**ABSTRACT**

**Objective:** To determine outcome and postoperative complications of trans-sternal thymectomy for myasthenia gravis.

**Study Design:** Experimental, prospective.

**Place and Duration of Study:** The study was conducted at Department of Surgery, Pakistan Institute of Medical Sciences (PIMS), Islamabad from June 2009 to June 2012.

**Materials and Methods:** We included 30 consecutive patients from all age groups either coming to Surgical outpatient clinic or referred from Neurology unit having generalized myasthenia gravis between 12-55 years of age, thymic mass on radiology or poor medical control of disease with no contra indications to surgery. Patients unfit for anaesthesia due to any reason or inoperable thymic tumour were excluded. We studied outcome and post-operative complications in all patients after total thymectomy through trans-sternal approach for 24-40 months. All patients were assessed for haemorrhage, transfusion requirement, shock, myasthenia crisis, respiratory infection, wound infection, delayed healing of wound and dehiscence and pulmonary embolism. Remission of disease was assessed according to De Filippi classification. The data was collected by post graduate trainees on a pre-designed proforma and analysed by SPSS 10. The descriptive statistics were applied and results were shown in percentage.

**Results:** In total 30 patients, mean age was 37±8.6 years. All patients needed at least two units of blood transfusion. We observed pleural damage in 20 patients (66.67%), respiratory infection in 20 (66.67%), myasthenia crisis in 8 (26.7%), minor wound infection in 6 (20%), mortality in 4 patients with thymic carcinoma(13.33%). Artificial ventilation discontinued within 24 hours in 22, at 7th day in 4 and at 14th days in 4 patients. Wound dehiscence occurred in 1(3.33%), cardiac arrest in 1 (3.33%). Mean hospital stay was 13.6 (7-45) days. Six patients (20%) were symptom free without drugs and 9 patients (30%) were symptom free with drugs at 2 years.

**Conclusion:** Trans-sternal total thymectomy provides good results for symptom control in benign thymic conditions. The major complication is haemorrhage needing transfusion. Other complications can be managed successfully by conservative treatment.

**Key Words:** Trans Sternal Thymectomy, Myasthenia Gravis, Thymic Tumour.

**Introduction**

Myasthenia Gravis (MG) occur due to formation of antibodies against acetylcholine receptors at myoneuronal junctions and presents with muscle weakness and fatigability. Most of patients develop generalized weakness involving bulbar, limb musculature, extensors of neck and diaphragm. Antibody to muscle-specific kinase (MuSK) may be positive in sero-negative MG patients and they develop involvement of respiratory muscles, shoulder and neck without ocular weakness. Treatment comprises of four methods: anticholinesterase drugs, immune-suppressive agents, removal of thymus, and immunotherapies, like exchange of plasma and intravenous immunoglobulin (IVIG). Blalock et al found the successful outcomes of thymectomy in MG in 1941. Since then surgery is widely being used as a for such patients. In fact, thymectomy is considered, by neurologists, as a first-line therapy in most patients with thymoma or generalized myasthenia to achieves sustained improvement or remission. About three fourth of such people have abnormality in thymus; of them, hyperplasia in 85% and thymoma in 15%. Thymoma is the most common mediastinal tumour (25%). Median sternotomy is considered safe and effective approach for...
thymectomy, especially for ectopic locations. Data of the efficacy and complications of thymectomy in patients with MG via median sternotomy is limited in Pakistan. The authors, in the current study, made an effort to determine the safety of median sternotomy in patients with MG and then outcome of thymectomy.

Materials and Methods

This experimental, prospective study was conducted between June 2009 and June 2012 in department of Surgery, Pakistan Institute of Medical Sciences (PIMS). We included 30 consecutive patients from all age groups either coming to Surgical Out Patient Department or referred from Neurology unit of PIMS with generalized myasthenia gravis having the disease for less than 5 years, thymic mass on radiology (mediastinal widening) or poor medical control of disease with no contra indications to surgery usually grade II B & III. The patients unfit for anaesthesia due to any reason or inoperable thymic tumour were excluded. The data was collected by post graduate trainees on a pre-designed proforma. After detailed history, thorough examination and routine investigations, specific investigations including Tensilon test, Electromyography (EMG), X-ray chest and CT Scan of chest to assess anatomical location, thymoma and vascular relationships were carried out.

All patients remained in care of a multidisciplinary team including surgeon, neurologist, pulmonologist, respiratory therapist, anaesthetist and intensivist. The patients were stabilized on drugs preoperatively but anticholinesterase drugs were stopped 6-8 hours before surgery. Patients taking oral steroids were tapered gradually. Plasmapheresis was done 3 days before surgery. Blood group, cross match, and ventilator in intensive care unit (ICU) were arranged and informed consent taken. The antibiotic prophylaxis consisted of three intravenous doses of 1g of Ceftriaxone, at induction, at 12 and 24 hrs post operative period respectively.

