



The role of plasmapheresis in Myasthenia Gravis

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Myasthenia Gravis

- ◆ S/S:

- 2/3 initial symptoms: Ocular motor disturbances, ptosis or diplopia.

- 1/6: Oropharyngeal muscle weakness

- 1/10: limb weakness

- ◆ severity of the weakness fluctuates

- ◆ orbicularis oculi muscle and jaw muscle weakness



Diagnosis

- ◆ Tensilon test: AChE inhibitor
2mg IV and monitored for 60 seconds.
Subsequent injections are 3 and 5 mg.
- ◆ EMG: decremental response to repetitive motor elective stimulation.
- ◆ AChR: titer not relative severity of MG
associated with thymoma
- ◆ CXR, CT: soft tissue mass at ant.
Mediastinum



Osserman`s classification

- ◆ I, ocular myasthenia.
- ◆ IIa, mild generalised myasthenia.
- ◆ IIb, moderate generalised myasthenia.
- ◆ III, acute severe myasthenia.
- ◆ IV, late severe myasthenia.



Pathophysiology

- ◆ autoimmune condition: antibodies to the AChR on skeletal muscle
- ◆ 10% to 15%: thymoma
- ◆ 80%: thymic hyperplasia



Treatment

- ◆ Thymectomy
benefit in 50% to 80%
max favorable response : 2 to 5 years
< 60 y/o poor response for thymectomy
- ◆ Extubation: within hours after surgery
- ◆ Repeat thymectomy: chronic, refractory
for residual thymic tissue or good response
to the original surgery.



Acetylcholinesterase Inhibitors

- ◆ Pyridostigmine bromide (Mestinon)
neostigmine bromide (Prostigmin)
- ◆ ½ to 1 tablet (60 mg) every 4 to 8 hours
- ◆ Side effect:
cholinergic crisis: persistent depolarization
of the muscle fiber, then muscle weakness
- ◆ GI complication:
loose stools, nausea, vomiting, abdominal
cramps, and diarrhea



Immune Modulation

- ◆ **Corticosteroids**

 - ocular MG, not respond to AChEI.**

 - initial dose 1.5 to 2 mg/kg/day**

 - excellent response in before or after removal
thymoma**

- ◆ **Azathioprine :initial dose 50 mg/day**

 - leukopenia, GI irritation, AST/ALT ↑2倍**



Immunosuppression

- ◆ Cyclosporine: initial dose 5 to 6 mg/kg/day
combined prednisone 10-20 mg qod
- ◆ Cyclophosphamide:
Alopecia and less common: leukopenia,
nausea, vomiting, anorexia, and
discoloration of the nails and skin



Intravenous Immunoglobulin

- ◆ 2 gm/kg infused over 2 to 5 days
- ◆ down-regulation of antibodies and symptom relief.
- ◆ Side effect: headaches, chills, and fever
less common: alopecia, aseptic meningitis, leukopenia, and retinal necrosis



Plasma Exchange

- ◆ short-term intervention for acute exacerbation
- ◆ rapidly improve strength before surgery
- ◆ postoperative deterioration
- ◆ chronic intermittent treatment for refractory disease.



Plasma Exchange

- ◆ Side effect:

cardiac arrhythmias, nausea, lightheadedness, chills, visual obscurations, and pedal edema, thromboses, thrombophlebitis, and subacute bacterial endocarditis.



Comparative effects of plasma exchange and pyridostigmine on respiratory muscle strength and breathing pattern in patients with myasthenia gravis

Thorax 1995;50:1080-1086



Patient list

Patients	Age (yrs)	Sex	Antibodies				Duration of both disease and treatment (yrs)	STD (mg × 10 ³)	Thymectomy
			AchR		SM				
			C	PE	C	PE			
1	68	M	20	8	1:160	<1:80	6	21.6	Yes*
2	63	M	54	42	1:160	<1:80	8	28.8	Yes*
3	65	F	85	52	-	-	4	21.6	No
4	57	M	44	25	1:160	<1:80	1	10.8	Yes*
5	22	F	35	15	-	-	1	10.8	Yes
6	30	F	18	7	-	-	2	14.4	Yes
7	33	F	15	10	-	-	4	21.6	Yes
8	38	F	28	13	-	-	1	10.8	Yes
9	30	F	64	29	-	-	5	27.0	Yes

AchR = acetylcholine receptor; SM = skeletal muscle; C = control; PE = plasma exchange; STD = steroid total dose (daily dose × 180 days × years).

