Original Article

Effect of Intraoperative Target Control End Tidal CO2 on Postoperative Recovery in Neurosurgical procedures; a Randomized Control Trial

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Abstract

Background: The long abated technique of hyperventilation is still desired by neurosurgeon in the era of end tidal CO2 monitoring in the management of neurosurgical procedure. However, its use remains controversial as there is evidence of its potential to cause cerebral ischemia attributable to vasoconstriction. It may be harmless in healthy brain, but under pathological conditions it may be harmful and worsen the neurological outcome of the patients. Therefore, we designed this study to evaluate the effect of two different range of end tidal carbon dioxide (ETCO2) by two modes of ventilation (Eu-ventilation and Hyper-ventilation) on perioperative outcome and cognitive recovery following neurosurgical procedure. **Methods:** Fifty adult patients with brain tumour were randomized into two groups according to computer-generated random number. In Group A, ETCO2 was maintained between range of 34±2 mmHg (Eucapnia group) and in Group B the ETCO2 between 26±2 mmHg (Hypocapnia group). Brain relaxation assessment was done during intra-operative period by four point scale. AVPU scoring system was used as indicator of mental recovery at the end of anesthesia. **Results:** Results revealed that the brain relaxation was almost equally maintained in both the groups. Brain relaxation assessment showed that 84% patient of group B scored grades ≤2, while 80% in Group A. However all recovery parameters as accessed by AVPU score were achieved earlier in Group A as compared to Group B. **Conclusion:** We concluded that even in neuroanesthesia maintaining euventilation and normocarbia during perioperative period is associated with prompt return of cognitive function following extubation.

Key words: Capnography, Neurosurgical procedures, Postoperative period.

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Introduction

Special anesthetic considerations in neurosurgery are the control of intracranial tension (ICT) and maintenance of cerebral perfusion. Arterial carbon dioxide levels (PaCO2) play an important role in governing the intracranial tension hence cerebral perfusion. PaCO2 levels can be well controlled by changing the strategies of ventilation that is by hyperventilation or hypoventilation.

Hyperventilation has been a frequent manoeuvre in the management of anesthesia in elective and emergency neurosurgical procedures.[1-3] However, its use remains controversial as there is evidence of its potential to cause cerebral ischaemia attributable to vasoconstriction. It may be harmless in healthy brain, but under pathological conditions it can be harmful and worsen the patients' clinical condition and prognosis.[1,4] Thus postoperative mental recovery and cognitive functions may vary due to PaCO2 levels.

Capnography is an essential monitoring tool used during neuro-anesthesia. It is a predictor of arterial CO2 tension (PaCO2). Anesthesiologists rely upon end tidal CO2 as the arterial sampling for PaCO2 by arterial blood gas analysis during perioperative period can sometimes be difficult and moreover frequent sampling has been required during surgery. The ETCO2 levels as an acceptable and constant predictor of arterial CO2 tension (PaCO2) during neurosurgery.[5] Also ABG autoanalyser are not available in operation theatre premises and the samples need to be sent to laboratory so our reliance upon capnography to guide intraoperative management is the only option for consideration.

In neuroanesthesia, it is the necessary to prevent increases in intracranial pressure (ICP) or to reduce ICP that is already increased due to pathology to maintain adequate cerebral perfusion pressure and to prevent the herniation of brain tissue between intracranial compartments or through the foramen magnum.[3] The Brain bulk assessment is one of the important clinical indicators suggestive of raised ICP during intraoperative periods, especially when assessment is done by experienced neurosurgeon or anesthetist, helps in guiding immediate therapeutic interventions.

This study was designed to evaluate the effect of end tidal carbon dioxide by two mode of ventilation (eu-ventilation or hyper-ventilation) during neurosurgical procedure and postoperative mental recovery of the patient.

Materials and Methods

As per institutional protocol written informed consent was obtained from the patients who were posted for craniotomy under general anesthesia. Fifty adult patients with brain tumor were randomized into two groups according to computer-generated random number. In Group A, ETCO2 was maintained between range of 34±2 mmHg (Eucapnia group) and in Group B the ETCO2 between 26±2 mmHg (Hypocapnia group). The patients were randomized to one of the two groups on the basis of study design as follows:

Group A (Euventilation)**:** End tidal CO2 maintained in the range of 34±2 mm Hg,

Group B (Hyperventilation): End tidal CO2 maintained in the range of 26±2 mmHg.

Treatment series was stratified according to a computer-generated random number (Group A or B). Finally, at the end of procedure the effect of end tidal carbon dioxide by two mode of ventilation (eu-ventilation or hyper-ventilation) was assessed in terms of mental recovery by APVU system. Eligible patients were between 18 and 60 years of age, ASA physical status II–III, well oriented to time, place and person and scheduled for elective craniotomy for excision of a supratentorial tumor. We excluded the patients from the study who were neurologically unstable or if the attending anesthesiologist incharge considered that the mass effect is too great to allow safe participation in the study. Patients with severe cardio-respiratory or other severe systemic disorders were also excluded. According to our routine clinical practice at the discretion of attending anesthesiologists and neurosurgeons the preoperative medications included the usual prescribed drugs as dexamethasone, antihypertensives and anticonvulsants, along with tablet alprazolam 0.5mg per oral night before surgery.

