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Safia Bano
KEMU, Lahore Pakistan, safiabano207@gmail.com

Muhammad Athar Javed
KEMU, Lahore Pakistan

Waqas Arshad
KEMU, Lahore Pakistan

OUTCOME IN PATIENTS WITH MYASTHENIA GRAVIS MANAGED WITH OR WITHOUT THYMECTOMY

Safia Bano[1], Muhammad Athar Javed[2], Waqas Arshad[3]
[1]Assistant Professor, Neurology department, MHL/KEMU, Lahore, [2]Professor, Neurology department, MHL/KEMU, Lahore,

Correspondence to: Safia Bano, *E-mail: safiabano207@gmail.com*

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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.

SETTING: Department of Neurology, Mayo hospital, Lahore. Duration: patients with myasthenia gravis from 2014 to 2017.

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 antimyasthenic 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.[3] 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.[4] 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.[5] Thymectomy is one of the treatment modality to treat MG.[6] 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.[7] We aimed to conduct this study to find the beneficial role of thymectomy for myasthenia Gravis patients in recovery from myasthenia.

We aimed to conduct this study to understand the potential benefits of thymectomy in our myasthenia gravis patients. We hypothesized that patients treated with thymectomy will have better clinical outcome, compared to the patients managed purely with pharmacological means.

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 in OPD 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 1years (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$\leq$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.[8] Mostly published literature on thymectomy has consisted of either non-randomized observational trials or case-control studies, mainly relying on remission rates.[9 10] 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.[11] 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.[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.[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.[14] However, the complete stable remission rate (26.0%) was less as compared to other reported series (14%-47%).[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.[18] In another trial, 42 patients with myasthenia gravis having thymoma were compared with 42 MG patients without thymoma using a modified Osserman classification. The mean Osserman 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.[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.[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.

Fig 1: criteria for assessment of Myasthenia Gravis patients after thymectomy (MGFA-PIS)

Complete remission: pt. no S/S of MG for one year and no medication

Remission CSR: no clinical weakness on examination
Pharmacological remission: same as CSR, taking medicine but no on cholinesterase inhibitors

MM: No symptoms but weakness on clinical examination

MM0: pt. did not receive MG treatment for one year

MM1: pt. is taking immunosuppression but no cholinesterase inhibitors

MM2: pt. is taking cholinesterase inhibitors <120mg pyridostigmine for a year

MM3: pt. is receiving both immunosuppressant and cholinesterase inhibitor

CHANGE IN STATUS

IMPROVED: a decrease in clinical manifestations or dose reduction in previous treatment Unchanged: no change in clinical manifestations or dose reduction in previous treatment

WORSE: increase in pre-treatment clinical manifestations or dose

EXACERBATION: pt who is fulfilling criteria of CSR or PR but showing clinical worsening

DIED: death of MG pt. either on treatment or after thymectomy

Fig 2: Comparison of outcome in both groups (p>0.05)

Fig 2: Comparison of long term outcome in both groups

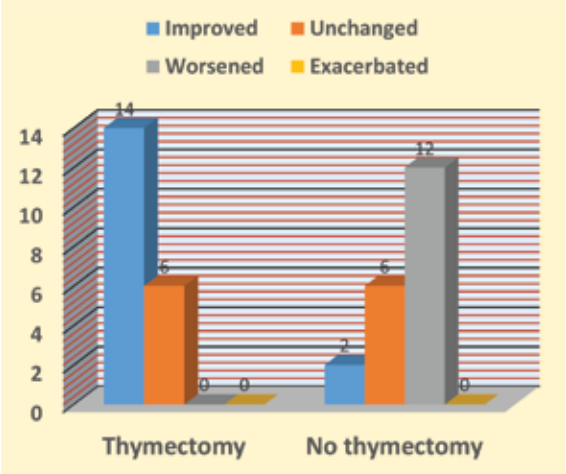
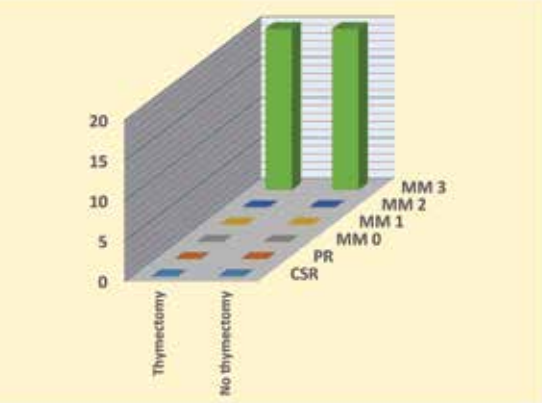


Fig 3: Comparison of long-term outcome in both groups



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Safia Bano; concept, data collection, data analysis, manuscript writing, manuscript review
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Waqas Arshad; data collection, data analysis, manuscript writing, manuscript review