ORIGINAL ARTICLE

A comparative evaluation of dexmedetomidine with midazolam as an adjuvant to propofol anesthesia for spinal surgical procedures under motor evoked potential monitoring

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ABSTRACT

Background: Intraoperative neurophysiologic monitoring helps to prevent neurologic morbidity from surgical manipulations. Anesthetic agents have a dose dependent adverse effect on the ability to record evoked potential responses. Evoked potentials are highly sensitive to fluctuations in physiological parameters. The main objective of the study was to compare midazolam and dexmedetomidine in producing minimum effect on motor evoked potential amplitude keeping consistent depth of anesthesia and to evaluate hemodynamic stability during the surgery.

Methodology: It was a double-blind, randomized control trial. A total of 60 patients, between 10-60 years of age, with ASA class I - II, undergoing spinal surgery under general anesthesia were enrolled and randomly divided into two groups; Group M received midazolam and group D received dexmedetomidine infusion in addition to a standardized anesthesia technique. Motor evoked potential amplitude and heart rate and mean arterial pressure were measured at different intervals in two groups and the results were compared by Chi-square test or Fischer exact test. The significant result was defined as bilateral MEP loss or ≥ 80 % fall in transcranial MEP.[1] For hemodynamic changes ≥ 20% fall from the baseline values was considered as the positive result for both the groups.

Results: In Group M 10 (33.3%) patients had fall in motor evoked potential as compred to 2 (6.7%) in Group D (p = 0.010). This difference was found to be statistically significant. Group D showed higher number of patients [7 (23.3%)] with ≥ 20% fall in heart rate as compared to 4 (13.3%) patients in Group M, but this difference was statistically not significant. Fall in mean arterial pressure (>20%) was noted in 9 (30.0%) vs. 2 (6.7%) patients in Group D and M respectively (p = 0.020). The difference was found to be statistically significant.

Conclusion: The use of dexmedetomidine is better in terms of minimum effect on motor evoked potentials, but is associated with more adverse effect on hemodynamic parameters as compared to midazolam, when used as an infusion in patients undergoing spinal surgery.

Key words: Motor evoked potential; Dexmedetomidine; Midazolam; Mean arterial pressure; Heart rate

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INTRODUCTION

Intraoperative neurophysiologic monitoring (INM) is becoming very popular, and in particular motor evoked potential (MEP) monitoring is being more commonly used in neurosurgery. Anesthetic agents have a dose dependent adverse effect on the ability to record evoked potential responses.[2] Various authors have tested many anesthetic techniques or combinations of techniques with predicted minimal effect on INM. Tod B. Sloan et al[3] described the effects of various anesthetic agents on motor evoked potentials. Van Der Walt JJN et al[4] described that all inhalational anesthetic agents decreased

MEP amplitude and increased latency. Bithal PK et al[5] in their article described that nitrous oxide (60–70 %) decreases the cortical amplitude by about 50 %, but does not alter the cortical latency and subcortical waveform. Barbiturates have been shown to suppress myogenic MEPs in a dose dependent manner, whereas etomidate increases amplitude of cortical sensory components following injection, with no changes in peripheral and sensory responses.[6-7] Midazolam has not suppressed myogenic MEP even at plasma concentrations sufficient for anesthesia.[8] Other authors showed that midazolam and other benzodiazepines moderately suppress the intraoperative EP, and dexmedetomidine has also been used as a component of TIVA during posterior spinal fusion without affecting neurophysiologic monitoring.[9-11] Evoked potentials are highly sensitive to fluctuations in physiological parameters such as peripheral and core body temperature, arterial blood pressure, hematocrit etc. Keeping in view all the above factors we planned this study to compare two combinations of anesthetic agents in producing minimum effect on MEP amplitude and on hemodynamic stability during the surgery.

