

Role of thymectomy in myasthenia gravis

Shende S¹, Potwar S², Nagle K³, Pohekar P⁴, Nathani R⁵, Nair H⁶

¹Dr Shweta Shende, Assistant Professor, Cardiovascular & Thoracic Surgery, ²Dr Sushrut Potwar, Assistant Professor Cardiovascular & Thoracic Surgery, ³Dr Kanak Nagle, Professor & Head of Department, Cardiovascular & Thoracic Surgery, ⁴Dr Pankaj Pohekar, Resident, General Surgery, ⁵Dr Rahul Nathani, Resident, General Surgery, ⁶Dr Hari Nair, Resident, General Surgery, all authors are affiliated with TNMC & BYL Nair Hospital, Mumbai, Maharashtra, India.

Address for Correspondence: Dr Sushrut Potwar, Email: sspotwar@gmail.com

Abstract

Aims and Objective: The aim of study is to show the effect of thymectomy with symptomatic improvement in patients and decrease in dose of medication requirement. To study the outcome of patients with respect to histology, duration of symptoms, remission of symptoms and post operative outcome. **Methods:** We prospectively analysed 28 patients with symptoms of myasthenia gravis with respect to patients profile, patients remission of symptoms with respect to age, and grade of disease, the response to thymectomy with respect to histology, and duration of symptoms. **Result and Conclusion:** Patients mainly present with easy fatigability, patients with mild disease respond well to surgery, hyperplasia is favorable histology for remission and lesser the duration of symptoms more are the chances of remission of disease.

Keywords: Myasthenia gravis (MG), Thymectomy, Thymus gland pathology

Introduction

Myasthenia gravis is an autoimmune disease of disordered neuromuscular transmission resulting in exertional fatigue and weakness of voluntary muscles, due to specific antibody directed against the acetylcholine receptor complex of the motor end plate [1]. This clinical disorder was described by Thomas Willis 300 yrs ago. Modalities of treatment available are

1. Acetylcholinesterase inhibitors
2. Steroids
3. Immunosuppressive drugs
4. Plasmapheresis & Immunotherapy
5. Thymectomy [2]

From the beginning of twentieth century, a relationship between the thymus gland and myasthenia gravis was suggested. In 1939, Blalock reported improvement in myasthenia gravis patients after removal of thymic tumour [3]. Thymectomy has emerged as a definitive form of treatment in myasthenia gravis. We study the result of thymectomy in 28 patients of myasthenia gravis.

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Aims & Objectives

28 thymectomies were done in patients of myasthenia gravis in the last 2yrs (2013-2015) at TNMC & BYL Nair Hospital, Mumbai. The aim of study is to show the effect of thymectomy with symptomatic improvement in patients and decrease in dose of medication requirement.

Materials & Methods

The study includes 28 non randomized patients who underwent thymectomy for myasthenia gravis in the cardiac surgery unit at Nair Hospital by trans-sternal route between October 2013 to 2015.

Inclusion criteria: Patients with myasthenia gravis.

Exclusion criteria – Patient not willing and not fit for surgery.

Most common clinical feature was generalized weakness and fatigability other symptoms are dysphasia, dysarthria, weakness of mastication muscles. Clinically myasthenia gravis patients were classified according to Osserman and Genkins classification [4].

- 1) Paediatric Myasthenia gravis
 - a) Neonatal group
 - b) Juvenile group
- 2) Adult Myasthenia Gravis Ocular
 - a) Generalized disease -Mild
 - b) Generalized disease-Moderately severe
- 3) Acute fulminating disease
- 4) Late severe disease

There was no patient with exclusively ocular symptoms in our study

All patients were evaluated by following tests.

- 1) Pharmacological tensilon (i.e.Edrophonium chloride) test.
- 2) Electrophysiological test:-
 - Repeated nerve stimulation test (RNS)
 - Single fibre electromyography (EMG)
- 3) Serological test - Anti Ach-R antibodies
- 4) Chest X -ray
- 5) Computed Tomography scan thorax
- 6) Routine blood investigations
- 7) Pulmonary function test.
- 8) Arterial Blood Gases and electrolytes
- 9) Electrocardiography

RNS test was positive in all patients. CXR & CT scan showed thymoma in four patients. Immunological testing was performed in all patients and anti Ach R antibodies were found elevated in all patients. In majority of patients from stage II b and III, pulmonary function test was deranged.

All patients were classified according to Osserman and Genkin's clinical classification and given.

- T. Mestinon 60 mg tds.
- T. Prednisolone 60mg/ day. Two patients from Osserman's class III required 5 cycles of plasmapheresis and then stabilized on above drugs. After stabilization patients were referred for thymectomy. Tab Mestinon was stopped from previous evening as it increases respiratory secretions as well as its response becomes erratic after surgery. Hydrocortisone was given intraoperatively.

Anaesthesia- The anaesthetic medications were minimized because of the risks of aggravating the

myasthenic symptoms. Muscle relaxants were avoided. Induction was done with thiopental and maintained on nitrous oxide and oxygen. Tracheal intubations and general anaesthesia was used in all patients. Postoperatively all patients were kept on ventilator for few hours and then extubated.

