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Intraoperative neurophysiologic monitoring in spinal cord surgery: a brief review

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Abstract

Spinal / spinal cord surgery involves a wide range of procedures with a potential risk of injury to neuronal structures. During major spinal reconstructions, such as for the correction of kyphoscoliotic deformity, structures such as the spinal cord and nerve roots are prone to transient or permanent injuries with significant morbidity and devastating medico-legal and economic consequences.MNIO is a monitoring technique capable of assessing in real time the functional integrity of neurological structures under potential risk of injury, allowing a correlation between surgical manipulation and the neurophysiological changes that precede injuries resulting from surgical trauma, at the time when these can still be reversed

Key words: Electroencephalography; Intraoperative neurophysiological monitoring;Motor evoked potential;Neurosurgical anesthesia;Somatosensory evoked potential.

Introduction:

Prior to the introduction of intraoperative neurophysiological monitoring (IONM) into clinical practice, the integrity of the spinal cord during high-risk procedures could only be confirmed with wake-up tests (Stagnara's test) during anesthesia**.**Several types of neurophysiological monitoring are currently available for use in the surgical environment and are capable of assessing the integrity of the ascending and descending neural pathways and their respective blood supply. The integrated use of somatosensory evoked potentials (SSEP), motor evoked potentials (MEP) and electromyography (EMG) is the most commonly used IONM technique and provides high sensitivity and specificity in the prevention of neurological injuries in the intraoperative period of spine surgery spine and spinal cord [1,2,3,4,5].

Somatosensory evoked potential (SEP or SSEP)

The somatosensory evoked potential (SEP or SSEP) record aims to evaluate the functional integrity of the ascending sensory neuronal pathways from the peripheral nerve, through the dorsal column, to the sensory cortex. The recording is carried out in regions corresponding to the stimulated nerves and areas susceptible to injury during the surgical procedure. The level of the surgery determines which neuronal pathways will be monitored. Typically stimulation is performed on the posterior tibial nerve and the median nerve.The data is processed and measured to determine latency and amplitude. Latency is a measure of time. Amplitude is a measure of strength and is characteristically more variable than latency. An increase in latency greater than 10% and a reduction in amplitude greater than 50% in relation to the registration performed before the beginning of the surgical procedure (baseline) are warning signs and potential damage to nervous structures. With the start of the use of SSEP monitoring in spine surgeries, multicenter studies have observed that postoperative paraplegia was reduced by more than 50% and false-negative results occurred in only 0.063% of cases.

SSEPs are altered in surgical procedures by mechanical factors, such as compression or injury to nervous structures, or secondary to local or global ischemic processes. The SSEP record can also change due to events not necessarily related to the damage to nervous structures, such as hypotension, anemia, hypothermia and hypoxemia. However, these changes occur globally in all measured potentials and not exclusively in the locations corresponding to the nervous structures at risk due to surgical manipulation [6,7,8].

Motor evoked potential (MEP)

The PEM record aims to assess the functional integrity of the descending motor neuronal pathways. The achievement of PEM by transcranial electrical stimulation is performed through electrical pulses applied on the skullcap at points representative of the motor area. These pulses initially stimulate the first motor neuron in order to cause multiple descending waves with sufficient power to reach the depolarization threshold of secondary motor neurons, leading to contraction of the corresponding muscle fibers or groups. The muscles are selected based on the surgical procedure performed and the medullary level involved. The muscles usually used to record PEM in the upper limbs include the tenen, hypothenar muscle and the first dorsal interosseous muscle of the hand. The muscles most used to record PEM in the lower limbs include the posterior tibialis and the abductor hallucis. Analogously to PESS monitoring, the PEM record has as alarm signs an increase in latency greater than 10% and a reduction in amplitude greater than 50% in relation to the values recorded in the baseline. The injuries can be due to ischemia, metabolic changes, mechanical trauma or compression.

The main disadvantage of monitoring PEM is the need for adaptations to the anesthetic technique, including the careful use of neuromuscular blockers, which should be minimized or even not used, and the choice of anesthetic agents with less interference in the recording of evoked potentials.

Active stimulation of the masseter and its vigorous contraction can produce tearing of the tongue, dental fracture or even fracture of the jaw. These risks can be minimized or eliminated with the proper use of bite blockers. It is important to note that direct stimulation of the cerebral hemisphere also poses risks. PEM registration is contraindicated for patients with epilepsy, cortical lesions, skull defects, increased intracranial pressure and using implanted intracranial

devices or pacemakers [9,10,11].