* Thymoma.



- ◆ Medication: menstin0on 1# tid or qid
prednisone 20-60 mg/day
- ◆ Plasma exchange:
 - (a) 750-1000 ml saline.
 - (b) 500 ml 10 percent colloidal solution of low molecular weight dextran in saline
 - (c) three Baxter electrolytic rehydrating Solution (300 ml) plus 5000 IU heparin
 - (d) four 50 ml vials of 20 percent human albumin



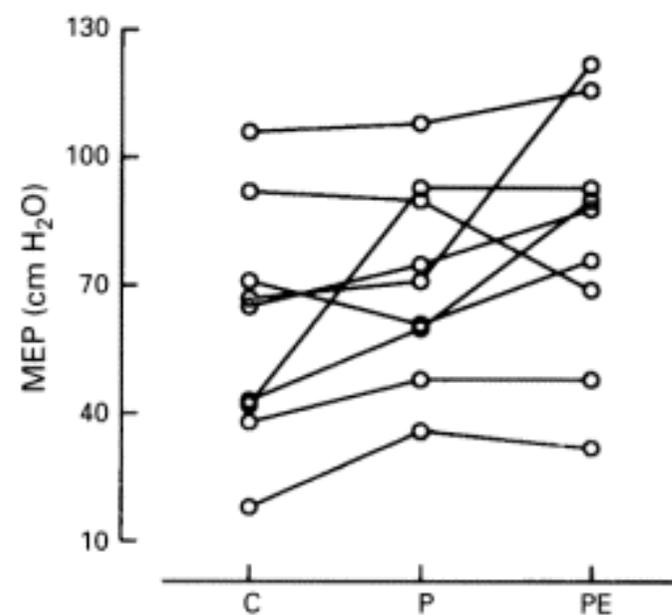
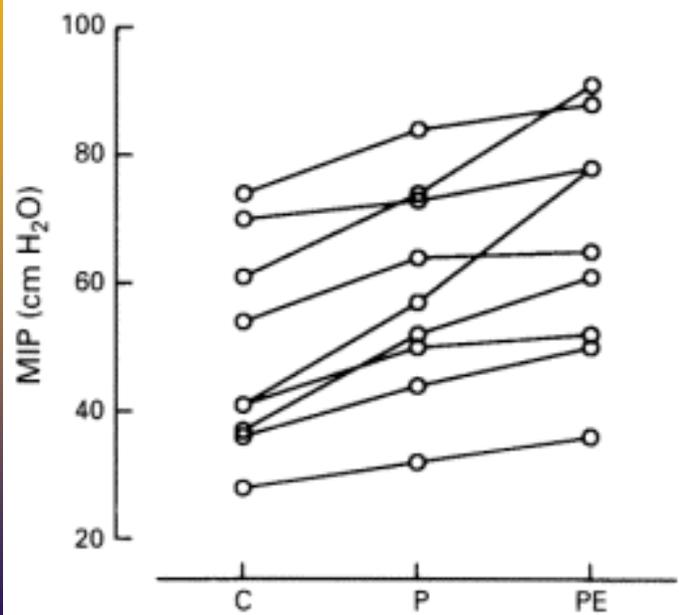
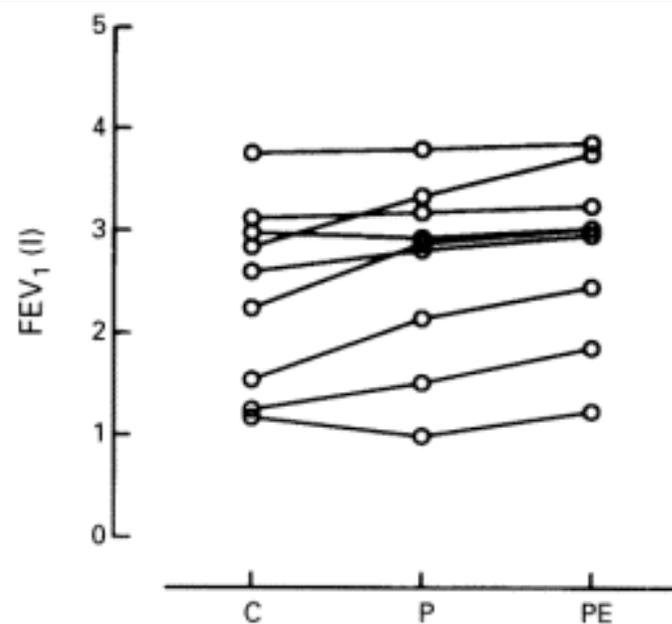
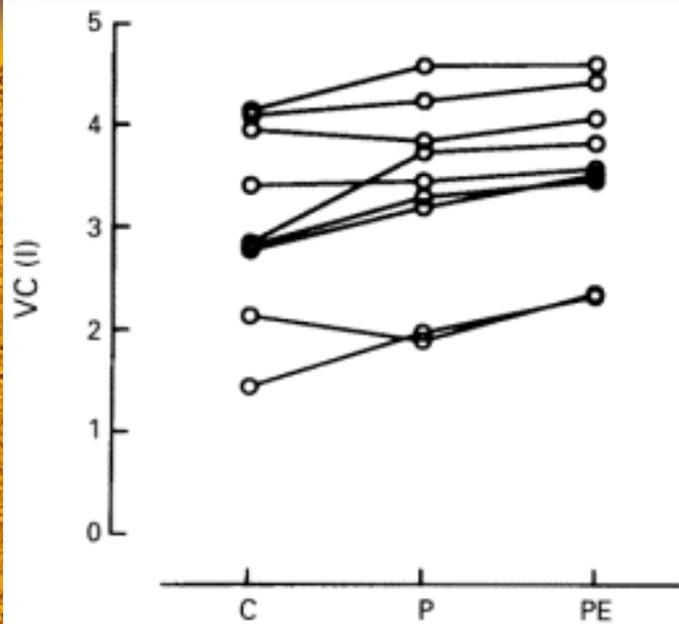
PROTOCOL

