Successful Intraoperative Spinal Cord Monitoring During Scoliosis Surgery Using a Total Intravenous Anesthetic Regimen Including Dexmedetomidine

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Summary: Intraoperative neurophysiological monitoring (IONM) during corrective spinal surgery is widely used. Because of the possible interference with the recording of evoked potentials by inhalational anesthetics, total intravenous anesthetic (TIVA) regimens have been advocated. TIVA regimens may be difficult to use in pediatric populations due to metabolic factors. We report on the results of multimodality IONM during 18 cases in which a TIVA regimen incorporating dexmedetomidine (Precedex, Hespira, Lake Forest, IL) was used. Monitoring techniques included sensory (SSEP) and motor evoked potentials (MEP), as well as pedicle screw stimulation. SSEPs were maintained within an acceptable range of baseline amplitude (50%) and latency (10%), and MEPs remained elicitable throughout each case. We therefore found that the anesthetic regimen did not significantly interfere with any of the monitoring modalities used and conclude that IONM in the presence of dexmedetomidine is feasible under appropriate conditions.

Key Words: Dexmedetomidine, Intraoperative neurophysiological monitoring, Motor-evoked potentials, Somatosensory-evoked potentials, Idiopathic scoliosis, Total intravenous anesthesia.

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Adolescents affected by spinal deformity may require surgery to correct the malformation. The surgical procedures used to rectify the scoliosis and/or kyphosis are known to pose a risk of postoperative neurologic deficit due to damage to the spinal cord. As a result, methods have been used to assess the integrity of a patient's spine intraoperatively. For the past 30 years, intraoperative neurophysiological monitoring (IONM) has become recognized as an accurate method of monitoring a patient during these surgical procedures (Nuwer et al., 1995; Pelosi et al., 2002). IONM in some combination of modalities has become routine during these procedures although exact monitoring techniques vary from institution to institution.

Because inhalational anesthetics including nitrous oxide are generally poor choices when intraoperative monitoring is desired (Chen, 2004, Sloan et al., 1995), a regimen consisting solely of intravenous agents can be used, a technique known as total intravenous anesthetic (TIVA). Medications included in a TIVA regime may include narcotics, such as fentanyl, which alter sensory (SSEP) and motor (MEP) evoked potential amplitude and latency minimally enough to permit recording, and in a dose-dependent manner (Kalkman et al., 1992); barbiturates, which elicit high sensitivity in MEP and SSEP response; and benzodiazepines. Propofol, a relatively new intravenous anesthetic agent, produces a dose-dependent depression of EEG. Unlike barbiturates, however, propofol is rapidly metabolized and may be titrated to accommodate MEP and SSEP recording. Studies have shown propofol to preserve cortical SSEPs well and consistently result in BIS values of less than 60 (Clapcich et al., 2004). Unfortunately, it has been our experience that the large doses that are often required by adolescents to assure adequate anesthesia depth may exceed the recommended "maximum dose" and result in difficulties awakening the patient postoperatively.

Dexmedetomidine (Precedex, Hospira) is a drug that is presently approved by the FDA as a sedative, anxiolytic and analgesic in an intensive care setting. It is an imidazole compound, which acts through α_2-adenoreceptor agonism, thereby activating pertussis toxin-sensitive G proteins and increasing potassium ion efflux. The drug is similar in action to clonidine, but with 8 times the affinity for the α_2-adenoreceptor. Administration of 1 μg/kg over 2 minutes to 6 healthy male adults caused reductions in blood pressure and heart rate consistent with a reduction in plasma adrenaline and noradrenaline levels (Bloor et al., 1992). Additionally, studies have shown that dexmedetomidine does not cause respiratory depression when administered over a 24-hour period of time. After metabolism in the liver, it is excreted as methyl and glucuronide conjugates, mainly via renal excretion (Mantz, 1999).

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Sedation studies have shown that use of dexmedetomidine significantly reduced the need for rescue sedation with propofol compared with placebo (Martin et al., 2003) and when used during intubation required 4 times less midazolam than placebo patients (Bachand et al., 1999). Analgesic effect was such that patients given dexmedetomidine required 50% less morphine than placebo patients, with 43% requiring no morphine, compared with 17% for placebo (Bhana et al., 2000). In a postsurgical setting, the use of dexmedetomidine has been shown to result in very cooperative sedation, in which patients can easily transition from sleep to a waking state (Martin et al., 2003). Additionally, because of the depression in heart rate that accompanies the administration of dexmedetomidine, it has been suggested that extubation and other stressful episodes can be performed with a lower risk of ischemic episodes (Venn and Grounds, 2000).

