“Neuromuscular management in multiple sclerosis”

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Introduction

In demyelinating diseases, multiple sclerosis is the most frequent, muscular weakness are due to abnormalities in the central nervous system, which leads to the need to minimize the possibility of postoperative residual neuromuscular relaxation, so we have to avoid postoperative morbidity and mortality as far as possible.

Multiple sclerosis

Demyelinating diseases are characterized by inflammation and selective destruction of myelin in the central nervous system, while the peripheral nervous system remains immune. In multiple sclerosis (MS) are the triad of inflammation, demyelization and gliosis, being able to have different evolutionary patterns, including relapsing remitting MS (RRMS, 85% of cases), primary progressive MS (PPMS, around 15% of cases) and secondary progressive MS (SPMS). It is necessary to emphasize in our environment is the second cause of neurological disability in the early or middle stage of life after trauma, presenting twice as often in women than in men and appearing between 20 and 40 years. In this disease there are weakness in the extremities that can manifest as loss of power or skill, fatigue or abnormal gait. The manifestation of weakness induced by exercise, typical of the upper motor neuron involvement is characteristic of multiple sclerosis and it is often accompanied with other signs such as pyramidal spasticity, hyperreflexia and Babinski. It is necessary to emphasize the weakness is the most frequent manifestation of the disease among the sensitive losses and the optical neuritis (1, 2). Motor deficits occur as a result of the involvement of the descending motor pathways, and may include paraparesis or paraplegia and less frequently weakness of the upper limbs. Amyotrophic due to disuse may also be present.

The typical signs of this disease are two, the first one is Lhermitte's sign, which consists of a transient electric-like shock extending down the spine triggered by flexing the head forward, and the other one is the Uhthoff phenomenon, which is the worsening of neurologic symptoms when the body gets overheated from hot weather, exercise or fever. The diagnosis is usually supported by radiological images and laboratory tests.

The McDonald criteria are also used to support it (3).

Multiple sclerosis and anesthesia

With a view to the anesthetic managing of this pathology, it is necessary to bear in mind the particularities of this disease even also the pharmacological treatment, because it is going to have important implications on the intraoperative behavior as well as on the metabolism and the sensibility of certain drugs. The withdrawal of the usual medication of the patient is controversial, there are studies that relate the discontinuity of the treatment with the appearance of new symptoms or the worsening of existing ones, especially in those patients who previously had high activity of the disease (4, 5, 6, 7).

Multiple sclerosis and neuromuscular relaxation

Respiratory dysfunction is very rare in ambulatory MS patients, while it is more frequent in MS patients with high disability. Characteristic of this disease is respiratory dysfunction in most patients in later stages, and in some of them, in the initial stages, although total lung volume and vital capacity may be normal, maximal inspiratory and expiratory efforts are often subnormal and may even approach 50% of normal values, which makes them especially susceptible for respiratory disorders secondary to residual neuromuscular paralysis. In this line, non-depolarizing blocking agents (NDBA) will be considered in two aspects, first one the interaction with the usual medication of this disease and the second one, the possible altered response to them. As we have mentioned before these patients suffer frequent spasticity, baclofeno must be the administered medication. This medicament can produce muscular weakness, provoking in the patient a extreme response to the action of the NDBA and, in addition it cannot be withdrawn sharply since it is capable of provoking agitation, delirium and seizures, not taking for granted that it has to be removed during two weeks at least. Thus, treatment with this drug in a patient involving emergency can become a big in problem handling with relaxation. In addition, selection of the anesthetic agents can prevent the exacerbation of MS symptoms after surgery, but some (poor) evidence exists only for epidural anesthesia, and that many controversies still exist (3,7,8,9). Moreover, apart from this consideration,

increased or decreased response to these agents is controversial; firstly there are studies that review resistance to their action based on an increase in the number of postsynaptic receptors and the action of certain drugs, especially, anticonvulsants such as carbamazepine. On the other hand, the muscular weakness and the decreased muscular mass in these patients can increase this response (7, 8, 10, 11, and 12). These forces to an exhaustive titration of the dose, monitoring the degree of relaxation, and closely vigilance of the neuromuscular blockade recovery.

The nerve twitch should be monitored, if possible, on an unaffected extremity so that factors will not lead to unintended overdoses (7).

