Peribulbar Corticosteroids for Ocular Myasthenia Gravis

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Background: Ocular myasthenia gravis is treated predominantly by oral medications, with the potential for systemic adverse effects. Successful treatment has been achieved using peribulbar dexamethasone. We assessed the effect of peribulbar dexamethasone or triamcinolone (40-mg Triesence), a longer-acting corticosteroid, targeting the peribulbar area as opposed to directly injecting the affected extraocular muscle. This more convenient and secure approach holds the potential for straightforward integration within clinical environments.
Methods: Retrospective chart review.
Results: Five patients were identified that were treated with peribulbar corticosteroids. In 4 of the 5 cases, ophthalmoparesis was unilateral. One case had isolated ptosis, and 4 had both ptosis and ophthalmoparesis. Three of these 4 cases reported complete resolution of symptoms within weeks of a single injection. Improvement lasted between 5 to 6 months, and all patients responded to repeated injections.
Conclusions: Peribulbar corticosteroids can be effective in ocular myasthenia gravis. We suggest that longer-acting agents such as triamcinolone are preferable, to reduce injection frequency.

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Ocular myasthenia gravis (OMG) can sometimes be successfully managed with cholinesterase inhibitors alone; however, oral immunosuppressive therapy is often required.[1] Systemic corticosteroids are often used in OMG, but their use is limited by adverse effects, especially long term.[2,3]

Successful treatment of ocular conditions using peribulbar dexamethasone has been achieved but requires repeated weekly injections for up to 6 weeks.[4] Repeated injections are inconvenient and increase the risk of orbital hemorrhage, particularly for patients who are concurrently receiving antithrombotic therapy.[5] As such, longer-acting agents, such as triamcinolone, may facilitate treatment with fewer injections, lowering the risk of complications.

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METHODS

Patients with acetylcholine receptor antibody–seropositive OMG presenting to the Hadassah Medical Eye Center between April 2021 and January 2023 were offered peribulbar corticosteroidal injection (PCSI) if pyridostigmine treatment failed either because of lack of efficacy or intolerable adverse effects. All patients were given detailed information about their condition and various treatment options including oral steroids and immunosuppressive agents. Declaration of Helsinki to conduct a retrospective chart review was obtained. All patients were treated with a peribulbar injection through the eyelid, generally in the inferior-temporal zone. To mitigate the risk of immediate complications, patients were monitored 20 minutes after injection using a slit-lamp examination to evaluate the anterior chamber, as well as measuring ocular pressure.

The primary objective was to induce remission of the ocular symptoms. All patients were followed up for a minimum of 6 months or at any sign of disease recurrence.

RESULTS

Five patients chose PCSI. Four patients had ocular symptoms of myasthenia gravis including ptosis, diplopia, and ophthalmoplegia, and one patient had isolated left eye ptosis. All had previously been treated with pyridostigmine, but reported clinically intolerable symptoms at recommended doses.

The first patient received peribulbar dexamethasone injections (0.75 mL of 4-mg/mL dexamethasone and 0.25 mL of 1% lidocaine). The following 3 patients were receiving antiplatelet therapy. To minimize the number of injections, we elected to substitute repeated dexamethasone injections for a single injection of triamcinolone (1.0 mL of Triesence, 40 mg/mL). All patients were able to discontinue aspirin one week before the procedure without thrombotic complications. The fifth patient was not on antithrombotic therapy but still preferred triamcinolone (1.0 mL of Triesence, 40 mg/mL) because of a desire to minimize injections. The results are summarized in Table 1.

Representative Cases

Case 1: A 90-year-old man was diagnosed with ocular myasthenia gravis. He initially presented with horizontal binocular diplopia, difficulty chewing, and right-sided face weakness. On a focused examination, the patient had marked left ptosis that obstructs the visual axis, which was alleviated after closing his eyes for 2 minutes. Treatment with pyridostigmine improved his vision, but he still