Dexmedetomidine's use as part of a TIVA regimen is contingent on the effect the drug has on IONM. This requires that the administration of dexmedetomidine be compatible with evoked potential acquisition. Studies in the rat model found that dexmedetomidine interferes minimally with the amplitude and latency of SSEPs (Li et al., 2003). Studies in humans confirm these findings, though it was noted that, while maintaining early cortical peaks, dexmedetomidine had depressive effects on later cortical peaks, which diminished as infusion of the drug was reduced (Bloom et al., 2001). The purpose of the present study is to evaluate multimodality IONM from cases where dexmedetomidine was incorporated into a TIVA regimen that includes propofol and narcotics.

TABLE 1. Subject Information

Subject	Sex	Age	Diagnosis	Procedure
1	F	17	Idiopathic scoliosis	T5-L1 segmental spinal fusion
2	F	15	Idiopathic scoliosis	T4-L11 segmental spinal fusion
3	F	16	Idiopathic scoliosis	T10-L4 segmental spinal fusion
4	F	18	Idiopathic scoliosis	T6-L4 segmental spinal fusion
5	F	27	Idiopathic scoliosis	T10-L2 inspection of fusion mass and revision of instrumentation
6	F	17	Idiopathic scoliosis	T4-L1 segmental spinal fusion and autograft
7	F	18	Idiopathic scoliosis	Segmental spinal fusion
8	F	17	Idiopathic scoliosis	High thoracic to L3 segmental spinal fusion
9	M	7	Idiopathic scoliosis	Extension of growing rod.
10	F	17	Idiopathic scoliosis, painful hardware	Removal of hardware, inspection of fusion mass
11	F	15	Idiopathic scoliosis	T4-L4 segmental spinal fusion
12	M	16	Idiopathic scoliosis	T4-T11 segmental spinal fusion
13	M	17	Idiopathic scoliosis	T11-L4 segmental spinal fusion
14	F	17	Idiopathic scoliosis	T11-L3 segmental spinal fusion
15	F	10	Idiopathic scoliosis	T4-L2 segmental spinal fusion
16	F	14	Idiopathic scoliosis	T5-L2 segmental spinal fusion
17	F	13	Idiopathic scoliosis	T4-L2 segmental spinal fusion
18	M	18	Congenital kyphosis	T4-L3 segmental spinal fusion

METHODS

Subjects

Table 1 illustrates the gender, age range, procedure being performed, and diagnosis for each of the 18 subjects.

TABLE 2. MEP Results

	Baseline MEP	Intraoperative MEP
1	AH, TA, VM, BF present bilaterally	No change
2	AH, TA, BF present bilaterally. VM present on right. VM on left had a bad electrode which could not be replaced.	No change
3	AH and TA present bilaterally.	Bilateral TA and right AH no change, left AH absent at closing (likely technical, see text)
4	AH, TA present bilaterally. VM and FDI on the right side only.	AH and TA responses on the left fluctuated in response to MAP
5	AH, TA, BF, FDI present bilaterally.	No change
6	AH, TA, VM present bilaterally	No change
7	AH, TA, BF,VM present bilaterally.	No change
8	TA bilaterally, AH on left.	No change
9	AH, TA, BF present bilaterally. VM on left only.	No change
10	AH, TA, BF,VM present bilaterally.	No change
11	AH, TA, BF, VM present bilaterally.	No change
12	AH, TA, FDI present bilaterally.	No change
13	AH, TA present bilaterally, BF on right.	No change
14	AH, TA, FDI present bilaterally.	No change
15	AH, TA, FDI present bilaterally.	No change
16	AH and TA present bilaterally.	No change
17	AH, TA, FDI present bilaterally.	No change
18	AH, TA, BF, VM present bilaterally.	No change

AH, Abductor hallucis; TA, tibialis anterior; BF, biceps femoris; VM, vastus mediales; FDI, first dorsal interosseous; MAP, mean arterial pressure.

With the exception of three subjects (18%) who were undergoing removal or revision of existing hardware, all subjects underwent segmental spinal fusion.

Anesthesia

One of Two Anesthetic Techniques Were Used for Induction:

1) Sevoflorane, N_2O, and O_2 by mask. On induction, two intravenous lines were placed, and the following infusions started: fentanyl, 3 μg/kg load with 1 μg/kg per hour infusion; propofol, 200 μg/kg per minute; dexmedetomidine, 0.5 μg/kg load over 20 minutes with infusion at 0.5 μg/kg per hour after loading. Sevoflorane and N_2O were discontinued with line placement, and intubation on 100% O_2. TIVA was continued with decreasing propofol to maintain a BIS of 35 to 45. In addition, elective hypotension to a mean arterial pressure (MAP) of 50 to 60 was achieved with a combination of β-blockade (esmolol and/or labetalol) and vasodilation (nitroprusside or nitroglycerin via intravenously infusion).
2) Intravenous induction with propofol (3 to 5 mg/kg), fentanyl (3 μg/kg), and dexmedetomidine 0.5 μg/kg. Infusions were then run as above.

