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Dexmedetomidine versus fentanyl in intraoperative neuromuscular monitoring using propofol based total intravenous anesthesia regimen in kyphoscoliosis correction surgery

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Abstract

Background: Intraoperative neuromuscular monitoring (IONM) is used to reduce the risk of postoperative neurological deficit in patients undergoing kyphoscoliosis correction surgery. Somatosensory evoked potentials (SSEPs) are among the several techniques developed by neurophysiologists to increase the sensitivity of intraoperative monitoring. We administered total intravenous anesthesia (TIVA) to 20 patients undergoing kyphoscoliosis deformity correction surgeries: group A: propofol and dexmedetomidine and group B: propofol and fentanyl. The primary objective of our study was to compare the effect of dexmedetomidine and fentanyl on intraoperative hemodynamic parameters and their interference with SSEP's readings. The secondary objective was to assess the total intraoperative requirement of inhalational anesthetic agents, quality of surgical field, and the cost-effectiveness of either regimen.

Results: Intraoperative hemodynamic stability, analgesia, surgical field, and cost-effectiveness (due to reduced requirement of sevoflurane) were better with dexmedetomidine than fentanyl. SSEPs were successfully recorded with both the drugs while the requirement of inhalation anesthetic agents was significantly reduced in the dexmedetomidine group than in the fentanyl group. There were no injuries while recording SSEPs. The latency and amplitude of SSEPs were maintained throughout either group. No intraoperative awakening or awareness was noted (bispectral index was maintained in the range of 40 to 60). No postoperative neurological deficit was noted in any patient.

Conclusions: Both dexmedetomidine and fentanyl can be successfully used in propofol-based TIVA for SSEP monitoring in kyphoscoliosis correction surgeries, but the better analgesic profile, ease of maintaining stable hemodynamics with a significant reduction in inhalational agent requirement, and opioid-sparing effect by dexmedetomidine make it a more desirable agent to be used in propofol-based TIVA.

Keywords: Dexmedetomidine, Fentanyl, Kyphoscoliosis, Propofol somatosensory-evoked potential (SSEP), Total intravenous anesthesia (TIVA)

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Background

The integrity of the spinal cord is potentially at risk during kyphoscoliosis correction surgeries. Intraoperative neurophysiological monitoring has been the standard of care and is considered mandatory in order to reduce the risk of damage to the neural pathways during such procedures. Continuous use of evoked potentials in the intraoperative period helps to prevent and reduce the incidence of neural injury (Holdefer et al., 2015).

We used propofol-based total intravenous anesthesia (TIVA) with either dexmedetomidine or fentanyl as adjuvants to minimize the use of inhalational agents which are known to interfere with neurophysiological monitoring. Propofol in contrast to inhalation agents causes minimal interference with SSEP recording.

Fentanyl is a synthetic opioid of the phenylpiperidine family and is structurally related to meperidine (Lalonde, 2015). It is highly potent with a rapid onset and a shorter duration of action. The intraoperative requirement of propofol for hypnosis is also reduced by the use of fentanyl (Somma, 2015). Higher doses of fentanyl, used to administer anesthesia, are also proven effective and safe for use in kyphoscoliosis correction surgeries.

Dexmedetomidine is an alpha 2 agonist with beneficial actions such as sedation, analgesia, and anxiolysis exerting an opioid-sparing effect which in turn reduces the minimum alveolar concentration (MAC) of inhaled anesthetics (Somma, 2015). It is a potentially useful drug in the TIVA regimen, facilitating neurophysiological monitoring as it does not interfere with SSEP recordings. Dexmedetomidine as an adjuvant in propofol-based TIVA has been suggested to alleviate postoperative pain also.

Methods

Institutional Ethical Committee approval (Reg No. ECR/275/Inst/MH/2013/RR-19) and written consent from

parents of all enrolled patients were obtained. The sample size was decided based on the previous study conducted by David et al. (Anshel et al., 2008). The patients who were posted for kyphoscoliosis correction surgery over a period of 1 year were randomly allocated ($n = 20$) in two groups (Fig. 1; group A ($n = 10$)—propofol and dexmedetomidine; group B ($n = 10$)—propofol and fentanyl). Our study was of a smaller sample size as our institute is not a spine specialty center, and the number of pediatric patients coming for kyphoscoliosis correction surgery in which SSEPs can be utilized is limited. All our patients belonged to ASA physical status II/III and were in the age group of 12–18 years with Mallampati classification I/II.

