

Effects of avoiding neuromuscular blocking agents during maintenance of anaesthesia on recovery characteristics in patients undergoing craniotomy for supratentorial lesions: A randomised controlled study

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ABSTRACT

Background and Aims: Neuromuscular blocking agents have been one of the cornerstones of anaesthesia. With the advent of newer surgical, anaesthetic and neurological monitoring techniques, their utility in neuroanaesthesia practice seems dispensable. The aim of this prospective, comparative, randomised study was to determine whether neuromuscular blocking agents are required in patients undergoing supratentorial surgery when balanced anaesthesia with desflurane, dexmedetomidine and scalp block is used. **Methods:** Sixty patients with the American Society of Anesthesiologists physical status I or II, aged between 18 and 60 years were included in the study. All patients received anaesthesia including desflurane, dexmedetomidine and scalp block. The patients were randomly allocated to receive no neuromuscular blocking agent (Group A) or atracurium infusion to keep train-of-four count 2 (Group B). The two groups were compared with respect to haemodynamic stability, brain relaxation scores and recovery characteristics. Haemodynamic parameters and time taken to achieve Aldrete score >9 and other secondary outcomes were analysed using Student's *t*-test. Non-parametric data were analysed using the Mann-Whitney test. **Results:** The mean arterial pressure was comparable between the groups. The intraoperative heart rate was comparable; however, in the post-operative period, it remained higher in Group B for 30 min after extubation ($P = 0.02$). The brain relaxation scores were comparable among the two groups ($P = 0.27$). Tracheal extubation time, time taken for orientation and time required to reach Aldrete score ≥ 9 were comparable among the two groups. **Conclusion:** The present study suggests that balanced anaesthesia using desflurane, dexmedetomidine and scalp block can preclude the use of neuromuscular blocking agents in patients undergoing supratentorial surgery under intense haemodynamic monitoring.

Key words: Atracurium, desflurane, dexmedetomidine, neuroanaesthesia, neurosurgery, scalp block

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INTRODUCTION

The goals during anaesthesia for neurosurgery are the maintenance of haemodynamic stability, optimal operative conditions, ensuring early emergence for neurological assessment and allowing electrophysiological monitoring. Keeping these goals in mind, the necessity of neuromuscular blocking agents

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may be debatable. Residual effects of neuromuscular blocking agents can produce post-operative respiratory complications with increased chances of hypoxia and hypercarbia, thereby increasing intracranial pressure (ICP). The analysis of electrophysiological monitoring can be confounding when neuromuscular blocking drugs are used. Neuromuscular blocking agents are required during maintenance of anaesthesia to keep the patient immobile, facilitate mechanical ventilation and ensure optimal operating conditions by paralysis of muscles. All these goals can be achieved using balanced anaesthesia with inhalational agents or target controlled infusion of propofol, alpha 2 agonists such as dexmedetomidine and regional blocks such as scalp block. Furthermore, there are no muscles in the scalp which require to be paralysed to improve surgical conditions. Desflurane, a volatile anaesthetic with low blood solubility, allows for early recovery after anaesthesia. In neurosurgery, it may facilitate early post-operative neurological assessment.^[1,2] Scalp block can blunt the haemodynamic response to noxious stimuli, decrease the amount of opioids and reduce post-operative pain^[3,4] facilitating smooth and early emergence. Dexmedetomidine provides good perioperative haemodynamic stability, decreases the requirement of intraoperative opioid and has minimal effect on ICP. This makes it a suitable adjuvant to neurosurgical anaesthesia.^[5,6] Dexmedetomidine has been shown to reduce the minimum alveolar concentration (MAC) of inhalation anaesthetics and the need of perioperative fentanyl.^[7-9]

The aim of our study was to assess the time taken for discharge from the Post-Anaesthesia Care Unit (PACU) by measuring the time taken to achieve an Aldrete score of 9 as the primary end-point and testing the hypothesis that omitting neuromuscular blocking agents can result in faster discharge from PACU.

METHODS

After the Institutional Ethics committee approval and written informed consent, sixty patients (30 in each group) of the American Society of Anesthesiologists (ASA) physical status I and II, age ranging from 18 to 60 years of either sex with a Glasgow Coma Score of 15, undergoing elective craniotomy for supratentorial lesions, were enrolled in this prospective randomised study in a tertiary care hospital. The patients were randomly allocated to either Group A (without use of neuromuscular blocking agent) or to Group B (with atracurium infusion

to keep train-of-four count 2). Randomisation was done by picking chits allocating the patient to either study group by a person not involved in the study. The patients, neurosurgeons assessing brain relaxation, nurses in the PACU and outcome assessors were blinded to the group allocation. The use of neuromuscular monitoring prevented intraoperative blinding of the anaesthesiologist managing the case. The criteria for exclusion were baseline heart rate (HR) <50 beats/min, pregnant and lactating patients, patient on β blockers, sick sinus syndrome and known hypersensitivity to drugs being used and/or refusal to consent. The criteria for withdrawal were defined as severe intraoperative bleeding and elective ventilation due to the surgical cause.

