

RESPIRATORY DYSFUNCTION IN PATIENTS WITH MYASTHENIA GRAVIS

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Abstract

Background: Myasthenia Gravis, a neuromuscular disorder causing skeletal muscle weakness involving respiratory muscles which some times sever enough to need assisted respiration. Approximately 30% of patients with MG develop some degree of respiratory weakness, myasthenic crisis most often precipitated by systemic infection (40%), thymoma (30%) and aspiration pneumonitis (10%).

Objectives: To evaluate respiratory function status with MG and to determine the triggering factors for respiratory dysfunction and effect of thymectomy.

Method: 50 consecutive cases of MG, 33 females and 17 males with an age range between 16–60 years old, 29 of them underwent thymectomy.

The study was done throughout the period October 1999 to June 2001 in Al-Kadhiymia Teaching Hospital.

Results: 46% of patients show respiratory muscles involvement. 47.82% of cases show respiratory involvement in the first 4 years. 68.9% of thymectomized patients show no respiratory muscles involvement while 66.7% of non-thymectomized show respiratory muscles involvement. Infection is the highest triggering factor (39%).

Conclusion: Respiratory dysfunction seems to develop in the first 4 years of the disease course. The incidence of respiratory dysfunction is less frequent in thymectomized patients. Infection is the main triggering factor.

Keywords: Myasthenia Gravis, Neuromuscular, Thymectomy, Respiratory failure

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Introduction

Myasthenia Gravis (MG) is a neuromuscular disorder characterized by fluctuating weakness and easy fatigability of the skeletal muscles that resolves with rest^[1]. It is an autoimmune disorder of neuromuscular transmission in which antibodies of IgG class reduce the functional status of acetylcholine

receptors at the neuromuscular junction^[2].

Myasthenic crisis defined as a marked clinical worsening of myasthenic weakness of the intercostals and diaphragmatic muscles leading to respiratory failure that requires intubations and mechanical ventilation^[1,3-6].

Approximately 30% of all patients with MG develop some degree of respiratory weakness. 15-20% will experience at least one crisis; one third of the patients who survive their first crisis will later experience a second one^[4].

Myasthenic crisis tends to occur early in the course of the disease. The median interval from onset of the myasthenia gravis to the first crisis is 8 months with almost 75% of cases occurring within

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the first 2 years of the disease onset and rarely a respiratory distress is the first manifestation of myasthenia gravis^[2-4,6]. Patients are often asymptomatic from the respiratory symptoms point of view in the early stages but as weakness progresses (VC < 30 ml/kg) atelectasis, reduced lung compliance, ventilation perfusion mismatch and hypoxia develop^[4].

Respiratory crisis is mediated through two mechanisms of equal importance, respiratory muscles weakness and oropharyngeal weakness which leads to aspiration, infection and inability to clear airway passages^[4,5]. Myasthenic crisis is most often precipitated by infection (40%), thymoma (30%), aspiration pneumonia (10%), change of medications (8%) and spontaneous exacerbation (no risk factor) (30%).

Myasthenic crisis can be avoided in many patients through immunosuppression and thymectomy^[4]. Pulmonary function tests (PFT) provide objective standardized measurements for assessing the presence and severity of respiratory dysfunction. The most common measurements of lung function through pulmonary function test are the ventilatory capacities (FVC, FEV1, and VC)^[7,8].

In MG the respiratory muscles involvement results in restrictive pattern of defect on PFTs^[4,6-8]. The best, simplest and most reliable way to evaluate respiratory functions in patients with MG is frequent measurement of VC^[9,10].

Normal VC value is 60-70 ml/kg, Patients below these values should be monitored and treated aggressively. Vital capacity of 15ml/kg (~ 1 liter) is generally considered the level of which intubations is needed^[4,6-8,10].

Aims of the study

1. To evaluate respiratory function depending on PFTs (VC) to recognize the cases where respiratory muscles are involved.
2. The relationship between respiratory dysfunction in patient with MG with onset of clinical presentation of respiratory dysfunction, thymectomy and the aggravating factors.

