



ORIGINAL RESEARCH PAPER

Anesthesiology

COMPARISON OF TWO COMBINATIONS OF ANAESTHETIC AGENTS WITH AND WITHOUT KETAMINE FOR MOTOR EVOKED POTENTIAL DURING SPINE SURGERIES
KEY WORDS:

Dexmedetomidine, fentanyl, ketamine, motor-evoked potential, propofol

Dr Shuchin Mangla

Post graduate Deptt of Anaesthesiology and Critical care National Institute of Medical Science Jaipur.

Dr Zara Wani*

Post graduate Deptt of Anaesthesiology and Critical care National Institute of Medical Science Jaipur. *Corresponding Author

Dr Meenaxi Sharma

Head of Department Deptt of Anaesthesiology and Critical care National Institute of Medical Science Jaipur.

ABSTRACT

Background: Anesthetic agents cause a dose-dependent effect on motor-evoked potentials (MEPs). We conducted a study to find whether addition of ketamine to the combination of propofol–fentanyl–dexmedetomidine has an effect on MEP monitoring and hemodynamic parameters in patients undergoing spine surgeries.

Materials and Methods: Sixty patients of American Society of Anesthesiologists Grade I–III undergoing spine surgery in general anesthesia were divided into two groups, P and K randomly. Written informed consent was obtained and all the patients were blinded to the interventions. After induction, anesthesia was maintained in Group P using propofol + dexmedetomidine + fentanyl infusion, whereas in Group K, ketamine infusion was added to the above combination. After taking baseline reading of MEP, heart rate (HR), and mean arterial pressure (MAP), mean of all the other readings was calculated and percentage fall in all factors was calculated. More than 80% fall in mean MEP and more than 20% fall in mean HR and MAP were considered significant.

Statistical Analysis: Analysis was done by SPSS 20.0 statistical system. Continuous normally distributed data were analyzed using Student's independent t-test.

Results: In Group P, percentage fall in MEP on the right side was 46.39 ± 24.19 , whereas in Group K, it was 37.98 ± 26.17 . Similar results were obtained on the left side. In Group P, percentage fall in HR in Group P was 17.68 ± 7.0 , on the other hand, it was 14.02 ± 7.7 in Group K. Finally, percentage fall in MAP was found to be 14.61 ± 6.37 in Group P, whereas in Group K, it was 9.51 ± 5.02 . On intergroup comparison of all factors, we found that difference in percentage fall in MEP and HR was insignificant whereas it was significant in case of MAP.

Conclusion: It was found that addition of ketamine in Group K led to better hemodynamics in patients undergoing spine surgery without affecting the MEP significantly.

Introduction:

The use of intraoperative neurophysiological monitoring (INM) for spinal procedures provides a challenge to anesthesiologists. Motor-evoked potential (MEP) monitoring is being widely used intraoperatively. The roles of anesthesiologists in INM include understanding the appropriate anesthetic techniques and applying the knowledge of medicine, surgery, physiology, and pharmacology to get the best possible outcome.[1]

Van Der Walt et al. described anesthetic implications for INM. Numerous investigators have attempted to find the most appropriate anesthetic technique with minimal effect on evoked potentials. To the best of our knowledge, there is no single drug or combination of drugs considered as ideal with insignificant effect on INM.[2]

Thus, it is worthwhile to study and compare single drug or combination of anesthetic agents that has minimal effect on MEP monitoring and also maintain hemodynamic stability to avoid the complications such as neurological deficits, for which patients and health-care providers fear the most.

Material and Method:

A double-blind, prospective randomized controlled trial was performed after obtaining approval from the institute's Ethics Committee. Sixty patients were randomly divided into two groups. Patients included in the study were of either sex, scheduled for elective spine surgical procedure, requiring oro-tracheal intubation, with the American Spinal Injury Association Score-D and American Society of Anesthesiologists (ASA) Grade I–III. Patients excluded from the study were those with contraindications for MEP monitoring such as epilepsy, cortical lesion, raised intracranial tension, cardiac diseases, intracranial electrodes, vascular clips/shunts, and with ASA Grade IV or more.

The patients were randomly allocated to one of the two groups. In

Group P, patients received oxygen (O₂), nitrous oxide (N₂O), propofol, dexmedetomidine, and fentanyl infusions. In Group K, in addition to the above-mentioned drugs in Group P, ketamine was added to propofol infusion in the ratio of 1:5 (in 60 ml syringe, 500 mg [50 ml] propofol and 100 mg [2 ml] ketamine were added, a total of 52 ml, to prepare a concentration of 9.6:1.9, i.e., 1:5). Written informed consent was obtained from all the patients. Furthermore, all the patients were blinded to the interventions. On the day of surgery, standard monitors including electrocardiography, pulse oximetry, and noninvasive blood pressure were attached and a wide-bore intravenous cannula was secured. Similar anesthesia regimen was used in both groups. Injection glycopyrrolate 0.005 mg/kg + injection fentanyl 1–2 µg/kg were administered for premedication. Induction was performed with injection propofol 1.5–2 mg/kg along with N₂O 50% + O₂ 50%. Intubation was done after giving injection rocuronium 0.6 mg/kg or alternatively, awake intubation with fiber-optic bronchoscope was done as required in the patient. Correct placement of the tube was confirmed with capnograph and bilaterally equal breath sounds. A soft bite block of appropriate size was placed and fixed to avoid tongue bite. A temperature probe was inserted in all the patients nasally. All electrodes for MEP and bispectral index (BIS) monitoring were placed. All anesthetics were discontinued for baseline readings.

