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THYMECTOMY IN MYASTHENIA GRAVIS;
ANAESTHETIC MANAGEMENT WITH PROPOFOL-TRAMADOL WITHOUT MUSCLE RELAXANTS ALLOWS EARLY EXTUBATION.

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ABSTRACT... roblnafirdous@hotmail.com Background Anaesthetic management for thymectomy in myasthenia gravis (MG) presents a significant challenge to the anesthesiologist due to neuromuscular involvement. One of the recommended techniques of general anaesthesia is to avoid the use of muscle relaxants and rely on propofol anaesthesia or a combination of propofol and an analgesic. Objectives: This study was undertaken to investigate the efficacy and safety of propofol-tramadol anaesthesia for transsternal thymectomy in MG and to find out whether it allows early extubation. Design of Study: Quasi-experimental/before-after type Setting: PMC, District Headquarter Hospital, Faisalabad. Period: From February 2004 to July 2005 Methods: Twelve consecutive myasthenic patients undergoing transsternal thymectomy were included in this study based on temporal sampling. Anaesthesia was induced with propofol-tramadol, without muscle relaxants and maintained with propofol infusion and toradol and tramadol boluses as required, together with ventilation with oxygen and nitrous-oxide. Results: Propofol-tramadol anaesthesia allowed early extubation of all the patients without any anaesthesia related complications. Conclusions: Propofol-tramadol anaesthesia is safe and allows early extubation.

Key words: Anaesthesia, myasthenia gravis, thymectomy, neuromuscular, muscle relaxants, propofol, tramadol, analgesic, extubation

INTRODUCTION

Myasthenia Gravis (MG), an autoimmune disease of the neuromuscular junction, results from the production of antibodies against the acetylcholine receptors of the neuromuscular synapse1. It is characterized by weakness and fatigability of skeletal muscles, with improvement following rest. The incidence is 50-142 cases per million population2. In a majority of patients with MG, the thymus gland is involved in the autosensitization process and about 40-90% of patients are benefited by thymectomy[3].

The perioperative management of a myasthenic patient undergoing transsternal thymectomy poses a significant challenge to the anaesthesiologist. The patient is unusually sensitive to non-depolarizing muscle relaxants commonly used during anaesthesia[4].

There is a risk of postoperative respiratory failure that may result from stress induced exacerbation of MG (myasthenic crisis) or
other adverse drug interactions[5].

Different techniques for Anaesthetic management of myasthenic patients undergoing thymectomy have been reported. The balanced technique of general anaesthesia which includes the use of muscle relaxants may be used if neuromuscular transmission is monitored[6].

This technique, however, involves some significant complications for myasthenic patients; the major concerns being the respiratory muscle weakness and adverse side effects due to the heavy dose of anticholinesterases. This limits the use of muscle relaxants in Anaesthetic management for transsternal thymectomy in myasthenic patients.

An approach based on anaesthesia management without using muscle relaxants should facilitate the perioperative management, allowing early recovery of muscle functions in myasthenic patients. Some anesthesiologists avoid the use of muscle relaxants in myasthenic patients and rely on deep inhalational Anaesthetics, such as halothane or isoflurane. But reports have shown that these inhalational Anaesthetics can depress neuromuscular transmission in myasthenic patients[7].

As an alternative to inhalational anaesthesia, total intravenous anaesthesia (TIVA) with propofol or a combination of propofol/remifentanil8, without muscle relaxants, has been employed for thymectomy in a few reported cases of myasthenia gravis. This management is safe and allows better lung function postoperatively.

The experience of the use of propofol or sevoflurane anaesthesia without muscle relaxants is though limited, the results have been encouraging. In a limited number of reported cases, anaesthesia induction with a combination of propofol and remifentanil has been smooth and effective for myasthenic patients.

This study was aimed at assessing the effectiveness of non-muscle relaxant technique using propofol-tramadol anaesthesia without muscle relaxants.

