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"TOTAL INTRAVENOUS ANESTHESIA (TIVA) AND EPIDURAL ANALGESIA FOR THYMECTOMY IN A PATIENT OF MYASTHENIA GRAVIS: A CASE REPORT."

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ABSTRACT Myasthenia gravis (MG), an autoimmune disease is characterized by fatigable weakness of the skeletal muscles as a result of an antibody-mediated immunologic response directed at the acetylcholine receptors in the postsynaptic membrane of the neuromuscular junction (NMJ). Anesthesia concerns for patients with MG include the disease treatment and the interaction of various anesthetic agents, particularly neuromuscular blocking agents (NMBAs). Patients with MG are sensitive to non-depolarizing NMBAs and resistant to succinycholine (Depolarizing NMBA). We present a case of trans-sternal thymectomy for myasthenia gravis using total intravenous anesthesia (TIVA) technique of anesthesia with propofol and fentanyl.

KEYWORDS : Myasthenia Gravis, Autoimmune, Neuromuscular Junction, Succinylcholine, Thymectomy, Total Intravenous Anesthesia.

INTRODUCTION

Myasthenia gravis (MG) is an autoimmune-mediated disease characterized by weakness and fatigability due to dysfunction of the neuromuscular junction from antibodies directed against the acetylcholine receptor (anti-AchR). The thymus has been regarded as the main site for the production of anti-AchR and the thymectomy has been accepted as the standard therapy in the treatment of MG [1].

MG is associated with unusual sensitivity to neuromuscular blocking agents and volatile anesthetics, and the risk of postoperative respiratory failure. Various anesthetic techniques, that eliminate the use of neuromuscular blocking agents to avoid these problems, have been reported in MG patients [1, 2]. Total intravenous anesthesia (TIVA) has been recommended for patients with MG, because it helps avoid the use of both neuromuscular blocking agents and volatile anesthetics [3,4].

This is a case of trans-sternal thymectomy for myasthenia gravis using total intravenous anesthesia (TIVA) technique of anesthesia (propofol and fentanyl) and Epidural Analgesia. No use of any muscle relaxant was employed. This technique provided a greater control over hemodynamic responses during surgery while allowing an early and smooth extubation on termination of anesthesia.

Case Report

A 67 year old, 60kg male with a 1 year history of myasthenia gravis was scheduled for trans-sternal thymectomy. Clinically his symptoms correlated with an Osserman classification [5] of IIa (Table 1). His principal complaints were of proximal limb muscle weakness in all four limbs with sparing of bulbar function. On examination he had bilateral ptosis, diplopia on upward gaze and limb weakness in all limbs with fatigue. Palatal and tongue movements were normal with no difficulty swallowing water. His preoperative treatment consisted of pyridostigmine 30 mg 8 hourly and Tablet Azathioprine 50mg 12 hourly. This provided symptomatic relief but had mild proximal limb weakness. There was no evidence of additional co-existing autoimmune disease.

Table 1: Osserman classification.

I	Ocular symptoms only.
IIa	Ocular symptoms and mild generalized disease.
IIb	Bulbar symptoms and moderately severe generalized disease.
III	Generalized disease, acute bulbar impairment, respiratory failure with or without dysphagia.
IV	Severe generalized disease, bulbar involvement and elderly.

Diagnosis had been established on the basis of the clinical picture, a positive edrophonium test (transient improvement in muscle strength after intravenous edrophonium 2 mg) and elevated acetylcholine receptor antibodies at >2 nmol/l (normal up to 0.25 nmol/l, positive >0.4 nmol/l). On CT THORAX a prominent thymus meassuring 26 × 25 mm in size is seen, which shows homogenous enhancement upto 50HU. His respiratory function was stable with preoperative spirometry as follows; FVC of 1.89 litres (predicted 2.31), FEV1 of 1.89 litres (predicted 1.66), FEV1/FVC of 71.86% (96%) and peak flow of 4.58 litres/ second (predicted 6.41 litres/second). His ECHO showed an Ejection Fracyion of 55-60% with normal functions. The patient was continued on Tablet Pyridostigmine 30mg TDS till day of surgery. However Azathioprine was omitted on the day of surgery. Premedication was given in the form of Tablet Alprazolam 0.25mg and Tablet Ranitidine 150 mg the night before surgery. The patient was kept nill per oral the night before surgery and a written informed consent was obtained. The patients airway was prepared using nebulisation with 5ml of 4% Lignocaine 30 min before induction. The patient was then shifted to the operating room with two working i.v. lines (16G and 18G) in B/L forearms with co-loading of 0.9% Normal Saline at 90ml/hour. All standard monitoring were attached and baseline parameters were recorded on a multiparameter monitor. Under local anesthesia an arterial line was secured in the left radial artery and invasive blood monitoring was started. A thoracic epidural was placed in the T8-T9 intervertebral space and a continuous infusion was started using Bupivacaine (0.125%) and Morphine (3mg) in a total volume of 180 ml kept at 4ml/hour. Then the patient was preoxygenated for 3 minutes and a premedication of Inj. Midazolam 1mg i.v. with Inj. Fentanyl 100 μg i.v. was given. Anesthesia was started intravenously through bolus Inj Propofol 1.5mg/kg followed by infusion of propofol 4 mg/kg/hour and Fentanyl 1 μg/kg/hour. After 2 minutes, 10% lignocaine was sprayed into the patient's airway and the trachea was intubated using video assisted laryngoscopy. Intubating conditions as assessed were; jaw relaxation—good, cord relaxation—fair and reaction to intubation—slight [6].