Pre-induction monitoring included electrocardiogram, oxygen saturation and non-invasive blood pressure. Infusion of dexmedetomidine (loading dose of 0.5 $\mu\text{g}/\text{kg}$ over 10 min followed by maintenance dose 0.2–0.7 $\mu\text{g}/\text{kg}/\text{min}$) was started as soon as intravenous (IV) access was established. IV preservative-free 2% lignocaine 1.5 mg/kg, midazolam 0.02 mg/kg and fentanyl 2 $\mu\text{g}/\text{kg}$ were administered before induction of anaesthesia with propofol 2 mg/kg. Tracheal intubation was assisted with atracurium 0.75 mg/kg. End-tidal CO_2 , respiratory gas monitoring with MAC monitoring and neuromuscular monitoring were initiated after induction. Anaesthesia was maintained on O_2 , N_2O , desflurane (MAC 0.8–1.0) and dexmedetomidine in Group A and O_2 , N_2O , desflurane (MAC 0.8–1.0) dexmedetomidine and atracurium infusion (4–6 $\mu\text{g}/\text{kg}/\text{min}$) to keep train-of-four count (TOF) of 2 in Group B. Scalp block with 0.25% bupivacaine was given to patients in both groups. In case of patient movement, propofol was started at 25 $\mu\text{g}/\text{kg}/\text{min}$ and titrated as per effect. Vital parameters were monitored every 10 min. After opening the dura, surgeon satisfaction with brain relaxation was gauged by Brain Relaxation Scoring Scale on a scale from 1 to 4 [Table 1].

Propofol and atracurium infusions were stopped at the end of dura closure. Dexmedetomidine and desflurane were discontinued at the end of skin closure.

Table 1: Brain relaxation scoring scale

| Brain relaxation evaluation | Score |
|----------------------------------------------------------------|-------|
| Excellent, no swelling | 1 |
| Minimal swelling but acceptable | 2 |
| Serious swelling but no specific change in management required | 3 |
| Severe brain swelling requiring some intervention | 4 |

Paracetamol 15 mg/kg was given IV at the time of dura closure. Only patients in Group B were reversed with glycopyrrolate 0.008 mg/kg and neostigmine 0.06 mg/kg at TOF count ≥ 3 . Patients were extubated when no fade was detected on double burst stimulus. The time taken for eye opening and extubation was noted. The total amount of dexmedetomidine and propofol used was calculated. The time taken for orientation and ability to call out name and city of residence were noted. Vital parameters were monitored every 15 min for 1st h and then at 60 min, 90 and 120 min after extubation. The time taken to reach modified Aldrete score of 9 was recorded. Bradycardia (HR <50/min) was treated with atropine 0.6 mg IV. Hypertension (>20% increase from baseline value) and tachycardia (HR >100/min) were first treated with increasing dose of dexmedetomidine and one dose of fentanyl 1 μ g/kg, if required, after 5 min. For persistent hypertension, 10 mg aliquots of esmolol were given, or nitroglycerine infusion was started depending on HR. Hypotension (defined as a decrease in mean arterial pressure [MAP] <60 mm Hg for >1 min) was managed with increased rate of infusion of crystalloids. If this was not effective, 6 mg aliquots of ephedrine were used.

Recovery from anaesthesia was the primary outcome and was assessed by measuring the time taken for reaching a modified Aldrete score of 9 after stopping desflurane and dexmedetomidine. The Aldrete score was assessed every 15 min after extubation in the PACU.

The secondary end-points included intraoperative and post-operative HR and MAP, tracheal extubation time, time taken for eye opening and orientation, surgeon's satisfaction with the intraoperative degree of brain swelling and requirement of dexmedetomidine, fentanyl and other drugs to maintain haemodynamic stability. Brain relaxation scoring scale was used for assessing the surgeon's satisfaction with the operative field.