With the help of ulnar nerve stimulation, wearing off of effect of muscle relaxant was confirmed and baseline transcranial MEPs were recorded on the left and right sides. The best baseline MEP recordings of the muscle group likely to be least affected by surgical procedure were chosen for monitoring. After satisfactory MEP (response), anesthetic agents according to our study were started for maintenance. Baseline readings of heart rate (HR) and mean arterial pressure (MAP) were also recorded.

After recording baseline MEP bilaterally, infusions of drugs were started at lower side of the dose range in both the groups. In Group P, injection propofol infusion at 50–150 µg/kg/min + fentanyl

infusion at 1–3 µg/kg/h + dexmedetomidine 0.5–0.8 µg/kg were injected over 30 min and pumped at 0.1–1.0 µg/kg/h with O₂ (50%) + N₂O (50%).

In Group K, anesthesia was maintained using injection propofol infusion at 50–150 µg/kg/min + fentanyl infusion at 1–3 µg/kg/h + dexmedetomidine 0.5–0.8 µg/kg injected over 30 min and pumped at 0.1–1.0 µg/kg/h + ketamine 10–30 µg/kg/min + O₂ (50%) + N₂O (50%).

Additional drugs used in both the groups were same and no muscle relaxant was used for maintenance in both the groups. All the patients were subjected to controlled ventilation. During surgery, the patient's end-tidal carbon dioxide was maintained between 35 and 45 mmHg and the BIS was maintained between 50 and 60. MEP monitoring was done using the Medtronic® NIM Eclipse™ system 68 L2128 neurophysiological detector. The stimulus intensity was kept between 200 and 350 V. The MEPs were recorded simultaneously from muscles bilaterally and five readings of the left and right sides were taken at the interval of 30 min simultaneously, keeping rest of the factors constant (BIS, voltage, and temperature).

Mean of all the five readings was calculated in both the study groups separately for the left and right sides. The same procedure was followed for hemodynamic parameters. Mean of HR and MAP of all the five readings were calculated. Subsequently, the percentage fall in MEP, HR, and MAP was calculated by comparing mean value with baseline values for further comparison in both groups. The significant result was defined as bilateral MEP loss or ≥80% fall in transcranial MEP.^[3]

For hemodynamic changes ≥20%, fall from the baseline values was considered the positive result for both the groups.

Statistical analysis

All the data were filled in a printed format for further analysis by SPSS 20.0 statistical system (Armonk, NY: IBM corp). Descriptive statistics of quantitative data were presented as mean and standard deviation. Continuous normally distributed data were analyzed using Student's independent t-test. For all comparisons, a probability of 5% was considered significant.

Results:

Sixty patients were included and the following observations were made. Scoliosis correction, posterior stabilization, decompression surgery in spinal cord injuries or tumor excision, etc., were the most common surgeries included. On an average, time taken by these surgeries was around 2 to 4 h.

In Group K, only two patients had more than 80% fall in MEP that too only on the right side, whereas in Group P, two patients had bilateral fall in MEP more than 80% and two patients had fall in MEP on the right side only. On intergroup comparison of the mean of percentage fall in MEP from baseline in both the groups, it was found to be insignificant (left side P= 0.908 and right side P= 0.201).

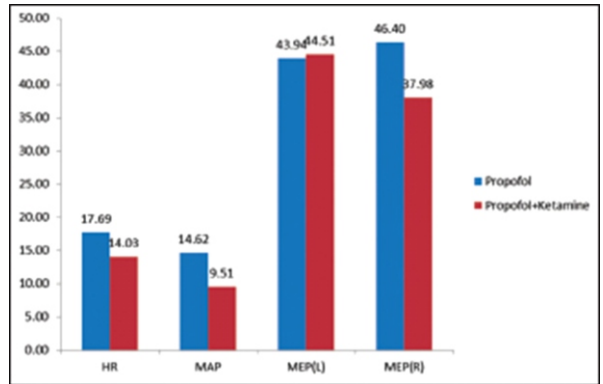
In Group P, eight patients had more than 20% fall in HR and seven patients had more than 20% fall in MAP from the baseline, whereas in Group K, four patients had more than 20% fall in HR and none of the patients had more than 20% fall in MAP. On intergroup comparison, the difference in mean of HR was found to be insignificant, whereas the difference in MAP in both the groups was statistically significant [Table 1] and Graph 1].