Patients in the study were reviewed by the neurologist prior to surgery. A detailed neurological evaluation along with history and examination was noted, and the INM was planned. Any neurological impairment including sphincter disturbances was documented. Preoperative SSEP studies were undertaken, in all patients.

After arrival to the operation theater, the NBM status was confirmed, a wide bore IV access was secured while the blood and blood products were reserved. Emergency resuscitation drugs, equipment and defibrillator, and difficult airway trolley were kept ready; multipara monitors (pulse oximetry, non-invasive BP monitoring, ECG, temperature monitoring) were attached; and warming blankets were used throughout the surgery.

Anesthesia regimen was standardized in all patients after the attachment of multipara monitors. Patients were preoxygenated with 100% oxygen for 3 min and then premedicated with intravenous glycopyrolate 4 mcg/kg, ondansetron 0.1 mg/kg, midazolam 0.05 mg/kg, and fentanyl 2 mcg/kg. Intravenous preservative-free 2% lignocaine 1 mg/kg was given 90 s before laryngoscopy. Anesthesia was induced with intravenous propofol 2 mg/

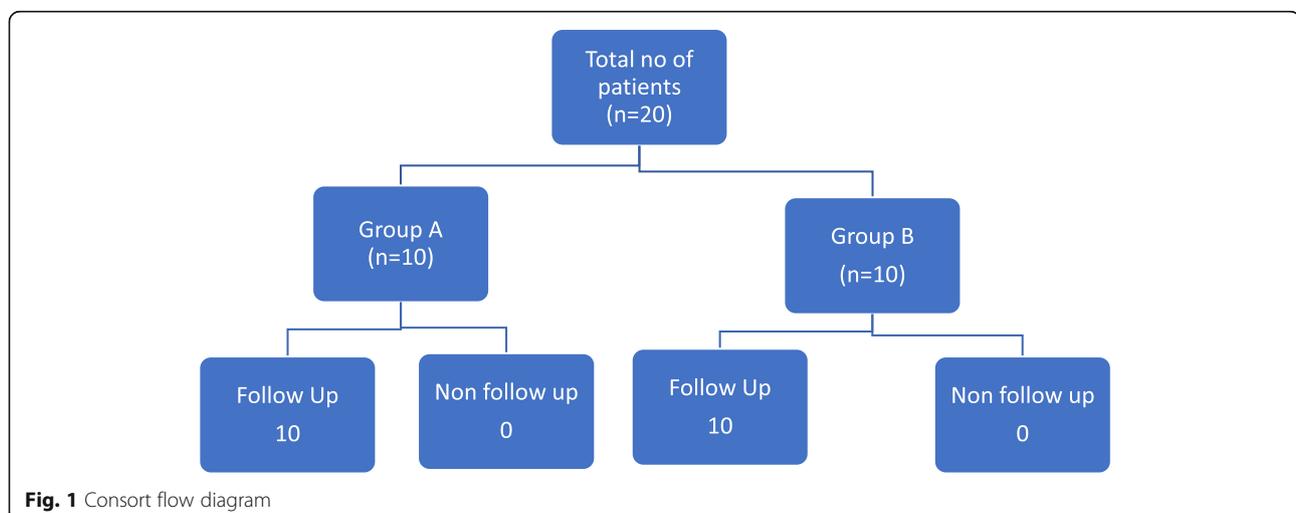


Fig. 1 Consort flow diagram

Table 1 Demographic distribution

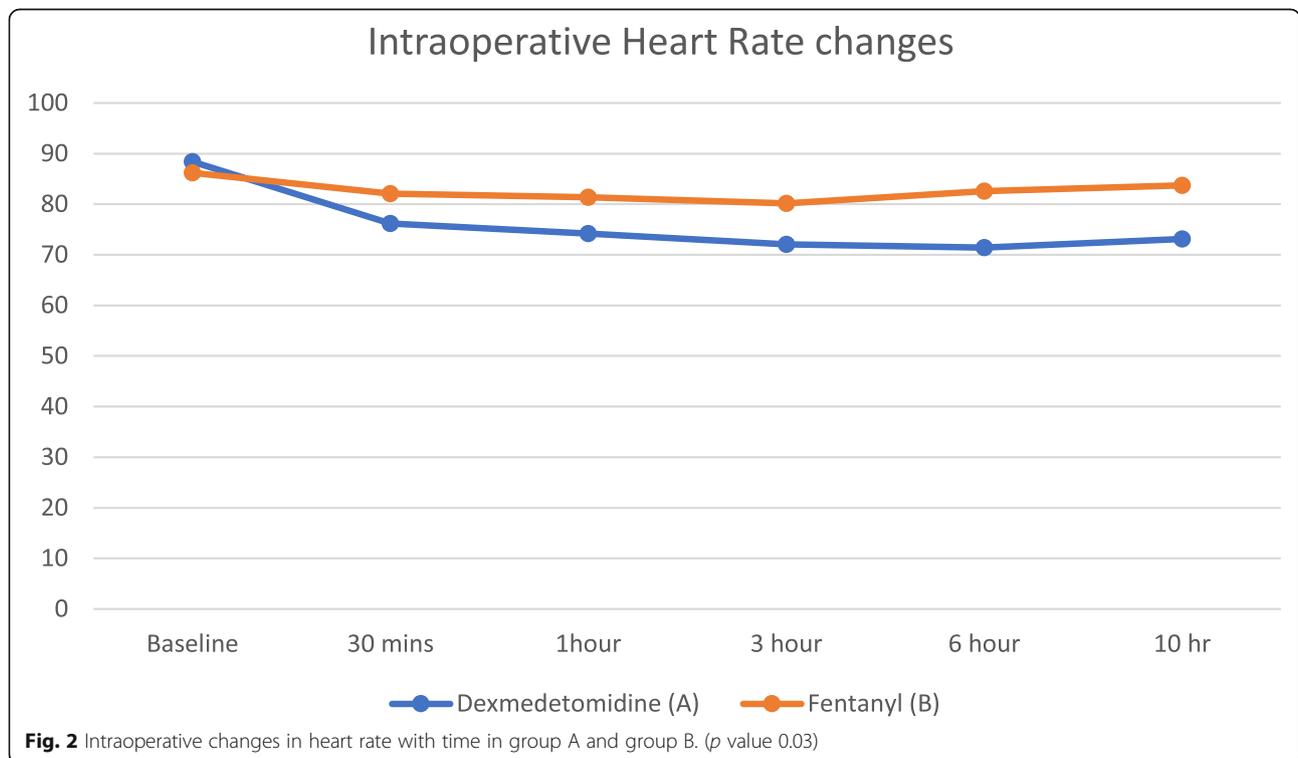
	Dexmedetomidine group	Fentanyl group	p value
Age (years)	13.7 ± 1.5	14.5 ± 2	0.24
