Abstract: Alpha 2 agonists are appreciated drugs designed for the peri-operative period, because of their anxiolytic, sedative and analgesic properties. However, they are usually avoided during scoliosis surgery, a long-lasting major procedure involving healthy patients, because of their potential effects on Somatosensory and Motor evoked potentials. The absence of recommendations suggests that their effects on evoked potentials are still unclear. Thus, we tried in this narrative review to identify the literature representative of the effects of clonidine and dexmedetomidine on evoked potentials, on human beings, published between 1988 and 2015 in English or French, using GOOGLE SCHOLAR and PUBMED. Paucity of literature prevented any conclusion about Clonidine’s effects on evoked potentials, but no data suggested a noxious effect of Clonidine on evoked potentials, used in oral premedication (300 µg) or during the procedure (2 to 5 µg/kg). If literature was more extensive for dexmedetomidine, studies were still controversial. Although the majority of the studies did not find statistically significant differences concerning the effects of this drug on evoked potentials (loading dose of 0.3 to 1 µg/kg followed by continuous infusion of 0.3 to 0.8 µg/kg/h), 2 case reports and 2 studies described substantial decreases. However, dexmedetomidine’s shorter duration of action allowed a quick return to basal situation within an hour. In conclusion, more studies are needed in order to evaluate the effects of alpha 2 agonists on evoked potentials and to assess the safety of their use in this setting.

Key words: Scoliosis; alpha agonists; evoked potentials; somatosensory; motor.

Introduction

Surgery for idiopathic scoliosis is a long-lasting major procedure, involving young and healthy patients. A multimodal approach to manage postoperative pain is usually required. Alpha 2 agonists, like clonidine and dexmedetomidine, have well known perioperative anesthetic and analgesic sparing effects (1) and these properties could be very beneficial for the postoperative pain management in this setting. However, alpha 2 agonists are usually avoided during scoliosis surgery because of their potential effect on neurophysiologic monitoring. Neurophysiologic monitoring, by the means of somatosensory and motor evoked potentials, is used to detect and thus prevent spinal cord injury and the consecutive neurological deficits. Paucity of literature and the absence of clear recommendations on this topic suggest that the effects of alpha 2 agonists on the motor and somatosensory evoked potentials are still unclear.

Methods

To identify the medical literature representative of the effects of alpha 2 agonist on evoked potentials, we searched articles on human subjects published between 1988 and 2015 in English or French with PUBMED and GOOGLE SCHOLAR. The search was conducted using keywords: scoliosis, spinal surgery, alpha agonists, clonidine, dexmedetomidine, evoked potentials, somatosensory, motor, sensitive.

Results and Discussion

Neuromonitoring

Neurological complications during surgery for idiopathic scoliosis are rare. These complications may occur from vascular, ischemic, metabolic or mechanical causes, like neural compression by implants or migration of bone graft in the spinal canal (2). In the 1980’s, the incidence of neurological complications ranged from 3.7 to 6.9% (3). With...
the development of neurophysiological monitoring techniques, these percentages decreased. According to the Scoliosis Research Society Morbidity and Mortality Reports, between 2002 and 2005, 0.8% of the patients presented neurological complications (4). In 2007, in a series of 1301 consecutive spinal fusions, Dahn et al. identified 0.69% of neurologic complications (5). The neurological complications commonly described were paraplegia, quadriplegia, and peripheral deficit. In order to avoid these spinal injuries, perioperative somatosensory and motor evoked potentials are now routinely used. Already in 1988 it was noticed that monitoring the somatosensory evoked potentials (SEP) reduced neurological complications after spine surgery (6), with a decrease of paraplegia from 6.9 to 0.7% in cervical spine procedures (7). The simultaneous monitoring of sensory and motor evoked potentials (MEP) to detect neurologic complications offers high sensitivity and specificity, 100% and 98% respectively (2).

Evoked potentials (EP) are the record of the electrical potentials produced by the stimulation of the nervous system by electrical, magnetic, cognitive or repetitive sensory stimulations. The response comes from action potentials or graded polysynaptic potentials while the impulses propagate, and may be recorded with surface electrodes or sub-dermal needles. These electrical signals are very discrete when compared with an electroencephalogram (EEG) and are usually artefacted by random electrical activity. To extract them, a computer system is used. The «post stimulation latency» is described in “ms” and represents the time elapsed between the application of a stimulus and the time window of interest (usual latency of the waited EP waveform). The «peak to peak amplitude», measured in “mV” or “µV”, compares the individual peaks in the waveform. A decrease in amplitude or a prolongation in latency are significant and suggest a compromise of the neurologic pathway. The peaks and valleys arise from specific neural generators, unestablished definitively but based on clinical humans and animals studies, clinic pathologic correlations and intra-operative studies (8, 9, 10).