- ◆ Study I: fasted and a single dose (120 mg) of mestinon, Functional evaluation after 30 min.
- ◆ Study II: underwent the first of 5-9 courses of plasma exchange, re-evaluated at the same time in the morning
- ◆ Study III: on-steroid or off-steroid day 30 minutes and two hours after a dose of 120 mg pyridostigmine.

Results

	<i>VC</i> (<i>SR</i>)	<i>FRC</i> (<i>SR</i>)	<i>RV</i> (<i>SR</i>)	<i>TLC</i> (<i>SR</i>)	<i>FEV₁</i> (<i>SR</i>)	<i>FEV₁/VC</i> (%)	<i>MIP</i> (%pred)	<i>MEP</i> (%pred)
C	-1.46 (1.88)	1.21 (1.26)	1.74 (1.96)	-0.14 (1.17)	-1.52 (1.65)	77.7 (16.3)	56.2 (19.5)	38.2 (18.8)
P	-0.80 (1.72)	1.23 (1.46)	1.14 (2.03)	-0.25 (1.18)	-0.96 (1.54)	76.8 (12.7)	68.5 (21.2)	45.2 (16.2)
PE	-0.35 (1.56)	0.775 (1.26)	0.77 (1.79)	0.10 (1.22)	-0.47 (1.43)	78.4 (13.6)	75.8 (21.3)	50.6 (16.5)
Analysis of variance								
F	12.71	6.99	4.79	2.21	10.43	0.28	30.35	4.013
p	0.0005	0.01	0.025	NS	0.002	0.76	0.0001	0.05
Bonferroni test (<i>p</i> values)								
P v C	<0.05	NS	NS	NS	NS	NS	<0.05	NS
PE v C	<0.05	<0.05	<0.05	NS	<0.05	NS	<0.05	<0.05
PE v P	NS	<0.05	NS	NS	NS	NS	<0.05	NS

