Original Article

Changes in Respiratory Condition after Thymectomy for Patients with Myasthenia Gravis

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Background: Anesthesia without muscle relaxants has been reported to be effective for early extubation after thymectomy, but postoperative respiratory status of the patients has not been studied intensively.
Methods: Fifty-two consecutive patients undergoing thymectomies for myasthenia gravis (MG) were evaluated.
Results: Forty-two (81%) of the 52 patients were extubated in the operating room, and 49 (94%) patients were extubated within 24 hours. However, 6 (12%) patients required subsequent reintubation for respiratory support. There was a sudden increase in the respiratory rate (RR) and $PaCO_2$. The mean value of the increase in $PaCO_2$ at the time of reintubation was 23 mmHg (12-58 mmHg). The mean value of the increase in RR above the preoperative level at the time of reintubation was 16/min (7-30/min). In univariate analysis, vital capacity (VC), %VC, the preoperative pyridostigmine dose and the duration of surgery correlated with reintubation, but with multivariate analyses, the pyridostigmine dose was the only significant factor related to reintubation.
Conclusion: The patients who received at least or more than 240 mg of pyridostigmine should be monitored carefully after tracheal extubation. (Ann Thorac Cardiovasc Surg 2003; 9: 93–7)

Key words: reintubation, thymectomy, myasthenia gravis

Introduction

The avoidance of muscle relaxants during thymectomies for myasthenia gravis (MG) has been performed successfully for early extubation.[1,2] The criteria of extubating those patients in the operating room or intensive care unit (ICU) have been well studied,[3,4] but respiratory conditions of the patients have not yet been studied after extubation, especially in the event of reintubation. Herein, we present respiratory changes that occur after extubation, especially on the first postoperative day.

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Patients and Methods

Fifty-two consecutive patients undergoing thymectomies for MG from 1997 to 2001 were retrospectively evaluated. Thirty six (69%) of the 52 patients were female. The mean age of the patients was 45 years (range: 13-79 years). The preoperative and postoperative respiratory statuses were studied.

Since 1997, the patients with MG have not received any muscle relaxant during thymectomy as a part of their anesthetic management.[1,2] For preoperative preparation before thymectomy, we generally used anticholinesterase. Preoperative anticholinesterase therapy was continued until the time of surgery. Five patients received steroids and 6 patients were treated with semi-selective immunoadsorption using Asahi IM-TR 350 (Asahi Medical, Tokyo, Japan).[5] In the operating room, epidural anesthesia was also used. The epidural catheter was inserted

Table 1. Patient characteristics

Characteristic	Score	Mean±SD
Males/females	16/36 (30.8%/69.2%)	
Age range (years)	13-79	44.7±18.0
Osserman grade	I 10	
	IIA 19	
	IIB 19	
	III 2	
	IV 1	
	V 1	
Duration of symptoms (years)	0.1-18.6	1.8±3.3
Pyridostigmine dose* (mg)	0-480	132±79
Duration of surgery (min)	110-295	184±51
Anti-AchR Ab (nmol/L)	0.2-726	57±119
Pathology		
Thymoma/non-thymoma	25/27	
Lung function		
VC (L)	1.38-4.83	2.81±0.82
%VC (%)	45-128	92.7±16.2
FEV_1 (L)	1.05-3.95	2.32±0.73
FEV_1% (%)	42.9-100	82.4±10.8
Preoperative arterial blood gas analysis		
PaO_2 (torr)	65-114	87.9±11.4
$PaCO_2$ (torr)	32.8-49.1	42.1±3.2

*One mg ambenonium corresponds to 8 mg pyridostigmine.
Anti-AchR Ab, anti-acetylcholine receptor antibody; VC, vital capacity; %VC, % vital capacity; FEV_1, forced expiratory volume in one second; FEV_1%, forced expiratory volume % in one second.

into the T 6-7 interspace. Bupivacaine hydrochloride (0.2%) with or without fentanyl citrate was continuously infused through the catheter. All of the 52 patients received extended thymectomies[6] through full sternotomy incisions.

The trachea was extubated in the operating room after observation for 10 minutes or more. Then the patients were awake and satisfied the standard criteria for extubation without any episodes of preoperative crises. When a particular patient did not meet the criteria,[7] he/she was transported (while intubated) to the ICU. After extubation, these patients were transferred to a general ward and were monitored using their vital signs and clinical conditions.

Clinical variables listed in Table 1 were examined to determine whether they correlated with postoperative reintubation. Regarding the administered dose of pyridostigmine, 1 mg of ambenonium chloride was given per 8 mg of pyridostigmine bromide.[8]

Analysis was first done using χ^2 and Fisher's exact-testing in contingency tables and an unpaired t test. Univariate and multivariate analyses were then performed using a logistic regression model. Significance was assigned for a p value less than 0.05.