After induction and intubation, an arterial line was placed in the radial artery for continuous pressure monitoring. The patient was then positioned prone for the surgical procedure. If needed, 0.2 mg/kg rocuronium was used for muscle relaxation during dissection through paraspinal muscles.

Intraoperative Neurophysiological Monitoring

All IONM was performed using an Epoch XP (Axon Systems; Hauppauge, NY). Intraoperative monitoring consisted of SSEP, MEP, and pedicle screw stimulation. Initial baseline SSEP and MEP samples were taken after intubation, before the first incision was made. A second baseline was then performed after spine exposure.

SSEP stimulating electrodes were placed over bilateral posterior tibial nerves behind the medial malleolus and over bilateral median nerves at the wrist. Stimulation intensity was 50 to 60 mA at a duration of 200 to 400 μs. Recording electrodes were placed on the scalp at locations C3′, C4′, Cz' (1 cm posterior to C3, C4, Cz), Fpz, and in a high cervical location. The posterior tibial cerebral P36/N45 components were detected by the Fpz-Cz' and C3′-C4′ derivations, and the cervical N31 component was detected by the Fpz-cervical derivation. The median cerebral N19/P21 components were detected by the Fpz-Cz' and C3′-C4′ derivations, and the cervical N14 component was detected by the Fpz-cervical derivation. The band pass was set at 30 to 1000 Hz; 250 trials were averaged per sample. SSEP changes of >50% amplitude or >10% latency were considered significant.

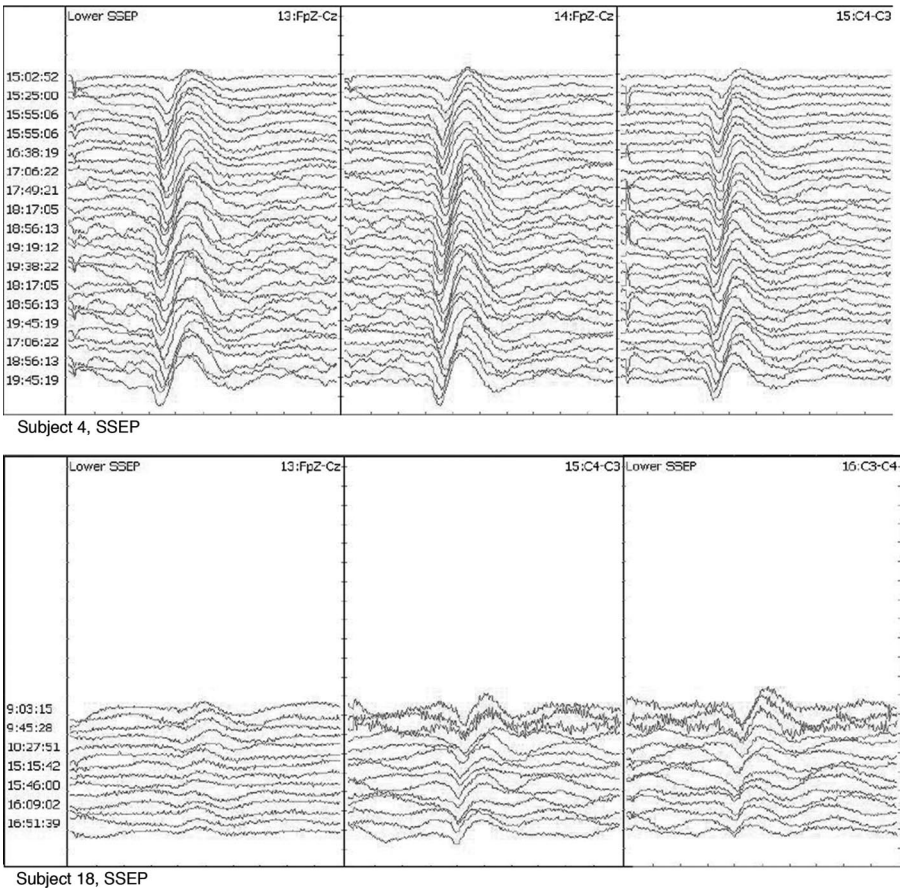

FIGURE 1. Sample tibial nerve SSEPs for two typical subjects over the course of their respective surgical procedures. Signals remained consistently reproducible throughout. Scale is 10 ms/division *x*-axis and 1 μV/division *y*-axis.

