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OUTCOME IN PATIENTS WITH MYASTHENIA GRAVIS MANAGED WITH OR WITHOUT THYMECTOMY

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ABSTRACT

BACKGROUND: Myasthenia gravis is a chronic acquired autoimmune disorder in which autoantibodies are produced against acetylcholine receptors present on neuromuscular junction. It results in neuromuscular transmission blockage hence muscle weakness occurs. Thymus gland is considered as having crucial role in development of these antibodies. Screening patients for thymoma and removal of the thymus gland with surgery has an important aspect in management of disease.

OBJECTIVE: To compare the clinical outcome of patients with myasthenia gravis treated with or without thymectomy.

MATERIAL AND METHODS: Study design: Retrospective observational comparative study.


Procedure: 40 Patients with myasthenia gravis Osserman stage from 1 to 4 treated from 2014 to 2017, irrespective of age and gender were included. Diagnosis of myasthenia Gravis was based on positive EMG study, acetylcholine receptor antibodies and Pyridostigmine test (as Edrophonium was not available). Records of 20 patients that underwent thymectomy and 20 patients which were managed conservatively were obtained. Outcome in patients having thymectomy was assessed on the basis of MGFA Post intervention status after 1year.

RESULTS: study sample (40 patients) includes 15 males and 25 females. The mean age of patients was 33 years (range 14 to 63, SD 11.2). In thymectomy group, 7 males and 13 females (age range 16 to 53years, means age 32, SD 10) that underwent thymectomy. With thymectomy, 14 patients improved, 6 remained unchanged while no patients showed worsening or exacerbation of their symptoms. There were 8 males and 12 females of age 14 to 63 years that were managed without thymectomy. Of them, 2 patients improved, 6 remained unchanged, and 12 had worsened symptoms while no patients showed exacerbated symptoms. The difference among the two groups was statistically significant (p<0.05).

Conclusion: After thymectomy there was a substantial dose reduction in antmyasthenic treatment with minimum or no exacerbation as compared to patients without thymectomy. So all patients of myasthenia gravis should be offered thymectomy as a part of treatment. This conclusion is in line with guidelines for the management of myasthenia gravis.

KEY WORDS: myasthenia Gravis, thymectomy, complete remission.

INTRODUCTION

Myasthenia gravis (MG) is a chronic acquired autoimmune disease of neuromuscular junction leading to muscular weakness. There are large number of molecules, including ion channels and various proteins, present at the neuromuscular junction, which can be targeted by autoantibodies resulting in blockage of neuromuscular transmission.1 Population-based studies of the epidemiology of myasthenia gravis have been conducted for over 50 years. A clear increasing trend has been reported. Recently, estimated prevalence is about 20 per 100,000 in United States.2 Patients with myasthenia gravis have fluctuating fatigability in voluntary muscles of body predominantly ocular, oropharyngeal, facial,
respiratory and limbs muscles. The role of thymus gland in pathogenesis of myasthenia gravis is incompletely understood, but consider as major driving factor for the production of acetylcholine receptor autoantibodies. Mostly patients with myasthenia gravis have thymic abnormalities, i.e. >50% is thymic hyperplasia, and 10–15% is a thymic neoplasm. Treatment is with pharmacological measures with or without thymic surgery. Medication consists mainly of acetylcholinesterase inhibitors (such as neostigmine, pyridostigmine) which reduce the breakdown of acetylcholine at the neuromuscular junction and hence increase the amount of acetyl choline available to act on the remaining post synaptic receptors. Alongside with this symptomatic therapy, immunomodulators are used to dumpen the autoimmune response. Thymectomy is one of the treatment modality to treat MG. The removal of thymus gland with surgery has been an alternative treatment modality for myasthenia gravis since Blalock had performed a successful thymectomy in young female with MG and thymus cysts. We aimed to conduct this study to find the beneficial role of thymectomy for myasthenia Gravis patients in recovery from myasthenia.

OBJECTIVE
To compare the clinical outcome of Myasthenia Gravis patients treated with or without thymectomy.

MATERIAL AND METHODS
Study design: Retrospective, observational comparative study.

Setting: Department of Neurology, Mayo hospital, Lahore.

Duration: Patients with MG treated from 2014 to 2017.

