Review Article

Safety of intraoperative neuromonitoring

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Abstract: The identification of laryngeal nerves during thyroidectomy procedures is considered the safest method to prevent variations in the motility of the vocal cords. However, the only visualization of the laryngeal nerves in many situations is not enough to ensure the result. In fact, anatomical wholeness does not always ensure the functional integrity. The number of endocrine surgery centers that use intraoperative neuromonitoring (IONM) is constantly increasing. Neuromonitoring techniques are currently considered safe methods; however, although infrequently, some complications and side effects related to the use of these methods have been reported. Recently, international guidelines on the use of IONM have been drafted and published to improve quality and safety. The aim of this work is to evaluate the safety of IONM by analyzing the complications reported in literature.

Keywords: Thyroid; thyroidectomy; intraoperative neuromonitoring (IONM)

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The identification of laryngeal nerves during thyroidectomy procedures is considered the safest method to prevent variations in the motility of the vocal cords; in fact, since 1938, when Lahey suggested the method of visualization and dissection of the inferior laryngeal nerve before the glandular dissection, this strategy has brought about a significant reduction in the percentage of recurring damages (1). Moreover, the only visualization of laryngeal nerves, in most situations, is not enough to ensure the result. In fact, anatomical wholeness does not always ensure the functional integrity (2). To respond to this need, in the last two decades, various devices have been used for intraoperative functional monitoring of the laryngeal nerves. These devices electrically stimulate the nerves, so as to conduct the signal up to the innervated muscles. The resulting muscle activity is then turned into acoustic and electromyographic signals; the information of neurophysiological signals can then be used for prognostic and medico legal purposes (3,4). Several techniques have been reported in the literature. Electromyographic signal recording (EMG) may include the use of needle electrodes inserted into the vocal cords endoscopically, the use of electrodes inserted through the cricothyroid ligament in the homolateral vocal muscle during surgical access or the use of surface electrodes endotracheal that can record the potential.

For several reasons, including non-invasiveness, safety, utility, ease of use and even the full market availability, systems with surface electrodes have found widespread and currently represent the most common format for monitoring equipment (5). The most recent acquisition is the continuous vagal monitoring, which requires the placement of electrodes even at the level of the vagus nerve, its continuous stimulation and recording of nerve signals, guaranteeing a "real-time" monitoring of the effects of manipulations during all phases of the surgery (6). Neuromonitoring techniques are presently believed to be safe methods; however, although infrequently, some complications and side effects related to the use of these

methods have been reported. The complications described may occur from displaced electrodes, from the obstruction of the endotracheal tube, from the drugs used for anesthesia and from the undesirable effects of the stimulation on the nervous structures and at the systemic level.

Complications related to the electrodes

The direct and cruent placement of the needle endolaryngeal electrodes can be complex and requires experienced operators; in addition, the needle electrodes, in general, can be displaced during muscle contraction, producing an EMG signal unstable. For surface contact electrodes instead—integrated into dedicated endotracheal tubes or externally applied to standard tubes—the problems of functioning may depend on the migration of the endolaryngeal tube or accidental detachment, so as to reduce the sensitivity of the method (7,8). In order to check the correct positioning of the electrodes, the impedance measurement can be used (9).

As for the placement of the tube, two aspects can be noticed: first, it is important that anesthesiologist and surgeon both offer help in the final check of the endotracheal tube; secondly, it is advisable that those checks are done after the patient has been put in the final position, not in a neutral position. The best option available for checking the correct placement of the tube is laryngoscopy. The anesthesiologist or the surgeon can visualize the glottis, after positioning the patient, by direct or fiberoptical laryngoscopy. The repetition of laryngoscopy after the definitive positioning of the patient is the most accurate method for evaluating the correct position of the tube.

Some authors believe that the needle electrodes in comparison with the superficial ones, while offering more information, can cause tearing of the vocal cords, bruises, infections, rupture of the Needles or damage to the endotracheal tube cuff (7,10). In a multicentre study of 8,534 patients, 112 (1.3%) damage to the cuff was seen after inserting needle electrodes into vocal muscle. This complication, which did not compromise the surgery, was not associated with wound infections, postoperative bleeding or increased postoperative pulmonary morbidity. In addition, damage to the cuff can be avoided by positioning the endotracheal tube more distally. In this study, therefore, no major complications related to the method have been shown (11). However, although reusable and cost-effective, the needle electrodes are less commonly used, because they represent a more invasive and more complicated method than the method which involves the use of dedicated contact surface electrodes.

Complications from tube obstruction

In a recent paper, Oysu and Demir described two cases of obstruction of an endotracheal tube studied for intraoperative neuromonitoring: at the 35th and 40th minutes of general anesthesia there was an abrupt and complete arrest of the ventilation (12). Checking the presidium on an animal trachea, it was noticed that the hyperinsufflation made the cuff herniate, causing obstruction of the tip of the tube. A 25-mm displacement outward contributed to this cuff herniation. In this case the collaboration of the anesthesiologist is fundamental: the endotracheal tube must be inserted considering the variations that involves the repositioning of the neck for the intervention, from the neutral position to the complete extension (13). The authors concluded that to solve the problem it was sufficient to slightly deflate the cuff and that, generally, the latter should be inflated to the minimum volume required; obviously, the operating team must pay the utmost attention to the stability of the endotracheal tube.

It may be said that cases of tube obstruction and tube misplacement are uncommon in this procedure and they can be managed with good medical practice by the anesthesiologist.