Sample size calculation, to achieve 80% power of the study, was on the basis of the previous study investigating the recovery characteristics of desflurane, which demonstrated the mean time to achieve Aldrete score ≥ 8 as 9.58 ± 6.13 min.^[1] We determined that 27 patients would be required for each group to detect 80% difference (8 min) in the time taken to achieve an Aldrete score of 9, using α and β values of 0.05 and 0.2. We chose to detect 80% difference as a smaller

change would be clinically insignificant. $P < 0.05$ was considered statistically significant. Gender, ASA grade and brain relaxation score were analysed using Chi-square test. Haemodynamic parameters and time taken to achieve Aldrete score >9 and other secondary outcomes were analysed using student *t*-test using Microsoft Excel 2010. Non-parametric data were analysed using the Mann-Whitney test.

RESULTS

Sixty patients were identified and randomised for the study. No patient had to be excluded from the study on the basis of withdrawal criteria. The age (Group A - 41.17 ± 11.83 years, Group B - 35.87 ± 11.58 years), sex (13 males and 17 females in both groups), weight (Group A - 54.47 ± 10.94 kg, Group B - 55.57 ± 10.62 kg), ASA status, type of lesion as well as duration of anaesthesia (Group A - 225.17 ± 47.86 min, Group B 231.67 ± 41.03 min) were comparable among the two groups.

There was no significant difference in the HR for most part of the intraoperative and post-operative period. The HR was significantly higher in Group B intraoperatively between 210 min and 260 min. The HR was significantly higher in Group B in the immediate post-operative period for first 30 min ($P = 0.024$) [Figure 1]. There was no significant difference between the MAP in the intraoperative as well as post-operative period [Figure 2]. No significant difference was found between the requirement of propofol, dexmedetomidine, fentanyl, atropine and ephedrine [Table 2]. The time taken for opening eyes, for extubation, for orientation and for achieving Aldrete score >9 was comparable among the two groups [Table 3]. Brain relaxation scores were also comparable ($P = 0.271$) [Figure 3]. One patient in each group was administered nitroglycerine for control of blood pressure. Two patients in Group A and four patients in Group B had transient fall in MAP up to 44 mm of Hg, which responded

Table 2: Comparison of dose requirement

| Drug | Group A | Group B | P |
|------------------------------------------------|-------------------|-------------------|------|
| Propofol (mg), median/IQR/range | 0/20/0-100 | 0/0/0-580 | 0.21 |
| Dexmedetomidine (μ g), mean \pm SD | 66.94 \pm 28.56 | 72.49 \pm 31.30 | 0.48 |
| Dexmedetomidine (μ g/kg/h), mean \pm SD | 0.33 \pm 0.08 | 0.3 \pm 0.126 | 0.62 |
| Additional fentanyl (μ g), mean \pm SD | 14.33 \pm 26.09 | 14.50 \pm 29.31 | 0.96 |
| Ephedrine (mg), mean \pm SD | 8.3 \pm 9.28 | 8.2 \pm 10.3 | 0.97 |
| Atropine (mg), mean \pm SD | 0.16 \pm 0.35 | 0.06 \pm 0.18 | 0.16 |