Table 1: Parameters with mean and standard deviation :

	GROUP	MEAN +- SD	P value
Percentage fall in Heart rate	PROPOFOL	17.68+- 7.00	0.059
	PROPOFOL + KETAMINE	14.02+- 7.70	
Percentage fall in MAP	PROPOFOL	14.61+- 6.37	0.001
	PROPOFOL + KETAMINE	9.51+- 5.02	

Percentage fall in MEP (LEFT)	PROPOFOL	43.93+- 23.43	0.918
	PROPOFOL + KETAMINE	44.51+- 19.44	
Percentage fall in MEP (RIGHT)	PROPOFOL	46.39+- 24.19	0.201
	PROPOFOL + KETAMINE	37.98+- 26.17	

P<0.05 is significant SD : Standard Deviation MAP : Mean Arterial Pressure, MEP : Motor Evoked Potential, HR : Heart Rate



Graph 1: Comparison of motor-evoked potential, mean arterial pressure, and heart rate in both the groups

Discussion :

In this study, we aimed to find the effect of ketamine and propofol on MEP so that the most dangerous complication of spine surgery can be avoided. We have selected standard dose of propofol for induction and maintenance in both the groups and ketamine was added in another group. Throughout the study, BIS monitoring was done and no gross changes were observed in BIS readings or hemodynamic parameters.

Tobias et al. in their study concluded that dexmedetomidine can be used as a component of total intravenous anesthesia (TIVA) during posterior spinal fusion without affecting neurophysiologic monitoring. We used dexmedetomidine in lower doses as infusion in both the groups as it has multiple actions.[4]

Penney et al. in their case report stated that dexmedetomidine and ketamine infusions as a combination can be used as an alternative to propofol-based TIVA during scoliosis repair surgery with intraoperative somatosensory-evoked potential and MEP monitoring. They also used 60% N₂O and 40% O₂ in their study which provided satisfactory conditions for the intraoperative neurophysiologic monitoring. In this study, we added ketamine to the combination of propofol and dexmedetomidine along with 50% N₂O and O₂ 50%. We also observed similar outcomes.[5]

Di Lazzaro et al. in their study demonstrated that low doses of ketamine can increase motor cortex excitability to transcranial magnetic stimulation by modulating the N-methyl-D-aspartate receptor transmission. Keeping in view these factors, we decided to add ketamine to our anesthesia regimen.[6]

Kawaguchi et al. in their study of 58 patients concluded that, if a train of pulses were used for transcranial stimulation, low-dose propofol can be effectively used as a supplement to ketamine-based anesthesia during intraoperative monitoring of myogenic MEPs. And also, they concluded that addition of propofol significantly reduced the ketamine-induced psychedelic effects. In this study, we also used very low dose of ketamine infusion in addition to propofol without affecting MEP monitoring.[7]

Frei et al. did a study on 108 children <18 years of age. MEPs were elicited by transcranial electrical stimulation and supplemented by temporal and spatial facilitation. The standard anesthesia regimen consisted of propofol, N₂O, and remifentanyl. Propofol was replaced with ketamine if no reliable MEPs could be recorded. The reliability of MEPs was improved by the use of a ketamine-based anesthesia. We thought it is worthwhile to add ketamine in our

study to anesthesia regimen so that MEP monitoring can be improved and complications can be avoided.[8]

Moustafa et al. did a study on 32 children and demonstrated that, during posterior spinal fusion surgery, the combination of ketamine and remifentanyl infusions in addition to propofol infusion as TIVA may provide more hemodynamic stability, satisfactory surgical requirements with reliable electrophysiological monitoring, and adequate postoperative pain relief. As remifentanyl is not available in our setup, we used fentanyl infusion along with other drugs and had similar results.[9]

Deepika et al. did a study on sixty patients using two different combinations of drugs and concluded that dexmedetomidine is a better adjunct to general anesthesia as compared to midazolam, when used as an infusion in patients undergoing spinal surgery, as it produces minimum effect on MEP, though it has more effect on HR and MAP, which itself may be beneficial in spinal surgery. In our study, we added ketamine to the above combination and found that effect on hemodynamic parameters was better without affecting MEP.[10]

Bruno bissonnette et al. emphasized on maintaining MAP for MEP monitoring. Decrease in MAP below autoregulatory pressure resulted in detrimental fall in MEP. MEPs are more sensitive than sensory-evoked potentials. In our study, it was observed that addition of ketamine in Group K led to less fall in MAP without affecting MEP significantly.[11]

Conclusion :

From this study, we conclude that ketamine infusion can be used along with propofol–fentanyl–dexmedetomidine combination without affecting MEP monitoring and HR and with significantly less fall in MAP which is an independent factor affecting MEP monitoring.

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