Complications related to anesthetic drugs

A fascinating aspect about complications of intraoperative neuromonitoring is that concerning the type of drugs to be used for the induction of anesthesia. In fact, the use of drugs that cause a neuromuscular block (neuromuscular blocking agents, NMBA), to make endotracheal intubation easier, can compromise the proper functioning of the method; for this reason, the usage of these drugs is not recommended during neuromonitoring. However, keeping in mind that the mechanical intubation and extubation procedures can themselves cause cord damage (14,15), some studies claim that the non-administration of NMBA, to make intubation easier, in adult patients is associated with a high number of local effects and laryngeal injuries (16). Nevertheless, in pediatric patients, intubation without the use of these drugs is common (17). In fact, by associating appropriate doses of propofol to an opioid, laryngeal relaxation and suppression of reflexes are sufficient to obtain a non-complicated intubation (18). In a recent retrospective study Birkholz

et al. compared laryngeal morbidity after thyroid surgery, associated with neuromonitoring in intubated patients, with the use or non-use of NMBA, without statistically significant differences between the two patient groups (19). Therefore, anesthesia induction is recommended with the use of NMBA with a short half-life, able to perform well only in the initial stage of intubation and in order to be disposed during the central stage of the surgery, when neuromonitoring is used rather than.

Furthermore, the availability of new drugs (such as Sugammadex) and the development of an anesthesiological technique that is increasingly suited to these needs could guarantee a successful tube position with no complications.

Complications of electrical stimulation

Scholars are debate on the safety of direct electrical stimulation of the nerve and on what the optimal intensity, frequency and amplitude are. With the stimulation of the laryngeal or vagus nerves a biphasic wave is obtained; in normal language the amplitude of the wave ranges from 100 to 800 μV, but during the surgery, the amplitude may change due to the presence in the operating field of fluids or blood, of tissues that cover the nerve, due to inadequate probe-nerve contact, due to the temperature or to the position of the electrodes (20). The threshold indicates the minimum electrical stimulus capable of producing an EMG response. The vagus nerve and laryngeal nerve are activated roughly between 0.3 and 0.4 mA, when the nerve is dry and exposed. The maximum stimulation of all the fibers is gained at 0.8 mA; beyond this threshold, the greatest stimulation does not correspond to a greater response to the EMG. As a consequence, the stimulus threshold for evaluating nerve function is 1 mA in many cases, while 2 mA stimuli are used for area mapping, where this technique is used for recurring nerve research and recognition (10). In a recent study, Choby *et al.* wanted to find the minimum threshold of stimulation of the recurrent nerve before and after thyroidectomy, using contact surface electrodes for the neuromonitoring. The actual results show that the average minimum intensity needed to stimulate the recurrent laryngeal nerve was 0.50 mA before thyroidectomy, whereas it was 0.47 mA after, with an average difference of 0.03 mA. None of these values was significantly related to postoperative cord palsy (21). This contrast in stimulation thresholds (22), can be explained by the reduction of pressure on the nerve, which can be stimulated with lower intensity of the current. In this respect, Wu *et al.* performed a study on pigs whose vagus and laryngeal nerves were stimulated with currents of 0.1 to 1.0 mA (with increases of 0.1 mA) and subsequently with stimuli of 1.5, 2.0, 2.5 and 3.0 mA. The stimulus lasted 10 μs and was repeated 4 times/second (4 Hz) for 10 minutes, with an interval of 2 seconds every minute to record the EMG signal. After 10 minutes the amplitude of the EMG signal was not significantly lower than that recorded at the beginning and the maximum amplitude was obtained with stimuli <1 mA, both for the recurrent nerve and for the vagus nerve (23). Therefore, the authors concluded that minimum currents (about 1 mA) are sufficient to generate the maximum response to the EMG and can be used to reduce the risks of nerve damage and cardiopulmonary side effects. Systemic side effects of nerve stimulation have generated great interest, mostly since continuous vagal monitoring has been introduced. For many years, the stimulation of the vagus nerve has been used to treat depression and epilepsy refractory to drugs. While long-term stimulations (weeks or months) seem to elicit voice and cough abnormalities, short-term ones are not usually related to complications (24-26). Although vagal therapeutic stimulation is conventionally recognised as a safe treatment, there have been cases in which it has resulted in cardiac arrhythmias and severe haemodynamic changes (27,28). In a 2004 publication, Ali *et al.* have described 3 cases of cardiac arrest in patients with refractory epilepsy who underwent a vagal stimulation implant, in the perioperative time, during the initial device test. For 6–15 seconds, these patients had a atrioventricular block, completely self-resolving resolved and compatible with the stimulation of the left vagus nerve (29). It was assumed that the causes of this phenomenon may have been represented by the centrifugal direct activation of the parasympathetic system with an inhibitory effect on the atrioventricular node, or by the centripetal activation of afferent pathways of the left vagus nerve, with effect on other central systems that affect heart rhythm. To establish the safety of vagal stimulation during neuromonitoring, Friedrich *et al.* have recently completed a non-randomized prospective study. Changes in heart rhythm and immunomodulatory effects induced by vagal stimulation were analyzed in 22 patients (30). In this study, in spite of a significant increase in vagal tone, no haemodynamic abnormalities were observed and no decrease in plasma levels of cytokines was observed or TNF-α.

Certainly, a correct preoperative evaluation and proper intraoperative monitoring could prevent side effects and minimize the risk of dramatic events at the cardiovascular level.

In conclusion, intraoperative neuromonitoring of the superior and inferior laryngeal nerves, even with vagal stimulation, can be considered a safe method for the complications related to it.

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