Sensory EP are produced from a stimulation of the sensory system. Three kinds of sensory EP are used for intra-operative monitoring: somatosensory evoked potentials (SEP), usually used during spine or spinal cord operations (11, 2, 12, 13), brainstem auditory evoked potentials (BAEP) and visual evoked potentials (VEP). BAEP appear as positive and negative waves, representing the transmission and the processing of audition from the ears to the brainstem. Their monitoring is particularly interesting in surgery such as resection of acoustic neurinomas, neural decompression, arterial and venous malformations, auditory implants and surgery of the posterior cranial fossa, during which the brainstem may be injured (14, 15, 16, 17). Finally, VEP are monitored in surgery involving optic chiasm, optic nerve or cranial base procedures (18, 19, 20).

MEP monitors the motor cortex and the descending pathways. They are recordings of depolarizing action potentials, from pyramidal neurons, and triggered by an electrical current. This one can be transcranial or directly activated on the cortex or the spine. They may be recorded at different points through the motor pathways (21, 8, 9).

During surgical correction of idiopathic scoliosis, SEP and MEP are regularly employed in order to assess the integrity of neuronal tracts. SEP evaluate the ascending sensory tracts and MEP evaluate the descending motor pathways.

SEP are divided in short latency (50 ms after the stimulus) and long latency (100-300 ms after the stimulus) evoked potentials and are obtained by electrical stimulation of peripheral nerves (commonly peroneal and posterior tibial nerves). They allow the evaluation of the dorsal column-medial lemniscus pathway, which defines fine touch and conscious proprioception. Short latency SEP are less influenced by environmental factors, like anesthesia (8, 10, 9).

SEP represent both large, fast conducting muscular afferent and cutaneous afferent fibers, situated in the spinal cord’s posterior column, and depend on their functional integrity. Thus, after mixed peripheral nerve stimulation, both of them contribute to the SEP.

Myogenic MEP are biphasic and large responses recorded over the muscle belly. Composed potentials are created by the addition of different muscular fibers’ potentials. The final amplitude depends on the number of motor fibers and by the number of the activated alpha motoneurons. De Haan et al. showed in animal models that myogenic responses seemed to be more sensitive to spinal ischemia than epidural; ischemia was produced with infra renal aortic balloon occlusion, and results were recorded from the lumbar epidural space and from the soleus muscle (22).

Finally, multi-pulse stimulation increases the amplitude of MEP, because it creates an addition of excitatory postsynaptic potentials in the anterior column of the spine’s cell, diminishing the anesthetic agents’ inhibitory effects (21).
Neurogenic MEP (NMEP) are the peripheral responses obtained after a spinal cord stimulation. They are resistant to anesthetic depression but non-specific to motor function, because the spinal stimulation activates both antidromic sensory tracts and orthodromic motor pathway (21).

For many authors, MEP recordings are considered to be stable if the modifications appear to be less than 50% in amplitude and less than 10% in latency (23, 24).

Anesthetic agents that modify SEP

Intravenous administrated or inhaled anesthetics can modify SEP (25, 26).

All volatile anesthetics may increase the latency and decrease the amplitude, as general anesthesia inhibits neurotransmission and therefore SEP. Volatile anesthetics may cause morphological changes of the waveforms (25). The new volatile anesthetics, like desflurane (27) and sevoflurane (28, 29, 30, 31) appear to modify less SEP than enflurane and isoflurane and this up to 1.5 MAC (32, 33, 34, 35). The reason why volatile anesthetics have different effects on SEP is not yet elucidated (8, 25).

Nitrous oxide depresses SEP and VEP when used with other gazes (35, 36) but, in moderate doses (Fi inf 65%), seems to be less suppressive than the other volatile agents (37, 38, 39).

Intravenous anesthetics have less effect on SEP than volatile anesthetics (25). Studies on thiopental have shown that doses up to 4 mg/kg preserved SEP and MEP (40).

