



Correlation between End-Tidal Carbon Dioxide Pressure and Arterial Carbon Dioxide Partial Pressure in Patients Undergoing Craniotomy

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Abstract

Background: End-tidal carbon dioxide pressure (ETCO₂) is commonly used as an indicator of arterial partial pressure of carbon dioxide (PaCO₂) which reflects adequacy of ventilation during major surgeries. While accurate determination of PaCO₂ level is an important aspect of anesthetic management of the patient it is all the way more important in neurosurgeries where changes in PaCO₂ can have a profound effect on cerebral blood flow. Moreover practice of reducing intracranial pressure by means of hyperventilation is often used to reduce intracranial pressure in neurosurgical patients. There has also been some controversy in recent anesthetic literature about whether end tidal CO₂ (ETCO₂) is an accurate reflection of PaCO₂. This study was aimed to evaluate the relationship between ETCO₂ and arterial PaCO₂ in neurosurgical patients undergoing craniotomy and to assess the predictive value of ETCO₂ as an indicator of PaCO₂ level.

Aims and Objectives:

1. To study the correlation in between arterial to end tidal CO₂ in neurosurgical patients undergoing craniotomy.
1. To study the correlation in between arterial to end tidal CO₂ in neurosurgical patients undergoing craniotomy.

Materials and Methods: This was a prospective study conducted on 30 patients aged between 18 to 60 years who were posted for elective craniotomy under general anaesthesia at a major hospital in an urban area. The patients were included in the study after approval of the institutional ethical committee and written informed valid consent obtained from the patient. Patients were taken to operation theatre and routine pre anesthetic examination was done. Vitals were noted. All patients were anaesthetized using standard balanced general anaesthesia as per attending anesthesiologist and set protocol for neurosurgery cases. PaCO₂ and PETCO₂ were recorded immediately after induction followed by every hourly till end of surgery. Data was collected and statistical analysis was done with the help of SPSS Software version 15.

Results: Total 30 patients were studied. Out of these cases 18 were males and 12 were females with a male to female ratio being 1: 0.66. The analysis of age group of the patients revealed that majority (36.66%) of the patients belonged to age group of 31-40 years. The percentage of patients in the age group of 21-30 years and 41-50 years was similar (20%). 12 (40%) patients belonged to ASA I category and 18 (60%) patients belonged to ASA II category. There was no patient belonging to other ASA categories as belonging to ASA I or ASA II category was the inclusion criteria of our study. Most common indication for surgery was meningioma which was seen in 15 (50%) patients followed by glioma, Cerebellopontine angle tumor,

schwannoma and glioblastoma which was seen in 6 (20%), 4 (13.33%), 3 (10%) and 2 (7.66%) patients respectively. All surgeries were uneventful. The analysis of PaCO₂ and ETCO₂ with respective to mean and standard deviations of pulse rate, Mean arterial pressure and central venous pressure during surgeries showed stable pulse rate, MAP and CVP throughout the surgical procedures thereby ruling out the fluctuations of these parameters as a cause of changes in PaCO₂ and ETCO₂. The data was analyzed for correlation between PaCO₂ and ETCO₂ at different intervals during craniotomy. Statistically significant correlation was found between PaCO₂ and ETCO₂ at baseline, 1hr, 2hr, 3hr and 4hr during surgery.

Conclusion: *In Our study there was a statistically significant correlation between PaCO₂ and ETCO₂ during elective neurosurgery patients undergoing craniotomy under general anaesthesia. Our study concludes that end-tidal CO₂ (ETCO₂) reflects arterial CO₂ with acceptable accuracy and hence capnometry can be relied upon as a reflection of arterial PaCO₂ in neurosurgical patients undergoing craniotomy.*

Keywords: *End tidal Co₂, PaCO₂, capnometry, Craniotomy.*

Introduction

In neurosurgery and neuroanaesthesia, continuous monitoring of ETCO₂ and intermittent monitoring of PaCO₂ is standard set protocol. Both PaCO₂ and ETCO₂ are indicators of ventilatory adequacy. It is important to know the PaCO₂ in neuroanaesthesia because of its effect on cerebral blood flow. ETCO₂ has been used as non-invasive estimate of PaCO₂ ^[1].

