Use of Dexmedetomidine and Ketamine Infusions During Scoliosis Repair Surgery With Somatosensory and Motor-Evoked Potential Monitoring: A Case Report

Rozanna Penney, CRNA, MSNA, CEN

Dexmedetomidine and ketamine infusions were the main anesthetics for a 15-year-old girl, who underwent scoliosis repair surgery with intraoperative wake-up test, somatosensory evoked potential (SSEP), and motor-evoked potential (MEP) monitoring. To achieve maintenance of anesthesia, dexmedetomidine and ketamine were administered concomitantly. The dexmedetomidine dose ranged from 0.9 to 1.2 µg/kg per hour throughout the case, and the ketamine dose ranged from 0.4 to 0.6 mg/kg per hour. The analgesic properties of dexmedetomidine and ketamine were complemented by the continuous fentanyl infusion at 1 to 2 µg/kg per hour. The sympatholytic properties of dexmedetomidine were balanced with the sympathomimetic properties of ketamine, and the patient required minimal vasoactive support (only 250 µg of phenylephrine was administered over the course of 12 hours of anesthetic care). This anesthetic regimen, as well as 60% nitrous oxide and 40% oxygen, provided satisfactory conditions for the intraoperative neurophysiologic monitoring. This case report discusses the use of dexmedetomidine and ketamine infusions as an alternative to propofol-based total intravenous anesthesia during scoliosis repair surgery with intraoperative SSEP and MEP monitoring.

Keywords: Dexmedetomidine, ketamine, motor-evoked potential, scoliosis repair surgery, somatosensory evoked potential.

Neurologic deficits associated with scoliosis repair are the complications that patients and healthcare providers fear the most. To prevent neurologic injury, multimodal intraoperative neurophysiologic monitoring of somatosensory evoked potentials (SSEP) and motor-evoked potentials (MEP) are frequently employed for these procedures. The use of total intravenous anesthesia (TIVA) has been advocated because volatile anesthetics depress MEP and produce dose-dependent increase in latency and a decrease in amplitude in SSEP. Even though propofol causes a dose-dependent depression of the amplitude in MEP, it provides better neurologic monitoring conditions than inhaled anesthetics, and is therefore used most frequently as the main component of TIVA. Ketamine is the only anesthetic that can be used as a continuous infusion that enhances MEP signals. Dexmedetomidine, when used as an anesthetic adjunct, does not affect SSEP or MEP monitoring. There are limited documented cases of the use of dexmedetomidine without propofol in TIVA. Since propofol provides dose-dependent depression of MEP, affects SSEP, and offers no analgesia, alternative anesthetic management for these cases may prove to be of benefit. This case report discusses the use of dexmedetomidine and ketamine infusions as an alternative to propofol-based TIVA during scoliosis repair surgery with intraoperative SSEP and MEP monitoring.

Case Summary
A 15-year-old girl weighing 48 kg, with a height of 162.5 cm, presented to the operating room for posterior thoracolumbar fusion with SSEP and MEP monitoring, as well as an intraoperative wake-up test. Her medical history showed idiopathic scoliosis, hypoplastic right lung disease, asthma, scarlet fever, and pneumonia. The patient had no known drug allergies. Her current medications included daily multivitamins and an albuterol inhaler that she used occasionally. Preoperative evaluation revealed clear lung sounds bilaterally, regular heart rate and rhythm, a Mallampati score of 2, and a thyromental distance of 3 fingerbreadths. Before induction, the surgeon and the anesthesia team discussed the intraoperative wake-up test with the patient.