Propofol has minimal effects on the latency and amplitude of SEP and MEP (41, 42). Used in high doses to induce burst suppression, it may inhibit later cortical responses. The primary cortical responses, which are used for neuromonitoring during spinal surgery, will not disappear (43). Studies concluded propofol (without nitrous oxide) could be used during spinal surgery when neurological monitoring was required (36). Its effects on evoked potentials are less depressive than those of sevoflurane (29) or isoflurane (41).

Opioids produce unimportant changes in evoked potentials waveforms, latency and amplitude of anesthetic or analgesic doses (25). A dose of 200 µg fentanyl does not affect SEP (9). The administration of fentanyl 3 µg/kg has the same minimal effects on MEP (9). An induction dose of 6 µg/kg and maintenance dose of 3 µg/kg/h fentanyl had minimal effect on the amplitude and latency of SEP (36). KALKMANN et al. observed the same unimportant changes on evoked potentials in a study comparing fentanyl, sufentanil and remifentanil (44). Even more, the combination of sufentanil and propofol had little effects on SEP (36). However, remifentanil in high doses (0.8 µg/kg/min) induces significant changes of the SEP amplitude (45).

Benzodiazepines have moderate depressant effects on SEP, 0.3 mg/kg of midazolam causes little changes in SEP amplitude and latency (46).

Etomidate increases cortical SEP amplitude up to 400% and decreases by 50% subcortical amplitude (47) while ketamine has negligible effects on cortical SEP (47, 36, 48, 49).

Anesthetic agents that modify MEP

MEP are sensitive to all anesthetics, especially inhalational agents. Volatile anesthetics inhibit in a

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Effects of principal anesthetic agents on SEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEP latency</td>
<td>SEP amplitude</td>
</tr>
<tr>
<td>Desflurane 1 MAC (34)</td>
<td>Increase</td>
</tr>
<tr>
<td>Sevoflurane 1.7-2.5 MAC (42)</td>
<td>Increase</td>
</tr>
<tr>
<td>Isoflurane 1 MAC (99)</td>
<td>Increase</td>
</tr>
<tr>
<td>Nitrous Oxyde 50-60% (100)</td>
<td>No change</td>
</tr>
<tr>
<td>Thiopental 2-3 mg/kg (40)</td>
<td>Increase</td>
</tr>
<tr>
<td>Etomidate 0.3 mg/kg (40)</td>
<td>Increase</td>
</tr>
<tr>
<td>Propofol 2.5 mg/kg (42)</td>
<td>Increase</td>
</tr>
<tr>
<td>Midazolam 0.1-0.3 mg/kg (46)</td>
<td>Increase</td>
</tr>
<tr>
<td>Ketamine 0.5 mg/kg (36)</td>
<td>No change</td>
</tr>
<tr>
<td>Sufentanil 5 ug/kg (101)</td>
<td>Decrease</td>
</tr>
<tr>
<td>Remifentanil 5 ug/kg + 1 ug/kg/min (102)</td>
<td>No change</td>
</tr>
</tbody>
</table>
Clonidine and neuromonitoring

Clonidine is an alpha-2 adrenergic agonist that binds to the central alpha 2 receptors and to the pre- and post-synaptic alpha 2 receptors in the spinal cord. Their activation inhibits adenylate cyclase activity, which in turn decreases the entry of calcium into the neuronal terminal and finally limits norepinephrine (NE) release. Clonidine also binds to the receptors which mediate the sympathetic-inhibitory actions of imidazolines (63, 64, 65). The sedative action is mediated by activation of descending inhibitory system in the locus coeruleus of the brain stem, and inhibits the spinal release of NE (66, 67).

Clonidine is an appreciated drug in the perioperative period because of its anxiolytic, sedative and analgesic properties (64, 63, 68). Clonidine has anesthetic sparing effects (69, 70, 71), antiemetic (72), antishivering (73) and antiepileptic properties (74). Clonidine’s effect of myocardial and renal protection is still debated (75, 76, 77, 78, 79). Clonidine could also decrease blood loss (80).

Clonidine modifies the electroencephalogram (EEG) by increasing the slow delta waves activity and decreasing the alpha fluctuations. Therefore it causes sedation and a significant decrease in the bispectral index (BIS), one explanation of its anesthetic sparing effect (71, 81).