Patients were kept fasted for at least 8 hours before surgery. In the pre-operative room, baseline cognitive function was assessed and patients who were not fully oriented to time place and person were not included in the study.

In the operating room, patients received noninvasive and invasive arterial blood pressure monitoring. An arterial cannula is inserted before induction of anesthesia for continuously monitoring blood pressure MAP) to estimate cerebral perfusion pressure (CPP) and to provides ready access for arterial blood gases measurement, hematocrit, serum electrolytes, glucose, and osmolality intraoperatively. Arterial blood gas measurement was done hourly to verify the adequacy of ventilation. Continuous electrocardiogram, pulse oximetry, temperature monitoring, urine output, and end-tidal CO2, inspired O_2 concentration and anaesthetic concentrations of inhalational anesthetic agents was done in all patients. Temperature was kept between 35°C and 37°C using warming blankets. Anesthesia was induced with propofol 1–2 mg^{-kg}. Inj. Vecuronium was administered to facilitate tracheal intubation. Anesthesia was then maintained in the two study groups (Group A & Group B) using oxygen along with isoflurane at an end-tidal concentration of 0.9–1.5 vol% or propofol infusion at a rate of 100–120 $\mu g.kg^{-1}min^{-1}$ according to clinical finding specially at time of bone flap removal or to keep the hemodynamic parameter within 20% of the basal level. Analgesia was achieved with inj. fentanyl 1-2 $\mu g.kg^{-1}$. Lungs were ventilated with tidal volume and respiratory rate set to maintain the targeted range of End tidal CO2 (EtCO2) according to groups assigned. All patients were placed in the supine position with a head-up tilt of 10° to perform the surgery. In a few cases the neck was rotated to 30-45° to get the adequate exposure to surgical site depending upon the requirement of the surgeon.

An arterial blood sample was obtained for blood gas analysis. Paco2 was measured at 37°C and corrected to patient's esophageal temperature. This was used to determine the difference between arterial and end-tidal carbon dioxide tension (Pa-ETCO2). Lung ventilation was then adjusted by varying tidal volume and respiratory rate to achieve the desired end-tidal CO2 tension (ETCO2). Airway pressure was kept below 22 cm H2O. Positive end-expiratory pressure was not applied. The neurosurgeon, unaware of the anesthetic and ventilatory management provided, was then asked to score the brain relaxation according to a four-point scale.[6] Brain relaxation was assessed by the surgeon immediately after opening the dura on a 4 point scale as follows: 1 = Adequately relaxed, 2 = Satisfactorily relaxed, 3 = Firm brain, 4 = Bulging brain. Scores 1 and 2 were taken as acceptable brain relaxation scores, while scores 3 and 4 as unacceptable brain relaxation scores.

During the entire study period, anesthetic delivery was maintained to stable hemodynamic to provide balance anesthesia. Specific or routine interventions required for brain swelling such as diuretic therapy with mannitol or furosemide was done as per intraoperative protocol.

The neuromuscular block was reversed with neostigmine bromide 0.05mg/kg and glycopyrrolate 0.01mg/kg IV when the TOF count was found to be 3 or greater.[7] Tracheal tube was removed after recovery of the neuromuscular block.

Neurological assessment is an essential component of post-operative recovery. Early warning scores for post-operative neurological recovery were investigated by two simple scales, which were used to identify seriously ill patients in the neurosurgical ward. The two scales were ACDU Score (Alert, Confused, Drowsy, Unresponsive) or by AVPU (Alert, responds to Voice, responds to Pain, Unresponsive) [8] .The AVPU system used in trauma ward was used in the present study to assess the mental functions following recovery from anesthesia. For this we modified it according to stages of recovery from anesthesia; named it as the modified AVPU Scoring System. Therefore, brain functions were mapped by modified AVPU Scoring System after extubation to access the mental recovery. The time count for AVPU scoring was started immediately after giving the complete dose of reversal agent. The brain mapping of cognitive function recovery after reversal of neuromuscular block was as following:

- A (Alert): time to return of cognitive functions as orientation to time place and person
- V: time of response to verbal commands & lifting limbs on command.
- P: time of response to painful stimuli after discontinuation of the anesthetics.
- U: How long the patient was unresponsive

All statistical analysis was performed using SPSS package (version 17, SPSS Inc., Chicago, IL, USA) software for windows. Data were recorded as mean ±SD or median and range as appropriate. Student's t-test was applied to the test the statistical significance. P-value <0.05 were considered statistically significant.

Results

Fifty five patients were recruited for the study, in which three patients were excluded from the study following intraoperative hemorrhage and hypotension and inability to maintain the desired end-tidal CO2 tension (ETCO2). Two patients having high intracranial tension and required intraoperative surgical drainage before tumor excision were also excluded from the study. Total of fifty patients were finally completed the study as per required assessment protocol. The two study groups were comparable with respect to gender, age, weight, and height [Table 1]. Intraoperative Brain-bulk was assessment in all the patients and grades were compared between two groups. The percentage of patient in Grade 1 and 2 was 84% in Group B while it was 80% in Group A [Table 2]. All recovery parameters as accessed by modified AVPU scoring system were achieved earlier in Group A as compared to group B [Table 3]. Intra-operative hemodynamic parameters did not differ in the two groups during the course of anesthesia [Figure 1].