The specific objectives of the study were:

1 . To evaluate the feasibility to extubate the patient in the operating room
2. To document perioperative complications

METHODS

From February 2004 to July 2005, twelve consecutive myasthenic patients, ten females and two males, underwent elective transsternal thymectomy at District Headquarter Hospital, Faisalabad. (Table I) After getting their informed consent, they were included in this study.
Anaesthetic Technique:

No patient was premedicated. Before induction of anaesthesia, Xylocaine 2% and 4% were used for topical anaesthesia of the pharynx and larynx. After 3-5 minutes of preoxygenation with 100% oxygen by face mask, anaesthesia was induced with tramadol 1 .5 mg kg'1, and propofol 1-2 mg kg'1.

During laryngoscopy, topical anaesthesia of the vocal cords and trachea was obtained with the application of 4% Xylocaine following which the trachea was intubated with an adequate sized single lumen endotracheal tube.

All patients received Ringer's Lactate solution 7-8 ml kg'1 hr1 during the procedure.

Mechanical ventilation was adjusted to maintain the end-tidal C02 (Et C02) 30-35 mmHg with respiratory rate of 14 breath/min, tidal volume of 8 ml kg1 and an inspiration-expiration ratio of 1:2. Anaesthesia was maintained with nitrous oxide and oxygen 70:30 respectively, and a continuous infusion of propofol 3-6 mg kg"1 hr1 supplemented by 2 boluses of tramadol 100 mg and a single bolus of toradol 30 mg as required.

Monitoring:
Infra-operative monitoring included electrocardiogram, blood pressure monitoring, pulse oximetry, and end-tidal C02. Neuromuscular transmission was monitored with (Train-of-Four) TOF Guard.

The forearm was immobilized in order to prevent interfering movements. The ulnar nerve was stimulated supramaximally at the wrist with train-of-four stimuli each of 60 mA for 200 ps at 30 s intervals and acceleration of the thumb was measured. Baseline twitch amplitude was established after the induction of anaesthesia.

T1 was recorded as a percentage of baseline measure and TR was recorded as ratio between the fourth and the first twitch (T4/T1). Skin temperature was monitored and maintained above 32˚C.

The evaluation of intra operative conditions included intubating conditions (jaw relaxation, laryngoscopy and vocal cords abduction).

Intraoperative haemodynamic changes and neuromuscular transmission were continuously monitored and recorded at times 0 (baseline) 30,60,90,120,150 minutes and at the end of anaesthesia.

Time from the end of anaesthesia to extubation (extubation), time from the end of anaesthesia to eye opening and recovery of consciousness (awake) were recorded.

All major complications such as respiratory depression, respiratory failure and cardiovascular events and other minor postoperative complications were recorded. At the end of surgery, all the patients were extubated in the operating room and transferred to the intensive care unit for monitoring.

Measurements and Statistics
The body surface area (BSA) of human body, male or female, was determined with a nomograph based on the formula9, BSA =, giving BSA in m2, while

W being the weight in kg, and H the height in m. Patient age, body surface area, preoperative pyridostigmine dosage (mg day4), intraoperative propofol administration, mean arterial pressure (MAP), heart rate (HR), and intraoperative neuromuscular transmission were recorded as mean with standard deviation (SD).

Preoperative FEV1, duration of surgery and anaesthesia extubation, awake, and ICU stay were also expressed as mean with standard deviation. Microsoft Excel was used for organizing and analyzing data.

RESULTS

Patients demographic and preoperative characteristics are listed in Table-l, and perioperative data are summed up in Table-ll. Intubating conditions were good in all the twelve patients.

There was no haemodynamic response to skin incision and no patient movement in response to surgery was observed.