The effects of alpha-2 agonists on SEP still remain unclear and the literature is poor: Gabriel et al. observed clonidine’s effects in 19 patients undergoing lumbar disc procedures. Two successive infusions of 5 µg/kg of clonidine were used. Total dose dependent manner motor neurons’ pyramidal activation in the spine, and therefore depress MEP’s amplitudes (50, 51). Nitrous oxide can be employed in doses up to 50% and is less depressant than the other volatile anesthetics (52).

Among the intravenous anesthetics, thiopental has depressive effects on MEP, while etomidate has minimal effects (21). Plasma propofol concentrations up to 3 mcg/ml preserve MEP, while at concentrations greater than 5 mcg/ml, their amplitude decreases, but is still recordable (53, 54). By monitoring its plasma level and increasing stimuli rates, MEPs are still maintained (55), with adequate recordings, with high doses (21, 9, 31).

Benzodiazepines seem to have little effects on MEP when used as premedication prior to the surgery or as part of a multimodal anesthesia, although some studies present controversial results. In animal studies, midazolam produced the attenuation of MEP (56) while in human beings, the continuous administration of 0.1 mg/kg/hour midazolam did not interfere with the MEP latency or amplitude (57), but a bolus of midazolam caused a 16% significant decrease in amplitude, persistent for 30 minutes (58).

Ketamine, administered as a single dose up to 0.5 mg/kg or as continuous infusion of 1 to 4 mg/kg/hour, has minimal effects during MEP recording (53, 54). Higher doses cause moderate depression of the amplitude in animal models (59).

Opioids have minimal effect on MEP (21, 60). Animal studies suggest that all opioids have the same effects on MEP, remifentanil being the least suppressive (61).

Muscle relaxants depress neural transmission and alter EMG responses, but correct MEP recordings are still possible if one or two twitches on Train-of-four are present (21, 62).

Clonidine and neuromonitoring

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| Table 2 | Effects of principal anaesthetic agents on MEP |
|-----------------------------------------------|
| **MEP latency** | **MEP amplitude** |
| Desflurane 1 MAC (30) | No change | Decrease |
| Sevoflurane 1.7-2.5 MAC (103) | No change | Decrease |
| Isoflurane 1 MAC (104) | Increase | Decrease |
| Nitrous Oxide 50-60% (105) | Increase | Decrease |
| Thiopental 2-3 mg/kg (21) | No change | Decrease |
| Etomidate 0.3 mg/kg (106) | Increase | No change |
| Propofol 2.5 mg/kg (26) | No change | Decrease |
| Midazolam 0.1-0.3 mg/kg (58) | No change | Decrease |
| Ketamine 0.5 mg/kg (26) | No change | No change |
| Sufentanil 5 µg/kg (61) | Increase | Decrease |
| Remifentanil 5 µg/kg + 1 µg/kg/min (106) | No change | No change |
EEG power decreased in 87% of the patients after the second dose of clonidine. At this dose, amplitude decreased by 10% and latency increased of 2% and the central conduction time increased from 6.47 to 6.92 ms. Clonidine had almost no effect on the amplitude of the cortical potentials and the BAEP (82). However, in this study, nitrous oxide was used for maintenance of anesthesia, and the dose of clonidine was higher than that normally recommended.

Porkkala et al. studied SEP during isoflurane anesthesia in 20 patients undergoing elective spinal surgery. They showed that the cortical SEP amplitude was attenuated and the peak latency increased during isoflurane anesthesia (1 MAC). However, the administration of 2 µg/kg of clonidine did not modify these findings and even more, the EEG effect of clonidine and isoflurane were not additive (83). This is supported by another study showing that clonidine by itself does not interfere with short latency SEP (84).

A report of 34 elderly patients undergoing cataract extraction under regional anesthesia, showed that oral premedication with 300 µg clonidine did not enhance the latencies of BAEP up to 120 minutes after surgery (85).

**Dexmedetomidine and neuromonitoring**

Dexmedetomidine is a higher selective alpha 2 adrenergic agonist (86, 87, 88, 89) which exhibits similar properties. Like clonidine, its effect on the perioperative evoked potentials has been the subject of a few studies.

In a retrospective review of prospectively collected data, the administration of 1 µg/kg of dexmedetomidine over 20 minutes followed by an infusion of 0.5 µg/kg/hour in 9 pediatric patients undergoing posterior spinal fusion showed no statistically significant difference in the recordings of MEP and SEP before and after the administration of dexmedetomidine (86).