Results

Forty-two of the 52 patients underwent extubations in the operating room, as 42 (81%) of the patients satisfied the criteria[7] for extubation and had no history of crisis. The remaining 10 patients (19%) were transferred to the ICU while still intubated for respiratory control, because of history of preoperative crises or failures to meet the extubation criteria. Seven of these patients, however, were extubated within 24 hours of surgery. Consequently, 49 (94%) of the 52 were extubated within 24 hours. Only 3 patients (6%) had respiratory support more than 24 hours; namely, for 2, 5 and 11 days, respectively. However, 6 (12%) of the 52 patients needed subsequent reintubation and respiratory support. Reintubations were performed for severe hypoventilation or difficulties in expectorating sputum. The mean time from the end of surgery to reintubation was 32 hours (range: 14-101 hours). Excluding one patient, who was reintubated on the fifth postop-

Table 2. Changing respiratory functions after thymectomy

	Reintubation	Non-reintubation	p value
Increase in RR* (/min)	15.7±8.5	7.9±7.1	<0.02
range	7-30	0-37	
Increasing rate of RR** (%)	77.0±33.2	43.3±37.8	0.043
range	29.2-120	0-206	
Increase in $PaCO_2$*** (mmHg)	23.1± 17.4	4.8±5.6	<0.001
range	12.0-58.2	0-14.8	
Increasing rate of $PaCO_2$**** (%)	58.3± 46.3	11.2±12.4	<0.001
range	27.9-150	0-39.3	

*=(RR at reintubation or max RR)–(RR before operation)
**=(increase of RR)/(RR before operation)×100
***=($PaCO_2$ at reintubation or max $PaCO_2$)–($PaCO_2$ before operation)
****=(increase of $PaCO_2$)/($PaCO_2$ before operation)×100
On unpaired t test.
RR, respiratory rate.

erative day, the remaining 5 patients were reintubated between 14 and 37 hours after surgery. The 6 reintubated patients had sudden increases in their respiratory rates (RR) and $PaCO_2$, compared to their preoperative baseline. The mean RR value at the time of reintubation was 36/min (range: 24-55/min). The mean $PaCO_2$ value at the time of reintubation was 64 mmHg (range: 52-97 mmHg). The mean value of the increase in the RR at the time of reintubation was 16/min (range: 7-30/min). The increase of the mean percentage value of RR at the time of reintubation compared to that before surgery was 77% (range: 29-120%). The mean value of the increase in $PaCO_2$ at the time of the reintubation was 23 mmHg (range: 12-58 mmHg). The increase in the mean percentage value of $PaCO_2$ at the time of reintubation compared to that before surgery was 58% (range: 28-150%). There were also increases of $PaCO_2$ and RR values in non-reintubated patients, but the reintubated patients experienced significantly higher increases in $PaCO_2$ and RR values than the non-reintubated patients (Table 2). None of the reintubated patients had complications during intubation nor thereafter, though one patient's $PaCO_2$ value increased to 60 mmHg after the second extubation. Re-reintubation was avoided using noninvasive positive pressure ventilation (NIPPV) in this case.

Vital capacity (VC, p=0.04), %VC (p=0.01), the pyridostigmine dose (p=0.01) and the duration of surgery (p=0.04) were extracted as factors correlating with reintubation by univariate analyses (Table 3). The duration of surgery of the reintubated group was 136 min, which was shorter than that of the non-reintubated group (190 min). There was a paradoxical correlation between the duration of surgery and reintubation. Multivariate analysis determined that pyridostigmine dose [p=0.049, odds ratio (OR) = 1.019, 95% confidence interval (CI) = 1.000-1.038] was the only significant factor among the following variables: VC, %VC, pyridostigmine dose, forced expiratory volume in one second (FEV_1), and Osserman grade (I, IIA, V vs. IIB, III, IV) (Table 4). Four of the 6 reintubated patients (67%) received 240 mg of pyridostigmine or more. In contrast, 93% of the non-reintubated patients received less than 240 mg (Fig. 1).

Discussion

Postoperative respiratory care after thymectomy for MG is an important problem. With progress in postoperative care, respiratory support and anesthetic techniques, almost all of the patients with MG were extubated without difficulty soon after surgery. In particular, anesthesia without muscle relaxants has been effective for early extubation.[1,2] Chevalley and colleagues[9] reported that postoperative ventilatory support was more frequently required when patients were given muscle relaxants. In the present study, 94% of the patients were extubated within 24 hours postoperatively. Eisenkraft and colleagues reported that 91% (84/92) of their patients were extubated within 3 hours after thymectomy without muscle relaxants.[7] Gorback and colleagues reported that 13 of 14 study patients were extubated within the first 25 postoperative hours without muscle relaxants.[4] Our extubation rate was slightly lower than those cited in previous reports.[4,7] This discrepancy might be attributable to the fact that the patients with an episode of crisis received respiratory sup-

Table 3. Preoperative variables and correlations to reintubation on univariate analyses

