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Myasthenia Gravis - Role of Thymectomy

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INTRODUCTION

Myasthenia Gravis as the name implies is a disease which effect muscle and has a poor prognosis. Grab et al reported that between 1940-1958 only 39% of patients with generalized myasthenia gravis improved under the treatment then available and mortality rate was approximately 30% [1] Various forms of treatment were given and are being given to these patients since it was first described by Thomas Willis in 1685[2].

Modern rational line of treatment was only possible after Dr. Mary Walker, a registrar in an obscure London Hospital started treating these patients with physostigmine. Her discovey of beneficial effect of anti cholinesterase agent provided evidence for defect of neuromuscular transmission in myasthenia gravis and led to use of similar drugs in the treatment of myasthenia gravis. With the modern management a great majority of patients are relieved of their symptoms and lead fully productive lives. Death as a consequence of myasthenia gravis has now become an extreme rarity. However, the ultimate goal of cure has remained elusive. Most patients must continue to take medication indefinitely despite the risk of adverse side effects.

Thymectomy is one form of treatment which has been thought to provide that elusive goal of cure. It has been in and out of fashion for last 50 years. Now it is an established form of treatment benifitting upto 75% of patients[4,5]. Its benifit appear in few week to few years[4]. Majority of the centres are performing this procedure as a treatment of choice for all the patients. However, few institute still use symptomatic treatment & reserve thymectomy for advanced cases of myasthenia gravis[5]. There have not been many trials and as far as we know no randomized trial have yet been conducted in Pakistan to determine the role of thymectomy and its benifecial role in Pakistani population. We are conducting this trial. We feel it is important because myasthenia gravis occurs in genetically susceptiable individuals. We present here data about eleven patients who had undergone thymectomy for myasthenia gravis.

MATERIALS AND METHODS

All patients were seen at Shaikh Zayed Hospital, Lahore. Most of them came through O.P.D. clinics except for one patient referred by a colleague in Faisalabad. Diagnosis of myasthenia gravis was made according to clinical criteria and were group from Group-I to Group-IV.

Group I ocular myasthenia gravis (symptom may remain persistently confined to the ocular muscles, particularly when 2 year have elapsed since the onset.

Grade II A. II B. mild or moderately severe generalized myasthenia gravis.
Group III acute severe (Fulminating) myasthenia gravis with respiratory muscle involvement.
Group IV Late (chronic) severe disease[6].

They were assessed and were put in the respective group. All of these patients were assessed for other immune disorders i.e Rheumatoid arthritis, pernecious anaemia, pemphigous, hyper and hypothyroid etc.

All the patients before undergoing thymectomy were on mestinon (pyridostigmine) and some of them were on steriods also. These patients underwent thymectomy and they were graded post operatively on Day-I. Day 7 and after 4 weeks. They were assessed whether their symptoms have improved or not. Requirement of steriods anti-cholinesterase amount was also assessed. Dosage of anti cholinesterase and steroids was calculated by taking the first dose as 100% and then subsequent of dosage as percentile of it.

RESULTS

Table 1 shows clinical data of these patients. In our study most of the patients were in Grade II and Grade-III, one patient was in group I. She was an 18 years old girl. All the patients were between the ages of 15-45. There were 4 male and 7 female patient. After thymectomy, 2 patients had myasthenic crisis. Both of them had to be placed on ventilator, for 48 hours. Rest of the patient had smooth post operative period. After

Table 1:

Group	Number of Patients	Thyroid Disorder	Other Immune Disorder	Thyroma	Thymic Hyperlasia	Male	Female	Age group
Group I	1	0	0	-	1	-	1	15-25
Group II-A	4	0	0	1	3	2	2	15-45
Group II-B	2	1	0	0	2	1	1	15-55
Group III	4	0	1 (R.A)	1	3	1	3	15-55
Group IV	0	0	0	-	0	-	0	

Table 2:

Six	Grade I	Grade II-A	Grade II-B	Grade III	Dose of Anti cholinestrase	Dose of steroid	Myasthenic crises	No. of patient on steroid
Pre-op.	1	4	2	4	100%	100%	-	7
Post of Day-1	1	4	2	3	80%	100%	2	7
Day-7	6	2	2	1	60%	75%	-	5
4th weeks.	6	2	3	0	30%	30%	-	3

7th day of operation almost all the patient showed signs of improvement. After 4th week, there were six patients in group I instead of one and there was no patient in group-III. Dose of anti cholinesterase and steriod was reduced by 70% each. Number of patient who were on steriod after 4 weeks were 3 instead of 7 pre-operatively.

It has been noted that in myasthenia gravis 72% have thymic hyperplasia 10% have thymoma and 18% have atrophy but no absences (7,8) In our study similar figures were found. In different studies it has been noted that thymectomy helps upto 75% of patient we have also acheived simlar results shown in Table 2.

