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Original Research Article

Evaluation of Effect of End Tidal Carbondioxide (Etco2) Monitoring on Patient's Safety during Propofol and Fentanyl Based Sedation for Short Surgical Procedures Compared to Standard Monitoring- An Observational Study

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Abstract:

Background: Currently, day care procedures are more frequently performed under procedural anaesthesia. It helps patient to tolerate unpleasant or painful procedures, avoiding intraoperative awareness. Compared to general anaesthesia, PSA may be linked with an even higher incidence of major sedation-related adverse events. Frequent monitoring is advised because sedation-induced depression of the central nervous system may compromise respiratory function. Even with low breathing frequencies, oxygen saturation is commonly maintained, and respiratory depression, hypoventilation, and apnoeic episodes are usually missed by pulse oximetry. With the aid of non-invasive EtCO2 monitoring, CO2 retention and hypoventilation can be identified early and appropriate action can be taken. However, in many places, EtCO2 monitoring is not a standard procedure during PS [2,3]. Hence, we have focused to evaluate the effect of EtCO2 on patients' safety in terms of CO2 retention and apnoeic events in propofol and fentanyl-based sedation for short surgical procedures as compared to standard monitoring.

Objective: To evaluate whether EtCO2 monitoring decreases the incidences of CO2 retention and apnoeic events in propofol and fentanyl-based sedation in short surgical procedures as compared to standard monitoring.

Methods: 80 patients between 18-65 years age of either gender with ASA status I and II posted electively for short surgical procedure and receiving total intravenous anaesthesia using propofol and fentanyl were selected. The patients were randomly divided into two groups. Group A: Patients monitored with end tidal CO2 in addition to standard monitoring. Group B: Patients monitored with standard monitoring. All patients were administered drugs according to the standard protocol. Baseline vitals were noted and ABG was done. Thereafter vitals were recorded at 5 min interval till 30 min and ABG at 15 min and end of the procedure.

Results:

CO2 retention occurred significantly less often in the EtCO2 monitoring group. In the standard monitoring group, the mean PaCO2 was more than 45mmHg and the pH was less than 7.35 at 15 min after induction of anaesthesia and at the end of the procedure. Both values were within the normal range in the EtCO2 monitoring group. The number of airway interventions performed was significantly higher in the EtCO2 monitoring group. Apnoea occurred less often in the EtCO2 monitoring group and recovery time was shorter.

Conclusion: The addition of EtCO2 monitoring to standard monitoring during propofol-based sedation can improve patient safety by decreasing the incidence of CO2 retention, and therefore the risk of hypoxaemia through early recognition of apnoea, and can also shorten recovery time.

Keywords: EtCO2, standard monitoring, propofol, fentanyl, short surgical procedure.

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Introduction

Procedural sedation (PS) refers to techniques, medications, and maneuvers performed to help a patient tolerate unpleasant or painful procedures, avoiding potential unwanted memories associated with such procedures.[1] Because the proper use of PS also aims to decrease the patient's perception of pain and is generally obtained through the administration of analgesics combined to a sedative, PS can also serve as procedural sedation analgesia (PSA).[2] Furthermore, PS also increases the like-

lihood of a successful procedure while decreasing the time required to perform it. Additionally, PS increases safety for the patient and personnel attending the patient.[3] According to the American College of Emergency Physicians (ACEP), PS is a 'technique of administering sedatives or dissociative agents with or without analgesics to induce a state that allows the patient to tolerate unpleasant procedures while maintaining cardiorespiratory function'.(4) The most common procedures associated with its use include orthopedic manipulations, dental procedures, colonoscopies, abscess incision and drainage, and wound debridement.[5]

PS is generally considered to include the stages of moderate and deep sedation of the continuum of anesthesia.[6] However, PSA is still associated with at the least the same or potentially even greater risk of serious sedation-related adverse events compared with general anesthesia.[7] Due to the potential that respiratory function may become impaired as a result of sedation-induced depression of the central nervous system, frequent monitoring is recommended.[6,8] Respiratory function is usually evaluated by observation of qualitative clinical signs (respiratory rate, depth and effort) and oxygen saturation monitoring.[8]

Capnography is a respiratory monitoring device that has become an accepted standard of care for PSA in many circumstances. For example, the American Society of Anesthesiology (ASA) standards for Basic Anesthetic Monitoring require the use of capnography for both moderate and deep sedation. In the UK, the Academy of Medical Royal Colleges Standards and Guidance for Safe Sedation Practice for Healthcare Procedures also include capnography as a developmental standard for patients receiving sedation where it has not already been implemented into practice.[8,9]