Similar results were reported in 18 patients undergoing surgical correction for idiopathic scoliosis who were administered a bolus of 0.5 µg/kg dexmedetomidine continued with an infusion of 0.5 µg/kg/h. Bispectral index was kept between 35 and 45. Authors observed that SEP were kept in an acceptable range and MEP remained unchanged through the procedure, suggesting that neuromonitoring was possible when dexmedetomidine was administered in this range of doses (90). This was confirmed by Lin et al. who reported similar results in a series of 36 patients using similar doses (91) and by another study which also reported minimal changes in the perioperative SEP and MEP monitoring with even higher doses of dexmedetomidine (0.6 µg/kg followed by 0.5 µg/kg/h) (92). The impact of even greater doses of dexmedetomidine on the SEP was analyzed. A loading dose of 6 µg/kg/h dexmedetomidine during 10 minutes followed by an infusion of 0.5 µg/kg during another 10 minutes produced no statistically significant changes in the amplitude or latency of SEP, but unfortunately, MEP were not monitored in this study (93).

However, Chen et al. concluded that if dexmedetomidine did not affect SEP and MEP in patients aged between 65 and 80, at a dose of 0.3 µg/kg followed by a 0.3 µg/kg/h infusion, it could inhibit MEP at higher dose: 0.8 µg/kg followed by a 0.8 µg/kg/h (94), suggesting that patients’ age (or its associated comorbidities?) could be an important factor.

In a series of 37 patients undergoing spinal surgery (95) Bala et al. monitored both upper- and lower-extremity MEP and right and left median and posterior tibial nerve SSEP after two infusions of dexmedetomidine with two different plasma targets: 0.3 or 0.6 ng/ml. Between the two infusions, a 20 minutes “wash out period” was foreseen to allow the plasma dexmedetomidine concentration to decrease to about 0.3 ng/ml or less. The results indicated that up to 6 ng/ml plasma concentration of dexmedetomidine had no effect on SEP, but they were unable to reject the hypothesis that it attenuated the MEP by an amount greater than 50%. This observation was confirmed by another study (96), where dexmedetomidine at plasmatic concentrations of 0.6 – 0.8 ng/ml with propofol really decreased MEP’s amplitude. However, the authors

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of Study</th>
<th>Number of cases</th>
<th>Dose</th>
<th>Other Agent</th>
<th>Effects on SEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gabriel et al. (82)</td>
<td>Prospective</td>
<td>19</td>
<td>5 µg/kg</td>
<td>N2O, Isoflurane, Diazepam, Fentanyl</td>
<td>NE</td>
</tr>
<tr>
<td>Porkkala et al. (83)</td>
<td>Prospective</td>
<td>20</td>
<td>2 µg/kg</td>
<td>Oxazepam, N2O, Isoflurane</td>
<td>NE</td>
</tr>
<tr>
<td>Kumar et al. (85)</td>
<td>Prospective</td>
<td>34</td>
<td>300 µg (premedication)</td>
<td>Facial and Retrobulbar Block</td>
<td>NE</td>
</tr>
</tbody>
</table>

NE = No effects.
The properties of the alpha 2 agonists make them interesting drugs for anesthesia and the perioperative period. However, dexmedetomidine and clonidine are rarely used during spine surgery when neuromonitoring is required. Rare and sometimes controversial literature describing the effects of alpha 2 agonists on the perioperative evoked potentials make the anesthesiologists avoid them in this setting. In particular, in such observational studies, measuring an observer-influenced outcome (such as change in waveforms), evidence base could be compromised. More studies, especially blinded randomized trials relying on important and clearly defined clinical outcomes, are needed in order to evaluate the effects of alpha 2 agonists on evoked perioperative potentials and to decide the safety of their use in this setting. However, dexmedetomidine’s short duration of action would be an advantage, allowing a quick return to the basal situation within one hour.

could not observe significant changes in cortical SEP amplitudes with high (0.8 ng/ml) concentrations. These results suggested different effects of this drug on MEP and SEP’s neural pathways, maybe at the level of spinal cord interneurons or alpha motor neurons.

Two case reports (97), where the authors describe that a dexmedetomidine infusion caused a decrease of the TcMEP amplitude of upper and lower extremities while ulnar and posterior tibial nerve cortical SSEP amplitudes and latencies remained within baseline range, further confirm the differential action of dexmedetomidine on SEP and MEP and also the robustness of SEP when compared with MEP. Important to notice, TcMEP reappeared within approximately 30 minutes after the end of the infusion of dexmedetomidine.