1. The usual reported difference between PaCO₂ and ETCO₂ in healthy awake patients is 3.6 to 4.6 mm of Hg ^[2].
2. A significant variability has been observed in mechanically ventilated neurosurgical ICU patients and in patients undergoing craniotomy in different positions ^[3].
3. There has also been some controversy in recent anaesthetic literature whether end tidal CO₂ (ETCO₂) is an accurate reflection of PaCO₂ ^[4].

Capnography is an accepted standard of care for intraoperative monitoring of mechanically ventilated patients and is often used during ventilation of critically ill patients with respiratory failure ^[5]. The respiratory rate, PETCO₂, and the respiratory waveform morphology are used to assess the presence of respiratory distress, ventilatory adequacy, and bronchial obstruction. ETCO₂ is used clinically as a positive indicator of endotracheal intubation, a disconnected alarm, and an estimation of PaCO₂. Capnography, which is based on the measurement of end tidal carbon

dioxide (ETCO₂), is a well-established method for intraoperative monitoring of respiratory function during routine anaesthesia ^[6]. ETCO₂ refers to the partial pressure of carbon dioxide at the end of expiration and reflects arterial carbon dioxide tension (PaCO₂). One of the treatment modality used by anesthesiologist for the management of raised intracranial pressure (ICP) in neurosurgical patients is hyperventilation, which reduces arterial PaCO₂ and hyperventilation is only effective when the PaCO₂ reactivity of cerebral vasculature is normal and intact ^[7]. It is well known that PaCO₂ correlates inversely with cerebral arterial resistance ^[8]. Therefore, it is important that an anaesthesiologist must be aware of PaCO₂ and ETCO₂ values during procedures where raised ICP is a potential problem ^[9]. Other methods to reduce raised intracranial pressure are – CSF drainage, ventriculostomy, diuresis (mannitol), cerebral metabolic rate compression (barbiturates, propofol), mean arterial pressure reduction (if dysautoregulation) and surgical control ^[10,11]. This study is undertaken to review our routine practice of obtaining PaCO₂ during craniotomy procedures and comparing it with the ETCO₂ at the same time. The objective is to see whether ETCO₂ reflected the PaCO₂ with acceptable accuracy.

Materials and Methods

After approval of the institutional ethics committee and written informed valid consent

obtained from the patient, 30 patients aged between 18 to 60 years who were posted for elective craniotomy under general anaesthesia at our hospital was chosen.

Inclusion Criteria:

1. Age 18 to 60 yrs.
2. Patients belonging to ASA I and II.
3. Elective craniotomies in supine and sitting position.
4. Patients who are conscious and oriented with time, place and person.
5. Duration of surgery 4-5 hrs.

Exclusion Criteria

1. Patients age < 18 yrs and >60 yrs.
2. Preoperatively intubated patients.
3. Patients with bleeding diathesis.
4. Patients with coexisting chronic bronchopulmonary disease and severe hemodynamic instability.
5. Intraoperative venous air embolism.
6. Patient's refusal.

This was a prospective study. All patients were anaesthetized using standard balanced general anaesthesia as per attending anesthesiologist and set protocol for neurosurgery cases.

Post induction arterial line was taken in all patients by cannulating radial artery (most commonly) as per the standard set protocol in all neurosurgery cases.

After patient positioning and achieving hemodynamic stability a baseline arterial blood sample was collected and PaCO₂ was measured by using blood gas analyzer and corrected to a temperature of 37⁰ Celsius, simultaneously PETCO₂ also recorded by using a side-stream capnometer which was connected by angle piece connector in between endotracheal tube and breathing circuit.

