Using methotrexate may reduce the negative impact of high treatment-related costs on patients with myasthenia gravis

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Myasthenia gravis (MG) is a rare autoimmune synaptopathy that is caused by the dysfunction of nerve cells and muscle fibers at the neuromuscular junction. The disease is characterised by pronounced muscle weakness and fatigue.

In the vast majority of MG patients, the disease is initially localised and limited to the eye muscles, causing drooping of the eyelid and double vision. Patients with untreated disease can experience severe weakness of respiratory muscles, leading to myasthenic crisis. In this situation, the patient can only survive through the use of mechanical ventilation and intubation.

Treatment of MG involves the administration of acetylcholinesterase inhibitors and corticosteroids. As it is an autoimmune condition, immunosuppressive therapies such as rituximab, tacrolimus, and Alexion's Soliris (eculizumab) have demonstrated efficacy in the management of patients with severe disease. However, the high treatment-related costs associated with biologics mean that patients from underprivileged backgrounds can have difficulty accessing Soliris, despite the fact that the drug is approved in more than eight countries.

One potential solution to this issue is to encourage the use of drugs such as methotrexate, which has notable advantages over other widely available immunosuppressants such as azathioprine and cyclosporine. Methotrexate tablets are taken once weekly, while azathioprine and cyclosporine tablets are both administered once daily. The potential teratogenicity of azathioprine is a subject of ongoing debate. Cyclosporine is associated with hypertension, gingivitis, renal dysfunction, and impaired insulin metabolism.

Conversely, clinical trials have shown that methotrexate is a safe, effective drug that is well tolerated by young patients and in people with comorbidities such as rheumatoid arthritis and psoriasis. Another clinical advantage is the fact that methotrexate can be injected subcutaneously and intravitreally for ocular indications. Methotrexate is an anti-neoplastic agent that prevents the proliferation of lymphocytes. In MG, these are responsible for the production of autoantibodies that inhibit the neurotransmission of acetylcholine, which is a key component of the autonomic nervous system.

Despite the widespread availability of generic methotrexate in countries such as the US, Italy, Germany, and Switzerland, the lack of formal approval for MG restricts its use for this debilitating and potentially fatal condition. Increasing the volume of clinical data to provide evidence of the drug's efficacy and safety profile in people with MG could be an important step toward making the treatment more affordable for socioeconomically disadvantaged patients. This is especially important for patients who are unable to be managed with non-pharmacotherapeutic strategies such as thymectomy and plasmapheresis.