Table-1. Demographic and preoperative characteristics of patients undergoing thymectomy	
No. Of patients	12
Gender: M/F	2/10
Age: (yr) (Range) [SD]	32(23-40)[11]
Height: (m) (Range) [SD]	1.59 (1.56-1. 7) [0.08]
Weight: (kg) (Range) [SD]	62.5 (50-90) [14]
Body surface area: (m2) [SD]	1.6 [0.29]
Osserman's staging	
I	0
Ila/IIb ..	8
III	4
Preoperative treatment	
Pyridostigmine (mg day 1) [SD]	240 [60]
Prednisolone (No. Of patients)	8
FEVI (% of the predicted value)	83
Data are expressed as mean [SD] FEVI: Forced expiratory volume in the first second	
Table-ll. Perioperative patient data	
Duration of surgery: (min) [SD]	167 [18]
Duration of anaesthesia: (min) [SD]	180(19]
A Extubation (min) [SD]	11 [4]
A Awake (min) [SD]	17.5 [7]
ABG 0.5 hr after surgery:	
Pa02(mmHg)[SD]	89 [3]
PaC02 (mmHg) [SD]	38 [2.5]
Postoperative complications:	
Respiratory insufficiency	0
Bleeding	1
Postoperative ICU stay (hr) [SD]	68 [15]
Rostoperative hospital stay (day) [SD]	9 [2]
Data are expressed as mean [SD] ABG: Arterial blood gases. Yr: Year, min: minutes	

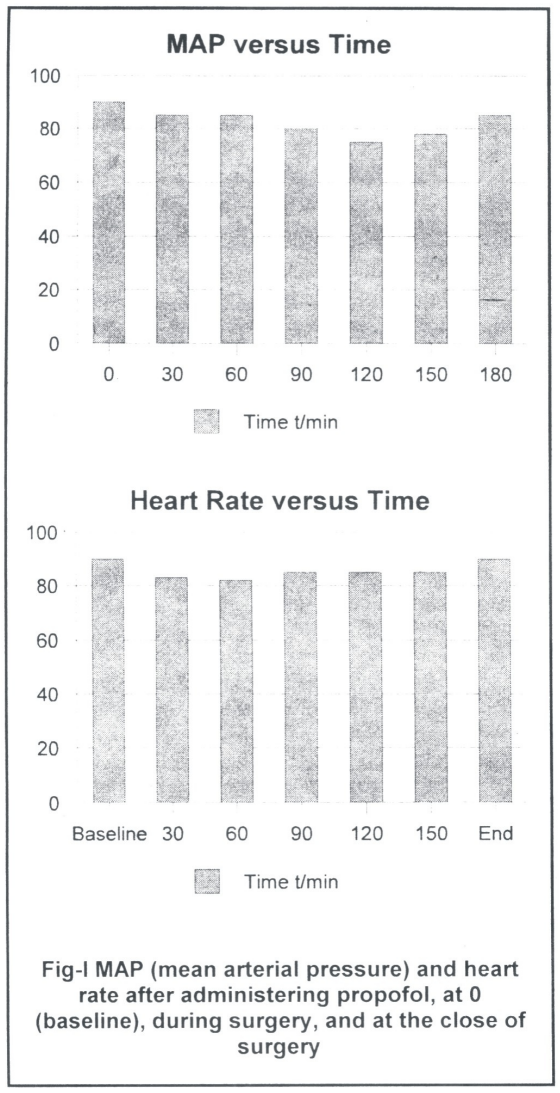

Fig-I MAP (mean arterial pressure) and heart rate after administering propofol, at 0 (baseline), during surgery, and at the close of surgery

DISCUSSION

The results of this study indicate that a non-muscle relaxant technique for Anaesthetic management of myasthenic patients undergoing transsternal thymectomy allows early extubation with no respiratory problem in intraoperative or postoperative period.

Anaesthesia induced with propofol-tramadol, and maintained with propofol infusion and toradol and tramadol boluses as required, together with

ventilation with oxygen and nitrous-oxide, brought about early extubation in the operating room.