Weight (kg)	39.4 ± 7.2	34.2 ± 8	0.19
Height (cm)	134 ± 10.2	138 ± 14.2	0.16
ASA 2	8	7	0.97
ASA 3	2	3	0.08
Average duration of surgery (h)	10 ± 2	11 ± 2	0.76
Cobb's angle (degree)	50 ± 10	48 ± 10	0.65

kg and after the loss of eyelash reflex and confirmation of ventilation, and intravenous succinylcholine 2 mg/kg was administered to facilitate intubation. Baseline SSEP was noted once the muscle paralysis by succinylcholine was weaned off. Intravenous paracetamol 15–20 mg/kg was used as an analgesic for all patients.

Anesthetic agents used for TIVA during surgery to facilitate SSEP recordings were intravenous propofol (5–10 mg/kg/h) (Dzikiti et al., 2010) and dexmedetomidine (0.5–0.7 mcg/kg/h) (Rozet et al., 2015) in group A and intravenous propofol (5–10 mg/kg/h) and fentanyl (0.01–0.03 mg/kg/h) (Dzikiti et al., 2010) in group B. No other neuromuscular blocking agent was used during surgery. We requested the neurophysiology team to notify whether there is a requirement to change the anesthetic regimen. Bispectral index was monitored and

maintained in the range of 40–60 by the anesthetist to aid in the evaluation of the depth of anesthesia. To maintain the bispectral index in the range of 40–60, a concentration of 0.2 to 0.4% sevoflurane was required in all patients. Hemodynamic parameters were recorded at regular intervals of 30 min throughout the surgery.

