Perioperative Management of Myasthenic Patients

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Abstract

Background: Myasthenia Gravis is an autoimmune disorder of the synaptic transmission. On the pre-operative visit, the presence of neurological symptoms and a careful review of used medications are of the most importance. Thymectomy is one of the most useful treatments in myasthenic patients.

Objectives: This review is aiming to make an update related with perioperative considerations in patients with Myasthenia Gravis.

General considering: General anesthesia for myasthenic patients scheduled for a thymectomy should be performed during stable phases of the disease and when patients require the less immunomodulatory drugs and are in optimal state. The preoperative use of acetyl cholinesterase inhibitors is controversial, it will improve muscle strength, patient comfort and decreases the risk of respiratory stress but will reduce cholinesterase activity, increase the risk of vagal responses and the need of higher doses of NDNMB agents.

Conclusion: Myasthenia gravis is a rare disease, but requires anesthesiologist specific knowledge and skills. The pharmacokinetics and pharmacodynamics of neuromuscular blockers are important for successful patient outcomes.

INTRODUCTION

Pathophysiology MG

Acetylcholine (Ach) is synthetized in the motor nerve terminal and stored in vesicles. The neural action potential determines that approximately 150 to 200 are released and combine with AChR, densely located at the peak of post synaptic folds [3,4].

In MG, the main pathophysiological features are the decrease in the number of available AChR at the post synaptic muscle membrane and the flattening of post synaptic folds, resulting in a decreased efficiency of neuromuscular transmission; therefore even if Ach is released normally it produces small end-plate potentials that may fail to trigger muscle action potentials.

The amount of Ach released per impulse declines on repeated activity, phenomenon known as presynaptic rundown [3], in the myasthenic patients the combination of the pathological features and the presynaptic rundown determine the main clinical symptom of myasthenic patients, muscular fatigue.

Immunological response to muscle specific kinase (MuSK) occurs in 40% of myasthenic patients negative to antibodies against AChR. Other patients, whose sera are negative to both antibodies, will be positive to antibodies against to a low density lipoprotein receptor related protein 4 (Lrp4) [4].

Thymectomy

Thymectomy is one of the most useful treatments for MG. It is done for surgical removal of a thymoma or as a treatment in patients with MG.

Although most of thymomas are histological benign, removal is necessary due to the risk of local spread.

In the absence of tumors, up to 85 % of patient’s experiences improvement after thymectomy, of these, approximately 35 % achieve drug free remission, improving long term outcomes [3].

It is a consensus that thymectomy should be performed in all patients with generalized MG who are between the ages of puberty and 55 years. Studies have [5] shown that patients with MuSK antibodies positive MG respond less well to thymectomy than those with ACh antibodies [3].

Thymectomy should never be done as an emergency procedure and the need of pre-operative plasmapheresis or intravenous immunoglobulin should be considered trying to avoid the risk of post-operative infections [3].

Objective

The objectives of this review are aiming to make an update related with perioperative considerations in patients with MG.
METHOD

An advanced search was performed on December 3rd, two thousand sixteen between eight hours thirty minutes and fourteen hours forty minutes in the PubMed databases of the National Medical Library of the United States (NLM) using the following descriptors in English: Perioperative management and Myasthenia gravis, Perioperative.

From a total of 69 articles, we excluded those more than five years ago, case reports, obstetric and pediatric patients and cardiovascular surgery.

When the filter was activated, human research we were obtain 62. Publication date in the last five years 13. Subsequently the filter was activated to full text nine appointments were obtained. The search was then restricted to systematic review and found two related articles and clinical trials 0 references appeared.

GENERAL CONSIDERING

Anesthetic considerations

General anesthesia for myasthenic patients scheduled for a thymectomy should be performed during stable phases of the disease and when patients require the less immunomodulatory drugs and are in optimal state.

Azathioprine can inhibit non depolarizing neuromuscular blocking agents (NDNMB) and might extend the effect of suxamethonium [4].

The preoperative use of acetyl cholinesterase inhibitors (ACI) is controversial, it will improve muscle strength, patient comfort and decreases the risk of respiratory stress but will reduce cholinesterase activity, increase the risk of vagal responses and the need of higher doses of NDNMB agents [5,6].

A cycle PLEX should be used in patients with acute exacerbations who must undergo to surgery urgently, but the use of this agent might be associated with prolonged action of suxamethonium and ester local anesthetics due to ACI like effect [5,6].