Patient variables	OR	95% CI	p value
Males/females	0.41	0.44-3.859	0.44
Age (years)	1.01	0.96-1.06	0.74
Osserman grade	8.53	0.92-79.26	0.06
History of crisis	4.10	0.59-28.39	0.15
Duration of symptoms	0.98	0.73-1.31	0.87
Pyridostigmine dose	1.03	1.01-1.05	0.011
Duration of surgery	0.96	0.919-0.997	0.037
Anti-AchR Ab	1.00	0.99-1.01	0.96
Thymoma	2.38	0.40-14.32	0.34
VC	0.998	0.997-1.000	0.039
%VC	0.895	0.82-0.97	0.01
FEV_1	0.999	0.999-1.000	0.061
FEV_1%	1.02	0.93-1.11	0.68
PaO_2	1.001	0.93-1.08	0.99
$PaCO_2$	0.86	0.66-1.12	0.26

OR, odds ratio; 95% CI, 95% confidence interval, Anti-AchR Ab, anti-acetylcholine receptor antibody; VC, vital capacity; %VC, % vital capacity; FEV_1, forced expiratory volume in one second; FEV_1%, forced expiratory volume % in one second.

Table 4. Preoperative variables and correlations to reintubations on multivariate analyses

Patient variables	OR	95% CI	p value
Osserman grade	1.077	0.04-29.31	0.965
Pyridostigmine dose	1.019	1.000-1.038	0.049
VC	0.998	0.991-1.005	0.542
%VC	0.915	0.775-1.082	0.300
FEV_1	1.002	0.995-1.008	0.598

OR, odds ratio; 95% CI, 95% confidence interval, VC, vital capacity; %VC, % vital capacity; FEV_1, forced expiratory volume in one second.

port in the ICU despite satisfying the extubation criteria.

In our study, 6 (12%) of the 52 patients underwent reintubation. Gracey and colleagues reported that 4 (8%) of their 53 study patients required reintubation.[3] Our reintubation rate exceeded 10%, and reintubations were performed from 14 to 101 hours postoperatively. Only one patient was reintubated on the fifth postoperative day. Gracey and colleagues[3] also reported that 43 patients with MG were extubated in the post-anesthesia recovery room, and 2 of the 43 patients required reintubation approximately 24 hours postoperatively. Therefore, patients extubated on their operative day should be monitored with respect to their respiratory condition, especially during the first operative day.

The predictors of reintubation in our study were VC, %VC and the administered dose of pyridostigmine upon univariate analyses. On multivariate analysis, the administered dose of pyridostigmine was the only predictor of reintubation. Four of the 6 reintubated patients received 240 mg or more of pyridostigmine bromide everyday before surgery. By contrast, only 3 patients of the non-reintubation group were administered 240 mg/day pre-

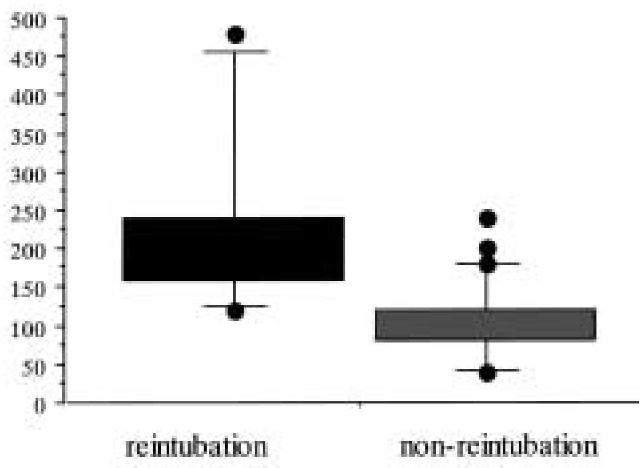

Fig. 1. Preoperative pyridostigmine dose (mg).

operatively. Leventhal and colleagues also reported that the pyridostigmine dosage (more than 750 mg/day for 48 hours preoperatively) was one of the predictive factors for postoperative ventilation.[10] The pyridostigmine dose must be an important factor for determining the respiratory care for patients with thymectomy.

There are a lot of different methods for performing thymecmoties and perioperative managing MG. As for the methods of thymectomies, transsternal thymectomy,[6] transcervical thymectomy[11] and recent video-assisted thoracoscopic[12] or mediastinoscopic[13] thymectomies have been reported. The postoperative respiratory status may be affected differently depending upon which of these modalities is used. Eisenkraft and colleagues[7] pointed out the possibility that transcervical thymectomy had a respiratory-sparing effect compared to transsternal thymectomy. Managements following thymectomy have been performed by different anesthetic and medical methods that have impacted patients' perioperative respiratory conditions.

In our study, one patient was saved from re-reintubation by increasing her $PaCO_2$ using NIPPV, nasal continuous positive airway pressure (n-CPAP) ventilation. NIPPV may be a powerful and effective treatment for patients with MG as well as for patients with other neuromuscular diseases,[14] if the patients have the ability to clear retained secretions by themselves. However, we will need to further examine the potential role of NIPPV in myasthenic patients with respiratory insufficiency.

It is necessary to carefully monitor the respiratory conditions of patients with MG at least through the first operative day. The preoperative dose of pyridostigmine (more than 240 mg) may alter the risk of reintubation.

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