Original Article

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A Comparative Study between Propofol and Thiopentone as Induction Agents in Myasthenia Gravis Patients for Thymectomy

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Abstract

Background: Anesthetic management of patients with myasthenia gravis is challenging, particularly in regards to the goals of respiratory function and extubation. We sought to compare two induction agents in patients undergoing trans-sternal thymectomy, evaluating the intra and post-operative conditions including extubation in the operating room.

Materials and Methods: Ten consecutive myasthenic patients undergoing trans-sternal thymectomy were prospectively randomized into two groups: Propofol and thiopentone. In the propofol, group anesthesia was induced with propofol (2 mg/kg) and intubation performed after topical anesthesia of the airway with lignocaine. In thiopentone group, anesthesia was induced with thiopentone (5 mg/kg) and intubation performed after topical anesthesia of airway with lignocaine. In both groups, anesthesia was maintained with isoflurane in oxygen and nitrous oxide. Fentanyl was used for analgesia in both the groups. Intubating conditions, hemodynamic changes, neuromuscular transmission along with postoperative intensive care unit stay were evaluated. Data were evaluated using ANOVA, Chi-square test, and Student's *t*-test.

Results: Intubating conditions were good in all patients. No significant hemodynamic changes are observed. Recovery was complete in all the patients, and all were extubated in the operating room. No other significant differences were observed between the two groups.

Conclusion: Both of these induction techniques allow early extubation of myasthenic patients in the operating room.

Key words: Myasthenia gravis, Propofol, Thiopentone, Thymectomy

INTRODUCTION

Myasthenia gravis is an autoimmune disorder of the neuromuscular junction. Autoantibodies against the α-subunit of the muscle-type nicotinic acetylcholine receptor destroy acetylcholine receptors of the neuromuscular junction and cause classic transmission failure with muscle weakness and fatigue. The number of active acetylcholine receptors get decreased either by a functional block, by increased rate of degradation of receptors or by complement mediated lysis.[1]

Sparing of other α-subunit of neuronal type nicotine acetylcholine receptors provides an explanation for the lack of autonomic or central nervous system involvement of the disease. In younger age groups, females are affected more often than males are, whereas in elderly age groups (>60 years), males are more frequently affected. There is a striking association between myasthenia gravis and hyperplasia of the thymus, with more than 70% of myasthenia gravis patients having thymus hyperplasia and only 10% having thymomas.

The diagnosis of myasthenia gravis is made by neurological examination and testing of the tendency to fatigue and exhibit increased weakness during exercise or

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repeated contractions. Pharmacologic treatment with anticholinesterases and immunosuppressants is aimed at manipulation of acetylcholine levels and the immune system, or by decreasing the circulating antibodies by plasmapheresis.[2,3]

Although the efficacy of thymectomy is based on retrospective data, it is a widely accepted therapy for myasthenic patients particularly those with thymoma and early-onset generalized myasthenia gravis.[4,5]

Post-operative complications may arise in these patients as a result of a stress-induced exacerbation of myasthenia gravis (myasthenic crisis) or due to an overdose of some drugs such as anticholinesterases (cholinergic crisis), antibiotics or antiarrhythmics.[6,7] Therefore, high-risk patients may require post-operative ventilators support in intensive care unit (ICU).[8]

Many anesthetic approaches have been reported in myasthenia gravis patients.[7,9,10] Here in this study, we compared two non-muscle relaxant anesthesia techniques in myasthenia patients undergoing trans-sternal thymectomy. The main objective was to evaluate the perioperative complications and feasibility of extubation in the operating room.

MATERIALS AND METHODS

The prospective study was conducted in NRI General Hospital on ten consecutive patients (7 male, 3 female) in the age group of 40-50 years who underwent elective trans-sternal thymectomy.

Preoperative Patient Demographics

Inclusion criteria: Osserman Stages I and II patients.

Exclusion criteria: Osserman Stages III and IV patients with concomitant respiratory complications.

According to the classification by Ossernman and Jenkins the clinical severity of myasthenia gravis myasthenia gravis was graded in five stages.

I - Only ocular muscle weakness
II - Mild weakness effecting other than ocular muscles
III - Moderate weakness effecting other than ocular muscles
IV - Severe weakness effecting other than ocular muscles
V - Defined by the need for intubation, with or without mechanical ventilation.

Besides routine tests, other pre-operative investigations included chest computed tomography scan, pulmonary functional tests, and detection of various circulating auto-antibodies (anti-acetylcholine receptor, anti-smooth cell, anti-nuclear factor).

All the 10 patients were divided into two groups: propofol and thiopentone. Before inducing the patients with propofol and thiopentone 10% xylocaine spray, is used for topical anesthesia of the pharynx and larynx. 3 min of pre-oxygenation with 100% oxygen by face mask was done, and propofol group is induced with fentanyl (2 μg/kg) and propofol (2 mg/kg). During laryngoscopy topical anesthesia of the vocal cords and trachea was obtained with the application of 4% xylocaine and intubated with adequate sized single lumen endotracheal tube. In thiopentone group, thiopentone 5 mg/kg was used, and the rest of the procedure was same.