TABLE 1. Summary of the 5-case series

Case	Age	Clinical Manifestations	Diagnosis	Previous Systemic Treatment	Aspirin Therapy	Length of Disease Prior to Injection	Type of Injection	Interval Between Injections	Total Injections	Clinical Outcome
1	90	Diplopia and ptosis	Seropositive AChR	Pyridostigmine	No	7 mo	Dexamethasone	6 mo and 5 mo	5 in single eye	6 mo and 5 mo of remission
2	75	Diplopia and ptosis	Seropositive AChR	Prednisone and pyridostigmine	Yes	4 mo	Triamcinolone acetonide	1 injection	1 single eye	4 mo of remission
3	79	Isolated left Ptosis	Seropositive AChR	Pyridostigmine	Yes	8 mo	Triamcinolone acetonide	4 mo	2 in single eye	4 mo of remission
4	72	Diplopia and ptosis	Seropositive AChR + sfEMG	None	Yes	5 mo	Triamcinolone acetonide	1 injection	1 single eye	No effect
5	59	Diplopia and ptosis	Seropositive AChR	Pyridostigmine	No	3 mo	Triamcinolone acetonide	6 mo	2 to each eye	6 mo of remission

AChR, acetylcholine receptor; sfEMG, single-fiber electromyography.

experienced horizontal diplopia in left gaze and intermittent diplopia in the evenings. Furthermore, he could not increase the daily dose beyond 300 mg because of disabling gastrointestinal side effects. He received 3 consecutive left-eye PCSI of dexamethasone and lidocaine, which resulted in a marked improvement in vision with minimal ptosis and no significant diplopia. The patient discontinued pyridostigmine and remained symptom-free for 6 months when a recurrence of diplopia occurred. He received another PCSI in the left eye. After 5 months, the patient developed slight diplopia with a limitation of left-eye abduction and received another PCSI. The patient remained diplopia-free for 9 months after the last injection.

Case 2: A 75-year-old man patient with a history of diabetes mellitus and aspirin treatment was diagnosed with OMG, based on positive serology and single-fiber EMG. The patient's symptoms were mainly manifested as a left ptosis and diplopia in nearly all directions except upgaze. Treatment with 60-mg pyridostigmine 3 times a day was ineffective and was discontinued because of severe diarrhea. Nearly 2 months after a left-eye injection of triamcinolone (1.0 mL of Triesence, 40 mg/mL), the patient reported significant improvement with complete resolution of ptosis and diplopia for 4 months.

Case 3: A 79-year-old man with OMG experienced a severe left ptosis, despite treatment with 300-mg-daily pyridostigmine, resulting in occlusion of the visual axis for the majority of the day. After discontinuing aspirin for one week, the patient received a left-eye triamcinolone injection (1.0 mL of Triesence, 40 mg/mL). Two months after injection, the patient reported no significant ptosis. However, 4 months later, the left fatigable ptosis had redeveloped, and the patient received a second left-eye injection. One month after the second injection, there was an improvement in the ptosis.

Case 4: A 72-year-old man with a history of hypertension presented with seropositive OMG manifested by a left ptosis, a left hypotropia, and limited left-eye elevation. He opted for PCSI over systemic treatment. After discontinuation of aspirin treatment for one week, the patient received a single left PCSI of triamcinolone (1.0 mL of Triesence, 40 mg/mL). However, as of 4 months after injection, the patient reported no significant change in the severity of the ptosis or diplopia, and thus, a second injection was not administered.

Case 5: A 59-year-old man with a history of hypertension and mild diabetes mellitus developed seropositive OMG characterized by diplopia and bilateral ophthalmoparesis. Pyridostigmine was not effective and poorly tolerated at 360 mg per day. Bilateral injections of triamcinolone (1.0 mL of Triesence, 40 mg/mL) were administered, resulting in a near-resolution of diplopia and significantly improved ocular mobility within one month after injection. The patient remained diplopia-free for nearly 5 months. Six months after the last injection, the patient received a second

round of bilateral injections and remained asymptomatic for 3 months.

All injections were well-tolerated by all patients, with no complications observed during or immediately after the procedure. Twenty minutes after injection, all patients were asymptomatic, and their ocular examinations revealed normal findings, including a normal anterior chamber and normal ocular pressures.

CONCLUSIONS

Our study contributes to evidence supporting the use of local corticosteroids for the management of OMG, while also shedding light on the potential advantages offered by triamcinolone over dexamethasone. Specifically, our research indicates that triamcinolone, a longer-acting corticosteroid, may serve as a favorable alternative to dexamethasone by minimizing the number of injections needed to induce remission of ocular symptoms.