Neuromuscular blocking drugs act by interrupting neuromuscular transmission at the level of the nicotinic acetylcholine receptors at the motor end plate. In myasthenic patients the sensitivity to non-depolarizing muscle relaxants is increased and the time course of effect is prolonged due to a reduced number of functional acetylcholine receptors at the neuromuscular junction. This sensitivity has been described in patients with minimal disease, in that in apparent remission and in those with subclinical undiagnosed myasthenia. The main complications associated with the use of neuromuscular blocking drugs in myasthenic patients are prolonged mechanical ventilation associated with respiratory depression, and atelectasis (collapsed areas of lung tissue). Although there are differences in the prevalence of these complications among various institutions, there is no evidence that aggressive treatment shortens the course of those complications

A reduced number of functional acetylcholine receptors are associated with increased sensitivity to NDNMB therefore intraoperative neuromuscular function monitoring is of paramount importance. Clinicians should be aware of a possibility to overestimate the degree of neuromuscular blockade at one site as will not always represent the level of block in other muscle groups.

As mentioned above the use of ACI, pyridostigmine, will impact on the use of NDNMB agents. Patients treated with pyridostigmine may have prolonged suxamethonium and ester local anesthetic effect, due to inhibition of plasma cholinesterase, and slower onset with a need of higher doses of NDNMB agents. Reversal might be difficult if the acetyl cholinesterase has been fully inhibited [6,7].

Myasthenic patient who are not taken ACI, will be resistant to suxamethonium and sensitive to NDNMB, due to a reduced number of AChR [6].

Thyroid function tests should be obtained in all myasthenic patients, hyperthyroidism occurs in 3 to 8% of patients 3, and may aggravates myasthenic weakness.

The chronic pre-operative use of glucocorticoids is associated with adrenal suppression and the need of pre-operative steroid supplementation should be considered.

Multimodal approach of post-operative pain control is a priority. Suboptimal pain management might precipitate a myasthenic crisis; the use of continuous infusion of Remifentanil with careful titration of responses is a valid option.

NDMB agents and MG: Mivacurium, Vecuronium, Atracurium and Cisatracurium have been used in myasthenic patients [7] (Table 1).

The author [8], have used doses of mivacurium higher than the doses recommended by previous publications [9], with similar findings on the neuromuscular patterns.

We have found that dose of cisatracurium equal to 15 μg/Kg [10], would decrease the clinical effect of this agent when compared with the dose classically recommended.

In a study done by the author [11], comparing rocuronium and vecuronium in patients scheduled for trans sternal thymectomy, a full spontaneous recovery was achieved at 71.3 minutes when was compared with vecuronium (96.3 minutes).

A rapid recovery of a neuromuscular function has been found in myasthenic patients receiving rocuronium when sugammadex (2 mg/Kg) was used for reversal, this combination seems to be a safe alternative in myasthenic patients for whom intraoperative neuromuscular relaxation is mandatory [12-14].

Regional anesthetic techniques are safe [6], with either use of amides or esters agents, but judicious dosing is essential as preparedness to manage worsening of muscle weakness safely.

Wolfe et al. [15], conducted the thymectomy trial in non-thymomatous myasthenia gravis patients receiving prednisone therapy, an international, randomized, single-blind (rater-blinded) trial, to determine whether extended transsternal thymectomy combined with a standardized prednisone protocol would be superior to prednisone alone after three years, with respect to lessening myasthenic weakness, lowering the total dose of prednisone, and enhancing quality of life. Extended
Induction with anesthetic of short duration as propofol

To calculate 25% of total dos is used in patient non myasthenic

Never to antagonize the neuromuscular blockers in mysthenic patient

Extubation only when the clinic recoveries are evident
If is posible monitorízate the neuromuscular function
the hight twitch ≥ 90 % o rate T4/T1 ≥ 90

Always that will be possible to monitorizate the neuromuscular function

Preoperative period

Plasmapheresis
Hyperimmune Immunoglobuline IV
Prednisone

Induction with anesthetic of short duration as propofol

To calculate 25% of total dos is used in patient non myasthenic

Mivacurium
Atracurium
Vecuronium

Extubation only when the clinic recoveries are evident
If is posible monitorízate the neuromuscular function
the hight twitch ≥ 90 % o rate T4/T1 ≥ 90

Always that will be possible to monitorizate the neuromuscular function

Plasmapheresis
Immunoglobuline inmune EV
Antibiotic therapy
Prednisone

Admites in ICU 72 hs

Without complications go to the hospitalization room

CONCLUSION

Myasthenia gravis is a rare disease, but requires anesthesiologist specific knowledge and skills. The pharmacokinetics and pharmacodynamics of neuromuscular blockers are important for successful patient outcomes.

REFERENCES