Recording electrode placement for MEPs varied among subjects, based on the procedure performed and was bilateral for all muscles monitored. All had a pair of needle electrodes inserted into the abductor hallucis (AH) and tibialis anterior (TA) muscles. Sixteen of the 20 (80%) subjects had electrodes placed in the vastus medialis (VM) muscle. Fifteen (75%) had electrodes in the biceps femoris (BF). Six (30%) had electrodes placed in the first dorsal interosseous muscles (FDI). A 5 pulse train was utilized with a stimulation pulse rate of 250 p/s, at a duration of 300 μs and an intensity of 200 to 300 V. The band pass was set at 30 to 1000 Hz. MEPs for each muscle were monitored as being present or absent. Needle stimulating electrodes were placed at C3 and C4.

Pedicle screw stimulation was performed using a nasopharyngeal electrode as cathode and needle anode placed in adjacent muscle. The triggered EMG threshold for reposition of screws was determined case-by-case, based on a combination of x-rays and threshold. EEG was performed for the purpose of monitoring for seizures.

RESULTS

Baseline SSEP cortical and cervical recordings had well-formed, reproducible waveforms from both upper and lower limbs in all of the 18 subjects. Well-formed SSEPs were continually elicited and remained within baseline limits (50% amplitude/10% latency) throughout the procedure for all patients.

Table 2 illustrates intraoperative MEP findings. All 18 subjects had baseline MEPs present bilaterally, which remained elicitable throughout the case. Only two cases showed a deterioration of MEP responses (subjects 3 and 4). In one case, there was a clear correlation with the mean arterial pressure (MAP) (subject 4). Responses could be obtained if the MAP was in the low 80s but were lost with a MAP in the low 60s. Subject 3 had bilateral AH and TA responses at baseline but lost the left AH response near the end of the procedure, with persistence of the left TA MEP. No definite reason was found for this. However, a technical factor is likely as stimulus artifacts were also lost from the AH channel. The patient had no postoperative neurologic deficit.

Sample SSEP and MEP stacks are shown in Figs. 1 and 2, respectively. They show that the quality of both SSEP and MEP signals was at least maintained, if not improved throughout these cases.

In all cases, baseline EEG was low to moderate amplitude in the delta and beta range, which remained consistent throughout surgery and gave no indication of seizure, including around times of transcranial electrical stimulation.