Procedure- Patient in supine position, anterior chest wall scrubbed. A midline sternotomy done from suprasternal notch to xiphoid cartilage. External retractor is passed and chest is spread. The margins of the dissection were from diaphragm to neck. Both cervico mediastinal lobes, supradiaphragmatic and mediastinal fat, fatty tissue in the neck was removed. All tissue were sent for histopathology testing.

Postoperative Care: Patient was kept on ventilator and adequate nursing care given.

Patients were evaluated by

1. Repeated arterial blood gases
2. Pulseoximetry
3. Electrolytes

Patients were gradually weaned off the ventilator and extubated. The mean extubation time was around 6 hrs. To prevent pulmonary atelectasis patients were given vigorous chest physiotherapy, incentive spirometry and good analgesic drugs. Aminoglycosides antibiotics were avoided. Mestinon was given in 3/4th of the previous day dose. Prednisolone was continued on the same dose and gradually tapered according to clinical response of the patients. All patients were discharged on Tab. Mestinon, Prednisolone for 1 month. Four patients developed wound infection and were treated with antibiotics, dressing and secondary suturing.

Follow up: Clinical examination was done and muscle strength monitored by single breath count and incentive spirometry. According to patient's symptoms the drug dosage was reduced and adjusted over 6 months to 1 year. Corticosteroid was tapered in 14 patients and omitted in 10 patients.

The response was assessed & categorized according to Osserman's response scale

A: Remission

B: Marked clinical improvement with decrease in the drug dosage.

C: Moderate clinical improvement without decrease in the drug dosage

D: Deterioration after thymectomy.

Observation & Results

All 28 patients were classified according to to Osseman's clinical classification. Out of 28 patients—

Stage IIa -14 patients

Stage IIb-10 patients

Stage III -4 patients

Table No 1: Response to thymectomy was assessed with respect to Osseman's clinical Stage.

	A	B	C	D
IIa	6	8	0	0
IIb	4	6	0	0
III	0	0	4	0
	10	14	4	0

Table no. 2 shows 10 patients went in to remission . Out of 10, 6 patients were from IIa stage and 4 patients from IIb. Out of 14 patients which showed marked clinical improvement with decrease in the drug dosage 8 patients were from IIa and 6 patients were from IIb. 4 patients from stage III showed moderate clinical improvement without decrease in the drug dosage.

Out of 10 patients who went into remission 5 were male and 5 female. Out of 14 patients, 10 males and 4 females showed marked improvement with decrease in drug dosage

Table 2: Response to thymectomy with respect to age

Age In Yrs	A	B	C	D
11-20	0	3	0	0
21-30	2	3	0	0
31-40	3	4	2	0
41-50	5	4	0	0
51-60	0	0	2	0
Total	10	14	4	0

In our study there were no patients from 1st decade of life and >60 yrs. Out of 10 patients who showed remission ,5 patients were from 5th decade,3 were from 4th decade,2from 3rd decade. Out of 14 patients with clinical improvement -4 patients were from 4th and 5th decade each and 3 patients were from 2nd and 3rd decade. 2 patients from 4th and 6th decade showed moderate clinical improvement without any decrease in the drug dosage.

Histology of thymus:

Table 3: The response to thymectomy with respect to histology was assessed.

HISTOLOGY	A	B	C	D
Normal or involuted	2	5	2	0
Hyperplasia	7	6	2	0
Thymoma	1	3	0	0
Total	10	14	4	0

In our study 15 patients showed hyperplasia, 4 showed thymoma, 7 showed normal or involuted histology. All thymomas were encapsulated. Out of 10 patients who went in to remission 2 patients showed normal or involuted histology, 7 showed hyperplasia, 1 showed thymoma. Out of 14, who showed marked clinical improvement, 5 showed normal or involuted histology. 6 showed hyperplasia and 3 showed thymoma.

Table 4: Response to thymectomy with respect to preoperative duration of symptoms.

Duration	A	B	C	D
3-6 months	6	8	0	0
6-12 months	2	2	0	0
>12months	2	4	4	0
TOTAL	10	14	4	0

In our series, 14 patients who underwent thymectomy had preoperative duration of symptoms 3-6 months. We noticed complete remission in 6 patients and marked clinical improvement with decrease in drug dosage in 8 patients. No patient showed deterioration after early thymectomy. 4 patients had duration of symptoms for 6-12 months and underwent thymectomy. 2 patients showed remission and 2 patients showed marked clinical improvement with decrease in the drug dosage. Total 10 patients had preoperative duration of symptoms of > 12 months. 2 patients went into remission, 4 patients showed marked clinical improvement with decrease in drug dosage and 4 patients showed moderate clinical improvement without any decrease in drug dosage.

Discussion

Study included patients from 2nd decade to 60 yrs. There were no patients from 1st decade of life and > 60 yrs of age. Common age of presentation was between 11-50 yrs with peak age of clinical presentation between 31 to 50 yrs.