Electromyography

In baseline conditions, where the nerve roots are intact, no muscle activity is recorded. Surgical manipulations that lead to traction or compression of nerves cause neuronal discharges, resulting in activity in the muscle group innervated by them. Monitoring this spontaneous electromyographic activity (spontaneous EMG) can help prevent postoperative radiculopathy during spinal surgery with instrumentation, including implantation of pedicle screws. This technique does not require stimulation and can be recorded continuously from pre-selected muscle groups based on nerve roots potentially at risk of injury. Spontaneous EMG has a high sensitivity for nerve root irritation. However, a false-positive result can occur during cold saline irrigation, cauterization and the use of a high-speed drill, since spontaneous EMG is also quite sensitive to changes in the temperature of the evaluated site. It is important to emphasize that the EMG signals may suffer interference in patients submitted to neuromuscular block and in patients with neuromuscular disorders such as myasthenia gravis or muscular dystrophy.

Intraoperative monitoring of induced electromyographic activity (induced EMG) detects irritation and nerve root damage after the violation of the medial pedicle by implantation of screws in spine surgery. The induced EMG uses the principle that the cortical bone would electrically isolate a well-implanted pedicle screw in relation to an adjacent nerve root. In the event of a violation of the medial pedicle, the pedicle screw would lose this isolation, altering the induced EMG and indicating nerve root damage. Thus, if the screw is stimulated with a constant voltage greater than 30 volts (V) without activation of EMG, it is unlikely that it has approached the vertebral cortex. However, the response to a stimulation below 20 V suggests a bone defect that provides a low impedance pathway to the nerve root [12,13,14].

Interference of anesthetic drugs in MNIO

Both PESS and PEM are affected by several pharmacological and physiological factors, and changes in PEMs occur more intensely than in PESSs. Since all anesthetic drugs alter neuronal excitability, through changes in synaptic function or axonal conduction, they can interfere with the assessment of evoked potentials, usually decreasing their amplitude and increasing latency. The impact of anesthetic agents on MNIO increases with the number of synapses in the monitored pathways. This fact explains the greater interference of inhaled anesthetic drugs in the evoked potentials measured at the cortical level than those measured at the subcortical (brainstem) and medullary levels.

When choosing the anesthetic technique, it should be taken into account that, in general, the effects of inhalation agents on evoked potentials are more pronounced than those of venous anesthetics. Despite this, both anesthetic techniques allow conditions for MNIO if they are properly conducted, being a fundamental point for the adequate measurement of the evoked potentials to maintain a steady-state in the alveolar or blood concentrations of the agents used. However, due to the possible muscle relaxation caused by halogenated inhalation agents, with a deleterious effect for the assessment of PEMs, inhalation anesthesia should be avoided when optimized monitoring of PEMs is aimed [15].

Effects of inhaled anesthetics on MNIO

Desflurane, sevoflurane and isoflurane produce a dose-dependent effect of increasing

latency and reducing the amplitude of the evoked potentials. This effect is apparently the result of the inhibition of pyramidal activation of spinal motor neurons at the level of the anterior horn of the spinal cord or of depression in synaptic transmission in the cerebral cortex. As the depressant effect of inhaled anesthetics is more intense in synaptic transmission than in axonal conduction, interference in the assessment of potentials is more evident at the cortical level than in subcortical areas.

PEMs are more easily abolished by halogenated inhalation agents than PESSs, and the use of alveolar concentrations of inhaled anesthetics above 0.5 MAC is incompatible with obtaining a reliable PEM. However, the D waves recorded in the epidural space, before the synapse in the anterior horn of the spinal cord or at the neuromuscular junction, are more resistant to the effects of inhaled anesthetics, being easily registered, even with high concentrations of these agents. Thus, the effects of anesthetics on the anterior horn of the spinal cord can be overcome by transcranial stimulation with multiple pulses of high intensity when alveolar concentrations of inhaled anesthetics below 0.5 MAC are used. Despite this, the best anesthetic plan would be to avoid the use of inhalation agents when aiming to optimize the monitoring of PEMs.

Nitrous oxide reduces the amplitude and increases the latency of the evoked potentials, without modifying the wave morphology, when used alone or in combination with halogenated inhalational anesthetics. The actual effect of nitrous oxide in obtaining the evoked potentials may vary depending on the other anesthetic agents used. For example, the addition of up to 50% N2O to less suppressive anesthetic drugs such as opioids, ketamine or low doses of propofol infusion does not cause significant interference in the evaluation of PEMs when the multi-pulse stimulation technique is used transcranial. However, when used in equipotent anesthetic concentrations, nitrous oxide produces more profound changes in cortical PEMs and PEMs obtained by transcranial stimulation than any other inhaled anesthetic agent. Therefore, its use is not recommended [16].