In 2011, the ASA recommended capnography monitoring during moderate and deep sedation based on a consensus document initiated by ASA Committee on Standards and Practice Parameters.[10] In contrast, the 2018 American Society for Gastrointestinal Endoscopy guideline for sedation and anesthesia states that "integrating capnography into patient monitoring protocols for endoscopic procedures with moderate sedation has not been shown to improve patient safety" but recommends considering capnography for deep sedation.[11]

Although oxygen saturation is routinely monitored, detection of hypoventilation may be delayed. Oxygen saturation is frequently maintained, even at a low breathing frequency, and pulse oximetry alone often fails to detect respiratory depression, hypoventilation, and apneic episodes, particularly when the patient receives supplemental oxygen. There is growing interest in the use of exhaled CO_2 to monitor respiratory status.[12] Noninvasive real-time CO_2 measurement like end-tidal carbon dioxide ($EtCO_2$) partial pressure can provide an early warning of impending hypoxemia and the need for prompt intervention.[13]

The ideal agent for PS should provide anxiolysis, analgesia and amnesia in a rapid, predictable manner, with minimal side effects, and should have a quick recovery phase.[14] PSA is usually the result of combining propofol or a short-acting benzodiazepine such as midazolam (sedative, amnestic, and anxiolytic properties but not analgesic effects) with an opioid (e.g., fentanyl), alone or in combination.[15] Propofol's pharmacodynamic profile including a rapid onset, rapid recovery time, and lack of active metabolites has accounted for its popularity in the arena of PS.[3,15] Reports regarding the use of propofol for PS in spontaneously breathing patients demonstrate a high incidence of respiratory adverse effects including hypoventilation, upper airway obstruction, apnea.[16] Opioids like fentanyl are equally capable of leading to respiratory depression when administered in equipotent doses. Opioids in combination with these agents have a synergistic effect on respiratory function, thereby significantly increasing the risk of hypoventilation, desaturation events, and apnea. [17,18] Noninvasive $EtCO_2$ monitoring helps to detect CO_2 retention, hypoventilation to take early necessary precautions. However, $EtCO_2$ monitoring is not currently standard practice during PSA in many areas, and there are no consistent results in the existing literature on $EtCO_2$monitoring for sedated patients.[2,3] Hence we have focused to evaluate the effect of $EtCO_2$ on patients safety in terms of CO_2 retention and apneic events in propofol and fentanyl based sedation for short surgical procedures as compared to standard monitoring

Material and Method

The study was performed in the Department of Anesthesiology, MGIMS, Sewagram, Maharashtra after approval of Institutional Ethical Committee. This was a prospective, randomized, open-label, observational study. The study was performed over a period of 2 years i.e., from December 2020 to October 2022. 80 patients between 18-65 years age of either gender with ASA status I and II posted electively for short surgical procedure and receiving total intravenous anaesthesia using propofol and fentanyl were selected. Patients who refused to sign informed consent form or with ASA class III and above, BMI >35 kg/m2, having any respiratory disorders, COPD, Asthma, or allergic to opioid or propofol, or having predicted difficult airway were excluded.

Also, pregnant, and breastfeeding females, chronic smokers and alcoholics were excluded. Patients were randomly and equally divided into two groups. Group A(n=40) Patients monitored with

end tidal CO2 + standard monitoring. Group B(n=40) Patients monitored with standard monitoring. A sealed envelope technique was used for randomization.

Characteristics studied included demographic characteristics such as age, gender, height, body weight, and body mass index (BMI), clinical characteristics included ASA physical status, modified Mallampati score, and vitals [heart rate (HR), systolic blood pressure (BP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP), oxygen saturation (SpO2), and respiratory rate (RR)] and end tidal carbon dioxide (EtCO2) was assessed in Group A. Perioperative characteristics included arterial blood gas analysis [ABG, partial pressure of carbon dioxide (PaCO2) and pH], PaCO2 retention, desaturation, apnoea, airway intervention, hypotension, bradycardia, and recovery time.

Patients who gave consent for the study were explained the study procedure in their native language. Pre-anaesthetic evaluation was done as per PAC protocol one day prior to surgery. Thorough systemic examination was performed. Basic preoperative laboratory investigations, including complete blood count, urine analysis, blood sugar, serum electrolytes, serum creatinine, ECG, and chest X-ray (as appropriate), were performed.