Contrarily to clonidine, it seems that during anesthesia conducted with isoflurane, dexmedetomidine further increases the effect of isoflurane on evoked potentials (98).

### Table 4

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of Study</th>
<th>Number of cases</th>
<th>Dose</th>
<th>Other Agents</th>
<th>Effects on SEP</th>
<th>Effects on MEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOBIAS et al.</td>
<td>Retrospective</td>
<td>9</td>
<td>1 ug/kg + 0.5 ug/kg/h</td>
<td>Propofol, Remifentanil</td>
<td>NE</td>
<td>NE</td>
</tr>
<tr>
<td>ANSCHEL et al.</td>
<td>Randomized</td>
<td>18</td>
<td>0.5 ug/kg + 0.5 ug/kg/h</td>
<td>Propofol, Remifentanil</td>
<td>NE</td>
<td>NE</td>
</tr>
<tr>
<td>LIN et al.</td>
<td>Randomized</td>
<td>36</td>
<td>0.5 ug/kg + 0.5 ug/kg/h</td>
<td>Etomidate, Fentanyl</td>
<td>NE</td>
<td>NE</td>
</tr>
<tr>
<td>ROZET et al.</td>
<td>Randomized</td>
<td>40</td>
<td>0.6 ug/kg + 0.5 ug/kg/h</td>
<td>Propofol, Remifentanil</td>
<td>NE</td>
<td>NE</td>
</tr>
<tr>
<td>KABIYAMA et al.</td>
<td>Prospective</td>
<td>8</td>
<td>1 ug/kg + 0.5 ug/kg/h</td>
<td>Propofol</td>
<td>NE</td>
<td>NE</td>
</tr>
<tr>
<td>CHEN et al.</td>
<td>Randomized</td>
<td>15</td>
<td>0.3 ug/kg + 0.3 ug/kg/h</td>
<td>Midazolam, Propofol, Fentanyl</td>
<td>NE</td>
<td>NE</td>
</tr>
<tr>
<td>CHEN et al.</td>
<td>Randomized</td>
<td>15</td>
<td>0.8 ug/kg + 0.8 ug/kg/h</td>
<td>Midazolam, Propofol, Fentanyl</td>
<td>DECAY &gt; 50%</td>
<td>NE</td>
</tr>
<tr>
<td>BALA et al.</td>
<td>Randomized</td>
<td>37</td>
<td>Pl. conc 0.6 ng/ml</td>
<td>Midazolam, Propofol, Fentanyl</td>
<td>NE</td>
<td>DECAY &gt; 50%</td>
</tr>
<tr>
<td>MAHMOUD et al.</td>
<td>Randomized</td>
<td>40</td>
<td>Pl. conc 0.6 – 0.8 ng/ml</td>
<td>Propofol, Remifentanil</td>
<td>NE</td>
<td>DECAY &gt; 50%</td>
</tr>
<tr>
<td>MAHMOUD et al.</td>
<td>Case reports</td>
<td>2</td>
<td>0.5 ug/kg/h</td>
<td>Fentanyl, Propofol, Remifentanil, Midazolam</td>
<td>NE</td>
<td>DECAY &gt; 50%</td>
</tr>
<tr>
<td>THORTON et al.</td>
<td>Randomized</td>
<td>9</td>
<td>Pl. conc 0.3 – 0.6 ng/ml</td>
<td>Isoflurane</td>
<td>NE</td>
<td>NE</td>
</tr>
</tbody>
</table>

NE = no effect ; Pl. conc = plasma concentration.

### Conclusion

The properties of the alpha 2 agonists make them interesting drugs for anesthesia and the perioperative period. However, dexmedetomidine and clonidine are rarely used during spine surgery when neuromonitoring is required. Rare and sometimes controversial literature describing the effects of alpha 2 agonists on the perioperative evoked potentials make the anesthesiologists avoid them in this setting. In particular, in such observational studies, measuring an observer-influenced outcome (such as change in waveforms), evidence base could be compromised. More studies, especially blinded randomized trials relying on important and clearly defined clinical outcomes, are needed in order to evaluate the effects of alpha 2 agonists on evoked perioperative potentials and to decide the safety of their use in this setting. However, dexmedetomidine’s short duration of action would be an advantage, allowing a quick return to the basal situation within one hour.
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