General anaesthesia without muscle relaxants and median sternotomy approach was used in all patients. The vascular pedicles tied and gland separated by blunt dissection from surrounding structures. Total thymectomy was done removing all tissue of thymus and mediastinal fat from the diaphragm and pericardium inferiorly to the thymic extension in neck superiorly upto thyroid and from one phrenic nerve to the other. Pleural damage, when occurred, repaired and chest drain placed in right chest wall, across the mediastinum and upto contra-lateral apex connected to under water seal. All surgeries were performed by one experienced surgeon with a dedicated team.

In post operative phase, all patients were monitored in ICU until their vital signs got stable and anaesthetist declared safe to shift to ward. Neurologists reviewed them and anticholinesterase drugs started if any signs of disease were found. We avoided, in all patients, sedatives, narcotics and muscle relaxants. We studied the post operative complications by assessment of haemorrhage, transfusion requirement, shock, myasthenia crisis, respiratory infection, wound infection, delayed healing of wound and dehiscence and pulmonary embolism.

On the basis of remission of disease according to De Filippipost operative classification, we assessed the outcome.

Class I: remission complete, without medication
Class 2: symptom free, less medication
Class 3: improved, decreased symptoms or medication
Class 4: no improvement
Class 5: worsening symptoms

Remission was defined as no symptom of myasthenia gravis or cessation of medical treatment without reappearance of any symptoms.

All patients were followed for 24-40 months (average 27) in surgical OPD and advised to consult on appearance of any of the signs and symptoms of myasthenia again. The data was analysed by SPSS 10. The descriptive statistics were applied and results were shown in percentage.

Results

Mean age of patients was 37±8.6 years. Neuromuscular blocking drugs, atropine and morphine were avoided during anaesthesia and no significant complication of anaesthesia was observed. Pleura was damaged in 66% of patients which was managed by chest intubation. Cardiac arrest occurred in one patient which was managed by internal cardiac massage and patient revived. Myasthenia crisis was observed in 8 patients, which was successfully managed in 4 patients. Three
patients died within 2 weeks and one survived for next 6 weeks. All 4 had carcinoma of thymus (Osserman’s group III). Respiratory infection was noted by symptoms of cough with sputum and irritation in throat in 6 (20%). All were successfully managed by medical treatment and physiotherapy. In post operative period, nasal endotracheal tube was kept for ventilation in ICU for 24 hours. In 22 patients, vital capacity was found to be 1.5-2 litres within 24 hours and artificial ventilation discontinued and patient ambulated. Endotracheal tube kept in place for further 3-4 days as a precaution. Four patients were extubated at 7th day while 4 patients needed re-intubation and ventilator support for next 14 days. Chest radiograph taken to exclude hemo/pneumothorax. Skin stitches removed on 7th-10th post operative day and patient discharged home.

Minor wound infection was observed in 6 cases (20%) and was managed successfully by local antiseptics. One patient on steroids for long period developed wound dehiscence, which was managed by pectoral myoplasty by a plastic surgeon. Mean hospital stay was 13.6 (7-45) days. Further results are in table I.

**Table I: Post operative complications (n= 30)**

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemorrhage needing transfusion 2 units</td>
<td>30</td>
<td>100</td>
</tr>
<tr>
<td>Pleural damage</td>
<td>20</td>
<td>66.6</td>
</tr>
<tr>
<td>Respiratory infection</td>
<td>20</td>
<td>66.6</td>
</tr>
<tr>
<td>Myasthenia crisis</td>
<td>8</td>
<td>26.7</td>
</tr>
<tr>
<td>Wound infection</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>Mortality</td>
<td>4</td>
<td>13.3</td>
</tr>
<tr>
<td>Wound dehiscence</td>
<td>1</td>
<td>3.4</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>1</td>
<td>3.4</td>
</tr>
</tbody>
</table>

**Table II: Symptoms control of myasthenia after thymectomy (n= 30)**

<table>
<thead>
<tr>
<th>Status of Symptoms</th>
<th>Number of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom free without drugs</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>Symptom free with drugs</td>
<td>9</td>
<td>30</td>
</tr>
<tr>
<td>Mild symptoms with drugs</td>
<td>9</td>
<td>30</td>
</tr>
<tr>
<td>Severe symptoms with drugs</td>
<td>1</td>
<td>3.3</td>
</tr>
</tbody>
</table>

**Discussion**

Thymectomy is one of the most effective treatment modalities to stop progression of symptoms in MG. The observations in different parts of the world, of the disease and the outcome of procedures are not the same.

In the study of Remes-Troche JM, mean age was 32.10 +/- 14.42 years. NiazHussain, found mean age at presentation to be 35.2 ± 14.5 years. Out of 22 patients, having persistent generalized or ocular myasthenia gravis, 16 (72.7%) were females and 6 (27.2%) males. Ali Soleimani, in a study of 110 patients in Iran, noticed mean age at thymectomy to be 30.3 ± 12.8 years. In our study, the mean age of patients presented for thymectomy was 37±8.6 years. The younger patients (<55 years) having MG for less than 5 years are most benefited by surgery. Trans sternal approach is considered standard and safe by many surgeons. In the current study, only median sternotomy was used to gain access to thymus and remained a safe technique. Kas et al found similar results. Pneumothorax was the most common minor complication. Very few patients developed any major or intra-operative complication. Zielinski et al reported no difference in morbidity after less invasive procedures like manubriotomy as compared to median sternotomy.