Induction of anesthesia was accomplished via mask inhalation with 6% sevoflurane in a mixture of 60% nitrous oxide and 40% oxygen. Following the induction of anesthesia, 2 peripheral 16-gauge and 18-gauge IV catheters were placed, as well as a 20-gauge radial arterial line. Once IV access was established, 250 µg of fentanyl, 1 mg of lorazepam, and 30 mg of rocuronium were administered intravenously followed by 90 seconds of continued mask ventilation. Laryngoscopy was accomplished, and the patient was intubated with a 7-mm cuffed endotracheal tube. Correct placement of the endotracheal tube was verified with positive end-tidal carbon dioxide and bi-
laterally equal breath sounds. A 16-French orogastric tube, esophageal stethoscope, and soft bite block (ie, tonsil balls between the teeth to protect dentition, tongue, and tubes during MEP monitoring) were placed at this time. Sevoflurane was discontinued while the 60% nitrous oxide and 40% oxygen mixture was maintained throughout the case. Intravenous anesthesia consisting of dexmedetomidine, 0.9 µg/kg per hour, and ketamine, 0.4 mg/kg, was started concomitantly per institutional protocol for spine surgery. The dexmedetomidine dose ranged from 0.9 to 1.2 µg/kg per hour throughout the case, and the ketamine dose ranged from 0.4 to 0.6 mg/kg per hour. The fentanyl infusion was started simultaneously at 1 µg/kg per hour and was maintained at 1 to 2 µg/kg per hour throughout the case. The neurologic monitoring technician applied all of the necessary equipment for SSEP and MEP monitoring and performed a baseline test.

After the patient was positioned prone on the Chick orthopedic table with meticulous attention given to proper positioning, the surgeon started the procedure. Muscle paralysis was not reversed but were off, as evidenced by 4/4 twitches by train-of-four. Additional doses of neuromuscular relaxant were not given. Thirty minutes before the wake-up test, the fentanyl infusion was stopped. Dexmedetomidine and ketamine infusions and nitrous oxide were turned off approximately 5 to 10 minutes before the wake-up test. The patient awakened promptly, and the wake-up test was performed successfully. As discussed with the patient before the induction of anesthesia, she squeezed her hands and moved her feet up and down and in and out like windshield wipers, on command. Following successful completion of the wake-up test, 50 mg of propofol and 1 mg of lorazepam were administered as a bolus, the dexmedetomidine infusion was restarted at 1.2 µg/kg per hour, the ketamine infusion was restarted at 0.5 mg/kg per hour, and the fentanyl infusion was restarted at 1 µg/kg per hour.

Total surgical time was approximately 9 hours, with an estimated blood loss of 1,100 mL. The patient received 1,000 mL of IV hetastarch (Hespan), 3,150 mL of Ringer's lactate solution, 1 U of autologous packed red blood cells, and 502 mL of autologous blood filtered through a blood recovery system (Cell Saver, Haemonetics, Braintree, Massachusetts). A total of 250 µg of phenylephrine was administered in 40- to 50-µg boluses for blood pressure support. The results of the intraoperative SSEP and MEP monitoring remained satisfactory throughout the case.

At the end of the surgery, the patient was ventilating spontaneously, and she opened her eyes, squeezed her hands, moved her feet, and lifted her head off the pillow to command. After demonstrating appropriate motor and sensory responses, the patient was extubated in the operating room. The patient was admitted to the pediatric intensive care unit (PICU) and, when interviewed the next day, had no recollection of the intraoperative wake-up test. She did not require any pain management intervention until 10 hours after admission to the PICU, at which time she was given 10 mg of diazepam (Valium) and 2 mg of morphine. She was discharged home 6 days later.

Discussion

The incidence of neurologic deficits associated with scoliosis surgery repair is 0.3% to 1.89%, increasing to 4% when spinal fusion is combined with segmental fixation. Electrophysiologic monitoring of the sensory mediated tracts in the spinal cord has been available since the 1970s, but the only way to monitor motor function was the wake-up test. The intraoperative wake-up test was first introduced by Stagnara and Vauzelle in 1973 to assess motor function. To this day, the wake-up test remains the gold standard for the assessment of motor function after applications of corrective forces to a rigid spinal canal. However, neurologic injury can occur at any time intraoperatively—from surgical maneuvers, instrumentation, vascular injury, or ischemia secondary to hypoperfusion of the spinal cord—and remain undetected for hours until the wake-up test is performed. In addition, the intraoperative wake-up test does not allow for the prompt identification of the specific surgical maneuver responsible for the spinal cord injury, which can be crucial to reversing the injury. Risks associated with the intraoperative wake-up test include damage to the spinal cord, dislodgement of instrumentation, extubation, hypoxia, and venous air embolus as a result of deep inspiratory efforts. In 1980, Merton and Morton described a successful recording of transcranial muscle evoked potentials, which was groundbreaking in the development of multimodal spinal cord monitoring. Multiple studies have documented the benefit of monitoring the integrity of specific ascending sensory and descending motor pathways by recording SSEP and MEP. In 1997, Paderg et al published a 10-year retrospective study of 500 patients who underwent corrective surgery for idiopathic scoliosis with combined SSEP and MEP monitoring. The study had 2 true-positives (0.4%), 7 false-positives (1.4%), and no false-negative results. The researchers concluded that such combined monitoring can eliminate the need for the intraoperative wake-up test. Subsequent, smaller studies supported these findings. Due to the safety, reliability, and sensitivity of combined SSEP and MEP intraoperative monitoring, it has become the preferred method for detection and reduction of intraoperative spinal cord injury.