In both the groups anesthesia was maintained with nitrous oxide, oxygen, isoflurane (End-tidal [ET] 1-1.5%), and propofol (3-10 mg/kg/h) infusion. Intraoperative monitoring included an electrocardiogram, invasive radial artery blood pressure monitoring, pulse oxymetry, $ETCO_2$, and neuromuscular transmission.

Baseline twitch amplitude of ulnar nerve is established after induction of anesthesia. First twitch (T1) was recorded as a percentage of baseline measure, and train of four was recorded as a ratio between the fourth and the first twitch (T4/T1).

During the intraoperative, we observed the intubating conditions (jaw relaxation and vocal cord abduction) and hemodynamic changes (mean arterial pressure and heart rate). After surgery, we recorded the ^T extubation (time from the end of anesthesia to extubation) and ^T awake (time from the end of anesthesia to eye opening). At the end of surgery, all patients were extubated in the operating room and transferred to the ICU for monitoring.

RESULTS

Demographic and preoperative characteristics of patients were depicted in Table 1. In the propofol group, mean arterial pressure and heart rate decreased 10% compared

Table 1: Demographic and preoperative characteristics of patients in the two groups

Patient characteristics	Propofol	Thiopentone
Gender: Male/female	4/1	3/2
Age (SD)	44.2 (2.68)	45.4 (2.30)
Body surface area (SD)	1.514 (0.04)	1.512 (0.08)
Osserman's staging		
II a	4	3
II b	2	1
Pre-operative treatment		
Pyridostigmine	5	5
Myasthenia gravis/day (SD)	240 (60)	240 (60)
Prednisolone (N)	2	2
FEVI (percentage of predicted value)	83	85

Data are expressed as mean (SD), FEVI: Forced expiratory volume in the 1st second, No: Number of patients, SD: Standard deviation

to baseline during surgery and returned to the preoperative value at the end of anesthesia. In thiopentone group, no significant change was observed in mean arterial pressure and heart rate (Graph 1a and b). The neuromuscular transmission remained stable in the propofol group, but in the thiopentone group single twitch and train of four decreased 15-20% compared to baseline intraoperatively ($P < 0.05$) and recovered completely after anesthesia (Graph 2a and b).

Since, we combined topical anesthesia for vocal cords with xylocaine along with induction agents propofol and thiopentone the intubating conditions were excellent in both the groups. As we used propofol for maintenance of anesthesia in both the groups, the most striking feature were fast recovery from anesthesia, the rapid orientation, and the minimal interference with psychomotor activity and coordination after prolonged anesthesia.

Duration of surgery and anesthesia, time to extubation, awakening, and postoperative complications are presented in Table 2. Arterial blood gas analysis was taken ½ h after extubation were also within limits. None of the patients experienced postoperative complications like respiratory insufficiency or bleeding for which they were observed 24 h in the ICU.

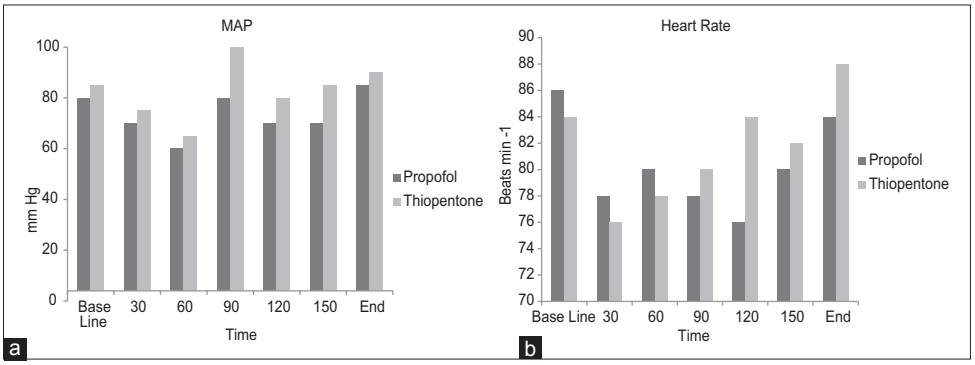
DISCUSSION

Blalock first successfully introduced thymectomy as a surgical treatment for myasthenia gravis.[11] Early,