Xiang-yang C reviewed 243 patients with MG who underwent thymectomy. Forty-four patients (18%) experienced postoperative myasthenic crisis within thirty days post thymectomy. Myasthenic crisis, in postoperative patients, was significantly higher in those having history of myastheniccrisis (P=0.016), thymoma (P <0.0001), and major postoperative complications (P <0.0001) than in patients without these three conditions. Ali Soleimani, in a study of 110 patients in Iran (76 cases done via trans-sternal approach and 34 done via trans-cervical route), showed that 32% developed myasthenia crisis. Lack of drug compliance and pneumonia causes were main triggering factors for myasthenic crises. Remes-Troche JM found myasthenic (9.3%) and cholinergic (2.7%) crises, the most serious complications. In our study, histopathology reports showed 16 cases of thymoma. Half of them (8 cases) had experienced crisis, which makes 26.7 % of total patients and 40% of those with previous history of...
crisis. Major postoperative complications related to thymectomy in the literature include pneumonia, pneumothorax, hydrothorax and ARDS. We found that the frequency of postoperative myasthenic crisis increases when the patients had severe postoperative complications. Multivariate logistic regression analysis in China revealed that major postoperative complications related to thymectomy are a predictor of postoperative crisis. In the work of Remes-Troche J et al in Mexico, no surgery-related deaths occurred in 75 patients. Marulli et al demonstrated the safety and efficacy of this procedure, after a review of 100 consecutive patients who underwent left-sided robotic thymectomy for MG. No deaths or intra-operative complications occurred. In our study, 3 patients died within 2 weeks and one survived for next 6 weeks. All 4 had carcinoma of thymus (Osserman’s group III).

Spath G et al operated upon 75 patients. Impaired wound healing was noticed in 6.7% of the patients, with complete sternal instability in one patient, while 5.3% developed pneumonia. Ali Soleimani showed that 20 of 110 (18%) developed attacks of respiratory failure. Niaz Hussain, out of 22 patients studied in Karachi, mentioned the most common major wound complication was sternal bleeding, encountered in 2 (9%) patients. This was followed by 1 case of disruption of the wound. Pneumothorax was the most common minor complication observed in 7 (31.8%), followed by wound infection in 4 (18%) patients, and 2 (9%) each of haemothorax, and seroma. We found wound infection in 6 (20%), and wound dehiscence in 1 patient (3.4%). Respiratory infection in 20 (66%). The wound complications are common in patients on long term steroids and pneumo / hemothorax is a common complication of surgery on thymus secondary to pleural damage. Spath G et al documented nerve paresis. Phrenic nerve in 2.7% and recurrent laryngeal nerve in 1.3%, noticed only in thymoma patients. Niaz Hussain reported that a total of 2 (9%) patients out of 22 had intra-operative complications including phrenic nerve and innominate vein injury. No long term morbidity occurred. In the current study, no nerve damage was noticed. Probably nerve damage is rare and associated with tumours.

Patients often experience some transient worsening of symptoms early in the postoperative period. Improvement usually is delayed for months or years. We followed the patients for next 24-40 months (average 27 months). Scott and Ditterbeck reported that 78% patients became better by one or more modified Osserman class and 69% had complete remission in Osserman class I, II and III. Takanami I found thymectomy to induce remission, more frequently in young patients with a short duration of disease, hyperplastic thymus, more severe symptoms, and a high antibody titer. We found remission of symptoms within 3 months. 20% became symptom free without drugs and 30% became symptom free with medication. Symptoms of further 30% became mild and only 1 patient (3.3%) remained unresponsive. All patients having complete remission were 45 yrs old or less. In a study by Nieto et al, the rate of remission in the presence of thymic hyperplasia was 42% compared to 18% in patients with thymoma. Shrager et al. reported an actual 50% complete remission with Kaplan-Meier estimate of 5 years of total remission of 57% in patients with ocular MG. After thymectomy there was no disease progression.

Masaoka reported a 46% remission rate at 5 years, 67% at 15 years and 90% overall palliation for the non thymoma group. They noted 32% remission rate and 82 % palliation rate for thymomas. The drug free remission was achieved primarily in early Osserman classes. According to Nason and Maddaus, thymectomy for thymomas results in improvement or resolution of symptoms only in 25% of MG patients. But patients with no thymoma, MG symptoms improve in 90% and 50 % have complete remission. Marulli et al demonstrated, after 5-year clinical follow-up of 100 consecutive patients who underwent left-sided robotic thymectomy, that 28.5% of patients had complete stable remission, and 87.5% showed overall improvement. Remission was significantly more likely in patients with preoperative class I to II MG according to standards of Myasthenia Gravis Foundation of America.

Conclusion
Trans-sternal total thymectomy provides good results for symptom control in benign thymic conditions. The major complication is haemorrhage needing transfusion. Other complications can be managed successfully by conservative treatment.
REFERENCES