Some institutions reserve the intraoperative wake-up test only for cases with abnormal electrophysiologic monitoring or when evoked potential data can not be obtained. A higher incidence of false-negative results than Paderg et al found was described by Iwasaki et al in 2003. The study reviewed 672 patients who underwent...
spinal surgery with SSEP and MEP monitoring. The overall results included 652 true-negatives, 12 true-positives, and 4 false-negatives. In an attempt to explain the false-negative results, Tsutsui et al performed a study, which revealed that selective insult to a limited area in the anterior horn of the spinal cord and to the single spinal root did not always change MEPs. After careful consideration of the risks and benefits, some orthopedic surgeons, as in our case, prefer the routine use of the intraoperative wake-up test in addition to electrophysiologic monitoring. Due to the complexity of the spinal cord function, experts recommend multimodal combinations for effective intraoperative neurologic monitoring.

Intravenous and inhalation anesthetic agents produce effects by altering neuronal excitability through changes in synaptic and axonal functional activities. The sensitivity of the SSEP and MEP monitoring to specific anesthetic agents depends on the neurologic pathways involved and the agent's mechanism of action. Volatile anesthetics depress excitatory and enhance inhibitory neurotransmission. When used at therapeutic concentrations, volatile anesthetics produce a dose-dependent increase in latency and decrease in amplitude during SSEP monitoring and are powerful depressants of MEP. Nitrous oxide has the least effect; however, when the other anesthetics are present its effect may vary.

Many authors advocate that the best anesthetic plan for optimal MEP monitoring, even when using a high-frequency stimulation technique, is to avoid inhalation agents. Barbiturates, benzodiazepines, and propofol act by enhancing the inhibitory effect of γ-aminobutyric acid (GABA). These agents bind to the GABA receptors, activation of which increases chloride conduction, hyperpolarizes the membrane, and produces synaptic inhibition. They produce a dose-dependent increase in latency and decrease in amplitude of SSEPs and depression of MEPs. Unlike barbiturates, propofol has a very rapid metabolism that allows for rapid adjustment of both anesthetic depth and the effects it has on evoked potential monitoring. The MEP amplitude depression observed with the use of propofol can be overcome by multipulse stimulation. Opioids activate specific opioid receptors (µ, κ, and δ). They have a minimal effect on SSEPs and MEPs, and are frequently used with propofol.

Etomidate and ketamine are different from the other anesthetic agents in that they can increase evoked potentials. Etomidate dramatically increases the amplitude of SSEPs and MEPs, which appears to coincide with myoclonus, suggesting heightened cortical excitability. Ketamine enhances the MEP amplitude and cortical SSEP without a change in latency, providing satisfactory monitoring conditions if used as a continuous infusion intraoperatively. When used as an anesthetic adjunct, dexmedetomidine does not affect the SSEP or MEP monitoring.

Dexmedetomidine is a relatively selective α2-adrenoceptor agonist that is 8 times more selective than clonidine. Alpha2 adrenoreceptors are found in the peripheral nervous system and central nervous system in presynaptic, postsynaptic, and extrasynaptic locations.

### Table. Effect of Anesthetic Agents on Somatosensory and Motor Evoked Potentials

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These receptors modulate norepinephrine release through a negative feedback mechanism. There are 3 α-adrenergic subtype receptors: α2a, α2b, and α2c. Stimulation of the α2b subtype, located mainly in the peripheral vasculature, causes vasoconstriction, and is responsible for the transient hypertension observed with rapid infusion of dexmedetomidine. Subtypes α2a and α2c are found predominantly in the central nervous system and are responsible for the hypotensive effects of dexmedetomidine. In addition, stimulation of the α2a subtype is responsible for sedation, analgesia, and sympatholysis, whereas stimulation of the α2c subtype is responsible for anxiolysis and contributes to spinal antinociception. A slow IV infusion of 10 to 300 μg/kg of dexmedetomidine can achieve α2 selectivity, but this effect is lost at high doses (>1,000 μg/kg) or with rapid administration.