METHODOLOGY

A double-blind, prospective randomized control trial was performed after approval by the institute ethics committee. All patients were administered general anesthesia with intubation. A total of 60 patients between 10-60 years of age, with ASA class I - II, undergoing spinal surgery under general anesthesia were enrolled. Patients, younger than 10 or older than 60 years, ASA grade III & IV, and those with contraindications for MEP monitoring, e.g. epilepsy, cortical lesion, raised intracranial tension, patients with intracardiac devices like pacemakers, vascular clips or shunts, neuromuscular disease were excluded from the study. Study patients were randomly divided into two groups. Patients of Group M received propofol, fentanyl and midazolam infusion, and Group D received propofol, fentanyl and dexmedetomidine infusion. Written informed consent was obtained from all of the patients.

Induction of anesthesia was performed by propofol 1.5-2 mg/kg IV and nitrous oxide 50% + oxygen 50%. Muscle relaxation was achieved by inj. rocuronium 0.6 mg/kg and intubation was done. Electrodes for INM and BIS monitoring were placed. All anesthetics were discontinued for baseline readings.

Wearing off of the effect of rocuronium bromide was confirmed with the help of ulnar nerve stimulation. Baseline transcranial motor evoked potentials were recorded. The best baseline MEP recordings or the MEP reading of the muscle group likely to be least affected by surgical procedure was chosen for monitoring. Baseline heart rate and mean arterial pressure were recorded. After satisfactory MEP (response), anesthetic agents (according to the study groups) were started for maintenance of anesthesia and patient positioning was made as per our protocol.

Anesthesia was maintained in Group M using injection propofol infusion at 50 -150 µg/kg/min, fentanyl infusion at 1-3 µg/kg/h , midazolam 0.05 - 0.1 mg/kg given as loading dose and thereafter infused at 0.5 – 1 µg/kg/min with 50% oxygen and nitrous oxide.

In Group D, anesthesia was maintained using dexmedetomidine 0.5 - 0.8 µg/kg injected over 30 minutes and infused at 0.1 - 1.0 µg/kg/h with 50% oxygen and nitrous oxide.

Additional drugs administered in Group D were same as in Group M and muscle relaxant was not administered in either of the groups. All of the patients were subjected to controlled ventilation at frequency of 14 - 16/min. During surgery, the patient's $EtCO_2$ was maintained between 35 and 45 mmHg and the bispectral index (BIS) was maintained between 50 and 60.

MEP monitoring was done using the Medtronic® NIM – Eclipse™ system 68L2128 neuro-physiological detector. The stimulus intensity was kept between 200 and 350 V. The MEPs were recorded simultaneously from muscles bilaterally. The MEP waveforms and amplitudes were analyzed on left and right side to determine the result. After recording baseline MEP bilaterally and starting infusions of drugs at lower side of the dose range five readings of left and right side were taken at the interval of 30 min simultaneously, keeping rest of the factors constant (BIS, voltage, temperature). Mean of all five readings was calculated in both of the study groups separately for left and right side. The same procedure was followed for hemodynamic parameters. Mean of heart rate and mean arterial pressure of all five readings were calculated. After that percentage fall in MEP, percentage fall in heart rate and percentage fall in mean arterial blood pressure were calculated for further comparison in both groups. The significant result was defined as bilateral MEP loss or ≥ 80 % fall in transcranial MEP. For hemodynamic changes ≥ 20% fall from baseline value was considered as the positive result for both the groups. For the patients that exhibited a significant result, surgery was reviewed to determine whether or not an intraoperative intervention had occurred; moreover, infusions were terminated. When a waveform could not be continually recovered, a wake-up test was conducted.

All the data was filled in a printed format for further analysis by SPSS 17.0 statistical system. Descriptive statistics of quantitative data was presented as mean and standard deviation. Continuous normally distributed data was analyzed using student's 't' test, both paired and unpaired. Proportions were compared by Chi-square test or Fischer exact test. For all comparisons a probability of 5% was considered as significant.

RESULTS

60 patients were included and following observations were made. Surgeries in most of the cases included scoliosis correction, posterior stabilization and decompression surgery in spinal cord injuries or tumor excision etc. Time taken in these surgeries was around two to four hours. The demographic data are presented in Table 1.