Effects of venous anesthetics on IONM

*O*pioids

Opioids are often administered intraoperatively and postoperatively as analgesic agents for spinal surgery. The effects of synthetic opioids used in anesthesia, such as fentanyl, alfentanil, sufentanil and remifentanil, on the evoked potentials are less intense than those obtained with the use of inhalation agents. When administered in the neuroaxis or intravenously, they generate little depression of the amplitude and latency of cortical potentials. This characteristic makes them important components of the anesthetic technique when aiming at monitoring the PESS and PEM. The main advantage of sufentanil and remifentanil used in continuous infusion is to maintain constant serum concentrations, with little interference in obtaining the evoked potentials, allowing a consistent measurement of them. This characteristic makes the use of these drugs one of the pillars of anesthesia for neurophysiological monitoring [17]..

Ketamine

The effects of ketamine on evoked potentials differ from those seen in most anesthetics: it generates an increase in the range of PESSs and PEMs in responses recorded in muscles and spinal cord. Because it causes an increase in the amplitude of the evoked potentials, ketamine is a good alternative for patients who have previous neurological injury and have low amplitude and high latency evoked potentials in the baseline assessment. Ketamine has the additional

benefit of providing adequate analgesia for patients with chronic pain who have undergone a high number of surgeries associated with severe pain in the postoperative period. However, its administration may lead to increased intracranial pressure and hallucinations, which may limit its use [18].

Barbiturates and Benzodiazepines

Barbiturates are not usually administered when MNIO is used in spine surgeries since the responses of the evoked potentials are sensitive to this class of drugs and their effects are prolonged. The decrease in amplitude and the increase in latency occur immediately after induction with thiopental. The latency of cortical waves is more affected, while minimal effects are observed in subcortical and peripheral responses. The complete loss of PEM responses occurs with doses of thiopental from 4 to 9 mg.kg-1.

Benzodiazepines can cause depression in the range of PEMs, but this effect is less than that of thiopental. Diazepam has shown little effect on the PEM latency and amplitude when used as a pre-anesthetic medication. Midazolam has the desirable property of causing amnesia and has been used to monitor cortical PESSs. In doses of anesthesia induction, and in the absence of other agents, midazolam produces a slight depression of the cortical PESSs and minimal effects on the subcortical and peripheral components. However, like the thiopental, it produces marked depression in the PEM.

Etomidate

With an effect similar to that of ketamine, etomidate increases the amplitude of cortical PESSs after bolus injection, with no changes in subcortical and peripheral sensory responses. This increase in amplitude seems to coincide with the myoclonus observed after administration of the drug. Etomidate produces minimal suppression of PEMs when compared to barbiturates or propofol. The administration of the induction dose leads to a mild and transient depression of the amplitude of the PEMs, without changes in their latency. Of all the intravenous agents studied, etomidate results in a lower level of interference in the amplitude of potentials after an induction dose or during continuous intravenous infusion. However, adrenocortical suppression following the administration of this drug limits its use in continuous infusion.

Propofol

Propofol induction produces a dose-dependent reduction in the amplitude of PESSs and PEMs, with minimal effect on their latency and rapid recovery after the end of the drug infusion. Propofol in continuous infusion is an excellent option for monitoring evoked potentials, as it has pharmacokinetic characteristics that make it possible to maintain serum concentrations of the drug at constant and expected levels, allowing adjustment of the anesthetic depth without prejudice to the monitoring of potentials. Comparing the effect of propofol on MNIO with that observed with the use of inhalation agents, it was concluded that propofol provides better conditions for recording PESS and PEM. This data corroborates the use of propofol in continuous infusion as the standard anesthetic approach for recording the evoked potentials during MNIO [18].

Alpha agonists 2

Clonidine, used alone or in combination with inhaled anesthetics, does not alter the

latency or amplitude of the evoked potentials. Dexmedetomidine changes the amplitude of PESSs in a clinically non-significant way, and can be used without harm to MNIO up to a dose of 1.0 mcg.kg-1.h-1[19].

Neuromuscular blockers

Neuromuscular blockers used in anesthesiology work at the neuromuscular junction and have little effect on the electrophysiological recording of PESS, since it does not require muscle activity for its measurement. However, deep neuromuscular block is incompatible with the PEM record. Some authors advocate that a partial neuromuscular block would have the benefit of reducing a substantial portion of the patient's movements, secondary to stimulation to obtain the PEMs, and would facilitate surgical procedures in which muscle relaxation was necessary to allow the manipulation of structures adjacent to the muscles . The maintenance of two of four contractions on the train-of-four (TOF) monitor, with the use of continuous infusion of muscle relaxants, would not be prohibitive for the measurement of PEM. However, there is no standardization of the ideal TOF value or basis in the literature that allows the use of neuromuscular blockers concomitantly with the measurement of PEM, without prejudice to its monitoring. Therefore, the current recommendation is to use muscle relaxants of short or medium duration during anesthetic induction, to facilitate orotracheal intubation,with subsequent reversal of their effect by specific antagonist drugs. The goal is to maintain a 100% TOF during the surgical procedure and measurement of PEMs, in order to increase the sensitivity of monitoring and reduce the chances of an undiagnosed neuronal injury[20].