Surgical field quality was assessed by Former's score (1, mild bleeding without any surgical nuisance; 2, moderate bleeding, without any interference to surgery; 3, moderate bleeding that moderately compromised surgical field; 4, bleeding, heavy but controllable, that significantly interfered the surgery; and 5, massive uncontrollable bleeding) (Hrishi et al., 2017). A score of 1 or 2 was acceptable while a score of 3 or 4 was not acceptable for all practical purposes. Postoperatively, all the patients were electively ventilated for 24 h.



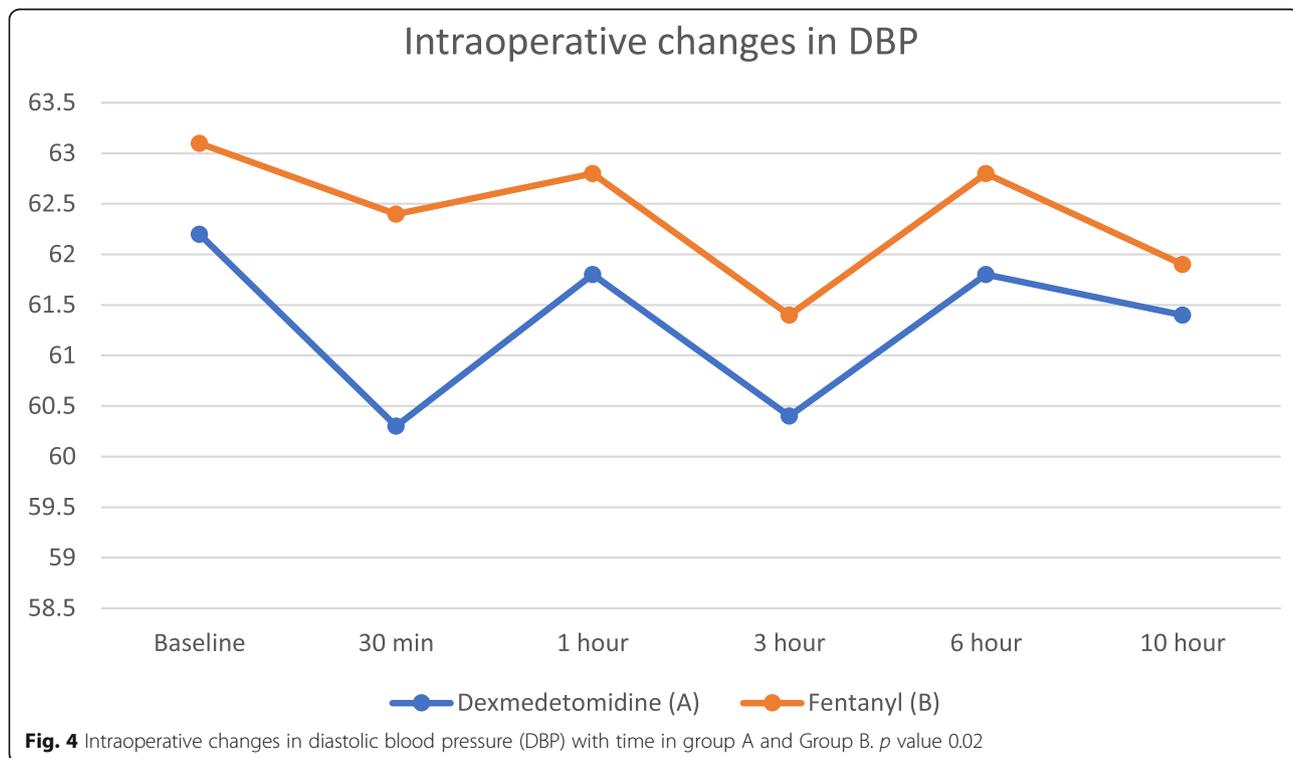
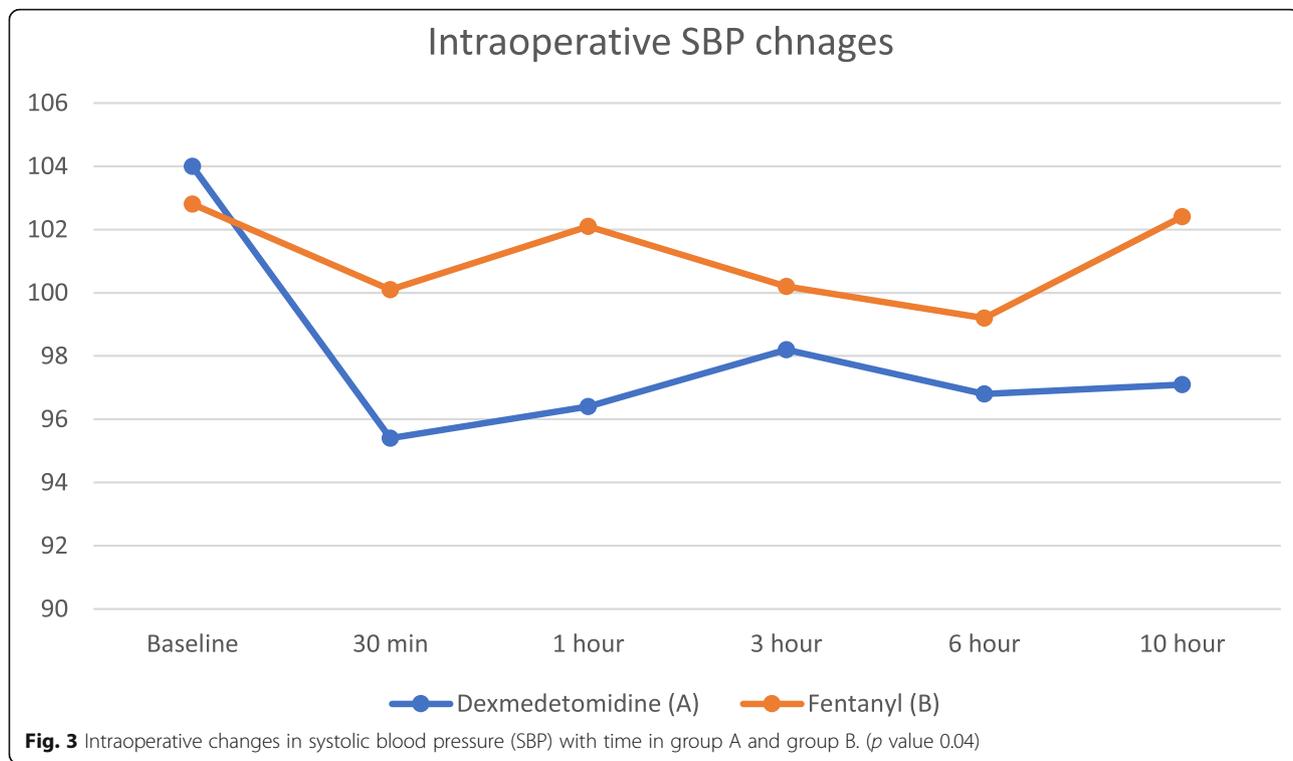