Sampling technique: Non-probability, consecutive sampling.

Selection criteria:
Inclusion criteria: all patients with myasthenia gravis, Osserman stage from 1 to 4 treated from 2014 to 2017, irrespective of age and gender.

Exclusion criteria: Patients with recurrent myasthenia Gravis, ocular myasthenia with normal thymus having disease less than one year, HIV patients.

Data collection: After taking approval from ethical committee, medical record of 40 patients was obtained. Diagnosis of myasthenia gravis was based on positive EMG/RNS study, acetylcholine receptor antibodies and Pyridostigmine test (as Edrophonium was not available). Record of 20 patients that underwent thymectomy and 20 patients that did not get thymectomy was obtained. Then patients were called for follow-up and clinical assessment was be done for myasthenia Gravis. Outcome in patients having Thymectomy assessed on the basis of MGFA Post intervention. Complete remission of disease was defined as patients with normal muscle strength, without medications for myasthenia gravis for at least 1 years (fig 1). Data was entered and analysed by SPSS 21. Both groups were compared for complete remission by using chi-square test and p-value≤0.05 was considered as statistically significant.

RESULTS
Study sample (total 40 patients) includes 15 males and 25 females. The mean age was 33 years (range 14 to 63, SD 11.2). Table 1 In thymectomy group, 7 males and 13 females (age range 16 to 53 years, Mean age was 32, SD 10) that underwent thymectomy. With thymectomy, 14 patients improved, 6 remained unchanged while no patients showed worsened or exacerbated symptoms. There were 8 males and 12 females of age 14 to 63 years that did not undergo thymectomy. Without thymectomy, 2 patients improved, 6 remained unchanged. The difference was significant (p<0.05). Fig 2 In both groups, complete stable remission was absent in all patients, pharmacologic remission was also nil while minimal manifestation status 3 was observed in all patients in both group (100%). Fig 3

DISCUSSION
Thymic abnormalities like Thymomas are present in 10% of patients with myasthenia gravis, and thymectomy is mandatory. Mostly published literature on thymectomy has consisted of either non-randomized observational trials or case-control studies, mainly relying on remission rates. The potential benefits of thymectomy in improving clinical outcomes in myasthenia gravis (MG) patients without thymic abnormalities is still under study, despite the fact that it is used in clinical practice for more than 60 years. Thymectomy improves various clinical parameters and reduces the need for pharmacological treatment in patients with myasthenia gravis. When combined with
standard immunosuppressive therapy, surgery gives more benefits as compared with steroids alone. Importantly it also decreases the requirement for steroids or immune suppressants, hence their side effects.\textsuperscript{12} In our study, we observed that patients in thymectomy group were improved clinically, pharmacological remission with minimal manifestation (MM3). Patients in non-thymectomy group had frequent exacerbations than thymectomy group. Regardless of MG condition, all patient should undergo thymectomy (with or without thymoma). Thymectomy is indicated in myasthenia gravis to improve clinical outcomes and reduce the need for immunosuppressive drugs in patients with myasthenia gravis.\textsuperscript{13} According to another trial, 26.0% patients were in complete stable remission, 35.6% patients were without symptoms on reduced medications, and 17.8% patients had clinical improvement even further dose reduction. Overall, 79.4% of patients benefited with surgery, 8.2% had unchanged clinical status in disease, and 12.3% showed worsening clinically.\textsuperscript{14} However, the complete stable remission rate (26.0%) was less as compared to other reported series (14.4%-47%).\textsuperscript{15-17} In another trial, 113 consecutive thymectomies were done in patients with MG, complications rate was 14%. Complete stable remission was noticed in 21% of patients, and significant improvement of MG in 54%, so total beneficial rate was 75% and 14% had unchanged status, and 11% (10 of 92) were worsened clinically.\textsuperscript{18} In another trial, 42 patients with myasthenia gravis having thymoma were compared with 42 MG patients without thymoma using a modified Osseman classification. The mean Osseman grades at time of diagnosis, 6 months, 5 and 10 years post-thymectomy did not differ among groups. Results indicate that thymoma should not be considered as major poor prognostic factor for the long-term outcome of MG.\textsuperscript{19} Thymectomy exhibits satisfactory long-term clinical benefits in patients with myasthenia gravis without thymic abnormalities. Although presence of anti-MuSK antibodies correlates with poor response to operation.\textsuperscript{20} Thymectomy improved clinical status over a 3-year period in patients with myasthenia gravis without thymic abnormalities.