IQR - Interquartile range; SD - Standard deviation

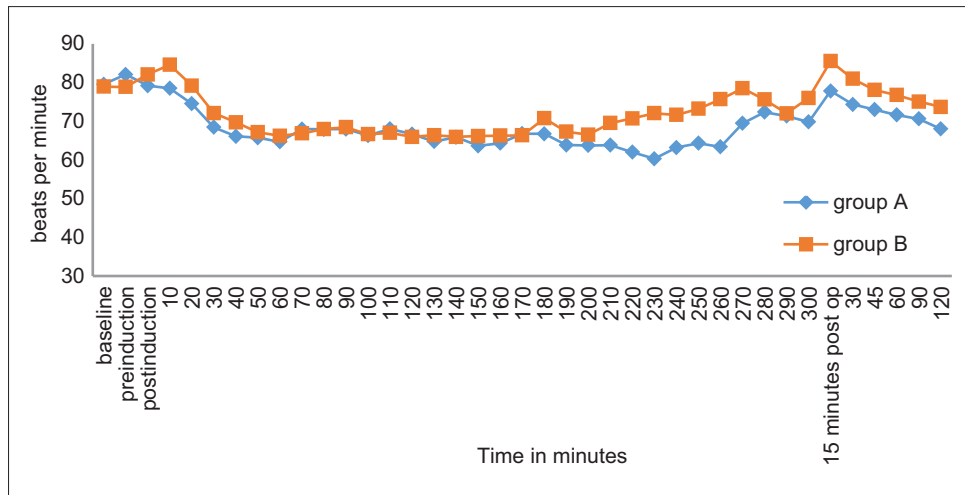


Figure 1: Comparison of mean heart rate

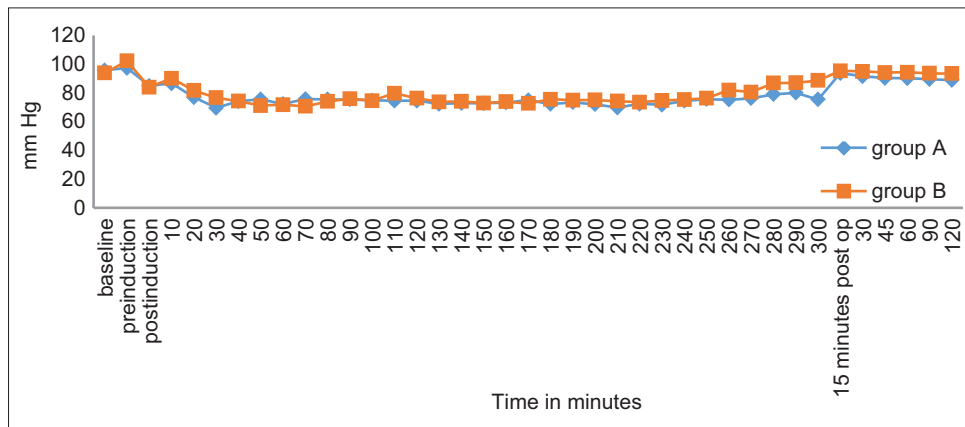


Figure 2: Comparison of mean arterial blood pressure

| Time taken for recovery | Table 3: Comparison of recovery time | | | | P |
|-------------------------|--------------------------------------|------------|---------------|-------------|------|
| | Group A | | Group B | | |
| | Mean±SD (min) | 95% CI | Mean±SD (min) | 95% CI | |
| Time for eye opening | 8.05±4.23 | 6.54-9.56 | 8.43±4.28 | 6.9-9.96 | 0.73 |
| Time for extubation | 9.17±4.23 | 7.66-10.68 | 10.6±5.1 | 8.78-12.42 | 0.24 |
| Time for orientation | 11.46±4.86 | 9.72-13.2 | 13.00±6.11 | 10.81-15.19 | 0.29 |

CI – Confidence interval; SD – Standard deviation

to fluid challenge and aliquots of ephedrine. Dexmedetomidine was stopped in four patients in Group A and three patients in Group B due to hypotension. However, hypotension was corrected promptly after stopping dexmedetomidine. No patient required inotropic support. All patients were extubated at the end of surgery without any neurological deficit attributable to hypotension. The incidence of minimal patient movement was same in both groups (three patients in each group). None of the patients desaturated or had convulsions in the post-operative period. One patient in Group B has post-operative nausea vomiting.

DISCUSSION

We observed from our study that there was no difference between the two groups in the recovery profiles, haemodynamic parameters or surgical conditions. The Aldrete score of 9 was achieved at 15 min (time of first assessment) in both groups and is similar to the time (9.58 min) obtained previously.^[1] The time taken for eye opening and orientation in both groups was not significantly different and it matched the time recorded (8.1 ± 7.0 min and 12.0 ± 8.2 min, respectively) in the previous study where a much higher dose of dexmedetomidine ($0.9 \mu\text{g}/\text{kg}/\text{h}$) was used.^[5] Desflurane-dexmedetomidine anaesthesia

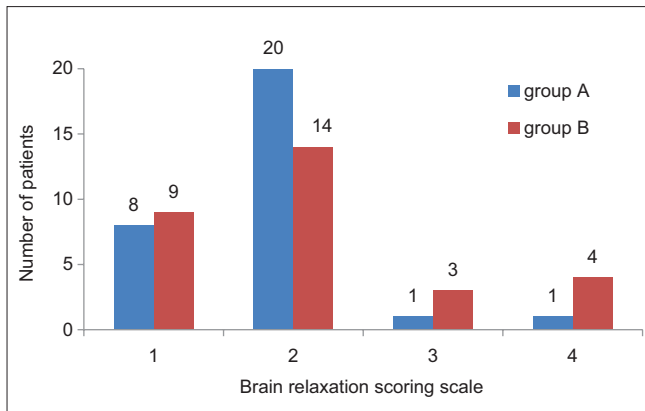


Figure 3: Comparison of brain relaxation score

offers faster eye opening, response to verbal commands and post-operative neurologic assessment than sevoflurane-dexmedetomidine or isoflurane-dexmedetomidine anaesthesia.^[5] Dexmedetomidine infusion provides faster recovery after anaesthesia without inducing respiratory depression after extubation as compared to fentanyl.^[10] Dexmedetomidine, when administered as a single dose IV before the induction of anaesthesia, shortens the period for recovery from the anaesthesia.^[11]