Table 2 Amplitude and latency of somatosensory-evoked potential at different time points (mean \pm SD) in groups A and B, p 0.37

Group	Measurements	T1	T2	T3	T4	T5
Group A (propofol + dexmedetomidine)	ULA (μ v)	2.0 \pm 1.1	2.1 \pm 1.1	2.1 \pm 1.0	1.8 \pm 1.0	1.9 \pm 1.2
	ULL (ms)	19.2 \pm 1.5	20.4 \pm 1.6	19.7 \pm 1.6	20.3 \pm 1.7	19.9 \pm 1.5
	LLA (μ v)	1.9 \pm 1.1	1.8 \pm 1.0	2.1 \pm 1.1	2.0 \pm 1.1	1.9 \pm 1.1
	LLL (ms)	19.4 \pm 1.8	19.2 \pm 1.7	20.4 \pm 1.5	19.4 \pm 1.6	20.3 \pm 1.6
Group B (propofol + fentanyl)	ULA (μ v)	1.6 \pm 1.1	1.7 \pm 1.0	1.8 \pm 1.1	2.0 \pm 1.0	1.8 \pm 1.1
	ULL (ms)	19.8 \pm 1.5	19.4 \pm 1.6	19.7 \pm 1.6	19.6 \pm 1.7	19.9 \pm 1.5
	LLA (μ v)	1.6 \pm 1.1	1.7 \pm 1.1	1.6 \pm 1.1	1.9 \pm 1.1	2.0 \pm 1.0
	LLL (ms)	19.0 \pm 1.7	19.2 \pm 1.7	19.8 \pm 1.5	19.4 \pm 1.6	19.3 \pm 1.6