Hans J.G.H. Oosterius from his study of 464 patients reported the age group ranging from 1-79 years and peak age of presentation was between 10 and 40 yrs. [4]

Age group of patient with myasthenia gravis is almost similar everywhere with minor variations.

Sex Distribution: Out of 28 patients, males outnumbered (17) female patients (11). In both sexes, peak age of clinical presentation was 2nd to 4th decade. In older age group (51-60 yrs) males were affected more than females. Williams H. Frist noticed from his study of 46 patients, 12 males and 34 females. The more common age of presentation was in 3rd and 5th decade and men were involved more in elderly group [5].

Clinical Presentation: In our series there was no patient suffering from ocular myasthenia gravis (stage I). Mild generalized myasthenia gravis (Osserman's stage IIa) was found in 14 patients (50%). Moderate generalized myasthenia gravis (Stage IIb) was found in 10 patients (35.70%). There were 4 patients (14.2%) from fulminating myasthenia gravis. The commonest clinical presentation was mild and moderate generalized myasthenia gravis. Grob D found 15% cases of ocular

myasthenia gravis & 85% cases of generalized myasthenia gravis [6].

Treatment Spectrum: All 28 patients were on corticosteroids and mestinon pre and post operatively. Out of 14 patients of mild generalized myasthenia gravis 6 (21.4%) patients went into remission, 8 (28.5%). patients showed marked clinical improvement with decrease in all the three drugs dosage and stabilized on that dosage. In moderate generalized myasthenia gravis (Stage IIb) out of 10 patients 4 patients showed remission with complete stoppage of all drugs, 6 patients showed marked clinical improvement with decrease in all 3 drugs.

4(14.28%) patient from stage III showed improvement without decrease in dose of medication. Mulder and associates found 85% remission in stage I, 36% in stage II, 20% in stage III and 12% in stage IV respectively [7]. Patients with mild generalized myasthenia gravis tend to revert to remission more than patients with generalized myasthenia gravis.

In our study patients in age group 4th decade showed remission. Oosterius H J et al reported patients between 10-40 yrs had better outcome after thymectomy than those older than 40 yrs [4]. In our study 15 patients showed hyperplasia of thymus, 4 patients showed thymoma (all cortical) and 9 showed normal or

involved histology. 7(25%) patients from hyperplasia

group went into remission, 2 (7.14%) patients from normal or involuted histology and 1 (3.57%) patient showing thymoma on histology went into remission. Out of 14 patients who showed marked clinical improvement with decrease in the drug dosage; 5 (17%) showed normal or involuted histology, 6(21.42%) showed hyperplasia and 3(10.71%) showed thymoma. Thus 46% patients with histology of hyperplasia of thymus showed favourable outcome for patients. Karbhase Jayant et al also noticed hyperplasia in 23 patients out of 25 patients 48% (12) patients had remission and 36% (9) patients had marked improvement with decrease with the drug dosage. [8,9] Yasumas Moden et al also found that remission rate in non-thymoma patients was 10% higher when compared with thymoma patients[10,11]. Rubin W Joseph et al reported 22 patients of myasthenia gravis after thymectomy; 13 patients had hyperplasia of which 7 patients had complete remission, more so patients with duration of less than 1 year. [12]

Relation of preoperative duration of symptoms to thymectomy: In our study out of 10 patients who showed remission-6 patients had symptoms for 3-6 month. All 8 patients who showed marked improvement had symptoms for 3-6 months. All 4 patients who showed moderate improvement without decrease in drug dose were having >12 months of duration of symptoms.

Yasumasa Moden reported serial follow up of patients underwent thymectomy with preoperative duration less than 1 year in one group and more than 1 yr in second group. He found remission rates in 1st group and second group were 14% and 5% respectively at 3 months after surgery 23% and 6% at 6 months, 38% and 13% at one year [10,11]. Gabriel Genkinsand Oosterius also reported early thymectomy in the patients of myasthenia gravis had better remission rates as we found in our study [4]. The explanation for better response to early thymectomy is on basis of injury to Ach-R occurs mainly during first year of clinical presentation [6]. Remission rate after thymectomy when compared with respect to sex, we found male and female (5 each) 17.8% went into remission. Donald G. Mulder reported female patients were found to be in remission 32.4% cases and male patients were in 23% cases [7].

As compared to Mulder study, our series both male and female showed equal remission rates (17.8%). In our study all patients who underwent early thymectomy had

good remission rate as in Oosterius and Yasumasa Moden et al study.

Conclusion

Thymectomy is very important treatment modality for patients with Myasthenia gravis. Early thymectomy after medical stabilization of patients helps to improve clinical state of myasthenia gravis patients. Duration of symptoms plays a very important role with this respect. Early presentation and early thymectomy keeps patient asymptomatic. Patients having thymoma or hyperplasia of gland with MG, thymectomy shows definite improvement in the clinical status.

Median sternotomy approach is good for exposure and dissection of thymus and extrathymic tissue. Thus thymectomy is definitive curative option for patients with myasthenia gravis.

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