The first post induction measurement was taken as a baseline and then repeated every 1 hourly until the end of surgery. Simultaneous measurement of blood pressure, heart rate, respiratory rate, central venous pressure, tidal volume, inspired O₂ fraction (FiO₂), peak inspiratory pressure were

recorded at each sampling time. All the other hemodynamic and respiratory parameters were recorded at the same time at the timing of collection of arterial sample for PaCO₂ and recording of ETCO₂ from capnometer from the same patient so that the values of PaCO₂ and ETCO₂ are not influenced by these parameters during respective intervals of collection of data throughout the surgical procedure. Data was collected and statistical analysis was done with the help of SPSS Software version 15.

Results

Overall 30 patients were studied in the age group of 18 to 60 years, 60% patients were male and 40% patients female (Figure 1).

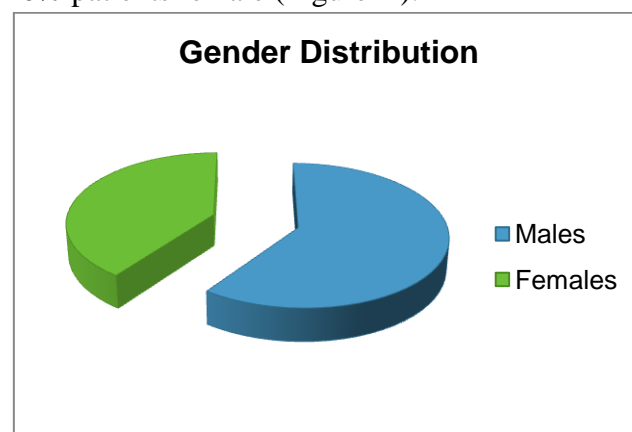


Figure 1: Gender distribution of the studied cases. In our study total 30 patients were studied from 18-60 years. These were distributed in different groups according to number of patients, out of these youngest patient was 23 years old and oldest was 59 years (Table 1).

Table 1: Age distribution of the studied cases

Age Group	Percentage of patients
21-30	20%
31-40	36.66%
41-50	20%
51-60	23.33%

Out of total patients 40% belongs to ASA I category and 60% belongs to ASA II category. All 30 patients involved in the study have undergone elective craniotomy for various

diagnoses as mentioned in the table and as given below (Table 2).

Table 2: Indication for craniotomy in studied cases

Diagnosis	Frequency	Percent
CP Angle Tumour	4	13.33%
Glioblastoma	2	7.66%
Glioma	6	20.00%
Meningioma	15	50.00%
Schwannoma	3	10.00%
Total	30	100%

During study, all surgical procedures were uneventful. Throughout surgical procedure standard cardiorespiratory monitoring was done. All the standard cardiorespiratory parameters such as Heart rate, Blood pressure, Mean arterial pressure, Central venous pressure, Respiratory rate, PaCO₂ and PETCO₂ recorded at regular interval of 1 hour after baseline sample. All the cardiorespiratory parameters were within normal limit [Table 3].

Table 3: Study parameters (Cardiorespiratory variables) during surgical procedure.