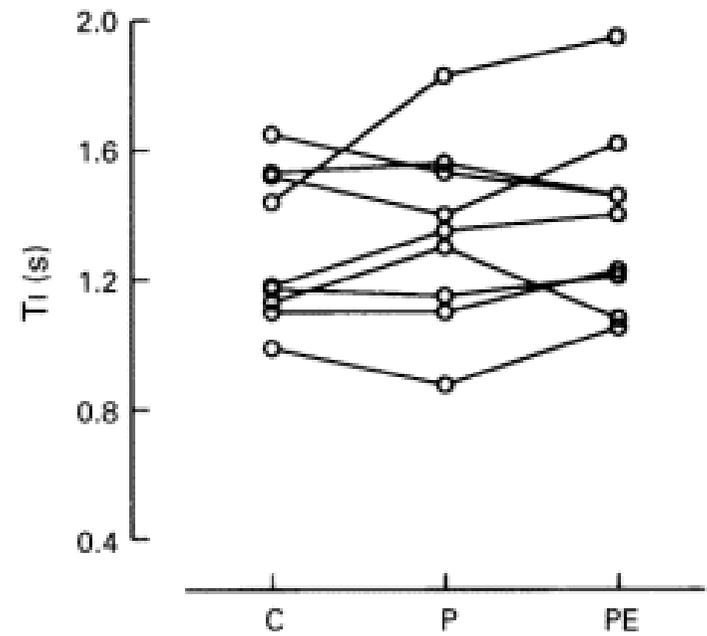
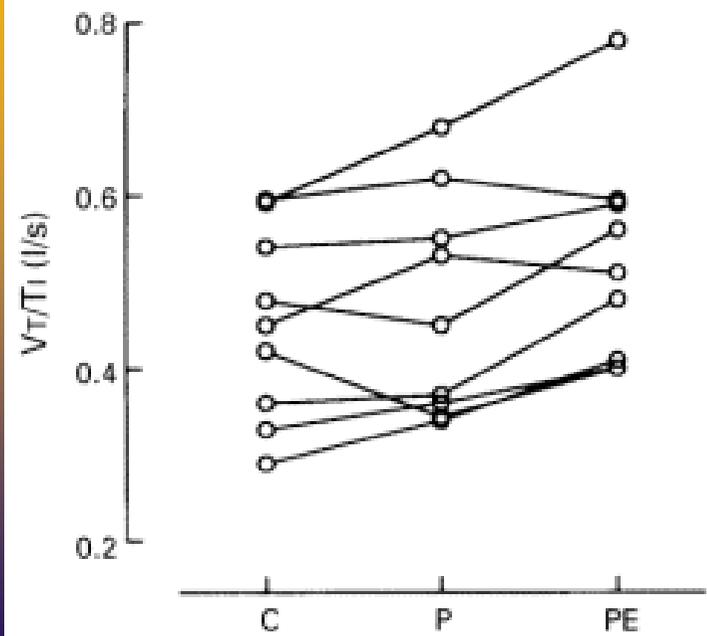
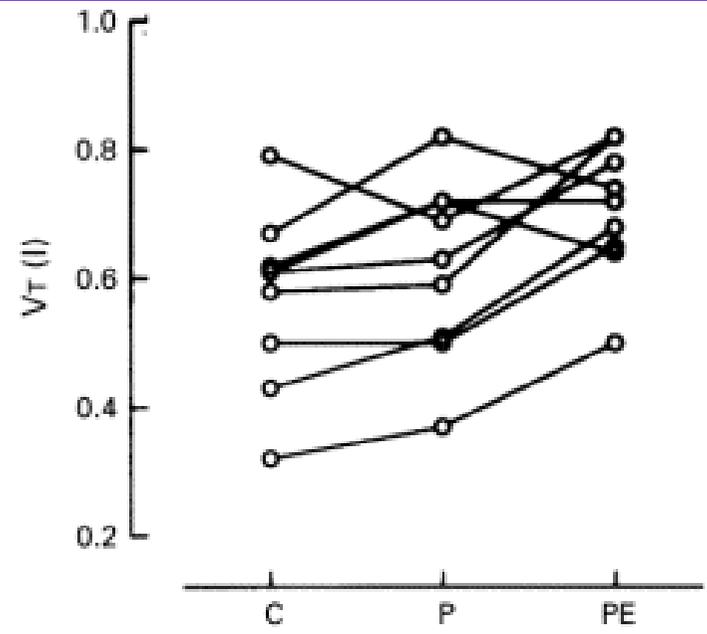
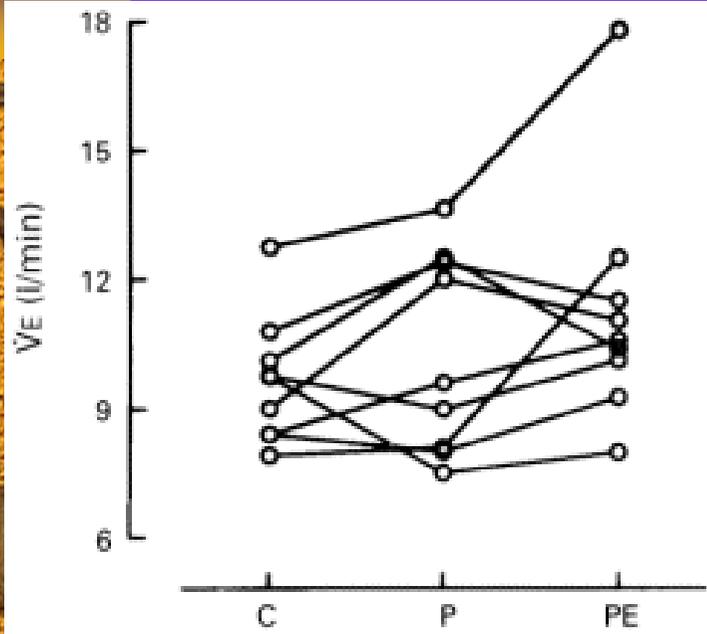
SR = standardised residuals; VC = vital capacity; FRC = functional residual capacity; RV = residual volume; TLC = total lung capacity; FEV₁ = forced expiratory volume in one second; MIP = maximal inspiratory pressure; MEP = maximal expiratory pressure.