Discussion

Maintaining ICP and facilitating surgical access was the main priority for which hyperventilation is being used. Hyperventilation can result in ischemia especially when baseline cerebral blood flow (CBF) is low commonly seen after injury.[9,10] In this study we found that maintaining ETCO2 between 34±2 mm Hg by normoventilation provided nearly same brain relaxation as ETCO2 between 26±2 mm Hg by hyperventilation. We have noticed that patient outcome and recovery was better in patient maintained normocapnia with ETCO2 between 34±2 mm Hg.

Table 1: Demographic Data.

Variables	Group A	Group B	P value
No. of patients	25	25	
Gender : male/female	12/13	14/11	>0.05
Age (years)	47±15	46±13	>0.05
Weight(Kg)	67±21	68±16	>0.05
Height(cm)	168±17	165±16	>0.05

Table 2: Brain Relaxation Assessment.

Variables	Group A	Group B
Grade 1	3	5
Grade 2	17	16
Grade 3	3	2
Grade 4	2	2

Table 3: Brain Function Mapping & modified AVPU Scoring System.

Variables	Group A (Mean ± S.D.)	Group B (Mean ± S.D.)	P value
A) Fully Alert (min)	3.82±2.1	8.6±5.208	<0.05
V) Response to verbal commands (min)	3.62±2.2	7.62±4.72	<0.05
P) Response to painful stimuli (min)	2.91±2.1	6.8±4.1	<0.05
U) Duration of unresponsiveness	2.04±2.2	5.23±3.3	<0.05

Muizelaar and colleagues[11] performed a study that incorporated a near normocapnic group in which PaCO2 was maintained at approximately 35 mm Hg, and a hypocapnic group in which PaCO2 was maintained in the vicinity of 25 mm Hg. Outcomes at 3 and 6 months after injury were not different. However, in a subset of patients with the best initial motor scores, outcome was better in the normocapnic group.[11]

Hyperventilation should not be used as routine maneuver in neuroanesthesia. Because of the low CBF state in SAH, hyperventilation is now widely avoided. Biochemical analysis showed reduced CBF in brain tissue beneath retractors.[12] Hyperventilation can further affect blood flow in these areas.

Its deleterious effect have been proven not only for the brain but also for other organs where perfusion is compromised.[9] Hypocapnia impairs cognitive function for upto 48 hours and elderly are more susceptible.[2,13] Hypocapnia raises the airway resistance due to bronchospasm and increase the permeability in the microvasculature.[2] Hypocapnia attenuates hypoxic pulmonary vasoconstriction worsening the intrapulmonary shunt and causing impaired systemic oxygenation.[2] Hypocapnia is also associated with development of arrhythmia, both in critical patients and panic attack.[3]

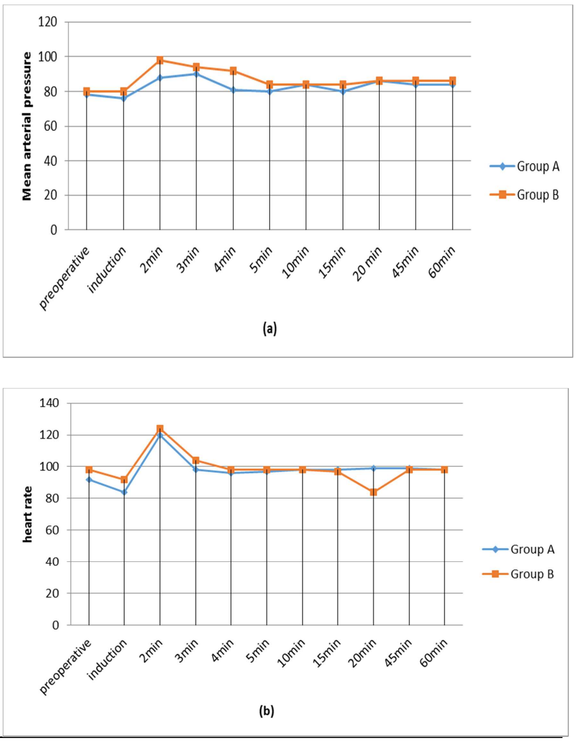

Figure 1: Change in intraoperative hemodynamic parameter. (a) Mean arterial pressure, (b) heart rate.

Conclusion

Thus we concluded that maintaining ETCO2 between 34±2 mm Hg is associated with better patient outcome in term of faster return of mental functions even in neurosurgical patients. It also provides nearly same brain relaxation as ETCO2 between 26±2 mm Hg. Thus, in neurosurgery hyperventilation may be used judiciously and only for short time interval and the target control end tidal CO2 with euventilation in the range of 34±2 mm Hg is to be maintained for better neurosurgical outcome.

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