Anesthesia was continued with infusions of propofol 4 mg/kg/hour and fentanyl 1 μg/kg/ hour, intermittent positive pressure ventilation using a low tidal volume (200ml), high respiratory rate (20 breaths/min) and oxygen to nitrous mixture (60:40). A nasal temperature probe was placed and the patient was kept warm using a lower body convection

heater. A nasogastric tube was also inserted. A triple lumen central line was placed in the left internal jugular vein under ultrasound guidance.

The continuous arterial pressure and pulse tracings were recorded (Figure 1) and two serial ABG's were taken at 60 min and 120 min intervals (Table 2). Significantly there were no changes in pulse rate or blood pressure to intubation, skin incision or sternotomy. Normothermia and normocapnia were maintained throughout the procedure which lasted ~ 120 minutes. During skin suturing the infusion rate of propofol was reduced to 2 mg/kg/hour and at the end of the procedure both infusions were stopped. The spontaneous respiration in the patient commenced within 15 minutes and the patient was extubated when the patient could no longer tolerate the tube and maintained a sustained head-lift for > 5 seconds. Oxygen therapy was continued using nasal prongs with 100% oxygen at 2 litres per minute maintaining a blood saturation of ≥ 98%. The patient was subsequently transferred to the intensive care unit for continuous monitoring.

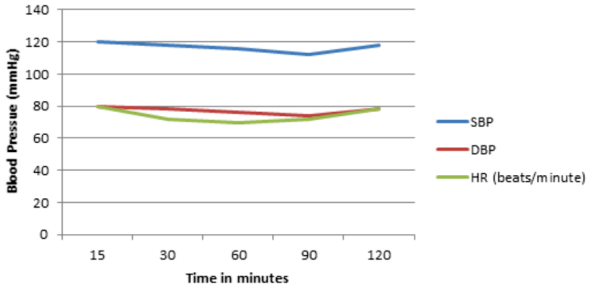

Figure 1: Intra-operative blood pressure and heart rate at various intervals.

Table 2: Intraoperative Arterial blood gases values.

Time in minutes from start of surgery	pH	PCo_2 (mmHg)	PO_2 (mmHg)	HCO_3^- (mmol/l)
60 min	7.265	64.51	160.63	29.52
120 min	7.312	57.03	204.1	29.11

Postoperative analgesia was continued using epidural analgesia technique for the next 12 hours. However, intravenous paracetamol (1g TDS) was added along with injection morphine 1mg i.v. bolus for breakthrough pain as and when required were also added additionally. Pyridostigmine was recommenced at 60 mg 8 hourly. Arterial blood gas monitoring was performed at 2, 6 and 12 hours after the procedure with the patient on oxygen 2 litres per minute via nasal prongs (Table 3). After 12 hours the patient was judged suitable for transfer to the open ward on oxygen 2 l/minute. Recovery was otherwise unremarkable.

Table 3: Postoperative Arterial blood gases values at 2litres/minute.

Time in hours from end of surgery	pH	PCo_2 (mmHg)	PO_2 (mmHg)	HCO_3^- 29.11
2 hours	7.32	52.50	187.51	28.46
6 hours	7.37	47.03	165.01	27.20
12 hours	7.38	45.30	142.51	26.40

DISCUSSION

The increased sensitivity of myasthenic patients to the action of a variety of nondepolarizing neuromuscular blocking agents has been well documented in the literature [7, 8, 9, 10]. Similarly the increased potency of the neuromuscular blocking properties of volatile anaesthetics has been noted, with Nilsson suggesting that in the case of isoflurane the presence of acetylcholine receptor antibodies and the HLA-B8 genotype may predict a more susceptible subgroup [11]. While the safe inclusion of both these groups of drugs in myasthenia gravis has been demonstrated, including non-relaxant techniques [12], neuromuscular transmission may be depressed as a direct result of their use. In addition the use of anticholinergic agents in reversing neuromuscular blockade raises the possibility of inducing cholinergic crisis [13]. The use of total intravenous anesthesia (TIVA) with epidural regional anesthesia technique appears to avoid both these hazards as has previously been reported [14]. The placement of propofol in TIVA is well established however, the introduction of fentanyl appears to offer an ideal companion for minimum impact at the neuromuscular junction and precise control of depth and duration of balanced anesthesia. Addition of epidural analgesia allows for impressive intraoperative control of cardiovascular responses to noxious stimuli such as sternotomy while achieving rapid emergence and early return of spontaneous ventilation.

Our case illustrates just such features with no significant rate or pressor responses during maintenance of anesthesia, while spontaneous respiration commenced nine minutes after cessation of the infusion with extubation after fifteen minutes. These times compare well with published data in subjects with normal neuromuscular function [15]. The use of such a "rapid offset" opioid does however require adequate provision of postoperative analgesia. The addition of epidural analgesia in anticipation of ongoing analgesic requirements in our case does not appear to have delayed return of ventilation, although it may have contributed to the modest postoperative hypoventilation as demonstrated by the blood gas values and the PaCO2 during extubation. While the use of a combined fentanyl/propofol total intravenous technique might avoid many pitfalls associated with anesthesia in the myasthenic patient, it still requires attention to detail, particularly with respect to immediate postoperative pain relief. Nevertheless we have been able to demonstrate that in this case the technique offered both excellent intra-operative conditions and early extubation.

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