	\dot{V}_E (l/min)	V_T (l)	T_I (s)	R_f (breaths/min)	V_T/T_I (l/s)	T_I/T_{TOT}
C	9.65 (1.5)	0.57 (0.1)	1.3 (0.2)	17.63 (4.2)	0.45 (0.1)	0.37 (0.06)
P	9.94 (2.2)	0.62 (0.14)	1.34 (0.3)	16.7 (4.6)	0.47 (0.12)	0.36 (0.06)
PE	11.2 (2.7)	0.7 (0.1)	1.4 (0.3)	16.1 (3.8)	0.52 (0.1)	0.37 (0.05)
Analysis of variance						
F	3.16	10.14	1.05	1.99	8.61	0.14
p	NS	0.002	NS	NS	0.005	NS
Bonferroni test (p values)						
P v C	NS	NS	NS	NS	NS	NS
PE v C	NS	<0.05	NS	NS	<0.05	NS
PE v P	NS	<0.05	NS	NS	<0.05	NS

\dot{V}_E = minute ventilation; V_T = tidal volume; T_I = inspiratory time; R_f = respiratory frequency; V_T/T_I = mean inspiratory flow; T_I/T_{TOT} = timing.





◆ Plasmapheresis:

FRC↑, RV↓, FEV1↑

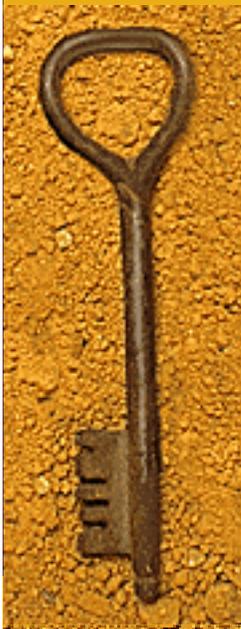
MIP↑, MEP↑

VT↑, VT/TI↑

◆ Mestinon:

FRC↑

MIP↑



Discussion

- ◆ increases in static and dynamic lung volumes and respiratory muscle strength in both.
- ◆ FRC is determined by the balance between lung and chest wall forces
decrease in plasma exchange, injection AChEI, not at oral AChEI.
- ◆ FRC~~MIP: no relation



- ◆ Post-mestinon 30min and 2-hours
- ◆ Low MIP, MEP---MG, corticosteroid myopathy.
- ◆ Corticosteroid on and off.
- ◆ Animal and human mode, II b fiber atrophy
- ◆ On change in TI.