Study Parameter	N	Mean	Std. Dev	Median	IQR	Minimum	Maximum
PaCO ₂ BL	30	37.13	1.85	37.60	1.78	32.80	39.80
PaCO ₂ After 1hr	30	36.74	1.49	36.80	2.37	34.50	39.90
PaCO ₂ After 2hr	30	36.49	1.61	36.80	1.68	32.10	38.90
PaCO ₂ After 3hr	30	36.62	1.55	36.60	2.90	33.80	39.70
PaCO ₂ After 4hr	30	36.61	1.81	36.80	2.45	32.70	39.90
EtCO ₂ BL	30	33.47	1.78	34.00	3.00	29.00	37.00
EtCO ₂ After 1hr	30	33.53	1.07	34.00	1.25	32.00	35.00
EtCO ₂ After 2hr	30	33.23	1.17	33.00	1.25	31.00	36.00
EtCO ₂ After 3hr	30	33.10	1.21	33.00	2.00	31.00	35.00
EtCO ₂ After 4hr	30	33.43	1.96	34.00	2.00	30.00	38.00
P(a-Et)CO ₂ BL	30	3.66	1.15	3.55	1.23	1.50	6.80
P(a-Et)CO ₂ After 1hr	30	3.20	1.31	3.65	1.43	-0.40	5.60
P(a-Et)CO ₂ After 2hr	30	3.26	1.73	3.75	1.33	-1.40	6.60
P(a-Et)CO ₂ After 3hr	30	3.52	1.49	3.80	1.95	0.60	5.80
P(a-Et)CO ₂ After 4hr	30	3.18	1.80	3.20	1.65	-0.30	8.10
PR BL	30	81.00	3.51	82.00	6.00	74.00	86.00
PR After 1hr	30	79.80	3.76	82.00	6.00	74.00	86.00
PR After 2hr	30	78.73	3.26	78.00	1.50	74.00	86.00
PR After 3hr	30	76.13	3.32	76.00	4.00	70.00	82.00
PR After 4hr	30	78.20	4.53	79.00	6.00	68.00	84.00
RR BL	30	12.00	0.00	12.00	0.00	12.00	12.00
RR After 1hr	30	12.00	0.00	12.00	0.00	12.00	12.00
RR After 2hr	30	12.00	0.00	12.00	0.00	12.00	12.00
RR After 3hr	30	12.00	0.00	12.00	0.00	12.00	12.00
RR After 4hr	30	12.00	0.00	12.00	0.00	12.00	12.00
SBP (mmHg) BL	30	128.87	3.85	128.00	6.00	120.00	138.00
DBP (mmHg) After 1hr	30	71.20	5.57	70.00	6.00	62.00	82.00
SBP (mmHg) After 2hr	30	125.67	2.47	126.00	4.00	120.00	132.00
DBP (mmHg) After 3hr	30	70.33	4.64	70.00	6.00	64.00	80.00
SBP (mmHg) After 4hr	30	126.47	2.96	126.00	4.00	120.00	132.00
DBP (mmHg) BL	30	68.93	4.92	69.00	8.50	60.00	80.00
SBP (mmHg) After 1hr	30	125.47	2.87	126.00	6.00	120.00	130.00
DBP (mmHg) After 2hr	30	68.53	4.23	68.00	6.00	64.00	78.00
SBP (mmHg) After 3hr	30	126.20	3.21	126.00	4.00	122.00	134.00
DBP (mmHg) After 4hr	30	68.27	4.69	68.00	6.00	60.00	80.00
MAP (mmHg) BL	30	90.42	3.67	90.33	4.67	84.00	98.00
MAP (mmHg) After 1hr	30	88.78	2.93	88.33	4.00	84.67	95.33
MAP (mmHg) After 2hr	30	88.11	3.30	88.67	4.83	82.67	94.67
MAP (mmHg) After 3hr	30	87.51	2.97	86.33	3.50	82.67	94.67
MAP (mmHg) After 4hr	30	87.58	3.25	87.33	4.50	82.00	95.33
CVP (mmHg) BL	30	6.83	0.91	6.50	2.00	6.00	8.00
CVP (mmHg) After 1hr	30	7.13	0.90	7.00	2.00	6.00	8.00
CVP (mmHg) After 2hr	30	6.70	0.88	6.00	2.00	6.00	8.00
CVP (mmHg) After 3hr	30	7.23	0.77	7.00	1.00	6.00	8.00
CVP (mmHg) After 4hr	30	6.97	0.96	7.00	2.00	6.00	8.00

Study of mean and standard deviations of Pulse rate monitoring during Craniotomy at regular intervals as respective with PaCO₂ and ETCO₂ measurements was studied. This showed stable pulse rate throughout the procedure and this does not influences the correlation between PaCO₂ and ETCO₂.

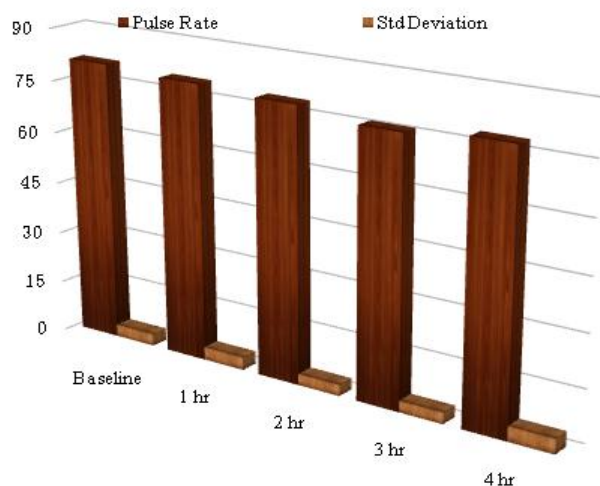


Figure 2: Pulse rate mean and standard deviations at regular intervals during craniotomy.