CONCLUSION

After thymectomy there is substantial dose reduction in anti myasthenic treatment with minimum or no exacerbation as compared to non-thymectomy patients. There are significant better results with thymectomy. So all patients of myasthenia gravis should be offered thymectomy as a part of treatment.
**INTRODUCTION**

10,000 cases of myasthenia gravis (MG) are present in the United States.2 Patients with MG have a recent estimated prevalence of about 20 per 100,000 in the United States. A clear increasing trend has been reported. 

**MATERIAL AND METHODS**

We aimed to conduct this study to understand the role of thymectomy in MG. Osserman stage from 1 to 4 treated from 2014 to 2016 was considered in this study. Inclusion criteria:

- Osserman stage from 1 to 4 treated from 2014 to 2016
- Thymectomy was performed
- Follow-up was maintained for at least 1 year

**RESULTS**

Thymectomy is indicated in MG to treat abnormal thymic abnormalities. Although presence of anti-MuSK autoantibody is associated with thymic abnormalities, the role of thymus in MG is still under study. Despite the fact that thymectomy improves various clinical parameters and reduces the number of PTU, the complete stable remission rate (26.0%) was observed in all patients in the thymectomy group. In another trial, 42 patients with MG were treated with thymectomy, and 113 consecutive patients with MG were treated with PTU. In the control group, 25 patients were treated with PTU, and 13 females (age range 16 to 53 years, Mean age 33 years) were treated with PTU, while no patients showed worsened or improved. The difference was considered as statistically significant (p<0.05). Fig 2 In both groups, complete remission of disease was noticed in 21% of patients, and complications rate was 14%. Complete stable remission was noticed in 21% of patients, and 14% had unchanged and 6 remained unchanged. The difference was considered as statistically significant (p<0.05).

**CONCLUSION**

Thymectomy exhibits satisfactory long-term clinical outcome, and the complete stable remission rate (26.0%) was observed in all patients in the thymectomy group. Regardless of MG condition, all patient should get thymectomy was obtained. Then patients were compared. Post intervention. Complete remission of disease was noticed in 21% of patients, and 14% had unchanged and 6 remained unchanged while no patients showed worsened or improved. The difference was considered as statistically significant (p<0.05). Fig 2: Comparison of long-term outcome in both groups.

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INTRODUCTION

Recently, estimated prevalence is about 20 per 100,000.7 Population-based studies of the epidemiology of myasthenia gravis since Blalock had performed a successful thymectomy exhibit an improved long-term clinical remission.8-10 Osserman stage from 1 to 4 treated from 2014 to 2017.11 This study intended to compare clinical outcome of Myasthenia Gravis (MG) treated with or without thymectomy. We hypothesized that patients treated surgically will have better clinical outcome, as thymectomy is one of the treatment modality to treat MG.12

MATERIAL AND METHODS

Thymectomy is one of the treatment modality to treat MG. Thymic abnormalities like Thymomas are present in 10–15% of myasthenia gravis patients.13 According to another trial, 26.0% patients have thymic abnormalities.14

Duration: Patients with MG treated from 2014 to 2017 in Lahore. Non-probability, consecutive patients treated with or without thymectomy. To compare the clinical outcome of Myasthenia Gravis patients, we hypothesized that patients treated with thymectomy will have better clinical outcome, as thymectomy exhibits satisfactory long-term clinical remission.15

Patient characteristics: In this study, 40 patients with MG were recruited and followed for 1 year post thymectomy. Data was entered and analysed by SPSS version 20, and p-value≤0.05 was considered as statistically significant.

Conflict of interest: Author declares no conflict of interest.

Funding disclosure: Nil

Author’s contribution:

Safia Bano: concept, data collection, data analysis, manuscript writing, manuscript review
Muhammad Ather Javed: data collection, data analysis, manuscript writing, manuscript review
Waqas Arshad: data collection, data analysis, manuscript writing, manuscript review

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