Patients & Methods

A prospective cohort clinical study; evaluation of fifty patients with MG, 33 females and 17 males with an age range between 16-60 years, 29 of them underwent thymectomy; throughout the period from October 1999 to June 2001 at Al-Kadhiymia Teaching Hospital

The diagnosis of MG is secured through clinical, tensilon test and neurophysiological assessments. Other investigations that were needed for the study, PFTs, TFT, CT scan or MRI of the chest, Chest X-ray, X-ray of the sinuses, CBP and ESR, vasculitic screening tests and other basic hematological tests

In this study, patients were classified according to their vital capacity into three groups: first, those patients with absent pulmonary function abnormality (VC > 80%), no ventilatory complaint. Second, those patients with mild to moderate impairment in pulmonary function test (V.C. 60-80%) of its predicted value, (V.C. 15-30 ml/kg), in which patients tend to have a low tidal volume and breath faster than healthy persons (RR 25-30 / minute). Third, those patients with severe pulmonary function tests impairment (VC < 60%) of its predicted value, (VC < 15 ml/kg), with RR > 35/minute clinically^[4,6,7,11, 12].

Results

Table 1: Percentage of Respiratory muscles involvement in M.G. patients depending on vital capacity

All patients with M.G.	VC> 80% Absent	VC 60-80% Mild -Moderate	VC <60% Sever	Total
Without respiratory muscles involvement	27	0	0	27 (54%)
With respiratory muscles involvement	0	16 (32%)	7 (14%)	23 (46%)

Percentage of patient without respiratory muscles involvement =54%

Percentage of patient with respiratory muscles involvement = 46%

Table 2: Time of onset of respiratory muscles involvement in relation to the time of onset of the disease

MG patients with respiratory muscles involvement	Presenting (respiratory failure)	1-2 years	3-4 years	>5 years
23	2 8.7%	11 47.82%	8 34.78 %	2 8.7 %

The onset of respiratory muscles involvement in relation to the time of onset of the disease is more frequent in

the first four years and rare after five years or as a presenting clinical feature (R.F.).

Table 3: Respiratory muscles involvement in relation to thymectomy

All patients with M.G.	Thymectomized		Non thymectomized		Total
	No.	(%)	No.	(%)	
Without respiratory muscles involvement	20	(68.9 %)	7	(33.3 %)	27
With respiratory muscles involvement	9	(31.1%)	14	(66.7%)	23
Total	29		21		50

Most M.G. patients with respiratory muscles involvement were not thymectomized, while most patients

without respiratory muscles involvement are thymectomized.

Table 4: Respiratory muscles involvement in relation to aggravating factors

All patients with respiratory muscles involvement	No.	Infection			Pregnancy			Surgery and stress	Drugs	Exercise	Mixed	Total
		UR	LR	Others	1	2	3					
Mild	6	1	0	1	1	0	0	0	1*	2	0	6
Moderate	10	2	1	0	0	1	0	1	0	1	4**	10
Severe	7	2	2	0	1	0	0	0	0	0	2***	7
Total	23	5	3	1	2	1	0	1	1	3	6	23
Total	23	9			3			1	1	3	6	23

*Steroid induced, ** Infection & exercise, *** Infection & surgery.

Infection > Exercise & Pregnancy > Drugs, stress & surgery.

Discussion

In this study, 46% of the cases showed respiratory muscles involvement (respiratory dysfunction) which is more

in contrast with other studies: Younger (1997) 16%^[13], Thomas et al (1997) 30%^[14], Fink (1993) 30%^[15], Michael et al (1981) 16%^[16].

This higher percentage of involvement in this study is due to, firstly delay in diagnosis and treatment of the disease itself, which leads to a more progression of the disease pathology and thus possibility of involvement of respiratory muscles, and secondly frequent infections in our patients, which is one of the main aggravating factors for myasthenic crisis.

This study shows that the onset of respiratory muscles involvement is more frequent at the first two years in the course of illness (47.82%), and less frequent at the (3-4) years of the course (34.78%) and rare to occur after 5 years of the disease course (8.7%) or as a presenting feature (acute respiratory failure) (8.7%) which agree with other studies^[14,17].

This high incidence of respiratory dysfunction in the first four years of the disease course is due to many factors which include: firstly the progression of the disease is more in the first three years, secondly most of the patients are not thymectomized at that time, and if they underwent thymectomy they may not get the full benefit of that operation early.

While low incidence of respiratory dysfunction after five years of the disease course is that, rarely the disease progress after five years and most cases are stabilized and in stationary state, and most patients are diagnosed and treated properly and were thymectomized and had the full benefit of it.