All patients were given tablet Alprazolam 0.5 mg orally on the night before the procedure and were kept fasting for 8 hours prior to surgery. Patients were wheeled into the operation theatre on the day of procedure. All standard ASA monitors like ECG, non-invasive blood pressure, and SpO2 were attached. In Group A, EtCO2 measuring cannula was also attached. EtCO2 monitoring was performed using a combined nasal cannula, one side of which was used to sample CO2 for measurement of EtCO2, whereas the other delivered low flow oxygen (3lt/min).

This cannula was designed to sample expired breath from the nasal prongs for continuous measurement of CO2 during oxygen delivery.(12) Baseline parameters was recorded as T0. Intravenous access was secured with 20 G IV cannula and started Ringer's lactate at 150ml / hour. Arterial line with 20G arterial switch cannula was secured after performing modified Allen's test and baseline ABG sample was sent.

In both the groups, all patients were premedicated with Inj. Glycopyrrolate 0.2 mg IV, Inj. Midazolam 1 mg IV, and Inj. Ondansetron 4 mg IV. After 5 mins, sedation was started with fentanyl 1 microgram/kg and propofol 1.5 milligram/kg. After that regular top-up was given as required. HR, BP, SpO2, and RR were observed at 5, 10, 15, 20, 25, 30 min and at the end of the procedure as T5, T10, T15, T20, T25, T30, and Tend respectively. ABG was done at 15 min and at end of the procedure. In Group A, EtCO2 was recorded at 5,10,15, 20, 25, 30 min and at the end of the procedure.

Patients were continuously monitored for respiratory movements throughout the procedure. If at any time apnoea is seen or CO2 retention is observed, the time interval was recorded and immediate O2 supplement respiration was started. For patients in apnoea, bag and mask ventilation was done with 100% oxygen and recovery time to spontaneous respiration was recorded.

Any sign of hypoventilation, apnoea, or oxygen desaturation (SpO2< 95%) prompted intervention for assisted ventilation, which consisted of changing the head position in case of obstruction, withholding medication, a chin lift or jaw thrust manoeuvre, and insertion of a nasopharyngeal tube.

We defined certain criteria for our study. Capnography criterion for apnoea was considered as absence of an EtCO2 waveform for 10 s. Hypoventilation on the capnograph was defined as High EtCO2 >50%,(19,20) bradypnea (respiratory rate <8 bpm) or tachypnoea (respiratory rate >30 bpm).(12) Desaturation was considered to be SpO2 < 90%.

Sedation-related adverse events like HR <50 bpm and SBP <80 mmHg after administration of sedation. In the event of bradycardia, atropine 1mg was injected intravenously. Ephedrine 6 to 12 mg or phenylephrine 50µg was administered in patients who developed hypotension. (12) Recovery time was considered to be the interval between the last dose of propofol and patient's eye opening after the procedure.

Sample Size Calculation

Sample size has been estimated to be 80 participants using Open Epi software with following assumptions:

Confidence Interval (2- sided): 95%

Power: 90%

Group A (n=40)

Group B (n=40)

Using the formula:

$$n_1 = \frac{(Z_{\alpha/2} + Z_{1-\beta})^2 \bar{p}\bar{q}(r+1)}{r(p_1 - p_2)^2}$$

Sample size was calculated to be 70, we rounded it to a total sample size of 80 with 10% attrition.

Statistical Analyses

Data was collected and graphics were designed by Microsoft Office Excel 2019. The data was analysed with SPSS (IBM, Armonk, NY, USA) version 23.0 for windows. The categorical and continuous variables are represented as frequency

(percentage) and mean (standard deviation, SD), respectively. The association between categorical and continuous variables was assessed with Chi-square and independent sample t-test, respectively.

A two-tailed probability value of < 0.05 was considered as statistically significant.

Results:

The demographic profile of the patients in terms of age, body weight, and male: female ratio, ASA status, Mallampati Class were comparable and no significant differences found among the three groups (P > 0.05). (Table 1)

Table 1: Comparison of demographic data between 2 groups

Parameters	Group A (n=40)	Group B (n=40)	p- value
Age (years)	38.23±12.13	39.78±6.91	0.485
Gender(m/f)	8/32	11/29	0.431
BMI (Body Mass Index)	22.37±1.91	22.93±1.69	0.169
ASA grade (I/II)	34/6	37/3	0.288
MPC grade(I/II)	8/32	12/28	0.302

