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Enhancement of muscle relaxant effect of rocuronium by intraseptal injection of a solution containing lidocaïne and epinephrine : a case report

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Abstract : *Introduction* : Various drugs and physiologic disturbances affect the action of neuromuscular blocking agents. If some are ignored by the anesthesiologist, e.g. in the absence of monitoring of neuromuscular function, the patient may be at risk of potentially severe consequences related to postoperative residual curarization.
Case presentation : A 67-year-old female patient underwent septoplasty under general anesthesia with basic monitoring (three-lead electrocardiogram, non-invasive blood pressure, end-tidal partial pressure of carbon dioxide and SpO_2) and a monitoring of neuromuscular function using acceleromyography of the adductor pollicis. General anesthesia was induced with propofol and sufentanil. After neuromuscular monitoring calibration, a single dose of rocuronium was given. Thereafter the trachea was intubated and anesthesia was maintained with sevoflurane. One hundred and two minutes after the administration of rocuronium, a 1% lidocaine solution containing 5µg/mL epinephrine was injected under the mucosa of the nasal septum immediately before the incision. Two minutes after this injection, the train of four ratio was significantly reduced. It took about 13 minutes to recover to the value recorded before the submucosal injection.
Conclusion : Epinephrine increases the degree of muscle relaxation achieved by rocuronium, even when neuromuscular function is recovering. Monitoring is the only mean to rule out a risk of postoperative residual curarization, given the numerous medications and factors interfering with the action of neuromuscular blocking agents.

Keywords : Rocuronium, Lidocaine, Epinephrine, Neuromuscular blocking agents, Postoperative residual curarization.

Introduction

Various patient factors (e.g., burns, age) or physiological disturbances may alter the action of muscle relaxants. Several drugs can also enhance or inhibit the response to neuromuscular blocking agents (NMBA). Halogenated anesthetics, antibiotics (aminoglycosides, tetracycline, clindamycine), and magnesium sulfate potentiate neuromuscular blockade. Antiepileptic drugs such as carbamazepine increase the clearance of NMBA while lithium and some other antidepressants prolong muscle relaxation by activating potassium channels pre-synaptically (resulting in the inhibition of the release of acetylcholine at the neuromuscular junction) and inhibiting butyrylcholinesterase, respectively (1, 2). We report an enhancement of neuromuscular blockade associated with a submucosal injection of a solution containing lidocaine and epinephrine.

The patient agreed to the publication of the case and signed an informed consent form.

Case presentation

A 67-year-old female patient (1,66 m height, 68 kg bodyweight), ASA PS 1, was scheduled for septoplasty under general anesthesia. She had no relevant medical history. Her physical examination was unremarkable. She was taking no medications and had no allergies. The patient was fasted for 8h before anesthesia. No medications were given before anesthesia. Upon admission to the operating theater, the patient was equipped with basic monitoring (ECG, SpO_2, NIBP, capnography). Neuromuscular function was assessed using acceleromyography of the right adductor pollicis (TOF Watch SX®, Organon, Swords Co., Dublin, Ireland). A preload device was attached to that hand (HandAdapter® ;

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Organon, Swords Co., Dublin, Ireland) in order to secure the position of the transducer. The arm was kept in the same position during the entire procedure.

Anesthesia was induced with sufentanil (10 µg) and propofol (2 mg/kg). After loss of consciousness, the acceleromyograph was calibrated using the implemented TOF-WatchSX® calibration mode 2. Train of four (TOF) stimulation was used. For the purpose of a clinical study, all data were stored on a laptop computer using a specific software (TOF-Watch SX®, version 2.2.). Then rocuronium bromide (0.6 mg/kg) was administered and the trachea was intubated. Anesthesia was maintained with sevoflurane and supplemental analgesia was provided by repeated administrations of sufentanil. No additional rocuronium and no other medication were given before mucosa infiltration by the surgeon. About 102 minutes after the injection of rocuronium, immediately before the incision, the surgeon injected 3 ml of 1% lidocaine hydrochloride solution containing 5 µg/ml epinephrine under the mucosa of the nasal septum. This long delay between rocuronium administration and the infiltration of the mucosa was related to the unavailability of the required surgical instruments. Two minutes after the injection, the TOF ratio began to decrease. It decreased for about 3 minutes by about 35% and then recovered. It took 13 minutes to return to the initial TOF ratio recorded at the time of injection (Fig. 1).

