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Original Article

Routine versus selective plasma exchange before thymectomy in myasthenia gravis

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Abstract

Background: Prethymectomy plasma exchange may improve the outcome of surgery; however, the technique is associated with an increased risk of complications. Therefore, the objective of this study was to compare selective versus routine plasma exchange before thymectomy in patients with myasthenia gravis.

Method: We conducted a prospective multi-center cohort study to compare two protocols for plasma exchange before thymectomy. We compared the routine plasma exchange in all patients undergoing thymectomy for myasthenia gravis (group I; n= 30) versus selective exchange (Group II; n= 30). Endpoints were the duration of postoperative mechanical ventilation, plasma exchange, and operative complications.

Results: There was no difference in age between both groups (30± 10.1 vs. 29± 9.2 years in Group I and II, respectively; p= 0.69). There were 17 females in Group I (56.67%) vs. 16 in group II (53.33%) (p= 0.8). Comorbidities are comparable between groups. All patients preoperative pyridostigmine, and 27 patients (90%) in Group I and 26 patients (87%) in Group II received glucocorticoids. There was no difference in pulmonary function tests between groups. Plasma exchange related complications were not different between groups. Immediate extubation was achieved in 29 patients (97%) in Group II, and after 6 hours in one patient (3.33%). In Group I, 28 patients (93%) extubated immediately, and two patients were ventilated for 7-12 hours. The mean ICU stay was 1.5 days in Group I and 1.4 days in group II (p= 0.615). The mean hospital stay was 8.5 days in Group I and 9.2 days in group II (p= 0.118). There was no significant difference in pathology between groups (p= 0.137).

Conclusion: Selective plasma exchange is feasible before thymectomy for myasthenia gravis. Selective plasma exchange may decrease exchange related complications without affecting the operative outcomes.

KEYWORDS

Plasma exchange; Thymectomy; Myasthenia Gravis

Article History

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Introduction

Several treatment options are available for the management of myasthenia gravis (MG), including medical and surgical treatment [1, 2]. The role of the thymus in the pathogenesis of MG is well-established [3], and thymectomy was found to be associated with sustained improvement in many myasthenic patients [4]. However, the

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postoperative complications after thymectomy, especially the need for mechanical ventilation, remain of concern [5]. Therefore, it is essential to optimize the patient's condition prior to surgery, especially in patients with severe myasthenic symptoms [6].

Plasma exchange (PLEX) before thymectomy appears to improve the postoperative outcome. However, several complications can occur following PLEX, such as infections. PLEX can be used selectively in high-risk patients before thymectomy to improve the surgical outcome and limit PLEX specific complications [7]. The use of preoperative PLEX was associated with a decrease in the duration of mechanical ventilation intensive care unit (ICU) stay [8].

Despite the widespread use of PLEX, there are several controversies about the indication, patients' selection, selective versus routine exchange. The effect of PLEX is short lasting [9], and repeated sessions are required within a short time, which can lead to the depletion of serum proteins, including coagulation factors. They may require several days for spontaneous recovery [10].

Therefore, the objective of this study was to compare selective versus routine plasma exchange before thymectomy in patients with myasthenia gravis.

Patients and Methods:

Patients and design:

We conducted a prospective multi-center cohort study to compare two protocols for plasma exchange before thymectomy. We compared the routine plasma exchange in all patients undergoing thymectomy for myasthenia gravis (group I; n= 30) versus selective exchange (Group II; n= 30). The study included 60 patients and was conducted between September 2016 and September 2019. Patients in Group I had routine plasma exchange before thymectomy, and in Group II, selective plasma exchange was performed for patients at high risk of prolonged postoperative mechanical ventilation. Assessment of high-risk patients was done according to the following criteria; forced vital capacity (FVC), forced mid-expiratory flow between 25% and 75% of the forced vital capacity (FEF25—75%), maximum expiratory flow at 50% of the forced vital capacity (MEF50%), and their percentages of the predicted as well as sex.

The diagnosis of myasthenia gravis was based on clinical presentation and laboratory investigations. The staging of MG was performed according to Osserman' s and Genkins' classification [11]. All patients received a neurological consultation preoperatively, for accurate detection of Esserman's class IIA or IIB symptoms. All patients had preoperative chest X-ray, chest computed tomography scan to exclude thymic tumors.

Patients were included in the study if they had MG Osserman' s class IIA and IIB in adult patients (older than 14 years old). Patients who had any contraindication to plasma exchange (infection, hemodynamic instability, and bleeding) were excluded from the study.