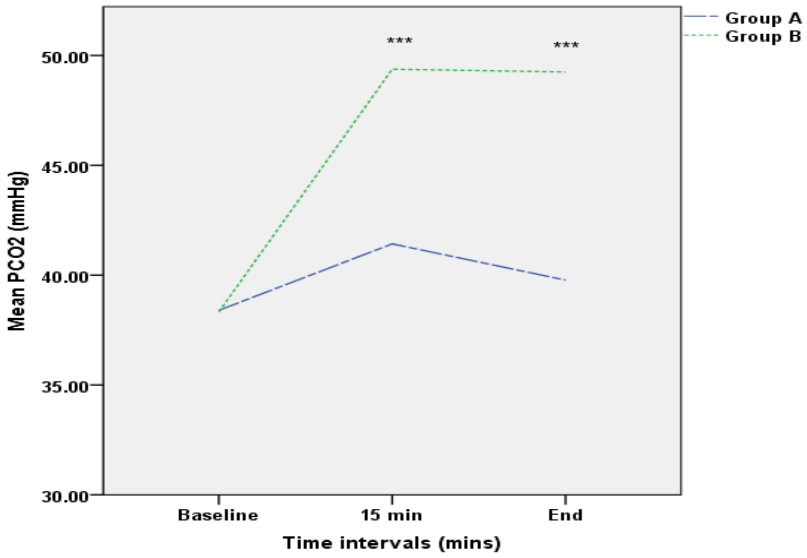

Figure 1. Comparison of partial pressure of carbon dioxide

Table 13 and Figure 13 depict the comparison of $PaCO_2$. On analysis, the groups did not differ at baseline (p-value = 0.886). However, mean $PaCO_2$ was significantly greater in Group B than Group A at 15 minutes and at the end of the study (both p-values < 0.0001).

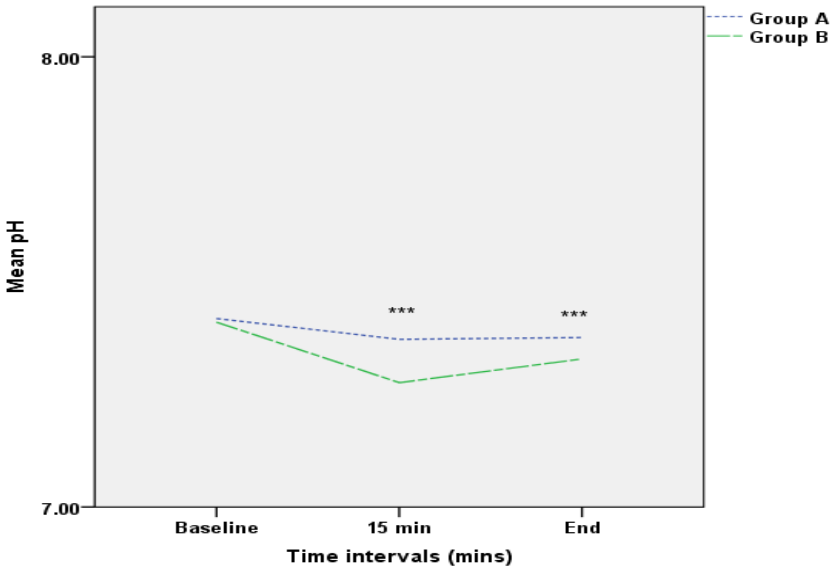

Figure 2: Comparison of pH

Table 14 and Figure 14 depict the comparison of pH. On analysis, the groups did not differ at baseline (p-value = 0.888). However, mean pH was significantly higher in Group A than Group B at 15 minutes and at the end of the study (both p-values < 0.0001).

