

The Influence of Thymectomy Over Acetylcholine Antibody Anti-receptor Concentration and Over the Clinical Manifestations on Myasthenia Gravis Patients

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Myasthenia gravis is an autoimmune disorder which presents a series of clinical manifestations which are generally motor. The hallmark of the disorder is muscle weakness, which typically worsens during physical exercise and improves upon rest. Approximately 80% of the patients presenting this affection test positive for Acetylcholine antibody anti-receptor (AChR-ab). Treatment of patients with myasthenia gravis consists of: administration of oral medication, immunomodulating treatment by removal of AChR-ab through plasmapheresis or surgical intervention (thymectomy). This article presents a retrospective study in which the authors attempted to identify factors which can influence the effect of thymectomy on AChR-ab titration and on the clinical presentation of the patients suffering with myasthenia gravis.

Keywords: myasthenia gravis, AChR-ab, thymectomy, Acetylcholine

Myasthenia gravis is an autoimmune disorder which presents a series of clinical manifestations which are generally motor, but there have been documented cases of patients with myasthenia gravis that presented non motor symptoms [1]. The hallmark of the disorder is *muscle weakness*, which typically worsens during physical exercise and improves upon rest [2,3]. Approximately 80% of the patients presenting this affection test positive for Acetylcholine antibody anti-receptor. (AChR-ab)[3,4]. However, recent studies demonstrate that there is no direct correlation between AChR-ab titration and the appearance of generalized myasthenia gravis [5,6].

Treatment of patients with myasthenia gravis consists of: administration of oral medication, immunomodulating treatment by removal of AChR-ab through plasmapheresis or surgical intervention (thymectomy) [6,7].

Although the role of the thymus is not yet fully understood in the pathogenesis of this disease, there are studies that correlated thymectomy and the reduction of AChR-ab concentration as well as symptomatic improvement [8,9]. Patients presenting with myasthenia gravis in association with thymoma were found to have a net favourable evolution after thymectomy, compared to patients that have not undergone the procedure [9,10].

Oral treatment consists in the administration of Cholinesterase inhibitors (Anticholinesterases), among which the first line of treatment is Piridostigmine [11,12]. In some specific cases, Neostigmine can be used. In patients that present moderate or severe forms of myasthenia gravis or which do not present a favourable therapeutic response to Cholinesterase inhibitors, glucocorticoids and/or immunosuppressive therapy are administered [13-15].

This article presents a retrospective study in which the authors attempted to identify factors which can influence the effect of thymectomy on AChR-ab titration and on the clinical presentation of the patients suffering with myasthenia gravis.

Experimental part

Materials and methods

The retrospective study was first approved by the Institutional Ethics Committee. The inclusion criteria was defined as patients diagnosed with myasthenia gravis with ages between 18 to 75 and with a titration of AChR-ab of minimum 1 nmol/L, presenting a thymic affection, confirmed with computer tomography for which there was surgical indication and hospitalized consecutively in the Thoracic Surgical department of the Pneumophysiology Hospital in Iasi, during the period 2014 – 2017.

Exclusion criteria was defined as patients presenting myasthenical manifestations, having a titration of AChR-ab less than 1nmol/L, and not having a surgical indication for a thymic affection.

Each patient was evaluated before the surgical procedure and 6 months post operative (thymectomy) according to clinical symptoms and titration values of AChR-ab. A patient was considered to be in remission whenever he didn't express the symptoms for a minimum of 3 months. These informations were introduced in the data base which were used to quantify post operative changes in myasthenia gravis.

Results and discussions

The study included 14 patients hospitalized in the Thoracic Surgical department of the Pneumophysiology Hospital of Iasi. They were included in the study based on the diagnosis of myasthenia gravis. They are evaluated

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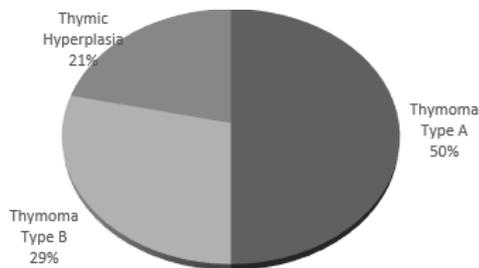


Fig 1. Repartition of thymic affection among patients with myasthenia gravis

based on the diagnosis of myasthenia gravis and the indication of thymectomy. Out of these patients, 71% were women, which corresponds to existent epidemiological studies [9]. The average age was 43.5 years old, ranging from 25 to 68.

Figure 1 presents the types of thymus affections in the case of preoperative patients.

The most common disease among these patients is Thymoma type A.

Figure 2 synthesizes the clinical manifestations observed preoperatively and 6 months post operatively, in the case of the patients included in the study.

The most common clinical manifestation was palpebral ptosis. This is also the most commonly found manifestation in other studies on this subject [10]. In this study, it is in these patients that the most substantial improvements were observed. On the other hand we have the patients that presented with dysarthria. This symptom was encountered at 6 months post operatively from thymectomy.

