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Review article

Optimal anesthesia protocols for successful intraoperative neuromonitoring during thyroid surgery

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There are several factors related to anesthesia that are required for successful intraoperative neuromonitoring (IONM) during thyroid and parathyroid surgery, including proper placement of endotracheal tube, adequate neuromuscular blockade, use of appropriate neuromuscular blockade reversal agent, and pain management. In this review, we summarize the anesthesia issues related to IONM during thyroid and parathyroid surgery.

Key words Intraoperative nerve monitoring, Thyroid surgery, Thyroid carcinoma

Introduction

One of the most serious surgical complications after thyroid surgery is recurrent laryngeal nerve (RLN) injury. The incidence of vocal cord palsy has been reported up to 5.2% for transient palsy, and up to 3.6% for permanent palsy[1,2]. Identification of the RLN is often difficult when the tumor is large or when localized inflammation is present. Evaluation of RLN functional integrity becomes even more challenging when relying on only visual inspection because traction injury can cause functional damage without leading to visual damage to the RLN[3]. Now days, intraoperative neuromonitoring (IONM) is widely employed during thyroid surgery to monitor the function of the RLN and the vagus nerve.

IONM involves two sequential actions: The first is the stimulation of the RLN or vagus nerve, and the second is the detection of electromyography (EMG) evoked by vocal cord movement. The surgeons receive audial or visual feedback from the IONM system allowing them to judge whether the nerves are functioning or not. IONM during thyroid surgery shows very high negative predictive value and relatively low positive predictive value[4]. A well- detected EMG signal predicts postoperative normal vocal cord function with high accuracy. However, the EMG signal cannot be detected during surgery, even when there is no nerve injury (false-positive). Successful IONM requires suitable EMG endotracheal tube placement, appropriate use of

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anesthetic agents, effective reversal of neuromuscular blockade, and a dry operative field. Most of these factors related to 'detection of the EMG signals' during IONM are closely associated with the area of anesthesiologists. Therefore close collaboration between the anesthesiologist and the surgeon is essential for successful IONM. In this review, we will discuss the anesthetic considerations and optimal protocols for successful IONM during thyroid surgery.

Various types of EMG detection sensors

The most common EMG detection method during IONM is detecting the EMG signal using an electrode attached to the endotracheal tube. Commercialized EMG endotracheal tubes as well as adhesive electrode can be used for this purpose. However, use of commercialized EMG endotracheal tubes or adhesive electrodes is limited because they are costly and there are insurance issues in some countries. Several trials have been conducted to overcome tube positioning issues. One study inserted a needle electrode into the laryngeal muscles. They reported that this approach was highly sensitive with a low false positive rate[5]. However, this approach is invasive and may cause complications, so it is not commonly used. Another study used adhesive skin electrodes attached to the anterior neck skin to detect a subtle EMG signal in the vocal cords. This method is non-invasive, cost effective, and easily applied. However, the authors reported that the evoked EMG amplitude was relatively low, which may result in a high false positive rate[6]. This is because the position of the skin electrode is relatively distant from the laryngeal muscle. Surgeons have different preferences regarding the method of detecting EMG signals depending on their expertise, experience with false negative or positive rates, and the surgical conditions. In addition, the surgeon must also consider non- medical issues including the patient's economic situation or the insurance system requirements when selecting their EMG signal detection method of choice.

EMG tube intubation and positioning

The most common reason for IONM failure is malposition of the EMG endotracheal tube[7]. Migration of the tube by just 1 cm in either direction can significantly decrease EMG signal detection[8,9]. This can cause inaccurate information to be conveyed to the surgeon which can jeopardize the patient's safety[10].

The favored surgical position for thyroidectomy is supine with the neck slightly extended. However, the endotracheal tube can migrate during positioning [10-16]. One previous study reported that tube migration more than 1 cm occurred in 12.7% of patients during patient positioning[17] and another reported that tube repositioning was required by 5% of patients for successful IONM in thyroid surgery[18]. Tube repositioning during surgery may cause bucking or hemodynamic changes such as hypertension or tachycardia. To avoid tube migration and improve IONM quality, patient positioning prior to intubation should be considered.

There are several technical issues related to tracheal intubation for a patient in an extended neck position. The ideal patient position for direct laryngoscopy or tracheal intubation has been discussed since the 1900's[19]. Magill introduced the 'sniffing position' as the ideal posture for tracheal intubation in 1936 and it has largely been uncontested ever since[20-24]. Unlike the sniffing position, the surgical position for thyroidectomy can cause difficulties in tracheal because the glottic view is not easily visible. Using a video-laryngoscope may help anesthesiologists obtain glottic visibility. In previous studies, we showed that tracheal intubation for a patient in the surgical position for thyroidectomy was feasible and rarely required tube repositioning[25-28].

Selecting neuromuscular blockade agent and reversal agent

There are numerous studies investigating NMB and reversal strategies for successful IONM. We would like to discuss five such strategies which are well established: (1) using relaxant- free approach, (2) using small dose of nondepolarizing neuromuscular blocking agents (NMBA) without a reversal agent, (3) using a depolarizing NMBA - succinylcholine, (4) using a nondepolarizing NMBA followed by a reversal agent including neostigmine , and (5) using rocuronium followed by sugammadex.

There are inherent disadvatages associated with the first four methods. The relaxant- free approach may cause difficult intubation conditions and complciations such as dental injury. Although a small dose of nondepolarizing NMBA (i.e., 0.3 mg/kg of rocuronium) without reversal agents is sufficient for tracheal intubation, it may cause delayed reversal of NMB for IONM. Use of a depolarizing agent such as succinylcholine is limited for muscle relaxation because of associated complications such as hyperkalemia, rhabdomyolysis, and malignant hyperthermia. Nondepolarizing NMBA followed by reversal agent, including neostigmine or sugammadex, can provide good conditions for both tracheal intubation and IONM without delayed reversal of NMB. While both neostigmine and suggammadex are reported to be effective for reversal of NMB, the effectiveness of the two agents have not been compared sufficiently.