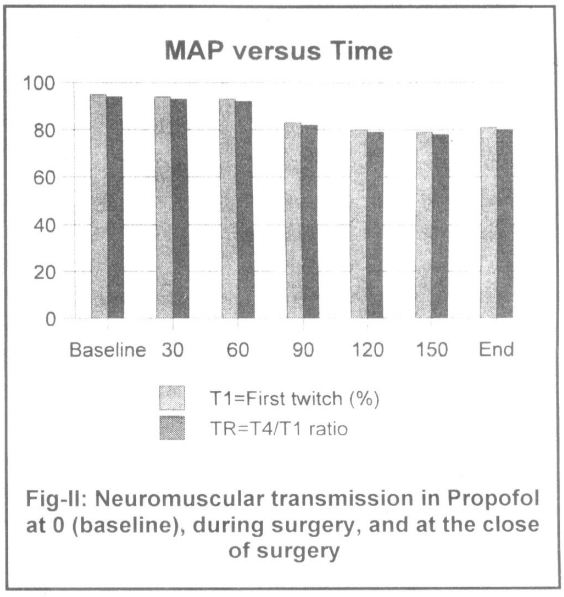

Fig-II: Neuromuscular transmission in Propofol at 0 (baseline), during surgery, and at the close of surgery

The intubating conditions were good in all the twelve patients. There were only minimal haemodynamic changes. None of the patients had to be intubated for postoperative respiratory depression. Neuromuscular transmission was slightly depressed but it recovered at the end of anaesthesia. Recovery was complete in all the patients at the end of the procedure. No postoperative complications related to anaesthesia were observed.

Two recommended techniques for general anaesthesia in myasthenic patients have been: the balanced technique which utilizes muscle relaxants, and the non-muscle relaxant technique. The use of muscle relaxants in myasthenic patients has been associated with (i) a higher rate of unsuccessful extubation, (ii) longer postoperative mechanical ventilation, and (iii) longer stay in hospital10. As the neuromuscular effects of non-depolarizing muscle relaxants are known to be prolonged in myasthenic patients, the use of muscle relaxants was avoided.

Chevalley and colleagues11 discussed the evolution of the perioperative management of myasthenic patients undergoing thymectomy and the possibility to predict the need for systematic postoperative ventilation. They observed that postoperative ventilation was more frequently required when a balanced technique involving muscle relaxants was employed. The results of the present study are in agreement with the observations made in the referred article because the employment of non-muscle relaxant technique allowed the early extubation of all the twelve myasthenic patients in the operating room.

The results of the use of propofol for thymectomy in myasthenia gravis have been described in the literature in small study groups or case reports. In their remarkable study, involving sixty-eight myasthenic patients undergoing transsternal thymectomy, Rocca and collegures12 concluded that propofol or sevoflurane anaesthesia without muscle relaxants allows the early extubation of myasthenic patients. By obtaining similar .results with propofol-tramadol anaesthesia without muscle relaxants, the present study supports and supplements the previous work.

The use of propofol in induction and maintenance of anaesthesia did not require postoperative respiratory support for the patient13. Propofol has been shown to obtund airway reflexes and allow a relatively easy intubation in the majority of the patients. The rapid elimination of propofol13 allowed fast recovery of consciousness, airway reflexes and respiratory function at the end of surgery, precluding a prolonged period of intubation and mechanical ventilation.

Thymectomy is generally performed in patients with initial symptoms of MG, so the majority of

patients in this study belonged to Osserman's Class Ha or lib, with no preoperative respiratory depression. It is debateable if the determinants of postoperative mechanical ventilation are the preoperative clinical condition14 (such as Osserman's Class), or the intraoperative use of muscle relaxants. Four out of twelve patients included in this study belonged to Osserman's Class III, and none of them suffered from respiratory complications.

In 1989, a case of opisthotonus following the Anaesthetic induction by propofol was reported. The patient was a woman with a known history of epilepsy16. Propofol should not be used in patients with a history of epilepsy.

CONCLUSIONS

This study concludes that anaesthesia induced with propofol-toradol and maintained with propofol infusion and toradol-tramadol boluses along with ventilation with oxygen and nitrous-oxide is a suitable non-muscle relaxant technique for thymectomy in myasthenia gravis. It offers smooth induction and rapid recovery, with no or minimal changes in neuromuscular function. Spontaneous ventilation is effectively restored at the end of the surgical procedure and there is no residual muscle weakness during the postoperative period.

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