ORIGINAL ARTICLE

Role of Preoperative Immunosuppressant Therapy in Prevention of Pot-ThymectomyMyasthenic Crisis

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ABSTRACT

Background: Myasthenia gravis is an autoimmune disease characterized by varying degrees of skeletal muscle weakness which worsens with exertion.
Aim: To observe the incidence of myasthenic crisis in patients with Myasthenia gravis with induction of complete remission via immunosuppressant therapy in the postthymectomy phase.
Methodology: This was a prospective interventional study. This study was undertaken at the Department of Thoracic Surgery, King Edward Medical University/Mayo Hospital Lahore between June 2009 and May 2017.
Results:132 patients, 83 females and 49 males in complete remission were thymectomized via trans-sternal approach. All these patients were observed for precipitation of myasthenic crisis in the post-operative phase. None of the patients had any clinical evidence suggesting myasthenic crisis or worsening of myasthenic symptoms in the early or intermediate post-operative phase.
Conclusion: It is hereby concluded that immunosuppressant therapy and induction of complete remission of Myasthenia Gravis ensures the prevention of Myasthenic crisis in post-thymectomy patients, which if precipitated can have significant morbidity and mortality in such patients.
Keywords: Thymectomy, myasthenia gravis, immunosuppressant therapy

INTRODUCTION

Myasthenia gravis is an autoimmune disease characterized by varying degrees of skeletal muscle weakness which worsens with exertion. Despite the fact that the cause of this disease is unknown, the pathophysiology of this disease revolves around production of antibodies directed primarily against acetylcholine receptors(AChR) at the post-synaptic end of the neuromuscular junction (NMJ), although Anti-MuSk(muscle-specific tyrosine kinase) antibodies[1] are also found in these patients. End plate potential (EPP) generated in normal NMJ is multiple times larger than the threshold needed to generate the postsynaptic action potential. This neuromuscular transmission "safety factor" is reduced in MG patients due to a decrease in number or activity of the AChR molecules at the NMJ which decreases the EPP, which may be adequate at rest; but the EPP may fall below the threshold needed to generate action potential when the quantal release of ACh is reduced after repetitive activity[2]. This is manifested by clinical muscle weakness, and when EPP at rest is consistently below the action potential threshold, it leads to persistent weakness. This is seen in moderate and severe generalized disease.

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Muscle weakness in this disease is worsened by heat, infection and stress[3]. This disease may be categorized clinically as ocular, mild generalized (26%), moderate generalized (36%)and severe generalized (39%), associated with bulbar symptoms and reduced FEV1[4]. Myasthenic crisis refers to a rapid deterioration in neuromuscular function which consequently leads to respiratory compromise due to ventilatory muscle insufficiency or weakness of upper airway musculature or both[5].

Myasthenia gravis is diagnosed using a number of tests, including Tensilon test[6,7], Ice pack test[8] and most diagnostic of all, Electrophysiological tests which include Repetitive Nerve stimulation test and single fiber electromyography[9.10](for occult Myasthenia gravis). Serological test for the diagnosis of Myasthenia Gravis measures the serum concentrations of Anti-AChR antibodies[11].

Once diagnosis is established and the disease has been categorized clinically, both medical and surgical managements are available. Medical management may be symptomatic (cholinesterase inhibitors),acute short term immunomodulating treatment (plasmapharesis and Intravenous immunoglobulins) and the more definitive disease modifying long-term immunomodulating therapy (corticosteroids and azathioprine). Surgical management involves removal of the thymus gland via VATS or the more conventional open method via transsternal approach, and it is highly recommended

in AntiAChRab- positive generalized myasthenia gravis in patients below 50 years of age[12].

Surgical stress has a tendency to precipitate an episode of Myasthenic crisis. This study focuses on the incidence of myasthenic crisis in the early and intermediate post-thymectomy period in patients with generalized Myasthenia Gravis in whom complete remission was induced preoperatively via both acute(plasmapharesis) and long-term (corticosteroids with or without azathioprine) immunomodulating therapy.