ULA Upper limb amplitude, ULL Upper limb latency, LLA Lower limb amplitude, LLL Lower limb latency

Medtronic NIM-ECLIPSE machine was used for INM. SSEPs were obtained in terms of amplitude and latency. Baseline readings were taken after the effect of succinylcholine was weaned off. For the assessment of any neurological deficit, SSEPs were monitored intraoperatively at baseline T0, at regular intervals (T1, T2, T3, T4, and T5), and at the completion of surgery T6.

SSEPs were evoked with constant stimulation of 20–50 Ma at 3–6 Hz, with a duration of each stimulus of 300 μ s. Display duration was 100 ms for the lower limb and 50 ms for the upper limb SSEPs. The site of stimulation included the median nerve at the wrist, the common peroneal nerve at the knee, and the posterior tibial nerve at the ankle. Evoked responses were monitored over the mastoid, scalp, and popliteal fossa electrodes. The changes in the latency and amplitude of the P37–45 component of the posterior tibial nerve and the N20–P24 component of the median nerve were recorded.

The statistical analysis of the data obtained from the study was carried out by the Statistical Package for the Social Science software version 21 (SPSS). All quantitative data was analyzed for normal distribution and homogeneity of variance. Descriptive statistics of quantitative data were presented as mean and standard deviation. The continuous normally distributed data was analyzed using the unpaired t -test. p value $<$ 0.01 was significant for the results.

Results

The data of 20 patients was included in the analysis, and there was no significant difference in demographic characteristics between the two groups (Table 1).

In our study, we observed that intraoperative hemodynamic parameters such as HR (Fig. 2), SBP (Fig. 3), and DBP (Fig. 4) were more stable in the dexmedetomidine group than in the fentanyl group (p $<$ 0.05). So, we conclude that the analgesic efficacy of dexmedetomidine is much better than fentanyl.

The latency and amplitude of SSEPs were slightly reduced in the fentanyl group than in the dexmedetomidine group, which was not statistically significant (Table 2; p

0.37), thus promoting opioid-free TIVA. In both groups, no intraoperative awakening or awareness was noted, and also, no postoperative neurological deficit was noted.

The requirement of sevoflurane was less in group A than in group B. The mean concentration of sevoflurane required (which is known to interfere with INM) in group A was 0.2%, and in group B, it was 0.4%. The SSEP monitoring was less interfered in group A than in group B, but the interference was not clinically significant. The cost of sevoflurane required in group A was less than in group B (p $<$ 0.01; Table 3).

Surgical field condition was better in group A than in group B which infers that hypotensive anesthesia could be better maintained with dexmedetomidine than fentanyl, further aiding in reducing blood loss in such major surgeries (Fig. 5).

