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THE ROLE OF VITAMIN D3 SUPPLEMENTATION ON MYASTHENIA GRAVIS COMPOSITE SCALE: A CASE REPORT

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ABSTRAK

Myastenia Gravis (MG) adalah penyakit autoimun kronis yang langka, yang dipicu oleh autoantibodi IgG patogenik dan komplemen. Gejala klinis yang sering dijumpai adanya kelemahan otot mata, kesulitan menelan, kesulitan berbicara, kelemahan pada otot ekstremitas, otot rangka hingga menyerang otot pernapasan. Perempuan usia 47 tahun mengalami ptosis unilateral, diplopia bilateral, disfagia, disfonia, disartria dan paresis pada ekstremitas atas dan bawah. MG composite scale (MGCS) mendapatkan total skor 31. Pemeriksaan elektromiografi mengonfirmasi diagnosis myastenia gravis dan pemeriksaan kadar vitamin D 25-OH mengalami defisiensi. Selama perawatan di rumah sakit, pasien mendapatkan terapi inhibitor kolinesterase, kortikosteroid dan suplementasi Vitamin D3 1x5000 IU selama sembilan hari. MGCS pasien mengalami penurunan hingga skor 19 sehingga kapasitas fungsional pasien meningkat.
Kesimpulan: Suplementasi vitamin D3 5000 IU/hari berpotensi memberikan manfaat klinis melalui penurunan skor MGCS, serta menurunkan risiko osteoporosis di masa mendatang sebagai sekunder dari defisiensi vitamin D 25-OH. Selain itu, perbaikan kondisi klinis pasien kemungkinan juga dipengaruhi oleh pemberian terapi inhibitor kolinesterase dan kortikosteroid.

ABSTRACT

The Role of Vitamin D3 Supplementation on Myasthenia Gravis Composite Scale: A Case Report. Myasthenia Gravis (MG) is a rare chronic autoimmune disorder triggered by pathogenic IgG autoantibodies and complement activation. Common clinical manifestations include ocular muscle weakness, dysphagia, dysarthria, dysphonia, limb muscle weakness, generalized skeletal muscle weakness, and respiratory muscle involvement. A 47-year-old female presented with unilateral ptosis, bilateral diplopia, dysphagia, dysphonia, dysarthria, and paresis of both upper and lower extremities. The Myasthenia Gravis Composite Scale (MGCS) score was 31. Electromyography confirmed the diagnosis of myasthenia gravis, and laboratory evaluation revealed 25-hydroxyvitamin D deficiency. During hospitalization, the patient received cholinesterase inhibitors, corticosteroids, and vitamin D3 supplementation at 5,000 IU once daily for 9 days. The MGCS score decreased to 19, indicating improved functional capacity. Conclusion: Vitamin D3 supplementation at a dose of 5,000 IU/day may provide potential clinical benefits, as reflected by a reduction in MGCS score, and may also reduce the future risk of osteoporosis secondary to 25-hydroxyvitamin D deficiency. However, the clinical improvement observed in this patient was likely also influenced by the concurrent administration of cholinesterase inhibitors and corticosteroids.

INTRODUCTION

Myasthenia Gravis (MG) is a rare chronic autoimmune disorder characterized by impaired neuromuscular transmission resulting from pathogenic IgG autoantibodies and complement-mediated damage at the neuromuscular junction.[1,2,3] Although MG is generally a treatable condition, it may lead to substantial morbidity and, in severe cases, mortality; these adverse outcomes are largely preventable through early diagnosis and appropriate management.[4,5,6] Globally, the incidence of MG ranges from 1.77 to 21.3 cases per million population per year, with an estimated prevalence of 15 to 179 million individuals.[7,8,9] However, the exact prevalence of MG in Indonesia has not yet been clearly established.[10] Epidemiologically, MG exhibits a bimodal age distribution among women, with incidence peaks around the ages of 30 and 50 years. Women are more frequently affected before the age of 40, with a female-to-male ratio of approximately 3:1.[4,11]

