase inhibitors, Glucocorticoid , which is currently recommended as a first-line treatment for MG, although it has drawbacks, including possible toxicity and inefficiency in patients with refractory MG and traditional immunosuppressants stay the standard treatments at present, but they have demonstrated limitations and often unsatisfactory efficacy so the target specific therapeutic interventions should therefore be directed against antibodies For example, Rituximab is a monoclonal antibody (mAbs) that could be more active and longer lasting with less serious side effects.

Keywords: myasthenia gravis, immunotherapy, monoclonal antibody, Rituximab.

Introduction:

Myasthenia gravis (MG) from Greek: myos = muscle, asthenos = weakness, and Latin: gravis = severe, is an autoimmune neuromuscular disease primarily mediated by antibodies (Abs) targeting either the nicotinic acetylcholine receptor (AChR), or the components of the postsynaptic membrane at the neuromuscular junction (NMJ) leading to impaired neuromuscular transmission.[1]

Standard treatment such as Cholinesterase inhibitors cannot completely relieve the symptoms of MG or prevent the progression of the disease, glucocorticoids are also widely used to treat MG often causing severe adverse effects, and immunosuppressant such as glucocorticosteroids , often used as first-line MG therapies but for long-term use of immunosuppressive agents, often leads to significant side effects.[1]

Fortunately, in recent years, with the rapid development of biological agents, target-specific monoclonal antibodies (mAbs) (e.g., rituximab) that target the CD20 antigen present in all mature B cells, which initiates complement-dependent cytolysis or antibody-dependent cell-mediated cytotoxicity. It depletes B cell populations but does not affect the recovery of B cells or the production of antibodies, that's why showed

good efficacy and safety in patients with refractory MG making it more appropriate for those who do not respond to immunosuppressive therapy.[1]

Aim of study:

The potential target monoclonal antibodies (mAbs) target-specific immunotherapy refers to the design of therapeutic drugs (biological agents) to modulate the immune system at different levels that have shown promising outcomes for refractory MG patients.

Material and method:

In this report , the data collected from the three published articles were the first study about eight patients with low-dose rituximab-treated refractory MG (600 mg/cycle: 100 mg on the first day and 500 mg on the next day).The quantitative MG score (QMGS), manual muscle testing (MMT) , MG-related activities of daily living (MG-ADL), MG-specific quality-of-life (QOL) , B cell levels and AChR levels were measured at 1, 3 and 6 months after rituximab treatment .[2]

Second study about 14 patients with refractory MG taking varying doses and cycles of rituximab were found after a mean follow-up of 22.6 months to have all experienced significant relief of all clinical symptoms. [2]

Third study was about the high risk of rituximab-induced progressive multifocal leukoencephalopathy (PML) which is caused by the John Cunningham virus (JCV).[3]

Result:

The result for first and second studies showed that symptoms began to improve after 1 month of treatment with 600 mg rituximab, 43% after 6 months. It was also observed that low dose rituximab could markedly reduce B cells and maintain them at low

levels for up to 6 months after the administration of treatment. Observing a lower dosage, MMT decreased after just one cycle of treatment, the amount of steroids and the number of plasma exchange or immunoglobulin (Ig) administration required is also greatly reduced. Therefore, based on the good clinical efficacy of rituximab confirmed by the aforementioned studies so, rituximab should be recommended for early treatment of refractory MG. [2]

Third study results reported only one case of death due to progressive multifocal leukoencephalopathy (PML) and no malignant tumors were observed MG. The risk of rituximab-induced PML and potential long-term drug-induced side effects for patients with mild refractory MG must be balanced against their therapeutic value. For patients with severe refractory MG, particularly those with anti-MuSK (muscle-specific tyrosine kinase) – positive MG, rituximab may be a more appropriate treatment, though the risk factors for PML (old age, male, multiple combined immunotherapy, and so on) remain important to consider before application. Finally, determining the presence of anti-JCV Abs prior to rituximab treatment may be a useful tool to predict the risk of PML development in MG patients weighing the benefits and risks of rituximab, though this remains to be scrutinized.[3]

Discussion:

The specific mAbs (rituximab) developed against CD20 antigens on the surface of B cells are relevant to MG immunopathogenesis and have been proposed to be promising therapeutic strategies. CD20 is a nonglycosylated phosphoprotein that presents in pre-B cells and mature B cells but not in normal plasma cells and does not circulate in plasma as a free antigen.[1]

The inhibition of CD20 by rituximab interferes with activation, differentiation, and proliferation of B cells, thereby reducing the number of circulating CD20+ B cells. This reduction of CD20+ B cells that affect T follicular helper (TFH) cells and short-lived plasma cells ultimately prevents a decrease in the number of AChRs in the postsynaptic membrane, and inhibits the autoimmune response in MG.[1]

Conclusion:

MG is a neurological autoimmune disease that seriously affects the quality of life that is usually treated with immunosuppressants but because it has side effects so the best treatment is rituximab, which is chimeric mAb against membrane-spanning four-domain protein CD20 targets and binding to CD20 on beta cells and mediate B cells lysis, that rituximab appears to be both a safe and effective treatment for MG.

References:

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