The present study shows that most patients with respiratory muscles involvement (66.7%) are not thymectomized, while most patients without respiratory muscles involvement (68.9%) were thymectomized which means that thymectomy is one of the protective measures against the development of respiratory dysfunction which agree with study done by Stephan (1997)^[4] who said that

thymectomy is a protective measure to avoid myasthenic crisis. In addition, this is in agreement with other studies about benefit of thymectomy in achieving remission^[18,19,20,21,22,23].

In addition, this study shows that infection is the main frequent aggravating factor for respiratory muscles involvement that includes upper respiratory tract infections, urinary tract infections and other infections for milder cases. URTI and LRTI like sinusitis and pneumonia are the main aggravating factors for moderate and severe cases. Some patients have mixed types of aggravating factors like infection, pregnancy and exercise.

Pregnancy (1st and 2nd trimester) was less frequent precipitating factor while drug induced, stress and surgery were the least frequent precipitating factors for respiratory dysfunction which agree with other studies^[1,3,14,16,24-27].

The pregnancy plays an important rule in the aggravation of myasthenic weakness and inducing myasthenic crisis especially in the first and second trimesters which is due to, frequent emesis during pregnancy which interferes with absorption of oral medications as drug treatment of myasthenia gravis. It also leads to hypokalemia which can aggravate myasthenic weakness, and the large uterus elevates the maternal diaphragm resulting in relative hypoventilation of the lower portions of the lungs, and lastly, expanded plasma volume and increased renal clearance may require that AchE medications be adjusted during pregnancy^[28].

Conclusions

1. The vital capacity as a part of PFTs is a simple test that can give a reliable idea about respiratory muscles involvement in patients with myasthenia gravis.

2. The respiratory dysfunction seems to develop early in the first years of the

course of the illness, while it is less frequent after five years of the course of the illness and rarely as a presenting feature (acute respiratory failure).

3. The incidence of respiratory dysfunction is less frequent in thymectomized patients compared to non thymectomized patients.

4. Infection is the main aggravating factor for the development of respiratory dysfunction followed by pregnancy, exercise, surgery and stress factors in sequence.

Recommendations

1. Patients with moderate or severe respiratory dysfunction should be kept under monitoring in RCU with frequent vital capacity assessment.

2. MG should be considered as differential diagnosis in patient with acute respiratory failure.

3. Thymectomy should be done as early as possible as one of the protective measures to prevent the occurrence of respiratory dysfunction.

4. Search and treatment of infection is essential as immunocompromised patients to prevent myasthenic crisis.

References

1. Drachman, D.B.: MG and other diseases of neuromuscular junction In: Braunwald, E., and Hauser, S.L. Harrison's Principles of Internal Medicine, 15th ed. New York, Mc Graw Hill 2001; p.p. 2515-20.
2. Hagon, J.A., and Cooper, J.D.: Surgical management of M.G. In Sabiston (chief editor). The biological basis of modern surgical practice. 15th ed. Philadelphia W.B. Saunders Company, 1997; p.p. 1933-41.
3. Adam, S.R., Victor, M., and Ropper, A.: MG and related disorders of neuromuscular transmission In: Adam, Victor, and Ropper. Principles of neurology. 6th ed. New York, Mc Graw Hill, 1997; p.p. 1441-2, 1459-75.
4. Stephan, A., and Mayer, M.: Intensive care of the myasthenic patient. Neurology, 1997; 48(Suppl.5): 70-5.
5. Shah, S.M., and Kelly, K.M.: Neuromuscular Disorders Acute Weakness Resulting from Neuromuscular Junction Disorders. In: Shah, S.M., and Kelly, K.M., Emergency Neurology,

Principles and Practice. Cambridge University Press, 1999; p.p. 85-90.