The pathophysiology of MG involves disruption of synaptic transmission due to impaired interaction between neurotransmitters released from presynaptic nerve terminals and postsynaptic receptors. Clinically, MG commonly presents with fluctuating muscle weakness, particularly affecting the ocular muscles (ptosis and diplopia), bulbar muscles (dysphagia and dysarthria), extremity muscles, and, in advanced cases, the respiratory muscles.[4,12]

Corticosteroids remain a cornerstone of MG management; however, long-term corticosteroid therapy is associated with an increased risk of osteoporosis, especially in patients with low serum 25-hydroxyvitamin D levels. Consequently, vitamin D3 supplementation has been proposed as a potential adjunctive therapy in MG.[13,14,15] Beyond its role in bone metabolism, vitamin D3 exerts immunomodulatory effects and contributes to skeletal muscle function, suggesting potential benefits in reducing muscle weakness in MG patients.[13,16,17]

Several studies have investigated the impact of vitamin D3 supplementation on disease severity in MG. One study demonstrated improvement in the Myasthenia Gravis Composite Scale (MGCS) following vitamin D3 supplementation at 800 IU/day for 2.5–10 months.[13] In contrast, Okparasta et al. reported that while vitamin D3 supplementation at the same dosage effectively increased serum vitamin D levels, it did not produce a significant improvement in MGC scores.[18] Despite these findings, evidence regarding vitamin D status and optimal supplementation strategies in MG remains limited and inconclusive. Based on the aforementioned considerations, this report will further discuss the role of short-term high-dose vitamin D3 supplementation administered during hospitalization, as well as the serial assessment of the MGCS to monitor therapeutic response.

CASE REPORT

History of Disease

One year prior to hospital admission, the patient complained of headache, postprandial vomiting, and generalized weakness that prevented her from standing. She was subsequently hospitalized at Hospital T for four days and was diagnosed with vertigo. During a follow-up visit, the patient reported binocular diplopia and consulted an ophthalmologist, who noted no significant abnormalities in ocular function. The patient later developed left-sided ptosis and was referred to a neurologist. Nerve conduction studies (NCS) and electromyography (EMG) were recommended to establish a diagnosis of Myasthenia Gravis (MG); however, these examinations were not available at Hospital T. The patient was therefore referred to an external facility, where the results were reported as inconclusive for the diagnosis of MG.

Four months prior to admission, the patient developed nasal and progressively hypophonic speech after prolonged talking. She returned to the neurologist and was advised to undergo an EMG at Hospital S. Following the EMG, the patient was diagnosed with MG and initiated on pyridostigmine (Mestinon). After starting treatment, her symptoms were better controlled, although intermittent limb weakness and recurrent ptosis persisted when medication was not taken. She denied nausea and vomiting, and her appetite remained good.

One day prior to admission, the patient experienced difficulty swallowing both liquids and solid foods and had several episodes of choking during meals. She also complained of dyspnea later that afternoon. Generalized weakness and worsening left-sided ptosis were also noted. These symptoms persisted despite adherence to medication. The patient had previously received corticosteroid therapy at an unknown dosage, which reportedly resulted in slight symptomatic improvement and allowed her to sleep. However, the following day, her dyspnea worsened, prompting her to seek medical care at Cipto Mangunkusumo National General Hospital.

Clinical Presentation and Examination

Physical examination revealed unilateral ptosis, bilateral diplopia, dysphagia requiring nasogastric tube (NGT) support, dysphonia, dysarthria, and paresis of both the upper and lower extremities. Functional capacity assessment using the MGCS yielded a total score of 31. Laboratory investigations demonstrated hemoglobin of 13 g/dL, platelet count of 360 × 10^3/µL, leukocyte count of 15.2 × 10^3/µL, sodium 132 mEq/L, potassium 3.6 mEq/L, chloride 100.3 mEq/L, urea 23.5 mg/dL, creatinine 0.70 mg/dL, estimated glomerular filtration rate (eGFR) 104.2 mL/min/1.73 m^2, and serum 25-hydroxyvitamin D level of 20 ng/mL. Single-fiber electromyography (EMG) confirmed the diagnosis of MG. A limitation of this case report is that testing for acetylcholine receptor (AChR) antibodies and muscle-specific kinase (MuSK) antibodies was not performed.

