Physiotherapy immediately after thymectomy in patients with myasthenia gravis.

Two cases and review of the literature

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Physiotherapy immediately after thymectomy in patients with myasthenia gravis. Two cases and review of the literature

AIM: *Myasthenia gravis (MG) is a rare autoimmune disease characterized by activation of autoantibodies against acetylcholine receptors: patients with MG typically experience muscle weakness and fatigue. The aims of the present study were 1) to describe immediate postoperative physiotherapeutic interventions in two MG patients who underwent thymectomy, and 2) to discuss postoperative rehabilitative issues in MG patients.*
MATERIALS AND METHODS: *This was a non-experimental study analyzing two subjects with MG who underwent thymectomy. Furthermore, to find evidence on postoperative rehabilitative intervention in MG patients undergoing thymectomy, four major databases were searched through August 2016.*
RESULTS: *All subjects were able to walk on postoperative day (POD) 1 and to climb at least one flight of stairs on POD 4. Pain was more intense on POD 1 than on PODs 2 and 4. Dyspnea was worse on POD 2 than on PODs 1 and 4. Regarding the literature review, 58 papers were identified. After removal of duplicates, 51 citations remained to be screened. After the full texts were read, one paper met the inclusion criteria and was included.*
CONCLUSIONS: *Our findings indicate that patients are willing to undergo immediate physiotherapeutic treatment in the ICU after thymectomy. It seems that physiotherapeutic intervention after thymectomy in MG-grade IIa middle-aged patients can be initiated immediately postoperatively in uncomplicated cases.*

KEY WORDS: Dyspnea, Myasthenia gravis, Outcome assessment, Pain measurement, Physiotherapy, Postoperative care, Rehabilitation, Thymectomy

Introduction

Myasthenia gravis (MG) is a rare autoimmune disease characterized by activation of autoantibodies against acetylcholine receptors, muscle-specific kinase, and lipoprotein-related protein 4. Patients with MG typically experience muscle weakness and fatigue [1]. Muscles of the face, throat, arms, and legs are most commonly affected, with symptoms worsening under repeated muscular effort and improving at rest [2]. Disturbance of coordination and balance, and difficulties with arm and leg movement are also common in MG patients [2]. Muscle strength in MG patients can be evaluated using dynamometry of the shoulder abductors, knee extensors, and ankle extensors; MG patients usually have considerably reduced knee extensor strength at diagnosis [3]. Diagnosis of the condition may also involve evaluation of muscle isometric strength, blood tests, and electromyography. Thymomas are associated with MG, and thymectomy is usually recommended for early-onset MG,

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particularly in young subjects [1]. The thymus gland may be surgically removed regardless of whether a tumor is present, as this can improve MG symptoms [2]. In this regard, a minimal thoracic approach has proven safe and feasible in these patients, resulting in a shorter operation duration and a reduced postoperative hospital stay [4,5]. To the best of our knowledge, no studies have investigated early postoperative physiotherapeutic intervention in MG patients who have undergone thymectomy. The aims of the present study were 1) to describe immediate postoperative physiotherapeutic interventions in two MG patients who underwent thymectomy, and 2) to discuss postoperative rehabilitative issues in MG patients.

Materials and Methods

This was a non-experimental study analyzing two subjects with MG who underwent thymectomy. Both subjects presented with a nodule in the thymus that captured contrast. Both patients provided informed consent.

CASE 1

A 49-year old man with a body mass index (BMI) of 25.1 (kg/m^2) with an anterior mediastinal nodule was referred to our institution for surgery. The patient had a 2-year history of diplopia. In the previous 3 months, he had experienced muscle weakness. He was diagnosed with generalized MG (Grade IIa)[6] after neurological evaluation and electromyography. Immunological examination showed an anti-acetylcholine receptor antibody level of 13.6 pmol/mL. An anterior mediastinal nodule (3.1 x 2.3 x 3.3 cm) that was highly suspicious of a thymoma was detected with chest computed tomography. Preoperative medical therapy was started with cholinesterase inhibitors (60 mg of pyridostigmine bromide four times a day), which improved the muscular weakness. Preoperative plasmaphoresis was performed just before surgery to avoid a myasthenic crisis. Thereafter, a radical thymectomy was performed through a median sternotomy. Pathological examination of the tumor identified it as a type A thymoma (Masaoka stage IIa). The patient did not receive postoperative adjuvant radiotherapy because the resection was complete.