Below graph shows mean and standard deviations of Mean arterial pressure (MAP) monitoring during Craniotomy at regular intervals as respective with PaCO₂ and ETCO₂ measurements. This shows stable MAP throughout the procedure and this does not influence the correlation between PaCO₂ and ETCO₂ (Figure 3).

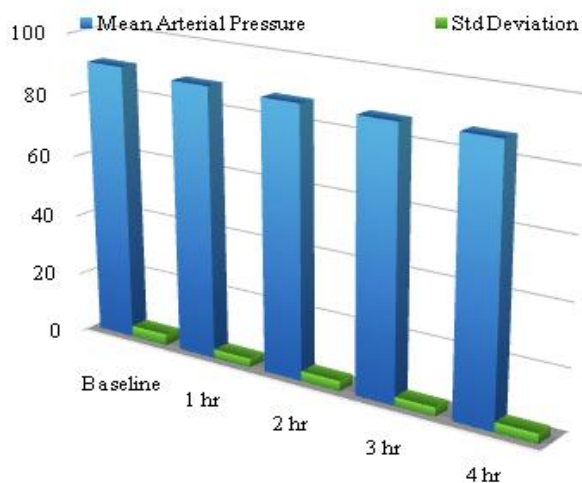


Figure 3: Mean arterial Pressures mean and standard deviations at regular intervals during craniotomy.

Graph below shows mean and standard deviations of Central venous pressure (CVP) monitoring during Craniotomy at regular intervals as respective with PaCO₂ and ETCO₂ measurements. This shows stable CVP throughout the procedure and this does not influences the correlation between PaCO₂ and ETCO₂

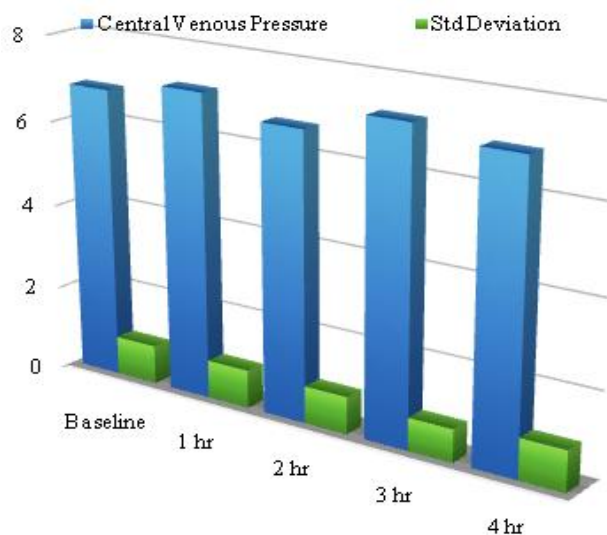


Figure 4 : Central Venous pressure mean and standard deviations at regular intervals during craniotomy.

The correlation between PaCO₂ and ETCO₂ was studied at different intervals during craniotomy . Data was analyzed by using Pearson’s correlation to see the relationship between PaCO₂ and ETCO₂ at regular interval during surgery such as baseline sample was obtained after induction of anaesthesia and achieving stable hemodynamics and after that after interval of 1hr, 2hr, 3hr and 4hr. A “P “value of < 0.05 is considered as significant. Data shows statistically significant correlation between PaCO₂ and ETCO₂ at baseline, 1hr, 2hr, 3hr and 4hr during surgery with Pearson’s correlation coefficients 0.799, 0.522, 0.582, 0.439 and 0.547 respectively and “p” values of 0.000, 0.003, 0.001, 0.015 and 0.002 respectively and all are < 0.05 and hence significant.