Table 1: Effects of drugs on amplitude and latency during IONM.Adapted from [15]

	SSEP		**MEP**	
Drug	**Lat**	**Amp**	**Lat**	**Amp**
Sevoflurane/Desflurane	Yes	Yes	Yes	Yes
Nitrous Oxide	Yes	Yes	Yes	Yes
Barbiturates	Yes	Yes	Yes	Yes
Propofol	Yes	Yes	Yes	Yes
Droperidol	No	No	Yes	Yes
Benzodiazepines	Yes	Yes	Yes	Yes
Opiates	No	No	No	No
α-2 agonists	No	No	No	No
Ketamine	No	No	No	No
Etomidate	No	No	No	No

Non-pharmacological factors that affect IONM

Hemodynamic changes

In addition to changes resulting from surgical manipulation of the nervous system and the effects of anesthetics, physiological homeostasis plays an important role in neuronal function. PESS and PEM are sensitive to events in the spinal cord produced by vascular ischemia or mechanical compression. However, as the sensory and motor tracts are topographically separated from each other, PESS and PEM can demonstrate different sensitivities to an ischemic event. Studies have shown a linear relationship between cerebral blood flow and evoked cortical responses. Under the effects of anesthetics, subcortical responses appear to be less sensitive than cortical responses to changes in blood flow. Local factors can produce regional ischemia not predicted by systemic hemodynamic parameters used in isolation. For example, during spinal surgery, the effects of hypotension on nerve roots can be exacerbated by traction. In this way, an acceptable limit of hypotension cannot be determined without the use of MNIO [21].

Hematocrit Levels and Intracranial Pressure

Due to its compressive effects on cortical structures, the increased intracranial pressure results in reduced cortical PESS responses. Thus, the increase in intracranial pressure is associated with reduced amplitude and increased latency of cortical SSPs. In relation to PEM, a gradual increase in the beginning of responses occurs as the intracranial pressure rises, until the response is no longer produced.

Changes in hematocrit can interfere with both the oxygen transport capacity and blood viscosity. It is known that a hematocrit between 30 and 32% provides the ideal conditions for monitoring evoked potentials.

Ventilation, Temperature and other Physiological Variables

The oxidative metabolism and the alteration of cellular homeostasis secondary to the critical reduction of neuronal tissue oxygenation, due to the decrease in inspired oxygen concentrations, inhibit the recording of PEM. Hypoxemia can lead to deterioration of the evoked potentials even before other clinical parameters are changed. PaCO2 levels below 20 mmHg cause excessive cerebral vasoconstriction and neuronal tissue ischemia, leading to changes in the cortical PESS and PEM records. In order to obtain an adequate record of PESS and PEM, it is necessary to maintain normocarbia and brain tissue oxygenation at normal levels.

Hypothermia can increase the false negative results of MNIO in spine surgery. Hypothermia is associated with changes in the registration of PESSs and PEMs, leading to increased latency and reduced conduction speed. With the core temperature below 28º C, the record of PESSs and PEMs disappears. Like the effects of anesthetic drugs and ischemia, changes related to hypothermia are more prominent in the cerebral cortex. Hyperthermia reduces latency and increases the conduction velocity of the evoked potentials. The amplitude of spinal PESSs does not change, however, cortical PEMs and PEMs deteriorate with central temperatures above 42º C. Due to the significant changes in the PEMs and PESSs latency with the increase or reduction of central temperature, it is recommended that the measures of evoked potentials are carried out

with a maximum variation of 2 to 2.5º C in relation to the measured basal temperature.

Changes in other physiological variables can interfere in obtaining the responses of the evoked potentials during MNIO. For example, changes in blood glucose, electrolytes, reduced circulating blood volume or increased pressure in the superior vena cava have been associated with changes in the recording of evoked potentials.

Discussion

IONM is a method of real-time evaluation of the functional integrity of neural structures used to prevent potential damage. The adequate use of IONM and the prevention of neural damage require dialogue, interdisciplinary cooperation and awareness of the interdependence between the anesthesiologist, the surgeon and the neurophysiologist.The combination of techniques increases the usefulness of monitoring and to some extent overcomes the limitations of each technique.

Conclusion

The current gold standard in IONM is total intravenous anesthesia (TIVA) without neuromuscular block, with propofol as hypnotic and remifentanil, sufentanil or ketamine as analgesic.

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