Local orbital steroid injections may initially appear counterintuitive in the treatment of OMG, as the pathophysiology suggests the need for a systemic approach. However, the intriguing findings by Shi et al challenge our current understanding of the underlying mechanism of autoimmunity against the extraocular muscles. In light of this, it is crucial to explore potential hypotheses that could explain the efficacy of local corticosteroids. One possibility worth investigating is the presence of lymphoid tissue within the orbit, such as the lymphoid follicles in the lacrimal gland and conjunctival-associated lymphoid tissue and among them B cells.[6] Those B cells have been shown to predominantly secrete immunoglobulin A (IgA) as expected from plasma cells in mucosa lining.[7] Although IgG antibodies are the primary type of antibodies involved in OMG, it is worth noting that other antibody types, such as IgA and IgM, may also be present in some cases in conjunction with IgG antibodies,s[8] and one can speculate they might be responsible in attacking the extraocular muscles. The notion that ocular myasthenia gravis may be due to local orbital autoantibody production is interesting because it would provide an explanation for the low sensitivity of serologic antibody detection because of local sequestration. Alternatively, it is conceivable that the antibodies do migrate into the orbit, but the administration of steroids somehow mitigates their damaging effects on the neuromuscular junction. Previous reports describe direct injection of corticosteroid injected into any extraocular muscles presumed to be weak.[4] This was the case in all but one of their 14 patients. We chose to deviate from this method and to exclusively perform peribulbar injections. Corticosteroids are fat-soluble and are therefore expected to spread throughout the orbit. Furthermore, local corticosteroid injection therapy has been successful for thyroid orbitopathy without directly injecting the palsied muscles.[9–11] Finally, we believe that a peribulbar injection is technically much easier and also safer. Our results suggest that it is an effective alternative.

Initially, we assessed the therapeutic efficacy of peribulbar dexamethasone injection in a single patient. Building on this proof of concept, we aimed at reducing the risk of serious orbital hemorrhage, resulting from consecutive weekly injections, particularly among individuals under antithrombotic therapy. Thus, we further tested the effectiveness of triamcinolone, a longer-acting corticosteroid in inducing remission of ocular symptoms. In 3 of the 4 cases, a single injection of triamcinolone was associated with a near-complete resolution of the symptoms within weeks and persisted for a duration of 4 to 6 months.

We believe that using triamcinolone for OMG not only offers advantages for patients receiving antithrombotic therapy[5] but also ensures enhanced safety for individuals at risk of clinical deterioration under systemic corticosteroid treatment. In fact, the use of systemic steroid treatment for purely ocular symptoms of MG requires a careful balance between potential benefits and the risks of serious side effects. Although steroid treatment can improve ocular symptoms in some patients, it can also cause significant systemic side effects, including weight gain, mood changes, increased blood pressure, and elevated blood sugar levels, as well as long-term complications.[2,3] Despite the potential benefits of steroid treatment, oral drug therapy with steroids or pyridostigmine has limited effectiveness in treating OMG symptoms. Only around 20% of patients achieve relief with these treatments, and symptom recurrence is common once steroid dosages are decreased.[12] Furthermore, none of the patients treated with pyridostigmine have experienced complete relief of ocular manifestations.[13]

Triamcinolone injections are successfully used for treating various conditions,[14] including orbital ophthalmopathy, but they carry the risk of potential complications.[9–11] These may include increased intraocular pressure, mild ptosis, and, in rare cases, central retinal artery occlusion (CRAO).[15,16] Unlike dexamethasone, a liquid steroid solution with a lower risk of CRAO, triamcinolone has been found to form larger and denser aggregates compared with other steroids.[17] These larger particles can potentially cause vascular occlusion by blocking smaller blood vessels in the eye.[18,19] To address concerns associated with CRAO, a recent study suggested a safer injection technique involving an intravenous cannula or a 24-gauge intravenous catheter for delivering triamcinolone.[20] This novel technique was successfully implemented in one patient (case 4) and holds promise for using triamcinolone with safer settings in the future.

This retrospective study revealed favorable outcomes with administration of dexamethasone or triamcinolone through PCSI in the management of OMG, supporting its use as an alternative to oral immunosuppressive agent. Nonetheless, the small number of cases included in the

study, the selection bias of patients, and the nature of retrospective design require more extensive clinical trials to assess whether this strategy should be implemented as first-line therapy for OMG.

STATEMENT OF AUTHORSHIP

Conception and design: M. Gotkine, J. Kruger; Acquisition of data: R. Lasry, J. Kruger; Analysis and interpretation of data: R. Lasry, M. Gotkine, J. Kruger. Drafting the manuscript: R. Lasry; Revising the manuscript for intellectual content: R. Lasry, M. Gotkine, J. Kruger. Final approval of the completed manuscript: R. Lasry, M. Gotkine, J. Kruger.

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