Table 1: Demographic data of the patients

Parameters	Group D	Group M
Mean age (years)	41.40 ± 20.08	48.50 ±19.39
≤ 50 years [n (%)]	19 (63.3%)	14 (46.7)
> 50 years [n (%)]	11 (36.7)	16 (53.3)
M:F ratio	17:13	18:12

In Group D, mean of all baseline MEP recordings of 30 patients was 2286.40 ± 864.12 and mean of all mean MEP recordings of 30 patients was 1835.77 ± 925.85 showing change of 450.63 ± 454.52 and percent change of 21.30 ± 19.08. So on doing intra group comparison this difference was highly significant ($p < 0.001$).

In Group M, mean of all baseline MEP recordings of 30 patients was 2544.80 ± 746.68 and mean of all mean MEP recordings of 30 patients was 1501.77 ± 1017.48 showing change of 1043.03 ± 763.70 and percent change of 43.56 ± 29.34. This difference was highly significant ($p < 0.001$).

On doing intergroup comparison between Group D and Group M, the difference of mean of all baseline MEP recordings between both groups was not significant ($p = 0.220$). Similar result was obtained for mean of all mean MEP recordings ($p = 0.189$), but percentage change between both groups was significant.($p = 0.001$). Similar results were obtained for the right side for corresponding patients. Group M showed more number of patients with fall (> 80%) in MEP of right side and this difference was found to be statistically significant ($p = 0.010$).

In Group D, mean of all baseline heart rate recordings of 30 patients was 100.80 ± 13.79 and mean of all mean heart rate recordings of 30 patients was 86.93 ± 20.01 showing change of 13.87 ± 10.65 and percent change of 14.42 ± 11.98. So on doing intra group comparison this difference was highly significant ($p < 0.001$).

In Group M, mean of all baseline heart rate recordings of 30 patients was 90.83 ± 12.03 and mean of all mean heart rate recordings of 30 patients was 81.27 ± 13.08 showing change of 9.57 ± 8.11 and percent change of 10.45±8.55. So on doing intra group comparison this difference was highly significant ($p < 0.001$). On doing intergroup comparison between Group D and Group M, the difference of mean of all baseline heart rate recordings between both groups was significant ($p = 0.004$), but the difference of mean of all mean heart rate recordings between both groups was not significant ($p = 0.199$) and percentage change between both groups was also not significant ($p = 0.145$).

In Group D, mean of all baseline MAP recordings of 30 patients was 94.93 ± 7.61 and mean of all mean MAP recordings of 30 patients was 80.53 ± 11.97 showing change of 14.40 ± 10.27 and percent change of 15.14 ± 10.62. So on doing intra group comparison this difference was highly significant ($p < 0.001$). In group M, mean of all baseline MAP recordings of 30 patients was 96.27 ± 5.82 and mean of all mean MAP recordings of 30 patients was 88.10 ± 9.43 showing change of 8.17 ± 7.62 and percent change of 8.49 ± 7.83. So on doing intra group comparison this difference was highly significant ($p < 0.001$). On doing intergroup comparison between Group D and Group M, the difference of mean of all baseline MAP recordings between both groups was not significant ($p = 0.449$), but the difference of mean of all mean MAP recordings between both groups was significant ($p = 0.009$). The percentage change between both groups was also significant ($p = 0.008$).

DISCUSSION

In our study we aimed to find out which drug out of midazolam or dexmedetomidine can maintain constant level of anesthesia and produce minimum effects on

Table 2: Comparison of both groups based on percentage fall in motor evoked potentials, heart rate, and mean arterial pressure

Parameters	Group D	Group M	Total	P value
Fall in motor evoked potentials (Left Side) (≥80%)	2 (6.7%)	10 (33.3%)	12 (20.0%)	p = 0.010*
Fall in heart rate (≥20%)	7 (23.3%)	4 (13.3%)	11 (18.3%)	p = 0.317**
Fall in mean arterial pressure (≥20%)	9 (30.0%)	2 (6.7%)	11 (18.3%)	p = 0.020*

*Significant; **Not significant

Transcranial Motor Evoked Potentials measured during Spine surgeries, besides maintaining hemodynamic stability.