Discussion

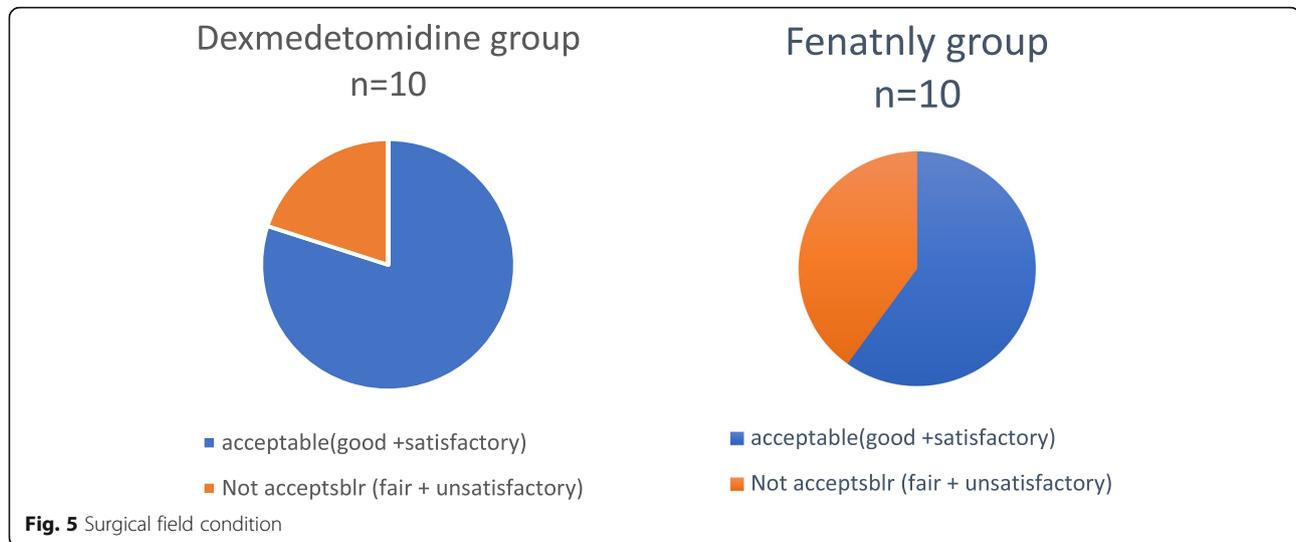
Recording of SSEPs is an effective and reliable method in patients for kyphoscoliosis correction surgery. This monitoring reduces the risk of postoperative neurological deficit and also the need for wake-up test. Incidence of neurological injury is increased many folds during kyphoscoliosis deformity correction surgery, which emphasizes the role of intraoperative neurophysiological monitoring.

INM is used to monitor neuronal integrity during many surgeries particularly kyphoscoliosis deformity correction procedures. An appropriate peripheral nerve was stimulated, and the responses were recorded at the somatosensory cortex; thus, a direct feedback is obtained testing the posterior columns of the spinal cord.

Table 3 Requirement of sevoflurane

	% concentration	Quantity (ml)	Cost (INR)	Egyptian pound	p value
Group A	0.2	24 ml	720	3355.2	$<$ 0.01
Group B	0.4	48 ml	1440	6710.4	

Fresh gas flow was 1.2 l/min in both groups. Indian rupee requirement (INR) of sevoflurane was more in group B than in group A (p value $<$ 0.01)



Changes such as a decrease in amplitude (> 50%) or an increase in latency (> 10%) indicate an interruption of the posterior column pathways. Though this sounds simple in theory, it requires particular skill and expertise as both amplitude and latency are affected by many anesthetic drugs. Several other factors that affect the SSEP are hypoxia, anemia, hypotension, hypothermia, nerve ischemia, and hypercapnia. SSEPs are recorded by electrical stimulation of the peripheral mixed nerves. Stimulation is provided most commonly with the surface electrodes (e.g., electrocardiogram electrodes) placed on the skin above the nerve or with the fine needle electrodes.

The amplitude is defined as the distance from the peak to the adjacent trough. The time from the stimulation to the peak in milliseconds is defined as the latency. Loss of or change in the waveform can indicate the need for modification of surgical strategy, patient positioning, or patients physiological management in order to prevent or minimize neurological injury. Specifically, a 50% reduction in amplitude or a 10% increase in latency of SSEPs, MEPs, and brain stem auditory evoked potentials (BAEPs) is considered to be of pathological significance (Sachdev et al., 2020). We used total intravenous anesthesia using propofol, dexmedetomidine, and fentanyl.

Sukhminder Jit Singh Bajwa found that propofol-ketamine and propofol-fentanyl can be used as an excellent combination in TIVA for both elective and day care surgery where minimal side effects and early recovery are desired (Singh Bajwa et al., 2010).

Several studies reveal that propofol affects SSEP to a lesser extent than other anesthetic agents like nitrous oxide, isoflurane, and sevoflurane making propofol a

recommended anesthetic agent of choice during INM. Inhalational agents affect the SSEPs more than the intravenous (IV) anesthetic agents (Lee et al., 2000).