The use of succinylcholine deserves special mention because of the risk of producing hyperkalemia, especially in cases of disease exacerbation. This risk also correlates with the progressive disease (13, 14). Levine y Brown has described a case of life-threatening hyperkalemia during an exacerbation of MS (15). In this case the patient had serum potassium levels of 3.7 mEq/L prior to the use of succinylcholine, which lift up dramatically, creating wide-complex arrhythmias. A new potassium test after treating with glucose and insulin, calcium and bicarbonate, reflected serum potassium levels of 6.4 mEq/L. The rise in serum potassium levels caused by succinylcholine, generally described as 0.5 mEq/L in patients without disease, can be up to 1.8 mEq/L in patients with neuromuscular disease (16). Therefore the use of succinylcholine must be avoided in this disease. However, it usually presents the necessity of a rapid sequence induction in relation with the depression of the pharyngeal and laryngeal reflexes due to risk of aspiration (8).

Considering the above, a blocking agent that disappears completely at the end of surgery is mandatory, preventing postoperative respiratory disorders, and at the same time can be used in a rapid sequence induction with an acceptable quality of intubation. Rocuronium only reaches this ultimate goal; meanwhile sugammadex solves the two handicaps.

Rocuronium

It is a non-depolarizing neuromuscular blocking agent of intermediate-acting with a rapid onset of action, which presents all the characteristic pharmacological actions of this kind of drugs (coraciiform). It acts by competing for nicotinic cholinergic receptors of the motor end plate.

It is indicated as an adjunct to general anesthesia to facilitate the tracheal intubation and in the induction of rapid sequence, as well as to obtain the relaxation of the skeletal musculature during the surgery. The standard dose of rocuronium in intubation is of 0.6 mg/kg, which provides suitable conditions of intubation in almost all the patients in 90 seconds. A dose of 1.0 mg/kg of rocuronio is recommended to facilitate tracheal intubation conditions in a rapid sequence induction, which provides suitable conditions of intubation in almost all the patients in 60 seconds. If a dose of 0.6 mg/kg rocuronium in rapid sequence induction is given, it is recommended to incubate the patient 90 seconds

after the administration of rocuronium (17). In the case of rapid sequence induction, doses of 1.2 mg/kg of rocuronium have not proved to be inferior to succinylcholine, finding the last reviews the shorter duration of the last as the only advantage over rocuronium (17). All these findings suggest rocuronium is a good option for patients with MS.

Sugammadex

It is a molecule indicated in the reversion of the residual paralysis induced for rocuronium or vecuronium and also in the immediate reversion after full dose of rocuronium. Sugammadex is a gamma cyclodextrin that is a "Selective Relaxant Binding Agent". It forms a complex with the rocuronium or vecuronium in plasma and thereby reduces the amount of neuromuscular blocking agent available to bind to nicotinic receptors.

A dose of 4 mg/kg of sugammadex is recommended when recovery has reached at least 1-2 post-titanic counts (PTC). A dose of 2 mg/kg of sugammadex is recommended if spontaneous recovery has occurred up in the reappearance of T2 at least, following rocuronium or vecuronium induced blockade. In case of clinical need for immediate reversal after administration of rocuronium, a dose of 16 mg/kg sugammadex is recommended. If there is a recurrence of neuromuscular blockade post-operatively after an initial dose of sugammadex, a repeat dose of 4 mg/kg sugammadex is adequate (19, 20).

Besides previously described, the safety in the use of sugammadex is higher than the use of other molecules like neostigmine which is not effective in all the circumstances and has a wider profile of undesirable effects (19).

Multiple sclerosis and sugammadex

As described above and as published in the literature, the choice of rocuronium as a relaxing agent and subsequent reversal with sugammadex should be used in general anesthesia patient with MS. Using this combination shall solved two problems posed by this situation, on the one hand the presence of residual neuromuscular paralysis resulting from the use of non-depolarizing relaxants and on the other the risk of hyperkalemia when using succinylcholine. Several case reports document the successful reversal of rocuronium with sugammadex, so their muscle function was quickly and reliably restored to the preoperative state (21). Many studies have shown the rocuronium-sugammadex combination works as fast as succinylcholine whereas the onset and the recovery time (22, 23, and 24). Although most publications support the need to avoid using succinylcholine, there are few studies describing the use of rocuronium. Furthermore have been reports where the use of mivacurium showing sufficient security (25), however its release of histamine makes us opt for rocuronium, owing to the hemodynamic problems caused by alterations in the autonomic nervous system in these patients. Although there are few publications, some of them discuss cases using rocuronium and sugammadex even repeatedly in the same patient with an excellent safety pattern (26, 27, 28, and 29).

Conclusions

Even though the methodological grade of the publications supporting the use of sugammadex and rocuronium is not optimal, it seems the best option. Hereby, and waiting for higher quality evidence and strength of recommendation, we suggest the use of this combination.

Conflict of Interest: None

Contribution: the entire article

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