The objective of this study was to observe the incidence of myasthenic crisis in patients with Myasthenia gravis with induction of complete remission via immunosuppressant therapy in the post-thymectomy phase.

PATIENTS AND METHODS

This was a prospective interventional study conducted in the Department of Thoracic Surgery, King Edward Medical University/Mayo Hospital Lahore between June 2009 and May 2017.A total of 132 patients 83 females and 49 males between ages 18 and 45 were registered in this study.Patients were evaluated clinically and history was taken on a pre defined questionnaire.

Inclusion Criteria

- All patients had extraocular Myasthenia Gravis with mild, moderate or severe generalized symptoms with or without Thymoma.
- All patients were put on immunosuppressant therapy (prednisolone with or without azathioprine) to induce complete disease remission.
- All patients were subjected to 2 to 5 plasmapharesis sessions in preoperative phase and were positively thymectomized within three weeks of the last session of plasmapharesis.

Exclusion criteria

- Patients not receiving immunosuppressant therapy
- Patients with any other co morbid conditions, e.g. ischemic heart disease, COPD etc.
- Patients with ocular Myasthenia Gravis

Data Collection: 132 patients were referred by the Department of Neurology, after medical management and induction of complete remission, to the Department of Thoracic Surgery. All patients underwent TranssternalThymectomy within three weeks of the last session of plasmapharesis. Patients were observed over the ensuing 2 weeks for any evidence of myasthenic crisis.

RESULTS

One hundred and thirty two patients, 83 females and 49 males in complete remission were thymectomizedvia trans-sternal approach. All these patients were observed for precipitation of myasthenic crisis in the post-operative phase. None of the patients had any clinical evidence suggesting myasthenic crisis or worsening of myasthenic symptoms in the early or intermediate post-operative phase. All these patients were followed over two weeks following surgery for this purpose. Two of the patients, both males over 35 years of age, however developed sternal dehiscence, one of whom required sternal rewiring via railroad technique, while the other patient recovered with conservative management via prolonged application of chest binder. Both these complications were attributed to the fact that both patients also had bronchial asthma which got precipitated in the post-operative phase. 12 patients, 7 females and 5 males had wound infection, which later on required removal of steel wires after three months of surgery. Rest of the patients had uneventful recovery.

DISCUSSION

Myasthenia Gravis is one of the most common autoimmune diseases causing skeletal muscle weakness ranging from ocular and bulbar muscle weakness to generalized weakness of the skeletal muscle system with eventual involvement of respiratory muscle leading to ventilatory failure precipitating a potentially life threatening condition referred to as Myasthenic crisis. Surgical removal of thymus continues to serve as a mainstay for the definitive treatment of this disease, which may act as a two-edged sword as surgical stress itself is a potential risk factor for precipitation of Myasthenic crisis.

This study establishes the importance of induction of complete remission of Myasthenic symptoms in preventing episodes of Myasthenic crisis in the post-operative period in thymectomized patients. For this purpose, all the patients included in this study were stabilized on cholinesterase inhibitor therapy and then put on immunosuppressant therapy, mainly oral prednisolone with or without azathioprine to induce complete remission of disease. All patients were subjected to plasmapharesis in the preoperative phase. Depending on the severity of symptoms and the duration of disease, 2 to 5 sessions of plasmapharesis on alternate days were performed and the patients were subjected to thymectomy within three weeks of the last session of plasmapharesis. Having followed this protocol, it was observed that not a single patient developed an episode of Myasthenic crisis, either at the time of reversal of

general anesthesia or during the two weeks following surgery. None of these patients required additional doses of pyridostigmine or corticosteroids and none of them required plasmapharesis in the post-operative phase. This was in stark contrast to another study in which 20 out of 110 thymectomized patients developed single or multiple episodes of Myasthenic crisis in the post-operative phase[14]. The only problems encountered by us in our study were sternal dehiscence in only two patients and surgical wound infection in 12 patients.

CONCLUSION

It is hereby concluded that immunosuppressant therapy and induction of complete remission of Myasthenia Gravis ensures the prevention of Myasthenic crisis in post-thymectomy patients, which if precipitated can have significant morbidity and mortality in such patients.

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