6. Weiner, W.J., and Shulman, L.M.: Neuromuscular Disorders MG. In: Weiner, W.J., and Shulman, L.M., Emergent and Urgent Neurology, 2nd ed. Philadelphia. A Walters Kluwer Company, 1999; p.p. 264-67.
7. Thomas, J.: Pulmonary function testing, In: Ronald, D.M. (ed.). Anesthesia 5th ed. San Francisco, 2000; p.p. 885-902.
8. Brakash, U.B.S.: Pulmonary diseases, Pulmonary function tests, In: Barakash, U.B.S., and Habermann, T.M., Mayo Internal Medicine Board Review, 2000-2001; printed in USA; Lippincott Williams and Wilkins, 2000; p.p. 771-3.
9. Crompton, G.K., Haslett, C., and Chilvers, E.R.: Diseases of the respiratory system, Lung function testing, In: Haslett, C., Chilvers, E.R., Hunter, J.A.A., and Boon, N.A.: Davidson's principles and practice of medicine, 18th ed., UK, Churchill Livingstone, 1999; p.p. 311-2.
10. Donald, J., and David, C.: Interpretation of blood gas measurements and respiratory function test. Medicine, Middle East, 1st series. Feb. 1980; p.p. 667-9.
11. Ferguson, I.T., Murphy, R.P., and Lascelles, R.G.: Ventilatory failure in myasthenia gravis. J Neurol Neurosurg Psychiat, 1982; 45: 217-22.
12. Abdulla, W.Y.: Guideline for ventilatory support in adults with respiratory failure, In: Principles of resuscitation and Intensive care, 1st ed., College of Medicine, University of Busra, Mosol, 1981; p.p 436.
13. Younger, D.S., Bradford, B., and Penn, S.A.: MG: Historical prospective and overview. Neurology, 1997; 48 (Suppl 5): 1-7.
14. Thomas, C.E., Mayer, S.A., Gungor, Y., et al.: Myasthenic crisis: clinical features, mortality, complications, and risk failures for prolonged intubation. Neurology, 1997; 48: 1253-60.
15. Fink, M.E.: Treatment of the critically ill patient with myasthenia gravis, In: Ropper A H, Neurological and neurosurgical intensive care, 3rd ed., New York; Raven Press; 1993; p.p. 351-62.
16. Cohen, M.S., and Younger, D.S.: Aspects of the natural history of myasthenia gravis crisis and death. Ann N Y Acad Sci, 1981; 377: 670-7.
17. Oosterhuis, H.J.: The natural course of myasthenia gravis: a long term follow up study. J Neurol Neurosurg Psychiat, 1989; 52: 1121-7.
18. Robinson, C.L.N.: The role of surgery of the thymus for myasthenia gravis. Ann Royal Coll Surgeon Engl, 1983; 65; 3: 145-50.

19. Monden, Y., Nakahara, K., Kagotani, K., et al.: Effects of preoperative duration of symptoms on patients with myasthenia gravis. *Ann Thoracic Surg*, 1984; 38 (3): 287-91.
20. Jaretzki, A.: Thymectomy of myasthenia gravis: Analysis of the controversies regarding technique and results. *Neurology*, 1997; 48 (suppl 5): 52-63.
21. Abdel-Kareem, A.M., Al-Kashab, S., Al-Nimer, M.S.M., and Niami, I.A.: Myasthenia gravis thymectomy; early outcome. *J Fac Med Baghdad*, 1993; 35 (4): 505-12.
22. Al-Shaikhly, K.I., Rustam, H.S., and Mussa, K.I.: Thymectomy in myasthenia gravis. *J Fac Med Baghdad*, 1994; 36 (4): 555-9.
23. Oosterhuis, H.J.: Observations of the natural history of myasthenia gravis and the effect of thymectomy. *Ann NY Acad Sci*, 1981; 377: 678-89.
24. Harber and Raw, Myasthenia gravis. *Clin Obs Gyne*, 1983; 26 (3): 599-604.
25. Bedlack, R.S., and Sonders, D.: How to handle myasthenic crisis, Essential steps in patient care. *Postgrad Med*, 2000; 107 (4): 211-4, 220-2.
26. Mazia, C.G., Schottlender, J., Menga, G., et al.: Invasive positive pressure ventilation in myasthenic crisis, The summary of the 1999 MGFA Scientific Session, Seattle, Washington, USA, 1999.
27. Masse, J.M.: Treatment of acquired myasthenia gravis, *Neurology*, 1997; 48 (suppl 5): 46-51.
28. Branch, D.W., and Porter, F.: Autoimmune disease; MG, In: James, D.K., Steer, P.J., Weiner, C., and Gonic, B., High risk pregnancy; Management options, 2nd ed., Philadelphia W.B. Saunders, 1999; p.p. 876-9.