Table 4 : Correlation between PaCO₂ and PETCO₂ during Craniotomy:

Correlations		EtCO ₂ BL	EtCO ₂ After 1hr	EtCO ₂ After 2hr	EtCO ₂ After 3hr	EtCO ₂ After 4hr
PaCO ₂ BL	Pearson Correlation	0.799	0.247	-0.062	0.430	0.235
	P Value	0.000	0.188	0.745	0.018	0.212
	Correlation is	Significant	30.000	30.000	30.000	30.000
PaCO ₂ After 1hr	Pearson Correlation	0.217	0.522	0.006	-0.166	-0.239
	P Value	0.248	0.003	0.975	0.380	0.203
	Correlation is	30.000	Significant	30.000	30.000	30.000
PaCO ₂ After 2hr	Pearson Correlation	-0.146	-0.015	0.582	0.015	0.031
	P Value	0.442	0.938	0.001	0.939	0.871
	Correlation is	30.000	30.000	Significant	30.000	30.000
PaCO ₂ After 3hr	Pearson Correlation	0.238	0.018	0.298	0.439	0.355
	P Value	0.206	0.924	0.110	0.015	0.054
	Correlation is	30.000	30.000	30.000	Significant	30.000
PaCO ₂ After 4hr	Pearson Correlation	-0.079	-0.299	0.290	0.269	0.547
	P Value	0.678	0.108	0.120	0.151	0.002
	Correlation is	30.000	30.000	30.000	30.000	Significant

Discussion

Ideally under stable physiologic conditions, with perfectly accurate monitoring gradient between Arterial to End-tidal Carbon dioxide P (a-ET)CO₂ should be close to zero, that is PaCO₂ values could be assumed precisely and repeatedly from ETCO₂ value [12,13]. Arterial blood gas measurement of PaCO₂ is the gold standard for monitoring changes in blood Carbon dioxide but it is invasive, expensive, and provides only intermittent measures of PaCO₂ whereas ETCO₂ provides continuous respiratory monitoring of changes in blood Carbon dioxide [14,15].

This study was carried out in 30 patients in the age group of 18 to 60 years undergoing elective craniotomy. In this study we studied the correlation of PaCO₂ and ETCO₂ during elective craniotomy operations.

Demographic data: In our study there were 30 patients included out of that 18 male and 12

female patients with mean age of 39.83±10.95 years. There is no significant correlation in demographic data and correlation between PaCO₂ and ETCO₂.

ASA grade: There were 12 patients belonging to ASA I grade and 18 patients belonging to ASA II. There is no significant correlation in ASA grading and correlation between PaCO₂ and ETCO₂.

Diagnosis: In our study elective craniotomy was carried out in patients having C P angle tumour (13.33%), Glioblastoma (7.66%), Glioma (20%), Meningioma (50%) and Schwannoma (10%). There is no significant correlation in diagnosis and correlation between PaCO₂ and ETCO₂.

Hemodynamic data: In our study hemodynamic parameters were measured with respective to the measurement timing of PaCO₂ and ETCO₂ at baseline, 1hr, 2hr, 3hr and 4hr till the end of surgery in all the 30 patients. Mean pulse rate (PR) were 81±3.51, 79.80±3.76, 78.73±3.26, 76.13±3.32 and 78.20±4.53 respectively. Mean

MAP measurements were 90.42 ± 3.67 , 88.78 ± 2.93 , 88.11 ± 3.30 , 87.51 ± 2.97 and 87.58 ± 3.25 respectively. Mean CVP measurements were 6.83 ± 0.91 , 7.13 ± 0.90 , 6.70 ± 0.88 , 7.23 ± 0.77 and 6.97 ± 0.96 respectively. There is no significant correlation between this hemodynamic parameters and correlation between PaCO₂ and ETCO₂.