MEP monitoring is widely used during neurosurgery, spine surgery, and thoraco-abdominal aorta replacement. Heike Gries studied on twenty patients in 2011, in the age group of 2 to 12 years and concluded that significant improvement of MEP and somatosensory evoked potential (SSEP) readings during neurosurgery occurs for pediatric patients while using dexmedetomidine as an adjunct to general anesthesia and therefore, improvement in clinical decision making.[2] Suren Soghomonyan et al[9] stated that midazolam and other benzodiazepines moderately suppress the intraoperative evoked potential and their use, whenever possible, should be avoided. Benzodiazepine induced evoked potential suppression was less pronounced compared to inhalational agents.[12]

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.[11] Sheng Lin et al did a study on effect of dexmedetomidine – etomidate – fentanyl combined anesthesia on somatosensory and motor evoked potentials in patients undergoing spinal surgery. They concluded that TIVA using combined agents as mentioned above may be safely administered in spine surgery as well as SSEP and MEP monitoring.[13]

Bithal PK et al in there article described that nitrous oxide (60 – 70 %) decreases the cortical amplitude by about 50 % , but does not alter the cortical latency and subcortical waveform.[5]

In a study, Suren Sohomogayan concluded that balanced general anesthesia with low doses of inhalational agents combined with low-dose constant infusions of remifentanil (0.05 μg/kg/min), propofol (50 μg/kg/min), or dexmedetomidine (0.003–0.005 μg/kg/min) may be recommended when EP monitoring is anticipated. Such an approach will provide stable anesthesia and reduce the incidence of adverse events encountered occasionally during total intravenous anesthesia such as patient movement and awareness. Midazolam and other benzodiazepines moderately suppress the intraoperative EP and their use whenever possible should be avoided.[9]

Similar results were shown in our study. The group using midazolam showed more number of patients with percentage fall in motor evoked potential on both sides while the group using dexmedetomidine produced minimum effect on MEP keeping consistent depth of anesthesia.

Bruno Bissonnette et al emphasized on maintaining mean arterial pressure for MEP monitoring. Decrease in MAP below autoregulatory pressure resulted in detrimental fall in MEP.[15]

In our study dexmedetomidine group showed more number of patients with fall (>20%) in MAP as compared to midazolam group and this difference was found to be statistically significant. Jyrson Guilherme Klamt did a study in 2010 in 32 children, comparing the hemodynamic effects of the combination of dexmedetomidine-fentanyl versus midazolam-fentanyl in children undergoing cardiac surgery with cardiopulmonary bypass and concluded that in both groups, systolic blood pressure and heart rate reduced significantly after one hour of anesthetic infusion, but the increase in systolic and diastolic pressure and heart rate to skin incision were significantly lower in the dexmedetomidine group. A significantly lower number of patients demanded supplementation with isoflurane in the dexmedetomidine group. After surgery, patients in both groups had similar hemodynamic responses.[16]

Another study compared the effect of dexmedetomidine and propofol on blood pressure and found that the incidence of hypotension in propofol was significantly higher than dexmedetomidine group. From subgroup analysis, in the age group ≤ 60 years, the incidence of hypotension also showed similar result. But the patients in the age group > 60 years, dexmedetomidine group showed greater tendency to develop hypotension and the incidence of hypotension in both groups was not significantly different.[17] This is well correlated with our study. The group using dexmedetomidine showed more number of patients with fall (>20%) in MAP and this difference was found to be statistically significant.

CONCLUSION

Based on the results of our study, we conclude 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 heart rate and mean arterial pressure, which itself may be beneficial in spinal surgery.

Conflict of interest: Nil declared by the authors

Authors' contribution: All the authors took part in the conduct of study. Literature search. Data analysis and manuscript preparation.

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