The cases of muscular weakness presented an important improvement following thymectomy. Also, positive results were noted in dysphagia and diplopia cases. In the case of the patients which presented with muscular weakness preoperatively, a total remission was observed in 4 out of 7 cases. In the case of patients with limb weakness, as well as those presenting axial muscle weakness, thymectomy yielded positive results, seen in fig. 2.

After a myographic study analysis, positive results were observed in the situations in which muscular weakness did not enter a remission stage. The latest dropped, on average, by 27%.

In two cases, the patients were admitted to the department with acute myasthenic crisis. They presented with severe respiratory events which prompted plasmapheresis treatment and which yielded fast positive results. Following thymectomy, both patients were free of respiratory manifestations at 6 months after surgical intervention.

Along side with thymectomy effect upon the clinical manifestations, the titration of AChR-ab was evaluated. In Fig 3 are presented the values obtained preoperatively and

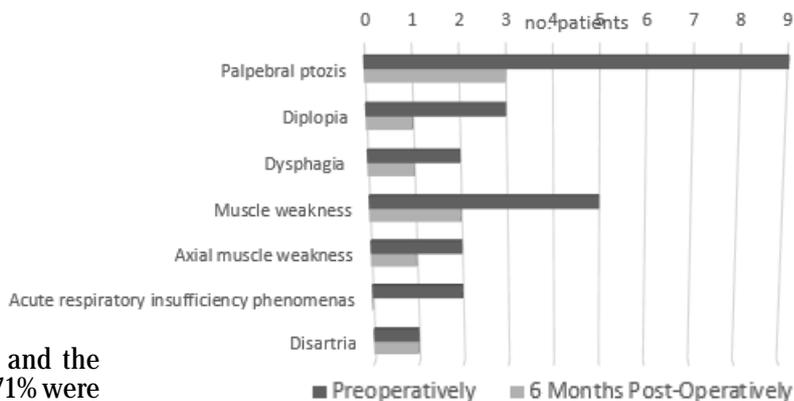


Fig 2. Clinical manifestations observed preoperatively / 6 months post operatively from thymectomy and the corresponding patient numbers

at 6 months post operatively. Also, table 1 shows the average values of AChR-ab according to the thymic affection associated, as well as the dynamics of this parameter in relation to the surgical intervention.

One can observe when analyzing figure 3 a significant decrease of patients with AChR-ab concentration under 10 nmol/L, at 6 months after surgical procedure, consisting of thymectomy, for patients evaluated with myasthenia gravis. Also, in table 1 one can observe that the patients with thymoma type B present the largest average titration of AChR-ab.

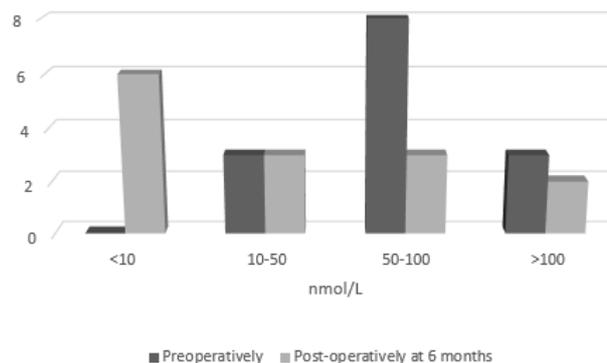


Fig 3. AChR-ab concentration dynamics in the first 6 months after surgical intervention

In table 1 there is a significant decrease of AChR-ab concentration at 6 months of the surgical intervention for all the 3 types of preoperatively thymic affections. Out of the patients included in the study, the best results were seen among patients with thymic hyperplasia.

Taking into consideration all of the above results from the study, a positive important effect can be seen following thymectomy, on the clinical manifestations of patients with myasthenia gravis and surgical indication for thymectomy, granted by the presence of a thymoma or a thymic hyperplasia. Also, there is a significant decrease of AChR-

Type of thymic association	AChR-ab (nmol/L)		
	PreOP	PostOPat 6 months	% difference
Thymoma type A (n=7)	73.48	27.3	-62%
Thymoma type B (n=4)	89.39	34.2	-61%
Thymic hyperplasia (n=3)	47.34	4.28	-90%

Table 1
AChR-ab CONCENTRATION DYNAMICS IN THE FIRST 6 MONTHS AFTER SURGICAL INTERVENTION IN RELATION TO THE TYPE OF THYMIC ASSOCIATED AFFECTION

ab titrations, with values up to 90% in patients presenting thymic hyperplasia.

Thus, it is necessary to continue to study the effects of thymectomy in the case of patients with myasthenia gravis associated with thymic diseases.

Conclusions

Although the role of the thymus is not yet fully understood in the pathogenesis of myasthenia gravis, thymectomy seems to yield positive results with respect to clinical manifestations observed in the evolution of the disease. Also, the decrease of AChR-ab concentration is evident in patients with myasthenia gravis.

According with the thymic affection associated, results of thymectomy vary, but positive results can be identified in the case of thymomas as well as those of thymic hyperplasias.

Future research on this subject could clarify new aspects related to the role of thymic diseases in the pathogenesis of myasthenia gravis.

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