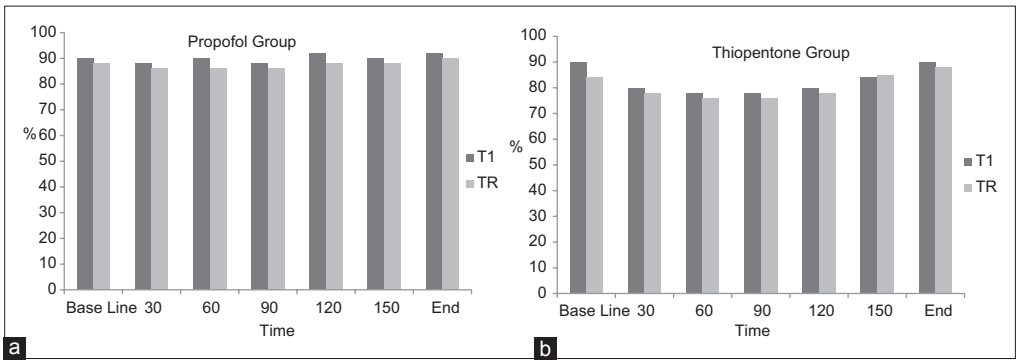
Table 2: Perioperative patient data

Observed parameters	Propofol	Thiopentone/ myasthenia gravis grade
Duration of surgery (min) (SD)	246 (24)	218 (28)
Duration of anesthesia (min) (SD)	278 (25.8)	270 (22.36)
^Extubation (min) (SD)	18.6 (2.60)	30 (3.80)
^Awake (min) (SD)	25.6 (3.78)	39.6 (3.64)
ABG 0.5 h after surgery		
Pao_2 (mmHg) (SD)	85.2 (2.28)	83.6 (1.67)
$Paco_2$ (mmHg) (SD)	38.8 (2.28)	38.4 (2.60)
Fio_2	0.4	0.4
Postoperative complications		
Respiratory insufficiency bleeding		
Post-op ICU stay (h)	24	24

Data are expressed as mean (SD), Magrade: Grade of myasthenia gravis (Osserman's staging), $F1o_2$: Inspired oxygen concentration, ICU: Intensive care unit, ABG: Arterial blood gas, SD: Standard deviation



Graph 1: (a and b) Mean arterial pressure and heart rate in the propofol and thiopentone groups at O (baseline), 30, 60, 90, 120, 150 min (during surgery) and at the end of surgery (end). *P* <0.05 compared to baseline, compared to end, and compared to the same moment in the propofol group



Graph 2: (a and b) Neuromuscular transmission in the propofol and thiopentone groups O (baseline), 30, 60, 90, 120, 150 min (during surgery) and at the end of surgery. T_1 = first twitch (%); TR = T4/T1 ratio, *P* < 0.05 compared to baseline, compared to end, and compared to the same moment in the propofol group

thymectomy is now the most preferable treatment of choice for most myasthenia gravis patients. The patient must ideally be admitted for thymectomy during the remission phase. As most of the patients are on pyridostigmine, the dose must be adjusted according to the individual need before surgery.

We observed in the present study, that using either propofol or thiopentone for induction and without using muscle relaxants throughout the surgery allows early extubation in the operating room without any postoperative complications. The intubating conditions were excellent in all patients, and no major hemodynamic disturbances were observed throughout the surgical procedure. Minimal changes were observed in the neuromuscular transmission throughout the surgery and showed complete recovery at the end of surgery in both propofol and thiopentone groups.

In myasthenia patients, use of muscle relaxants led to prolonged recovery time and increased the duration of postoperative ventilation.[8,12] Hence, non-depolarizing muscle relaxants were avoided in our study and to facilitate intubation we used the anesthetic spray to the vocal cords for better relaxation. Adequate surgical conditions were also provided intraoperatively during the entire procedure with the use of continuous propofol infusion and isoflurane. Propofol also attenuates skeletal muscle contractions by presynaptic inhibition of acetylcholine release thereby providing better surgical conditions intraoperatively. Though it is better to avoid muscle relaxants, several studies have reported the use of short-acting muscle relaxants (vecuronium, atracurium, cisatracurium) in association with short-acting inhaled anesthetics (sevoflurane, desflurane) provided early recovery and extubation.[13-15]

As myasthenia gravis patients are more sensitive to neuromuscular depression by the volatile agents,[16] we used low-fat soluble isoflurane in our study, so that it can be rapidly eliminated by the lungs and ensure complete neuromuscular recovery.

We compared two anesthetic techniques in ten myasthenia gravis patients coming from thymectomy. Good intubating conditions with acceptable jaw mobility and vocal cord relaxation were observed in the propofol group.[17] Good hemodynamic stability throughout the intraoperative period and mean time to awake and extubation were similar in both groups.

The patients in our stuffy group belong to Osserman's Class I or II, which have no preoperative respiratory involvement. Whether the determination of postoperative mechanical ventilation imply, preoperative Osserman's classification,[18] or the use of intraoperative muscle relaxants is debatable.

In our study, the management of myasthenia gravis patients with standardized anesthesia technique (without muscle relaxants) provided optimal intubating and operating conditions and also avoided the need for postoperative ventilatory support and shorter duration of hospital stay.

CONCLUSION

This study with propofol and thiopentone as induction agents without the use of muscle relaxants throughout the surgical procedure for myasthenia gravis patients provided satisfactory anesthetic conditions for intubation and also allowed early extubation after the procedure.

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