

## Changes in respiratory muscle function after neostigmine injection in patients with myasthenia gravis

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*Changes in respiratory muscle function after neostigmine injection in patients with myasthenia gravis. L. Radwan, M. Strugalska, A. Koziorowski.*

**ABSTRACT:** In sixteen patients with myasthenia gravis, the weakness of respiratory muscles, especially of expiratory, caused some disturbances in lung function. Thirty minutes after injection of neostigmine, general improvement of muscle function was accompanied by an increase of strength and endurance of respiratory muscles. The mean value of maximal inspiratory mouth pressure (P<sub>imax</sub>) increased by 33%, maximal expiratory mouth pressure (P<sub>Emax</sub>) by 23.5% and maximal voluntary ventilation (MVV) by 21%. As a consequence of these changes amelioration of lung function indices was found, vital capacity increasing on average by 13% and residual volume decreasing by 12.5%. We concluded that patients with generalized myasthenia gravis have disturbances in lung function which may be partially improved by neostigmine injection or other anticholinesterase agents.

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It is well known that in patients with generalized myasthenia gravis respiratory muscles are involved to some extent. Weakness of respiratory muscles may be the reason for respiratory symptoms in some myasthenic patients and may lead to more or less pronounced disturbances in pulmonary function [7, 8]. In our previous paper [6], an improvement in respiratory muscle function and lung function indices several months after thymectomy was demonstrated.

The aim of this study was to investigate the effect of a single injection of neostigmine (powerful anticholinesterase agent) on the functional state of respiratory muscles and some lung function indices in a group of patients with generalized myasthenia gravis.

### Materials and methods

The study was carried out on sixteen patients with myasthenia gravis, aged 24-49 yr (mean  $34.8 \pm 6.8$ ) without lung diseases. There were fifteen women and only one man. All of these patients presented a generalized form of the disease *i.e.* group IIa and IIb according to OSSERMAN [5] and were receiving anticholinesterase agents. The patients arrived at the laboratory in the morning and during the 12 h before examination, anticholinesterase therapy was withheld.

The respiratory muscle and lung function indices were performed before and 30 min after intramuscular injection of 0.5 mg of neostigmine (Polfa). We measured: 1) maximal inspiratory (P<sub>imax</sub>) and expiratory (P<sub>Emax</sub>) pressures at the mouth against occluded airway; 2) maximal voluntary ventilation

(MVV) measured during 30 s, as an approximate index of respiratory muscle endurance; 3) static lung volumes including thoracic gas volume (TGV) measurement in a whole body plethysmograph ('Bodytest', Jaeger); 4) airway resistance and peak expiratory flow.

Maximal inspiratory and expiratory pressures at the mouth were measured with the use of an electromanometer, which was calibrated over the range -23.5 to +23.5 kPa before examination. P<sub>imax</sub> was measured at residual volume (RV) after maximal expiration and P<sub>Emax</sub> at total lung capacity (TLC) after maximal inspiration. The best value of at least three measurements was taken. Maximal inspiratory and expiratory pressures at the mouth were referred to the data WILSON *et al.* [9]. A small control group consisting of 21 men (19-55 yr) and 15 women (24-55 yr) from the hospital staff was studied in our laboratory.

Maximal inspiratory pressures were on average  $-11.07 \pm 3.1$  kPa in men and  $-8.62 \pm 2.45$  kPa in women. Maximal expiratory pressures were on average  $13.81 \pm 4.01$  kPa in men and  $10.29 \pm 2.25$  kPa in women. These values are very similar to those found by WILSON *et al.* [9]. The predicted values for lung volumes were taken according to BERGLUND *et al.* [1]. Differences of functional indices before and after injection of neostigmine were assessed using paired t-test.