Treatment and Follow-up

The patient received Mestinon at a dose of 60 mg three times daily and methylprednisolone at a dose of 16 mg once daily during hospitalization. Vitamin D3 supplementation at 5,000 IU once daily was initiated on the second day of hospitalization and continued until day 10.

The patient's Myasthenia Gravis Composite Scale (MGCS) was 31 on the first, second, and third days of hospitalization. On days 4 and 5, the MGCS score decreased to 27. On days 6 and 8, the score further declined to 25, followed by a reduction to 22 on day 9. The patient was discharged on day 10 with an MGCS score of 19.

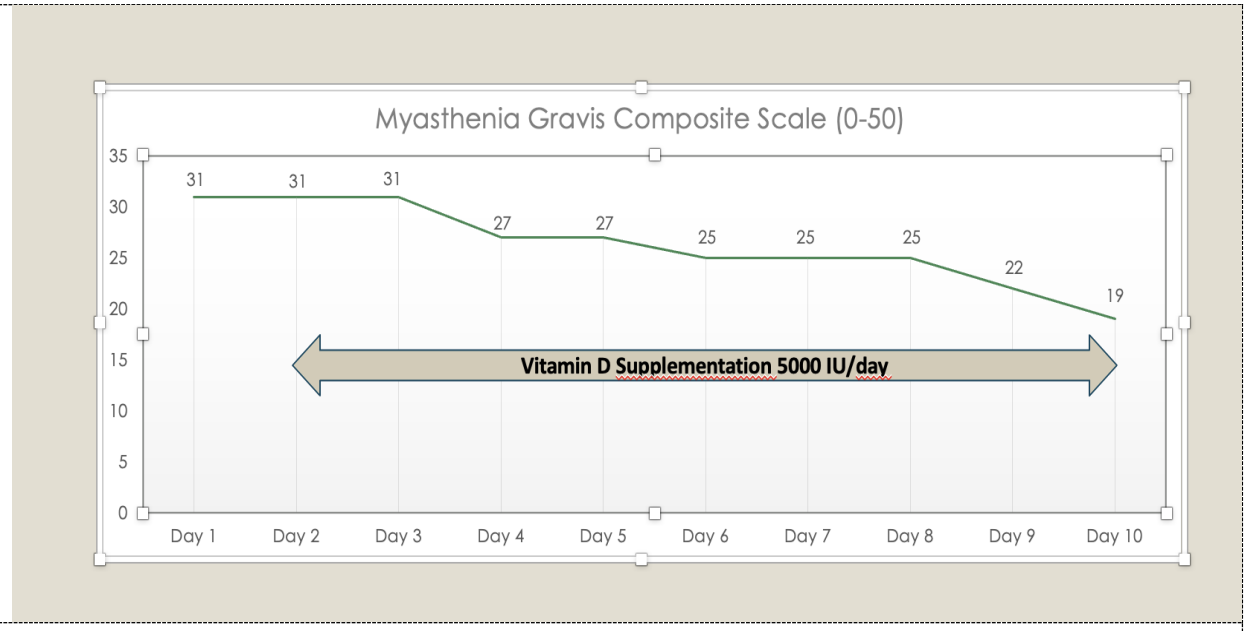

Figure 1. Myasthenia Gravis Composite Scale

DISCUSSION

Myasthenia Gravis (MG) is a rare chronic autoimmune disease characterized by dysfunction and structural damage at the neuromuscular junction, triggered by pathogenic IgG autoantibodies and complement activation.[1,2] The etiology of MG is closely related to individual immune system dysregulation.[19,20,21] In patients with MG, a type II hypersensitivity reaction occurs, in which IgG autoantibodies react with intra- or extracellular antigens, leading to damage of target organs.[4] The majority of MG patients harbor autoantibodies against the acetylcholine receptor (AChR), while a smaller proportion are seropositive for antibodies directed against muscle-specific kinase (MuSK), low-density lipoprotein receptor–related protein 4 (Lrp4), or agrin.[4,22]

The hallmark clinical manifestation of MG is fatigable muscle weakness that worsens with physical activity and improves with rest. The most common initial presentation involves ocular symptoms, including diplopia and ptosis.[4,12] In the present case, the patient experienced diplopia and ptosis for approximately one year prior to disease generalization. Up to 80% of patients presenting with ocular MG progress to generalized disease, typically within the first two years after symptom onset.[4] A study conducted at the Mayo Clinic reported that 51% of patients initially presenting with ocular symptoms subsequently developed generalized MG, with 55% progressing over time.[23] Consistent with these findings, the patient in this case developed generalized MG approximately one year after the onset of ocular symptoms.