Usha et al. studied the effect of nitrous oxide and isoflurane on SSEP monitoring and suggested that the morphology of SSEPs is maintained when nitrous oxide is avoided (Devadoss et al., 2010).

Parthiban et al. observed that propofol anesthesia lead to the generation of more successful baseline MEPs (74%) when compared with isoflurane anesthesia (50%) (Velayutham et al., 2019).

An important advantage of propofol in general anesthesia is its property of allowing rapid emergence. Hence, the idea was to use another adjuvant having sedative and analgesic properties with propofol that could reduce the requirement of propofol and also inhalational agents.

David et al. also concluded that dexmedetomidine when used as a TIVA regimen offers analgesia along with anesthetic properties without hindering the recording of either sensory-or motor-evoked potentials (Anshel et al., 2008).

We found that dexmedetomidine reduces the dose of propofol and deepens the plane of anesthesia without increasing the propofol requirement (Gehdoo et al., 2013).

Mahmoud et al. found that dexmedetomidine as an anesthetic adjuvant to propofol-based TIVA significantly attenuated the amplitude of transcranial electric MEPs (Mahmoud et al., 2010).

Hwang et al. also concluded that dexmedetomidine displayed superior efficacy in alleviating pain in the post-operative period after PLIF than remifentanyl as an adjuvant to propofol and our study also shows similar results (Hwang et al., 2015).

Rozet et al. observed that there was no difference in SEPPs and MEPs between the dexmedetomidine and placebo groups (Rozet et al., 2015).

Anshel et al. found that SSEPs were maintained within an acceptable range of amplitude 50% and latency 10% with dexmedetomidine; therefore, they concluded that anesthetic regimen did not significantly interfere with INM (Anshel et al., 2008). The results of our study were also concurrent with theirs.

Lee et al. concluded that the combination of propofol and fentanyl or ketamine used for TIVA is a very useful method in spine surgery under SSEP monitoring (Lee et al., 2000).

Conclusions

Dexmedetomidine and fentanyl both can be successfully used in propofol-based TIVA for SSEP monitoring in kyphoscoliosis correction surgeries, but the better analgesic profile and ease of maintaining hemodynamic stability with a significant reduction in inhalational agent requirement and opioid-sparing effect by dexmedetomidine make it the more desirable agent to be used in propofol-based TIVA.

Limitation

Limitation of our study was that of less sample size as our institute is not a spine care center. We suggest more studies with larger sample sizes to be conducted to support our results.

Abbreviations

INM: Intraoperative neurophysiological monitoring; SSEP: Somatosensory-evoked potential; TIVA: Total intravenous anesthesia; MAC: Minimum alveolar concentration; ASA: American Society of Anesthesiologist; NBM: Nil by mouth; ECG: Electrocardiography; BP: Blood pressure; HR: Heart rate; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; IV: Intravenous; MEP: Motor-evoked potential; IONM: Intraoperative neuromuscular monitoring

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Dr. Shardul Soman (spine surgeon)

Authors' contributions

NAP conceived and designed the analysis, performed the analysis, wrote the paper, approved the submitted version that involves the author's contribution, and agreed with the authors' own contribution. JVK conceived and designed the analysis, performed the analysis, approved the submitted version that involves the author's contribution, and agreed with the authors' own contribution. TLP collected the data, contributed to the data or analysis tools, performed the analysis, wrote the paper, approved the submitted version that involves the authors' contribution, and agreed with the authors' own contribution. UPB collected the data, contributed to the data or analysis tools, performed the analysis, wrote the paper, approved the submitted version that involves the authors' contribution, and agreed with the authors' own contribution. All authors have read and approved the final manuscript.

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Availability of data and materials

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Declarations

Ethics approval and consent to participate

This study was approved by the ethics committee of Smt. Kashibai Navale Medical College and General Hospital [Institutional Ethics Committee] with approval number, registration No. ECR/275/Inst/MH/2013/RR-19. Written consent from parents of all enrolled patients was obtained.

Consent for publication

Consent for publication was obtained from all the parents on the institutional consent form.

Competing interests

The authors declare that they have no competing interests.

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