Balanced anaesthesia without neuromuscular blocking agents appears to achieve the goals of neuroanaesthesia as seen in our study. The average age-adjusted MAC value to maintain BIS between 45 and 50 for desflurane has been found to be 0.65 ± 0.04 .^[12] Hence, desflurane with nitrous oxide with a MAC between 0.8 and 1.0 was chosen for our study. Maintenance of perioperative haemodynamic stability is an important goal of neuroanaesthesia practice. Hypertension can result in intracranial haemorrhage and cerebral oedema and hypotension may exacerbate neuronal injury in hypoperfused areas of the brain. In our study, the haemodynamic profile was similar in both groups at most points of observation during the study period. The HR was significantly higher in Group B intraoperatively between 210 min and 260 min. However, only 11 patients in Group A and 20 patients in Group B had surgeries lasting beyond 210 min. The sample size of the study was not calculated to detect changes in HR and MAP as the primary end-point. Hence, there is a possibility of error in evaluation of the significance of haemodynamic results. The HR in the immediate post-operative period is higher in Group B. This can be attributed to the effect on glycopyrrolate administered at the time of reversal only in Group B. The absence of significant difference in the MAP among the two groups indicates the efficacy of this

combination in maintaining target haemodynamic parameters. Scalp block with 0.25% bupivacaine is an effective adjuvant for maintaining stable haemodynamics for patients undergoing craniotomy during general anaesthesia.^[13] Dexmedetomidine administered during neuroanaesthesia reduces the requirement of opioids, antihypertensive treatments and offers better haemodynamic stability.^[6] Similarly, low concentration of desflurane combined with remifentanyl or fentanyl provides good control of blood pressure in patients who underwent intracranial surgery for vascular or space-occupying lesions.^[14]

A slack brain provides a good surgical field and reduces the need for brain retraction. We used the brain relaxation scoring scale as a surrogate for ICP monitoring as described earlier.^[1] We did not find any significant difference between the scores of the two groups. Dexmedetomidine has been shown to provide good operating conditions.^[15] Propofol, sevoflurane and desflurane have the same and acceptable effects on the brain relaxation scores at various stages of surgery.^[16] Dexmedetomidine is not sufficient to suppress haemodynamic responses but decreases the requirement of inhalation agents and provides brain relaxation and good surgical field exposure conditions without any side effect in patients undergoing supratentorial craniotomy.^[5]

The necessity of neuromuscular blockade in supratentorial surgeries has not yet been studied extensively. To the best of our knowledge, there has been no study which has analysed the use of desflurane-dexmedetomidine without using neuromuscular blocking agents in neurosurgical cases. The incidence of patient movement was same between both groups and could have been possibly due to inadequate depth of anaesthesia. The movement did not occur during the main surgical procedure with the microscope. Maintaining adequate depth of anaesthesia eliminated the problem in both groups.

There were few limitations of the study; intraoperative blinding could not be established due to neuromuscular blockade monitoring. The major concern with omitting neuromuscular blocking agents is that the higher concentration of anaesthetic agents required to maintain anaesthetic depth may lead to haemodynamic instability/depression requiring inotropic support.^[17] However, we did not encounter any major haemodynamic issue. We did not have depth of anaesthesia monitoring. Use of

Bispectral Index® or Entropy® could have guided the titration of anaesthetic agents better. The study was not designed to study the effect of desflurane-dexmedetomidine combination on intraoperative haemodynamic parameters. Hence, there can be an error in evaluating the incidence of hypotension that has been encountered. Furthermore, we did not have the facilities for evoked potential monitoring. The exact utility of omitting neuromuscular blocking agents in the presence of such monitoring could not be assessed. Further research utilising the protocol with evoked potential monitoring will render more information as it has been previously reported that with evoked potential monitoring, no neuromuscular blockade is preferred over the partial neuromuscular blockade.^[18]

CONCLUSION

Goals of anaesthesia for supratentorial surgeries can be achieved with balanced anaesthesia with desflurane-dexmedetomidine and scalp block. We would like to highlight that supratentorial craniotomies can be performed by avoiding relaxants. This may help anaesthesiologists in the decision regarding the use of neuromuscular blocking agents during neurosurgery.

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Conflicts of interest

There are no conflicts of interest.

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