### Results

The functional characteristics of examined myasthenic patients are given in table I and II. The force of

Table I. - Functional characteristics of 16 myasthenic patients - mean values

decreased P <sub>imax</sub>	65±15% pred.
decreased P <sub>E</sub> max	44±14% pred.
reduced MVV	48±16% pred.
slightly reduced VC	85±21% pred.
increased RV	153±44% pred.
normal FRC	97±12% pred.
normal TLC	96±12% pred.
normal FEV <sub>1</sub> %VC ratio	85±5.5%

inspiratory muscles was decreased in the majority of patients and mean value of P<sub>imax</sub> was 65% of that predicted. The force of expiratory muscles was decreased in all patients and mean value of P<sub>E</sub>max was 44% of that predicted. The more pronounced weakness of expiratory muscles is also evident in figure 1. Maximal voluntary ventilation was also decreased in all patients and mean value was 48% of the predicted value.

As a consequence of decreased strength of respiratory muscles, vital capacity decreased in the majority of patients (10 out of 16) and mean value of VC was slightly lowered, being 85% of predicted. Residual volume was increased in the majority of patients (mean value was 153% of that predicted), but functional residual capacity was normal (97% of predicted).

In table II, most of the functional indices before and after injection of neostigmine are presented. Maximal inspiratory pressure increased significantly from mean initial value of -4.73 to -6.31 kPa, which is an increase of 33%. At the same time maximal expiratory pressure increased significantly from mean initial value of 4.17 to 5.15 kPa, which is an increase of 23.5%. Maximal voluntary ventilation

Table II. - Functional indices of respiratory muscles and lung function (mean values) in myasthenic patients before and after intramuscular injection of neostigmine

	P <sub>imax</sub> kPa	P <sub>E</sub> max kPa	MVV l/min <sup>-1</sup>	VC l	VC % pred.	RV l	RV % pred.	TLC l	TLC % pred.	RV/TLC %
before	-4.73 ±1.14	4.17 ±1.35	45.6 ±15.4	3.26 ±0.91	84.7 ±20.6	1.66 ±0.45	152.8 ±44.0	4.93 ±0.81	96.2 ±12.3	34.1 ±10.2
after	-6.31 ±2.21	5.15 ±1.62	55.0 ±13.5	3.70 ±0.85	95.9 ±17.6	1.51 ±0.37	133.7 ±39.0	5.20 ±0.85	101.3 ±11.1	29.3 ±7.9
p <	0.01	0.001	0.001	0.001	0.001	0.05	0.05	0.001	0.001	0.001

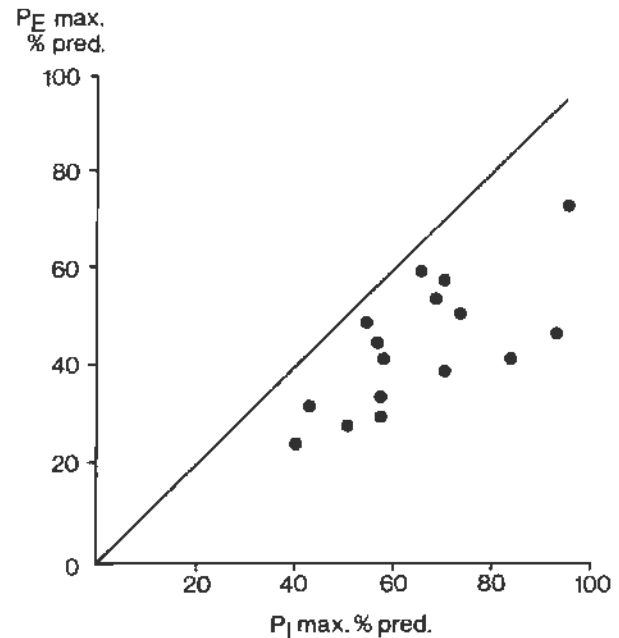


Fig. 1. The values of maximal inspiratory and expiratory pressures at the mouth (per cent of predicted) in 16 patients with myasthenia gravis.