Correlation between PaCO₂ and ETCO₂: The mean difference between PaCO₂ and ETCO₂ during Craniotomy at baseline, 1hr, 2hr, 3hr and 4hr are 3.66 ± 1.15 , 3.20 ± 1.31 , 3.26 ± 1.73 , 3.52 ± 1.49 and 3.18 ± 1.80 mm of Hg respectively. There is a significant correlation between PaCO₂ and ETCO₂ during Craniotomy with Pearson's correlation values at baseline, 1hr, 2hr, 3hr and 4hr are 0.799, 0.522, 0.582, 0.439 and 0.547 respectively. In this study a "P" value of < 0.05 is considered significant with "P" values during Craniotomy at baseline, 1hr, 2hr, 3hr and 4hr are 0.000, 0.003, 0.001, 0.015 and 0.002 respectively showing significant correlation between PaCO₂ and ETCO₂ throughout Craniotomy. In our study we found the statistical significant correlation between PaCO₂ and ETCO₂ at 5% level of

significance at baseline and after 1, 2, 3 and 4 hours during Craniotomy throughout the procedure in hemodynamically stable patients. Garfield B. Russel et al in their study of 35 patients undergoing craniotomies studied correlation of PaCO₂ and ETCO₂ [16]. They found a significant positive correlation between PaCO₂ and PETCO₂ and P (a-ET)CO₂, and PaCO₂. Changes in the study population of PaCO₂, and PETCO₂ correlated statistically. in 1996 Kerr M E et al [17] studied consecutive sample of 35 severe head-injured patients with a Glasgow Coma Scale score of < or = 8. In this study authors observed that end-tidal CO₂ monitoring correlated well with PaCO₂ in patients without respiratory complications or without spontaneous breathing. Fauzia khan et al [18] In their study of 50 patients could show a moderate association between PaCO₂ and ETCO₂ in neurosurgical patients undergoing craniotomy. Similar results were found in studies conducted by Husaini et al [19] and Lee et al [20] in their studies. Table below shows the comparison between different studies which studied the correlation between PaCO₂ and ETCO₂ during craniotomy (Table 5).

Table 5: Correlation between PaCO₂ and ETCO₂ during craniotomy in other studies

Author	No Of Patients	P (a-ET) CO ₂ (mean) mm of Hg	Correlation coefficient	P Value	Correlation
Garfield B Russel et al (1995)	35	7.2 ± 3.3	0.632	< 0.05	Significant
Fauzia Khan et al (2007)	50	4.09 ± 3.0	0.496		Moderate correlation
Husaini et al (2008)	35				
1.10 min after induction.		3.84 ± 2.13	0.571		Significant Significant
2. Prior to Dural Incision.		4.85 ± 5.78	0.559		Significant
3. Start of dural closure		3.91 ± 2.33	0.629		
Lee S W et al (2009)	66	Considered normal is -5 to 5	0.666	<0.001	Significant

Our study showed that ETCO₂ is a measure for the PaCO₂ in neurosurgical patients undergoing craniotomy which was consistent with the studies mentioned above. Thus we conclude that the End tidal Carbon dioxide (ETCO₂) reflects Arterial partial pressure of Carbon dioxide (PaCO₂) with a

statistically significant accuracy and thus can be used as measure for PaCO₂. These conclusions are similar to various studies

Conclusion

In this prospective observational study of 30 patients, in the age group of 18- 60 years, under

ASA I and II category, we observed significant correlation in between PaCO₂ and ETCO₂ during elective neurosurgery patients undergoing craniotomy under general anaesthesia.

Thus, this study shows that end-tidal CO₂ (ETCO₂) reflects arterial CO₂ with acceptable accuracy. So, we can rely on Capnometry for CO₂ measurement over arterial CO₂ measurement in neurosurgical patients which is simple, continuous and non-invasive Carbon dioxide monitoring as compared to arterial Carbon dioxide monitoring which is expensive, intermittent and includes invasive intervention.