CASE 2

A 48-year old man with a BMI of 24 (kg/m^2) was admitted to our institution due to an anterior mediastinal mass; no comorbidities were detected. Computed tomography of the chest showed a round anterior mediastinal mass that measured approximately 7.2 x 4.3 x 5.3 cm. The patient had exhibited cervical muscle weakness and diplopia over the previous 8 months. Generalized MG (Grade IIa)[6] was diagnosed via neurological evaluation and electromyography. The immunological examination showed an incremental anti-acetylcholine receptor antibody titer of 25.9 pmol/mL. Preoperative medical therapy was initiated with cholinesterase inhibitors (60 mg of pyridostigmine bromide three times a day), and plasmaphoresis was performed just before surgery. A radical thymectomy was performed, with the excision of a portion of the right mediastinal pleura through a median sternotomy. Pathological examination of the tumor identified it as a type B thymoma (Masaoka stage IIa modified). The patient did not receive postoperative adjuvant therapy because the resection was complete.

PHYSIOTHERAPEUTIC TREATMENT

A single mediastinal drain was placed at the end of surgery and removed on postoperative day (POD) 1 in both subjects. Patients were treated as soon as they arrived to the intensive care unit (ICU). Early physiotherapy was planned postoperatively. Manual respiratory exercises were also carried out on the day of intervention. Depending on the level of patient cooperation, 10 to 15 deep breathing exercises were encouraged as soon as subjects were awake and extubated. One patient was extubated in the operating room after surgery. Physiotherapeutic treatment was administered during the recovery period (Fig. 1). On POD 1, postural transfers (supine–sitting–standing) were executed, as well as walking on the ward. Furthermore, incentive spirometry exercises were explained to the subjects, who were encouraged to perform 8–10 repetitions, four times daily. Physiotherapy was administered for 20–30 minutes once a day. As soon as the subjects were able to walk unassisted for at least 300 meters and to climb a flight of stairs, physiotherapeutic treatment was stopped, as long as no other complications to rehabilitation were detected. There were no adverse effects related to physiotherapy during hospitalization.

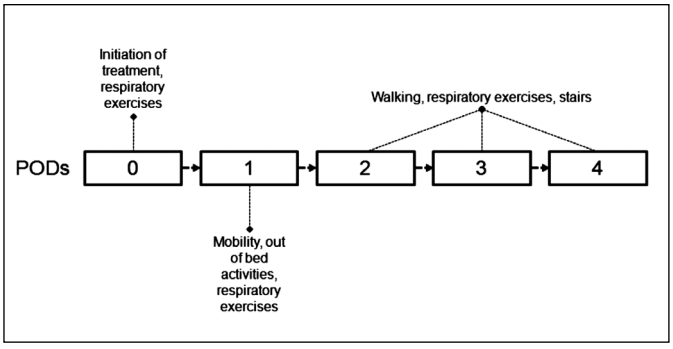

Fig. 1: Timeline and treatment progression.

Legend: PODs: postoperative days.

Outcome Measures

Pain intensity was evaluated using a 0–10 numerical rating scale (NRS), where 0 represented the absence of pain, and 10 represented the maximum level of pain ever experienced. Measurements were taken on PODs 1, 2, and 4. Dyspnea was also evaluated on PODs 1, 2, and 4 by having patients rank their level of breathlessness on a 10-cm visual analogue scale (VAS) [7]. The walked distance (WD) was also assessed during the physiotherapeutic sessions by calculating meters walked [8]; on PODs 2 and 4, patients' ability to climb one flight of stairs was also checked. Furthermore, the Italian version of the Barthel Index was used to evaluate patient autonomy levels over the recovery timeframe [9]; measurements were taken on PODs 1 and 4.

Literature Review

To find evidence on postoperative physiotherapeutic intervention in MG patients undergoing thymectomy, four major databases were searched through August 2016: PubMed, Scopus, Web of Science, and LILACS. Search terms were "myasthenia gravis," "thymectomy," "rehabilitation," and "physiotherapy" (Fig. 2). We did not apply limits to the publication date or gender. The search included the title, abstract, topic, and keyword fields. Citations were accepted if they discussed postoperative physiotherapeutic treatment in patients with MG who underwent thymectomy.

Studies were excluded if they were written in languages other than English, French, Spanish, or Italian; or if they constituted opinion pieces, conference proceedings, or editorials.

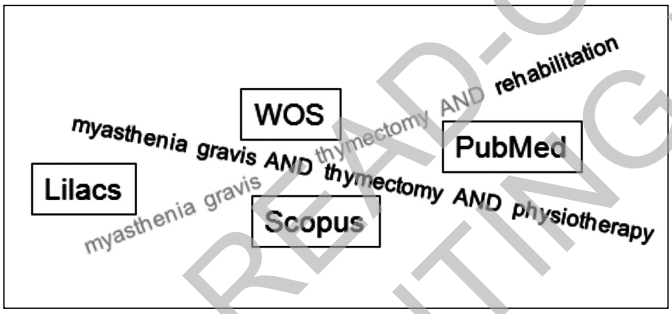

Fig. 2: Databases and search strings

Legend: WOS: Web of Science.