Ethical approval was obtained from the Research Ethics Committee of the participating centers, and patients' consent was obtained before enrollment.

Endpoints:

Postoperative extubation time was the primary endpoint, and secondary endpoints were plasma exchange and operation complications and duration of hospital stay.

Data collection:

For each patient enrolled in the study, we collected the preoperative variables, including age, gender, Osserman' s grade, preoperative medical treatment and the dose, number of preoperative PLEX session(s) and its complications, preoperative pulmonary function test (PFT) and their percentages from the predicted values and the results of the serological tests. Operative variables include the type of anesthesia and the use of neuromuscular blocking drugs. Postoperative data included the duration of mechanical ventilation, ICU, and hospital stay.

All patients in Group I received the preoperative PLEX and 17 patients in Group II. The

mean number of sessions for each patient was three, and the last session was 48 hours before thymectomy. Each session lasted for 1.5- 2 hours, and the aim was to remove 1-2 L of plasma at each session. COBE Spectra (COBE Laboratory, Lakewood, CO, USA), was used for PLEX.

Anesthetic management

Patients continued pyridostigmine and steroid until the day of surgery. Diazepam or lorazepam was used as a premedication at least 2 hours before surgery. Fentanyl- thiopentone were used for induction with sufentanil propofol in 41 patients. Thoracic epidural anesthesia was used in 47 patients. The neuromuscular blockade was used in 50 patients (83%). Nitrous oxide and isoflurane were used for anesthesia maintenance, and sevoflurane was used in 21 patients.

Surgical procedure

The basic principle for thymectomy is to remove all parts of the thymus gland with the surrounding fatty tissue and pericardial fat patch. In patients who underwent thymectomy via median sternotomy, phrenic nerves were the lateral landmarks of dissection. In patients who had video-assisted thoracoscopic thymectomy, we identified the right phrenic nerve, and the fat was removed until the left mediastinal pleura was clearly identified. All patients had video-assisted thoracoscopic thymectomy, and conversion to sternotomy was required in 3 patients.

Extubation in the operation room was planned in all patients depending on clinical and respiratory conditions. Patients with adequate neuromuscular function, with spontaneous breathing and tidal volume more than 5ml/ kg and inspiratory force of -20 cm H2O were amenable for early extubation. After surgery, all patients were transferred to ICU and continued the preoperative medications at the same dose. There were no operative or hospital deaths and no phrenic or recurrent nerve injuries in this patient population.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS version 20.0) (IBM Corp, Chicago, IL, USA) was used to perform the statistical analysis. Qualitative data were represented as number and percentage, and quantitative data as mean ± standard deviation (SD). The difference and association of qualitative variables were assessed using the Chi-square test. Differences between quantitative independent groups were assessed using a t-test or Mann Whitney test for non-normally distributed variables. P-value was set at <0.05 for significant results.

Results

Preoperative data:

Sixty patients with MG were enrolled in this study, all patients were divided into two groups, Group I (n= 30) had performed routine plasma exchange and group II (n=30) had selective plasma exchange before thymectomy in 17 patients. The study was performed from September 2016 to September 2019.

There was no difference in age between both groups (30± 10.1 vs. 29± 9.2 years in Group I and II, respectively; p= 0.69). There were 17 females in Group I (56.67%) vs. 16 in group II (53.33%) (p= 0.8). Comorbidities are comparable between groups. (Table 1)

Table 1: Dosage of the preoperative medications (Continuous data are presented as mean± SD, binary data as number and percentage)

	Group I (n= 30)	Group II (n= 30)	p
Hypertension	1 (3.3%)	2 (6.7%)	>0.9
Diabetes	1 (6.7%)	2 (6.7%)	>0.9
Hyperthyroidism	0	1 (3.3%)	>0.9
Pyridostigmine mg\day	215± 54.04	207± 53.34	0.566
Prednisone mg\day	16.33± 7.9	14.56± 6.4	0.344
Azathioprine mg\day	30± 12.6	34.34± 12.32	0.183

All patients preoperative pyridostigmine, and 27 patients (90%) in Group I and 26 patients (87%) in Group II received glucocorticoids. (Table 1) Preoperative assessment with pulmonary function tests was done in all patients. There was no difference in pulmonary function tests between groups. (Table 2)

Table 2: Preoperative pulmonary function tests (Data are presented as mean± SD)

	Group I (n= 30)	Group II (n= 30)	p
FEV1 (L)	1.7± 0.5	1.8± 0.9	0.5
FVC (L)	2.7± 0.5	2.5± 0.5	0.127
MEF50% (L/s)	3.6± 0.7	3.8± 1	0.373

FEV: Forced expiratory volume; FVC: forced vital capacity; MEF: maximum expiratory flow

The mean number of plasma exchange sessions in Group I was (3.2 ± 0.9) and (2.7 ± 1.1) in Group II (p= 0.059). Plasma exchange related complications are presented in Table 3.