also increased significantly by 21%. The injected drug also improved lung function indices. There was an increase in VC from 84.7% of predicted to 95.9% *i.e.* by 13%. Mean value of RV decreased from 153 to 134% of predicted, *i.e.* by 12.5%. At the same time RV%TLC ratio decreased significantly from mean initial value of 34 to 29%. The mean value of functional residual capacity (FRC) was normal and did not change after injection of neostigmine. Peak expiratory flow increased significantly from a mean value of 5.8 to 6.8 l·s<sup>-1</sup> producing an increase of 17%. Mean value of airway resistance was 0.13 ± 0.04 kPa·l<sup>-1</sup>·s<sup>-1</sup> and only slightly increased to 0.15 ± 0.06 kPa·l<sup>-1</sup>·s<sup>-1</sup> after the drug.

### Discussion

In the patients examined respiratory muscle weakness was more pronounced in the expiratory muscles.

This fact was also observed in our previous group of myasthenic patients treated by thymectomy [6]. This is in accordance with the data of RINGQUIST [7], and ROCHESTER and ARORA [8] that in myasthenic patients, inspiratory muscles which are the more important for ventilatory capacity were involved to a smaller extent than expiratory muscles. The endurance of respiratory muscles, as measured by MVV, was reduced. Although maximal voluntary ventilation is not as accurate a method of evaluation of endurance as maximal sustainable ventilation, their values are closely related [8].

As a consequence of a decrease in strength of respiratory muscles, vital capacity was in the majority of patients slightly reduced. It is known that in subjects without pathologic changes in lungs, the measurement of vital capacity may be a useful indicator of respiratory muscle function [4]. Nevertheless in our study, the decrease in strength of respiratory muscles was greater than the changes in vital capacity. This is in accordance with the data of BLACK and HYATT [2] who postulated that maximal static respiratory pressures can be abnormal even though the results of spirometry are normal.

Residual volume was increased in the majority of patients mainly due to expiratory muscle weakness [8], but at the same time, functional residual capacity was within normal limits. Similar results were found in our previous group of seven myasthenic patients examined before thymectomy [6], which suggested that resting end expiratory position (FRC) was not changed.

After injection of neostigmine we found an increase of strength and probably endurance of respiratory muscles. Many patients stated that they could breathe better and they had greater vital and total lung capacities and smaller residual volume. Also their peak expiratory flow increased. All of these changes indicated an improvement of their ventilatory capacities in a short time. It seems that the changes in pulmonary function after injection of neostigmine resulted only from the increase in respiratory muscle force. Similar results were found by De TROYER and BORENSTEIN [3] in a group of more disabled myasthenic patients after injection of another anticholinesterase agent, namely pyridostigmine. They found an

increase of FRC after pyridostigmine suggesting that respiratory muscle activity contributes to the relaxation characteristic of the chest wall in normal awake man. This finding was not confirmed in our previous [6] and present studies, probably because of the different muscular involvement in the groups of myasthenic patients examined.

Despite this, the De TROYER and BORENSTEIN study [3] as well as our own clearly show that the reversibility of pulmonary function disturbances after injection of anticholinesterase agent is a good example of the importance of respiratory muscles in determining some indices of lung function.

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**RÉSUMÉ:** Chez 16 patients myasthéniques la faiblesse des muscles respiratoires, et particulièrement des expiratoires, entraîne des anomalies fonctionnelles respiratoires. Trente minutes après injection de néostigmine, l'amélioration de la fonction musculaire générale s'accompagne d'une augmentation de la force et de l'endurance des muscles respiratoires. P<sub>max</sub> augmente en moyenne de 33%, P<sub>emax</sub> de 23,5% et MVV de 21%. Il en résulte une augmentation moyenne de la capacité vitale de 13% et une diminution du volume résiduel de 12,5%. On peut conclure que les indices fonctionnels respiratoires peuvent être améliorés chez les myasthéniques par une injection de néostigmine ou d'autres agents anticholinestérasiques.