Table I - *Demographics and clinical characteristics*

Variable	
AGE (mean, SD)	48.5±0.71
Gender male, (n)	2
BMI (kg/m^2), (mean, SD)	24.6±0.78
PT outset (hours after surgery), (mean, SD)	2.5±0.7
PT sessions, (n)	4
LOS, (days)	6±0

Legend: BMI: body mass index SD: standard deviation PT: physiotherapy LOS: length of stay.

Results

Demographic characteristics of the two subjects in the present study are shown in Table I. Their age, gender, and BMI were similar. During hospitalization, each patient completed four physiotherapy sessions, which ended 2 days before hospital discharge. Physiotherapy was initiated at 2.5 hours post-operatively in the ICU. All subjects were able to walk on POD 1 and to climb at least one flight of stairs on POD 4. Pain was more intense on POD 1 than on PODs 2 and 4. Dyspnea was worse on POD 2 than on PODs 1 and 4. On POD 1, subjects were almost autonomous, as shown in Table II.

Regarding the literature review, 58 papers were identified. After removal of duplicates, 51 citations remained to be screened (Fig. 3). After the full texts were read, one paper met the inclusion criteria and was included. In that paper, three subjects with MG who underwent thymectomy were observed. The main results are shown in Table III.

Discussion

In the study examined in the literature review [10], the authors found that MG patients who underwent thymectomy were able to tolerate an intensive rehabilitation program, and subjects' functional status improved following the postoperative rehabilitative therapy summarized in Table III. In the two cases reported in the present study, low-grade dyspnea was observed starting from POD 2,

Table II - *Results*

Variable	POD 1	POD 2	POD 4
MOTOR ACTIVITIES			
WD (meters), (mean, SD)	240±113.1	340±198	600±141.4
Stairs (yes, no)	–	1y, 1n	y
FUNCTION			
BI, (median, min-max)	72.5 (60-85)	–	95 (95-95)
PAIN			
NRS, (median, min-max)	1.5 (0-3)	0 (0-0)	0 (0-0)
DYSPNEA			
VAS, (median, min-max)	1.5 (0-3)	6 (0-12)	4 (0-8)

Legend: POD: postoperative day WD: walked distance SD: standard deviation BI: Barthel Index NRS: numerical rating scale VAS: visual analogue scale.

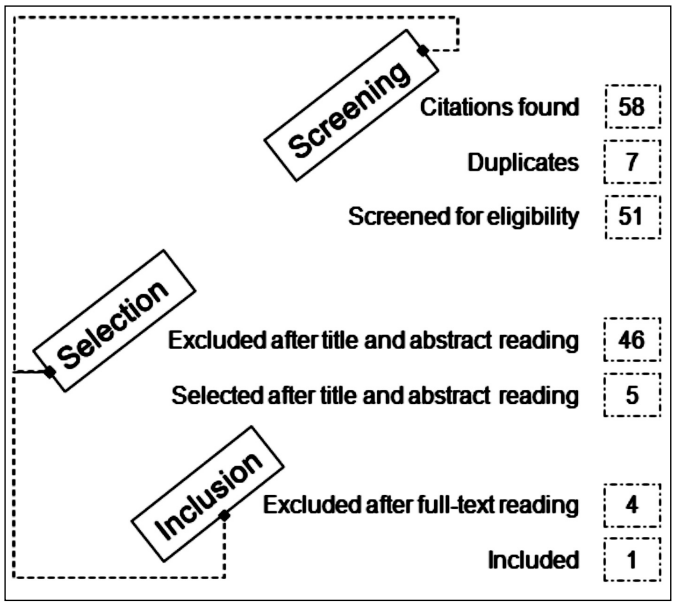

Fig. 3: Flow chart.

likely because exercise intensity and the WD were higher than on POD 1. However, the VAS values decreased on POD 4, although the WD increased by 76% (from 340 to 600 meters) and patients were able to climb stairs. These data indicate that dyspnea does not represent a major concern postoperatively. At the same time, neither the intensity of pain nor the level of postoperative physical autonomy hindered complete recovery in the first postoperative days. In fact, dyspnea and function did not seem to limit the progression of treatment. In light of this, we would argue that these patients do not present particular challenges during the rehabilitative postoperative course.

Are the results reported here directly related to the early initiation of physiotherapy? Although our results suggest that an immediate postoperative approach greatly contributed to substantial cooperation from patients, the nature of the present study prevents additional conclusions, and we are not able to directly relate the clinical outcomes to the characteristics of the physiotherapeutic interventions.

Limitations

As mentioned in the previous paragraph, the present study bears some limitations.