In the prospective study by Gurbet et al, patients who received a dexmedetomidine infusion intraoperatively during abdominal surgery required significantly less morphine in the postoperative unit without any increase in side effects. A meta-analysis performed by Kid et al concluded that intraoperative administration of dexmedetomidine improved postoperative pain status after major and minor surgeries performed under general, regional, and local anesthesia. Our patient did not require any pain management intervention until 10 hours after her admission to the PICU.

Initially approved for sedating patients in the intensive care unit, dexmedetomidine is gaining popularity in the operating room due to its ability to provide sedation, analgesia, and sympatholysis without causing respiratory depression or the vascular effects of the α1 receptors. Dexmedetomidine has been used successfully for sedation during awake fiberoptic intubation, awake craniotomy, and awake carotid endarterectomy, and as an adjunct to general and regional anesthesia. Ramsay and Luterman described the use of dexmedetomidine as the sole anesthetic at higher-than-recommended doses (up to 10 μg/kg per hour) with no adverse hemodynamic effects in 3 cases for which difficult airway management was anticipated. Mahmoud et al described a case in which general anesthesia was administered with a laryngeal mask airway using an infusion of dexmedetomidine, 2 μg/kg per hour, after a bolus of 2 μg/kg of dexmedetomidine and 30 mg of ketamine (in 5-mg increments) for biopsy of a large anterior mediastinal mass. Dexmedetomidine has been used as a component of propofol-based TIVA without compromising neurophysiologic monitoring and allowing for a decrease in the patient’s propofol requirements. When used with fentanyl and ketamine infusions in rabbits, dexmedetomidine allowed for MEP monitoring. Bala et al concluded that dexmedetomidine, used as an anesthetic adjunct to desflurane and remifentanil at target plasma concentrations up to 0.6 ng/mL, does not change SSEP or MEP responses during complex spine surgery. There are limited documented cases of the use of dexmedetomidine without propofol in TIVA, and because propofol provides dose-dependent depression of MEP and offers no analgesia, the alternative of ketamine and dexmedetomidine infusion should be considered.

In this case, dexmedetomidine, infused at 0.9 to 1.2 μg/kg per hour concomitantly with ketamine at 0.4 to 0.6 mg/kg per hour, allowed for successful intraoperative SSEP and MEP monitoring. Ketamine, an N-methyl-D-aspartate receptor antagonist and a dissociative anesthetic agent, has been recognized for its intense analgesic properties and has been documented to enhance the MEP signals. The analgesic properties of ketamine and dexmedetomidine also were complimented by the continuous infusion of fentanyl. The sympathetic properties of dexmedetomidine were balanced with the sympathomimetic properties of ketamine, thereby requiring minimal vasoactive support (ie, only 250 μg of phenylephrine administered over the course of 12 hours of anesthetic care). This regimen, along with the use of 60% nitrous oxide and 40% oxygen, provided satisfactory conditions for intraoperative SSEP and MEP monitoring.

Conclusion

Combined SSEP and MEP intraoperative monitoring is the standard of care for individuals undergoing correction of scoliosis. Considering that most anesthetics affect SSEP and MEP to some degree, anesthetic management of these cases often can present a challenge. In this case, successful intraoperative neurologic monitoring was performed using dexmedetomidine, ketamine, and fentanyl infusions plus nitrous oxide. As demonstrated in a few studies, dexmedetomidine has minimal effect on evoked potentials and ketamine enhances MEP signals. Both drugs have substantial analgesic properties, possibly decreasing postoperative narcotic requirements. When used together, they offset each other’s side effects on the sympathetic nervous system. Possibly, TIVA using dexmedetomidine and ketamine infusions during SSEP and MEP monitoring might provide a valuable alternative to the standard propofol-based TIVA, but further research is necessary.

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ACKNOWLEDGMENTS
The author thanks her husband Jason Penney for his continuous support. She also thanks her friend, Anne Marie Lewis, RN, MSN; her preceptor, Laura Bassi, CRNA, MSNA; former program director, Jonathan Cormwell, CRNA, MSNA; and program director, Anne Tierney, CRNA, MSNA, for their help, guidance and support.