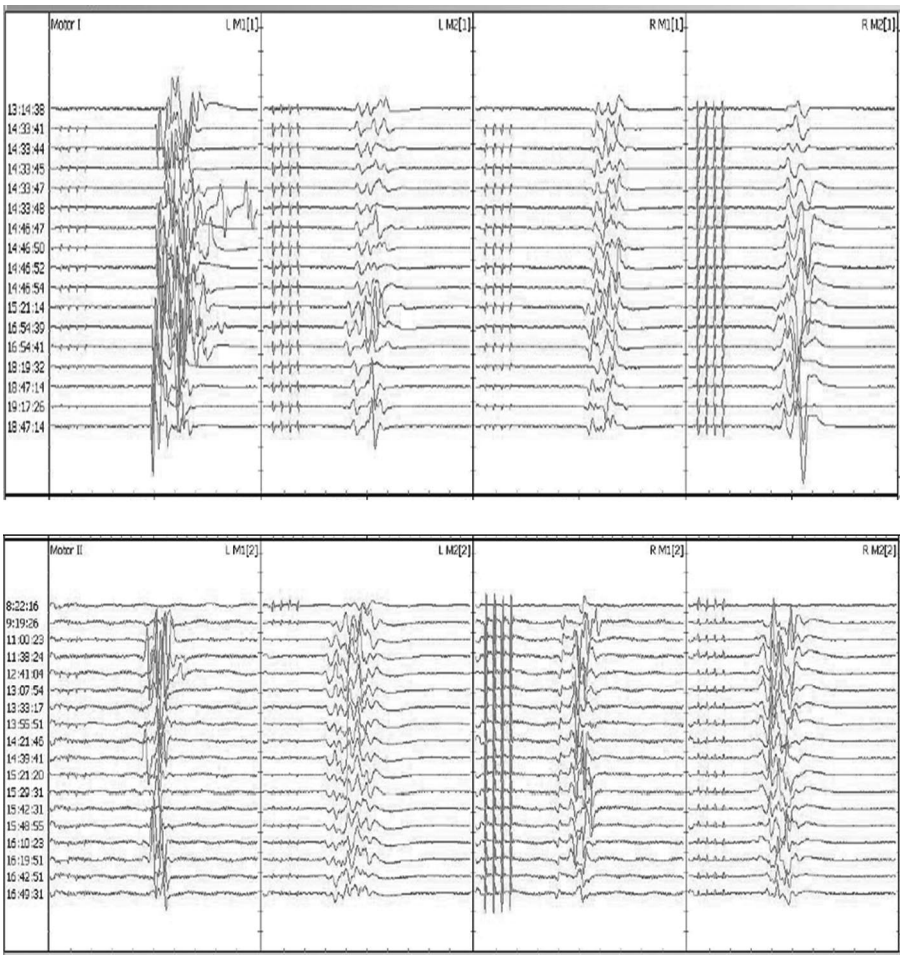

FIGURE 2. MEPs from two subjects illustrating signals collected from bilateral abductor hallucis and tibialis anterior muscles. Both subjects show reproducible complex waveforms throughout the case. Subject 13 displays an increase in amplitude on the right side. Scale for subject 13 is *y*-axis = 200 μV/division; subject 18, *y*-axis = 50 μV/division for LM1 and RM1, 100 μV/division for LM2, and 75 μV/division for RM2. *x*-axis = 10 ms/division, *x*-axis for all tracings.

Five (28%) of the 18 subjects underwent pedicle screw stimulation. A total of 68 screws were stimulated. Three screws had triggered responses at ≤10 mA; 15 had thresholds at ≤15 mA. No repositioning or removal of hardware was deemed necessary. There were no postoperative radiculopathies.

DISCUSSION

Until recently, the anesthetic, anxiolytic, and analgesic properties of dexmedetomidine have been used primarily in a postoperative setting in adults. It has been shown that dexmedetomidine provides a level of sedation that allows for easy arousal when necessary and preserves cognitive integrity (Bloor et al., 1992; Ebert et al., 2000; Hall et al., 2000). The present study has shown that dexmedetomidine as part of a TIVA regimen allows for successful multimodality IONM.

Our results indicate that in the present study subject population, multimodality IONM is possible in the presence of dexmedetomidine. In this case series, we found no evidence of interference with SSEP or triggered EMG recordings. Our MEP recordings were adequate to monitor corticalspinal tract function in all cases within this series. Mahmoud et al. (2007) have recently reported a loss of MEPs associated with dexmedetomidine during pediatric spine surgery in two cases. Those investigators report they "often use dexmedetomidine as an adjunct to TIVA in procedures requiring intraoperative neurophysiologic monitoring (200 to 250 cases per year) because of its sedative, analgesic, and neuroprotective properties." This suggests that dexmedetomidine may interfere with MEPs during one in every several hundred cases. Although, subsequent to the present 18 case series, we have continued to perform similar procedures and have not yet observed such an association. The advantages of easier wake up and postoperative pain management reported by Mahmoud et al. is similar to our own observations and that of others (Martin et al., 2003; Venn and Grounds, 2001).

The amount of propofol required to achieve a sufficient depth of anesthesia was reduced when dexmedetomidine was added, providing the benefit of an adequate maintenance of anesthesia accompanied by a less stressful and more rapid emergence and extubation allowing for patient assessment soon after completion of surgery and return to supine positioning.

Although our preliminary results look promising, dexmedetomidine's compatibility with IONM is not fully understood. In addition to the findings of Mahmoud et al. suggesting interference with MEPs, it is known that dexmedetomidine reduces the seizure threshold in rats, thus requiring additional precaution when using transcranial electrical stimulation (Mirski et al., 1994). Initial reports of the effects of dexmedetomidine in humans has shown that it can decrease mean arterial pressure without decreasing central venous pressure or pulmonary artery pressure, as well as depression in heart rate, cardiac output, and stroke volume (Ebert et al., 2000; Housmans, 1990; Schmeling et al., 1991). Some studies have also suggested a need to avoid bolus administration as there may be a transient increase in blood pressure and a reflex decrease in heart rate (Bloor et al., 1992; Ebert et al., 2000).

CONCLUSION

Dexmedetomidine, when used as part of a TIVA regimen, offers the characteristics of both an anesthetic and analgesic, while at the same time our results suggest that the use of dexmedetomidine does not significantly hinder the recording of either sensory or motor evoked potentials. This allows for the collection of evoked potentials as required during pediatric spine surgery and provides the patient with a relatively easy awakening and recovery postoperatively. A prospective case-control study would be valuable to further define the role of dexmedetomidine during multimodality IONM.

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