Now, it is well known sugammadex is effective as an NMB reversal agent, especially for NMB by rocuronium. However, there are several issues that clinicians should be aware of. First, because sugammadex was introduced to the market only about 10 years ago, unknown side effects pose noteworthy potential risks. In particular, researchers have reported concerns that sugammadex overdose could lead to complications such as severe bradycardia, interaction with setroids, coagulopathy, and neuronal damage. Several human studies have investigated the use of various doses of sugammadex combined with different doses of rocuronium for IONM during thyroid surgery[26,30-34]. Until recently, combination of 0.6 mg/kg rocuronim and 2 mg/kg sugammadex was recommended for IONM during thyroid surgery or parathyroid surgery[30,31,34]. However, NMB does not need to be as fully reversed for IONM during thyroid surgery as it does for extubation, so this dose of sugammadex may be excessive. It should be taken into account that recovery from NMB until train of four (TOF) $\geq$ 0.9 is not essential to ensure successful IONM[26,28]. A recent randomized controlled study showed that a low dose of sugammadex (1 mg/kg) following 0.6 mg/kg of rocuronium provided good conditions for IONM with fewer intraoperative bucking events compared with 2 mg/kg of sugammadex[26].

While it is clear that the timing of sugammandex administration should be optimized, to the best of our knowledge, no research or guidelines have been published about the optimal timing of sugammadex administration to reverse NMB for IONM during thyroid surgery. Therefore, further studies are necessary to address this issue.

When sugammadex is used for the reversal of NMB, re-establishment of neuromuscular blockade by rocuronum or vecuronium, particularly shortly after reversal, such as in case of immediate reoperation or reintubation must be challenging. In such cases, cisatracurium or succhinylcholine could be the drugs of choice. A previous study indicated that sufficient dose of cisatracurium (2 × ED95 for tracheal intubation, equivalent to 0.1 mg/kg) provided better conditions for tracheal intubation than 0.05 mg/kg of cisatracurium without disturbing IONM[35].

Selecting maintenance anesthetic agents

Traditionally, total intravenous anesthesia (TIVA) is the standard method of general anesthesia used for evoked potential monitoring during neurosurgery. For example, a combination of propofol and remifentanil is widely used during brain or spine surgery with evoked potential monitoring. In those surgeries, TIVA is preferred over inhaled anesthetics because inhaled anesthetics can suppress neurinal response to stimulation. In line with this concept, a recent study investigating IONM quality during thyroid surgery reported that time to first satisfactory EMG signal in patients who were administered inhaled anesthetic agent was longer by about 4 minutes compared to those who received TIVA[36]. However, the EMG response to electrical stimulation of the central nervous system, such as the brain or spinal cord, might be different to that of the peripheral nervous system, such as the RLN. In general, the common consensus among clinicians seems that the quality of IONM during thyroid surgery is not affected by the type of anesthetic agent employed, but there is a paucity of evidence to indicate which anesthetic agent is superior. Further studies are required to elucidate the impact of the type of anesthetic agents on the quality of IONM during thyroid surgery.

Pain control for IONM during thyroid surgery

Balanced anesthesia or TIVA, with a continuous infusion of opioids is widely used to achieve stable hemodynamics during surgery and prevent involuntary movement during highly stimulating surgeries. Intraoperative bucking movement because of spontaneous recovery or recovery by reversal agents generally requires increasing the level of anesthesia by using a bolus of opioid or increasing the infusion rate of opioid with or without additional NMBA administration. In such cases, anesthesiologits manually ventilate the patient to diminish or eliminate spontaneously respiratory movement, while increasing the anesthesia level. This phenomenon of reversal from neuromuscular blockade is different from recovery of consciousness. It is recommended that the surgeon halt the operation for a few minutes until the patient's movement ceases. Clinicians should understand how to manage involuntary patient movement during thyroid surgery using IONM without the adiministration of additional NMBA.

Role of train of four (TOF) during IONM

TOF monitoring with a peripheral nerve stimulator is used to assess the recovery of neuromuscular transmission at the adductor pollicis muscle which has the slowest recovery among all muscles. The recovery of neuromuscular transmission in the adductor pollicis muscle suggests recovery of spontaneous respiration[37]. While TOF monitoring has advantages to evaluate extubation timing, its usefulness for IONM during thyroid surgery is debatable. One study reported that the cricothyroid muscle twitch-response and V1 (initial EMG signal from the vagus nerve before initiating thyroid resection) and R1 (initial EMG signal from the RLN before initiating thyroid resection) signals were present even when TOF was less than 4/4[28]. Furthermore, the mean amplitudes of V1 and R1 were 985.3 ± 471.6 μV and 1177.2 ± 572.7 μV, respectively, while 16% of the patients still had a TOF of 0%[28]. This is expected because reversal of NMB varies depending on the muscle type[37,38]. Therefore, TOF monitoring at the adductor pollicis muscle may be of little value for IONM during thyroid surgery, and results should be carefully interpreted.

Conclusion

Appropriate anesthetic management is essential for effective IONM during thyroid surgery, and necessitates close collaboration between the surgeon and anesthesiologist. Surgeons and anesthesiologists should be aware that there are several factors related to anesthesia that can influence IONM quality and should understand how to detect and manage such issues if the IONM system fails.

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Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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