Optimization of passive transfer model for Myasthenia Gravis

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Myasthenia gravis (MG), one of best understood autoimmune disorders, is caused by autoantibodies targeting the neuromuscular junction leading to loss of AChR and AChR-associated proteins (1). As a result, MG patients experience muscle weakness and fatigue. In passive transfer animal models for MG (PTMG) monoclonal antibodies are administered to evoke an autoimmune response against the neuromuscular junction and induce MG. The standardized guidelines describe intravenous (IV) or intraperitoneal (IP) administration of the pathogenic antibodies (2). Even though both methods are effective, they are accompanied with complications such as discomfort and the inability to notice errors and verify correct placement. We hypothesize that subcutaneous administration is a more robust and humane approach to induce MG in the PTMG model. In order to prove this, female Lewis rats (10-12 weeks old) will be injected intraperitoneally or subcutaneously with mAb35, a monoclonal antibody targeting the acetylcholine receptor (AChR). Within 48 hours the animals are expected to show clinical symptoms such as hunched posture, muscle weakness, tremor and respiratory distress, which are scored using EAMG scoring. Muscle weakness and fatigue are measured using the grip strength test. At the end of the experiment, prior to euthanasia, the AChR content is determined with electromyography during curare infusion. Post-mortem analysis of muscle AChR content will confirm clinical observations and identify subclinical cases.

Keywords: myasthenia gravis, passive transfer, autoimmune antibodies

References

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