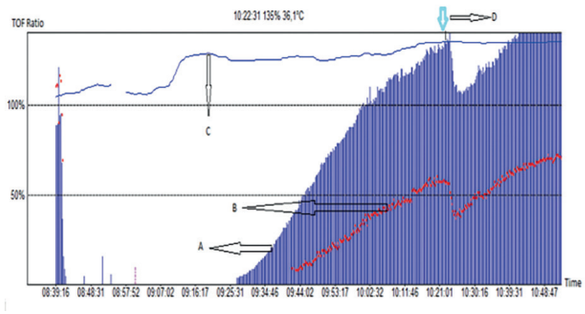

Fig.1. — Acceleromyographic recording of the effect of 0,6 mg/kg rocuronium showing the enhancement of the block by epinephrine and lidocaine solution. A: T1 (amplitude of the first response to TOF) ; B: TOF responses ; C: Muscle temperature at the site of monitoring ; D: Injection of the epinephrine and lidocaine solution.

Discussion

In ear, nose and throat surgery, infiltration of the surgical field with a solution of local anesthetic and epinephrine is common practice. In the case we report, a potentiation of the rocuronium-induced neuromuscular block was observed by the injection of 3 ml of lidocaine 1% containing 5 µg/ml epinephrine under the mucosa of the nasal septum. Two minutes after the injection of the lidocaine-epinephrine mixture, performed while neuromuscular blockade was recovering, the TOF ratio lessened by about 35% and took about 13 minutes to recover the value recorded just before the injection by the surgeon (Fig. 1). Previously published case reports have suggested that intravenous or nebulized epinephrine has the potential to alter rocuronium-induced neuromuscular blockade (3, 4).

These observations stress the impact of the administration of epinephrine on the neuromuscular blockade and the risk of postoperative residual curarization (PORC).

The case we report is consistent with the results of a small and poorly known study (5). In that study, the oral mucosal injection of lidocaine (6 mg) and epinephrine (mean dose 85.6 µg) resulted in an enhancement of the rocuronium-induced neuromuscular blockade (5). The effects of the administration of epinephrine and/or lidocaine on muscle relaxation induced by neuromuscular blockers have been assessed in several animal and human studies. In anesthetized feline, paralyzed with tubocurarine, the intravenous administration of epinephrine has a dual effect on neuromuscular blockade (6, 7). Initially, at low concentration, epinephrine reverses muscular relaxation, likely through an alpha-adrenergic effect at nerve endings (6). Thereafter, at higher concentrations, epinephrine enhances muscle relaxation. This enhancement is related to beta-adrenergic effects that result in hyperpolarisation of the end phase (6). The latter result is consistent with findings from a human study showing that the onset times of rocuronium are slowed by esmolol and accelerated by ephedrine (8).

The effects of lidocaine on neuromuscular blockers induced relaxation have been a matter of controversy for a long time. However, the last publications on the effects of lidocaine on muscle relaxation induced by neuromuscular blockers showed no effect. In humans, Cardoso found that an intravenous bolus of lidocaine (1.5 mg/kg) prolonged the early blockade recovery stage of rocuronium-induced muscle relaxation. However, it did not alter the onset or late recovery stage (9). Another human study failed to find any significant effect of intravenous lidocaine (1,5mg/kg bolus followed by a continuous infusion of 2 mg/kg/h) on rocuronium-induced neuromuscular block (10). The latter is consistent with another study that concluded

that lidocaine does not alter recovery from cis-atracurium-induced muscle relaxation (11). Also, it is worth noting that doses of lidocaine administered to the patients of the aforementioned studies were much higher than those administered in our patient (0.44 mg/kg).

All by all, the contribution of lidocaine to the alteration of the rocuronium-induced neuromuscular blockade observed in our patient seems to be minimal if any. Conversely, the enhancement of this neuromuscular block is most probably related to the vascular absorption of epinephrine. In order to prove that epinephrine was effectively responsible for the observed effect, a prospective controlled study would be necessary. Also, this case report highlights the paramount importance of monitoring neuromuscular function in anesthetized patients who are given muscle relaxants (12). Indeed, numerous drugs and conditions have the potential to alter the effects of neuromuscular blocking agents and their duration of action. Postoperative residual neuromuscular blockade is associated with the impairment of pulmonary and upper airway function. Such impairment can lead to postoperative adverse respiratory events including aspiration of gastric contents, upper airway obstruction, hypoxemia and ventilatory failure (13). In order to be as safe as possible and prevent any PORC or re-paralysis in the post-anesthesia care unit when drugs such as epinephrine are used shortly after extubation, it is important to reverse muscle relaxation to a TOF of 90% or better 100% measured at the thumb before tracheal extubation.

Conclusion

Given the numerous medications and factors interfering with the action of neuromuscular blocking agents and in order to avoid PORC and its potentially severe complications, a monitoring of the neuromuscular function should always be utilized when NMBA are used. Obtaining a TOF of 100% at the thumb before emergence from anesthesia is the only way to ascertain that the neuromuscular block is fully reversed.

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