Regarding the literature review, only one study with a very small population size was included; furthermore, it did not cover the specific topic in question, as it was conducted in a different setting and in an undefined temporal frame, as shown in Table III. These features prevented us from obtaining a wider point of view on this topic. However, the included study did contribute some background information.

Table III - *Included study*

Authors (year), study design	Patients and Intervention	Main outcomes measures	Main results	Key points
Milazzo et al. (2007) case series (evidence level: IV)[§]	3 subjects (mean age 53.3±10.4 yrs.) completed a 3 weeks rehabilitation program (2 daily sessions) which consisted of: - respiratory exercises - cyclette - treadmill - ROM exercises - GPR	- FVC - FEV_1 - 6MWT - Borg Scale - BBS - RMI - SF-36v2	FVC and FEV_1 improved in 1 patient out of 3. Walked distance (6MWT), rate of perceived dyspnea (Borg Scale), BBS and RMI improved in all subjects after the postoperative rehabilitative intervention. In 1 patient out of 3, all the SF-36v2 domains improved after participation in the postoperative rehabilitation program. In 2 subjects out of 3, the GH domain of the SF-36v2 did not improve significantly.	This was the first study investigating the effects of a postoperative rehabilitation program following thymectomy in patients with MG. From the study was not possible to understand when the patients had initiated physiotherapy. Physiotherapy consisted in two daily sessions lasting three hours each, for three weeks: from these data it could be surmised that the rehabilitative intervention was proposed in a non-acute phase of the postoperative recovery, when subjects were likely more tolerating an intensive physical activity.

Legend: ROM: range of motion GPR: global postural reeducation FVC: forced vital capacity FEV_1: forced expiratory volume in 1 second 6MWT: six-minute walk test BBS: Berg Balance Scale RMI: Rivermead Mobility Index SF-36v2: short form-36 version 2 GH: general health MG: myasthenia gravis [§]Please see http://tinyurl.com/ochdj3q.

Regarding the two patients described here, a major limitation is represented by the absence of a follow-up after hospital discharge. Nevertheless, the purpose of our study was to evaluate clinical variables during the early in-hospital phase after surgery. Despite the above mentioned limitations, the present study answered our initial questions.

Conclusions

Our findings indicate that patients are willing to undergo immediate physiotherapeutic treatment in the ICU after thymectomy. We found that manual respiratory exercises could be proposed as soon as the patient is awake, and physiotherapy can be initiated in the early postoperative period. In addition, incentive spirometer exercises can be proposed to MG patients postoperatively to maintain pulmonary expansion, and motor activities can be introduced as early as POD 1 in MG-grade IIa patients who have undergone thymectomy.
In the cases reported here, the early physiotherapy was limited to four sessions, and no complications occurred after surgery or during the hospital stay. Motor and respiratory function were well conserved postoperatively, and the two subjects were pain-free from POD 2. It seems that physiotherapeutic intervention after thymectomy in MG-grade IIa middle-aged patients can be initiated immediately postoperatively in uncomplicated cases.

Riassunto

La miastenia gravis (MG) è una malattia rara autoimmune, caratterizzata dall'attivazione di autoanticorpi contro i recettori dell'acetilcolina: le persone con MG sono in genere affette da debolezza muscolare ed affaticamento. Gli obiettivi principali del presente studio sono stati quelli di 1) descrivere le caratteristiche del precoce intervento fisioterapico post-operatorio in due pazienti affetti da MG e sottoposti a timectomia, e 2) approfondire le conoscenze di background sul tema della fisioterapia post-operatoria per questa specifica classe di utenza. Oltre all'analisi dei due casi clinici, è stata condotta una revisione della letteratura al fine di trovare evidenze sul trattamento fisioterapico post-operatorio in pazienti con MG sottoposti a timectomia: quattro principali database sono stati interrogati.
I due soggetti descritti nel presente studio sono stati in grado di camminare nella 1a giornata post-operatoria (GP) e di salire e scendere almeno una rampa di scale nella 4a GP. L'intensità del dolore era maggiore nella 1a GP rispetto alla 2a e 4a GP. L'intensità della dispnea era maggiore nella 2a GP se comparata con quella percepita nella 1a e nella 4a GP. Per quanto riguarda la revisione della letteratura, sono state identificate 58 citazioni. Dopo la rimozione dei duplicati sono state valutate 51 citazioni e successivamente incluse 5 pubblicazioni. A seguito della lettura dei full-text, 1 articolo è stato incluso rispondendo ai criteri di inclusione stabiliti.
I risultati del presente studio sembrano indicare che la fisioterapia post-operatoria in soggetti adulti con MG (Grade IIa) sottoposti a timectomia possa essere avviata nell'immediato post-operatorio in casi non complicati da aggravamenti post-chirurgici.

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