Postoperative data:

Immediate extubation was achieved in 29 patients (97%) in Group II, and after 6 hours in one patient (3.33%). In Group I, 28 patients (93%) extubated immediately, and two patients were ventilated for 7—12 hours. The mean ICU stay was 1.5 days in Group I and 1.4 days in group II (p= 0.615). The mean hospital stay was 8.5 days in Group I and 9.2 days in group II (p= 0.118).

There was no significant difference in pathology between groups (p= 0.137). In Group I, the thymus was normal in 2 patients (6.7%), atrophic in 23 patients (76.7%) and hyperplastic in 5 patients (16.7%). In group II, the gland was normal in 5 patients (16.7%), atrophic in 24 patients (80%), and hyperplastic in 1 patient (3.3%).

Discussion

Thymectomy for the management of MG achieved good results, and the remission rate reached 75% at 15 years in non-thymomatous MG [7]. The thymus plays an important role in the pathogenesis of MG; hence thymectomy improved the outcomes. Most patients with MG had thymus hyperplasia, and 10% had associated thymoma [12]. However, in our study, the main pathology was atrophic; this can explain the different results in our study compared to others. Good outcomes were reported using the sternotomy approach [13]. The principal of surgical resection is to remove all thymic tissue, which could be achieved either using a sternotomy or minimally invasive approach [13]. Some studies showed no improvement in the symptoms if thymus tissue was left behind [14].

Preoperative optimization is essential to improve the outcomes and decrease the need for prolonged mechanical ventilation. Plasma exchange is used in patients prior to thymectomy; however, the technique has its own complications. Additionally, it is not known if all patients will benefit from preoperative plasma exchange [7].

Therefore, we compare routine versus selective plasma exchange in patients who underwent thymectomy for MG. Patients had selective plasma exchange based on Naguib and colleagues' criteria [15]. This model predicts patients who may require postoperative mechanical ventilation. Selective plasma exchange may benefit this patient group and avoid the plasma exchange complications in patients who will not benefit from it.

Table 3: Plasma exchange related complications (Data are presented as number and percent)

	Group I (n= 30)	Group II (n= 30)	p
Hypotension	3 (10%)	2 (6.67%)	>0.9
Coagulopathy	2 (6.67%)	1 (3.33%)	>0.9
Infection	1 (3.33%)	0	>0.9
Venous access complications	2 (6.67%)	0	0.492

Prethymectomy PLEX was performed in 47 patients in our series, and complications rates were comparable between groups. This result is similar to what was reported by Vucic and colleagues [16]. There was no difference in plasma exchange related complications between groups, which could be attributed to the small sample size. Generally, plasma exchange may have life-threatening complications such as anaphylactic reactions [17], but none was reported in this study.

Hypotension is a possible complication of plasma exchange, which was reported in 8% of our patents. This result is comparable to other series [18], and this complication could occur due to excessive fluid withdrawal.

Access site complications of plasma exchange were reported in 3% of our patients. Catheter-related complications may increase morbidity and mortality [9, 19] by causing severe bleeding. We did not any mortality related to access site complications in our series. Recently, ultrasound-guided venous access was introduced to decrease the complications [20].

We did not find significant differences in the postoperative mechanical ventilation and complications between groups. These results indicate that selective plasma exchange is feasible and did not increase the operative risk. Yeh and colleagues [21] and Nagayasu and coworkers [22] demonstrated a significant effect of the preoperative plasma exchange in patients who underwent thymectomy. El-Bawab and colleagues reported similar findings to our results regarding the role of selective plasma exchange [7].

Study limitations

The major limitation was the sample size; however, this is accepted since the disease is not common. Additionally, most patients had plasma exchange, and this may lead to difficulty in detecting the difference between groups.

Conclusion

Selective plasma exchange is feasible before thymectomy for myasthenia gravis. Routine plasma exchange did not affect operative outcomes and did not increase exchange or operative related complications. This gives the rationale to select patients for plasma exchange before thymectomy for myasthenia gravis.

Conflict of interest: Authors declare no conflict of interest.

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