Conflict Of interest: None

References

1. Benallal H, Busso T. Analysis of end-tidal and arterial PCO₂ gradients using a breathing model. *Eur J Appl Physiol* 2000; 83:402-8.
2. Nunn JF: In Nunn JF Applied Respiratory Physiology. 3rd edition London: Butterworths, 1987, pp 207-34.
3. Russell GB, Graybeal JM. End-tidal carbon dioxide as an indicator of arterial carbon dioxide in neurointensive care patients. *J Neurosurg Anesth* 1992; 4:245-9.
4. Isert PR. Arterial to end-tidal CO₂ difference during neurosurgical procedures. *Can J Anesth* 1996; 43:196-7.
5. McCarter T, Shaik Z, Scarfo K, Thompson LJ. Capnography Monitoring Enhances Safety of Postoperative Patient-Controlled Analgesia. *American Health & Drug Benefits*. 2008;1(5):28-35.
6. Casati A, Salvo I, Torri G, Calderini E. Arterial to end-tidal carbon dioxide gradient and physiological dead space monitoring during general anaesthesia: effects of patients' position. *Minerva Anesthesiol*. 1997 Jun;63(6):177-82.
7. Gelb AW, Craen RA, Rao GS, Reddy KR, Megyesi J, Mohanty B, Dash HH, Choi KC, Chan MT. Does hyperventilation improve operating condition during supratentorial craniotomy? A multicenter randomized crossover trial. *Anesth Analg*. 2008 Feb;106(2):585-94.
8. Yoon S, Zuccarello M, Rapoport RM. pCO₂ and pH regulation of cerebral blood flow. *Frontiers in Physiology*. 2012;3:365.
9. Puppo C, Fariña G, López FL, Caragna E, Biestro A. Cerebral CO₂ reactivity in severe head injury. A transcranial Doppler study. *Acta Neurochir Suppl*. 2008; 102:171-5.
10. Rangel-Castillo L, Gopinath S, Robertson CS. Management of Intracranial Hypertension. *Neurologic clinics*. 2008;26(2):521-541.
11. Dennis LJ, Mayer SA. Diagnosis and management of increased intracranial pressure. *Neurol India*. 2001 Jun;49 Suppl 1:S37-50.
12. Agus MS, Alexander JL, Mantell PA. Continuous non-invasive end-tidal CO₂ monitoring in pediatric inpatients with diabetic ketoacidosis. *Pediatr Diabetes*. 2006 Aug;7(4):196-200.
13. Owen R, Castle N. EtCO₂: the key to effective prehospital ventilation. *Emergency Medicine Journal: EMJ*. 2006;23(7):578-579.
14. Xu A-J, He Z-G, Xia X-H, Xiang H-B. Anesthetic management for craniotomy in a patient with massive cerebellar infarction and severe aortic stenosis: a case report. *International Journal of Clinical and Experimental Medicine*. 2015;8(7): 11534-11538.
15. Ferber J, Juniewicz HM, Lechowicz-Głogowska EB, Pieniek R, Wroński J. Arterial to end-tidal carbon dioxide difference during craniotomy in severely head-injured patients. *Folia Med Cracov*. 2001;42(4):141-52.
16. Garfield B. Russell, MD, FRCPC, and John M. Graybeal *Anesth Analg* 1995;81:806-10.

17. Kerr ME, Zempsky J, Sereika S, Orndoff P, Rudy EB, “Relationship between arterial carbon dioxide and end-tidal carbon dioxide in mechanically ventilated adults with severe head trauma.” Crit Care Med. 1996 May; 24(5):785-90.
18. Fauzia Khan, Mueenullah Khan, Shemila Abbasi, Department of Anaesthesia, Aga Khan University, Karachi, studied “Arterial to End-Tidal Carbon Dioxide Difference in Neurosurgical Patients undergoing Craniotomy: A Review of Practice”. JPMA 57;446:2007.
19. Husaini J , Y C Choy, “End-tidal to arterial carbon dioxide partial pressure difference during craniotomy in anaesthetised patients.” Med J Malaysia , 2008 Dec;63(5):384-7.
20. Lee SW, Hong YS, Han C, Kim SJ, Moon SW, Shin JH, Baek KJ, “Concordance of end-tidal carbon dioxide and arterial carbon dioxide in severe traumatic brain injury.” J Trauma 2009 Sep;67(3):526-30.