DISCUSSION

Rational treatment of Myasthenia Gravis depends on an understanding of the pathogenesis of the disease. The basic abnormality is a reduction in the number of available acetylcholine receptors at neuromuscular junction, resulting in impaired neumomuscular transmission and hence weakness and fatigue.

Humoral auto immune mechanisms play a key role in the pathogenesis. The auto-antibodies which are detected are directed against acetylcholine receptors and these decrease the number of receptors by three possible mechanism (a) accelerating the degradation of acetylcholine receptors through a sequence that involves cross-linkage of the receptors by the antibodes (b) blocking the receptors active sites and (C) damaging the acetylcholine receptors possibly in collaboration with compliments.[9]. Antibodies to the acetylcholine receptors are produced by B lymphocyte which are dependent on helper T lymphocyte.

The factors that trigger the auto immune response in myasthenia gravis are not yet known. It has been suggested that an impairement of thymic dependent normal mechanism allows the immune system to respond to self antigen the acetyl choline receptor in an inappropriate way [10]. There are different hypothesis about this role of thymus in pathogenesis of myasthenia gravis.

1. Human thymic cell contain acetylcholine receptors (11) and thymosin (12) but they do not contain myofibils these substances are present in both hyperplastic and in atrophic thymus in myasthenia patients. The role of these substances acting as an antigen site containing foreigonoid material has been raised (the foreigonoid material means one that is infested by virus mycoplasma etc.) This has been substiantated by many different studies[12,13,14] and not by many others.

2. Thymosin which is present in thymus has been incriminted in playing as a faciltative role in myasthenia gravis[11].
3. T Lymphocyte with abberant functions have also been found in myasthenia gravis.

In summary if genetically susceptable individual with abberant T lymphocyte along with thymic dependent auto antibodies he/she will suffer from myasthenia gravis. It can also be said like pitutary thymus even containing few cells will be controlling the pathogenesis of myasthenia gravis[14,12,4].

The experience in our institute also supports the role of thymectomy in myasthenia gravis in various age groups as supported by various studies [14,8,15]. The only contra indications to surgery are the hazards of surgery.

REFERENCES

1. Grob D, Brunner N.G, Namba-T. The Natal course of Myasthenia Gravis and effect of theraputic means. Annals NY acvad Sci 1981; 377:652-69
2. Adams R.D Kakulas: Dizeases of Muscle Pathological foundation of clinical neurology. 4th Ed. Philadelphia Harper Row 1985)
3. Rowland L.P: Contraversis about the treatment of myasthenia gravis. J.Neurol Neurosurg Psychiatry 1980 43:644-659.
4. Engel WK, Festoff BVV, Pattern BM, et al. Myasthenia gravis An Intern. Med. 1974 81:255-246,.
5. Stump WJ,Adoranto BT, Engle WK, et al: Thymectomy i myasthnia gravis (MG) Neurology 1978 28: 372
6. Jhon Newsome-Davis; Myasthenia Gravis Medicin International. 6: 1988-1991.
7. Arnason BGW: Myasthenia gravis. In clinical immunolog; Vol.II edited by CW Paster, Philadiphina WB Saunders 1980 1088-1105.
8. Paptestas AF, Alpert LI, Osserman KE, et al studies in myasthenia gravis effects of thymectomy. Result on 185 patients with non-thymomatous and thymamotous myasthenia gravis Am.J.Med ,1971 50: 465-474.
9. Drachman D.B, Adams R.N, Stanley EF, Pestroonka Mechanism of Acetyl Choline receptors loss in Myasthenia Gravis. J Neurol Neurosurg psychiatry 1980: 43:601-10.
10. Penn As Immunological fertures of myasthenia gravis. In Agvayr AT, Karpati G. eds: Current topics in Nerve and muscle research selected papers of symposia held at the IVth International Congress on Neuro muscular diseases, Montreal Canada; sept. 17-21 1978.
11. Engel WK, Troher JL, Mc.Farlin DE, Mcintosh Cl: Thymic epithelial cell contains acelecholine receptors.
12. Dalkas MC, Engel WK, Mc Clure J, et al. Thymosin a,localization in normal and myasthenic gravi thymus N. Eng J. Med, 1980 19:1091.
13. Castleman B. The pathology of thymus gland in myasthenia gravis. Ann Ny.Acad Sci .1966 135:496-503.
14. Twomey JJ, Levis VM, Pattern Bm, et al:Myasthena gravis, Thymectomy and serum urguril hormone activity. Am. J. Med, 1979 66:639-43.
15. Shore A,Linatibul S,Dosh H-M,et al: Indentification of two serum componentns regulating the express of T-lymphocyte function in child hood myasthenia gravis .N.Engl J. Med. 1979; 301: 615-629.
16. Slater G.Paptestas.AE,Genkins G. et al Thymomas in patients with myasthenia gravis Ann.Surg.188:171-174,1978.
17. Genkins G. Paptestase AE,Horwitz SM, et al Studies in myasthenia gravs Am.J.Med. 1975 58: 517-24.