Bulbar muscle involvement is also common in MG and may result in flaccid dysarthria, dysphagia, and weakness of the facial and masticatory muscles. Axial muscle weakness may occur, with neck flexor weakness more frequently observed than neck extensor weakness.[4] Limb muscle weakness is typically symmetrical and predominantly affects proximal muscles, leading to complaints such as difficulty climbing stairs, rising from a seated position, or lifting the arms overhead. In addition, approximately 15–20% of patients with AChR antibody–associated MG may develop respiratory muscle weakness requiring mechanical ventilation, known as myasthenic crisis.[4] In this case, the patient reported dyspnea but did not require mechanical ventilatory support.

Vitamin D has a potential association with MG through two primary mechanisms: modulation of autoimmune responses and maintenance of muscle function via vitamin D receptors expressed in skeletal muscle.[24,25,26] The patient in this case was found to have vitamin D deficiency, with a total serum 25-hydroxyvitamin D level of 20 ng/mL. Previous studies have reported that up to 88% of MG patients exhibit vitamin D insufficiency or deficiency, compared with 62% in healthy control populations.[13] The high prevalence of vitamin D deficiency among MG patients is likely attributable to reduced physical activity due to muscle weakness and limited sunlight exposure resulting from functional impairment.[27,28]

The patient received vitamin D3 supplementation at 5,000 IU once daily during hospitalization and demonstrated improvement in MG Composite Scale (MGCS) scores. In a previous study, MG patients who received vitamin D3 supplementation at a dose of 800 IU/day for 2.5–10 months (mean duration of 6 months) showed favorable effects on immune response and MGCS scores; however, this dosage was insufficient to achieve substantially higher serum 25-hydroxyvitamin D levels compared with healthy controls not receiving supplementation.[13] In contrast, a study by Okparasta et al. reported that vitamin D3 supplementation at 800 IU/day increased serum vitamin D levels but did not result in a significant improvement in MGCS scores.[18]

High-dose vitamin D supplementation in autoimmune diseases remains controversial due to limited long-term safety data.[24,29] Several clinical trials are currently evaluating supraphysiological doses of vitamin D in multiple sclerosis, while comparable studies in other autoimmune conditions remain scarce.[24] Current MG management guidelines published in 2022 do not provide specific recommendations regarding vitamin D supplementation, and the optimal vitamin D status in MG patients remains uncertain. Available literature suggests that patients receiving long-term high-dose vitamin D supplementation, typically ranging from 80.000 to 120.000 IU/day, do not experience serious adverse effects.[24] Nevertheless, robust evidence supporting the routine use of higher vitamin D doses is lacking, underscoring the need for further research.

This case report demonstrates the potential effectiveness of vitamin D3 supplementation in improving functional capacity in a patient with Myasthenia Gravis, as assessed using the MGCS. However, the specific contribution of vitamin D3 supplementation remains inconclusive, as multiple factors may influence clinical improvement and functional outcomes in patients with MG, including standard MG therapy, level of physical activity, serum 25-hydroxyvitamin D levels, and the type of physical exercise performed.[30,31]

CONCLUSION

Vitamin D3 supplementation may improve functional capacity in patients with Myasthenia Gravis, as reflected by reductions in the MGCS. However, the observed clinical improvement is likely multifactorial and may also be attributable to concomitant treatment with cholinesterase inhibitors and corticosteroids. Routine assessment of serum vitamin D levels should be considered as part of comprehensive patient management. Moreover, maintaining adequate 25-hydroxyvitamin D levels may help mitigate the long-term risk of osteoporosis associated with vitamin D deficiency.

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