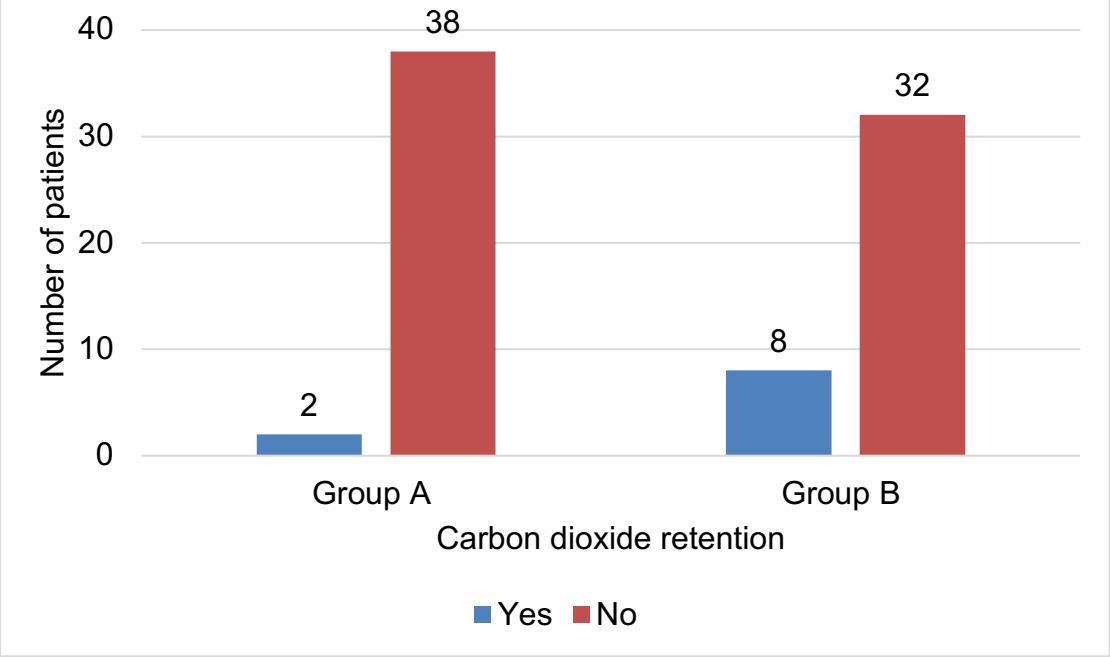

Figure 3: Comparison of patients with carbon dioxide retention

CO2 retention was observed in 2 subjects in group A whereas it was observed in 8 subjects in group B. On analysis, statistically significant greater proportion of patients in Group B than Group A had CO2 retention (p-value = 0.043).

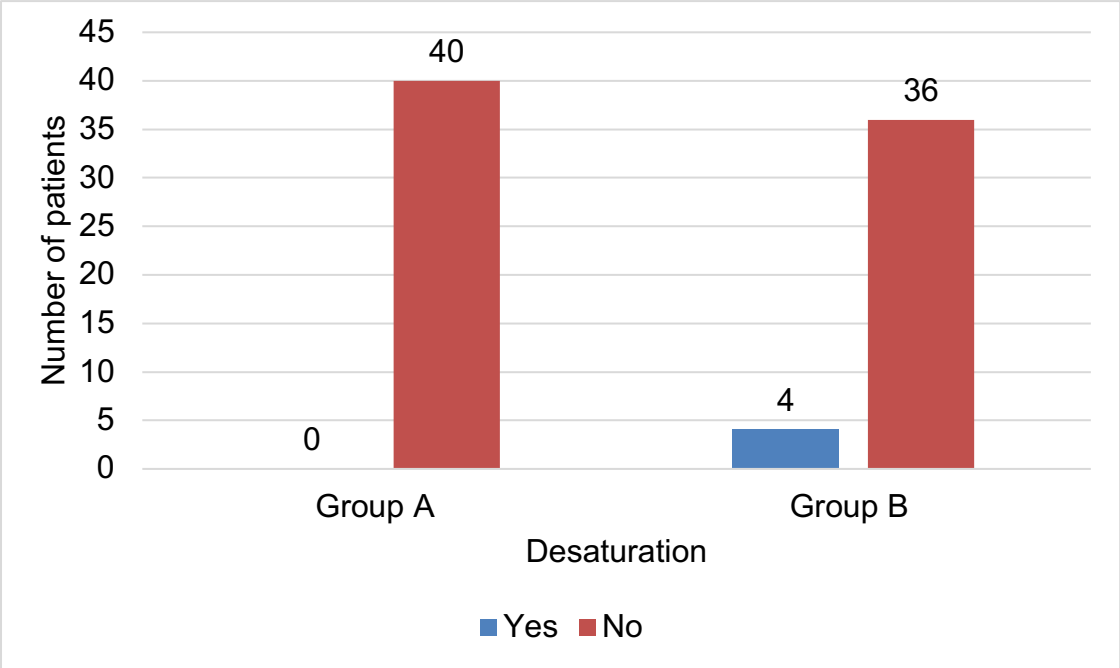

Figure 4: Comparison of patients with desaturation

In group A no subject suffered desaturation whereas desaturation occurred in 4 subjects in group B. On analysis, statistically significant greater proportion of patients in Group B than Group A had desaturation (p-value = 0.040).

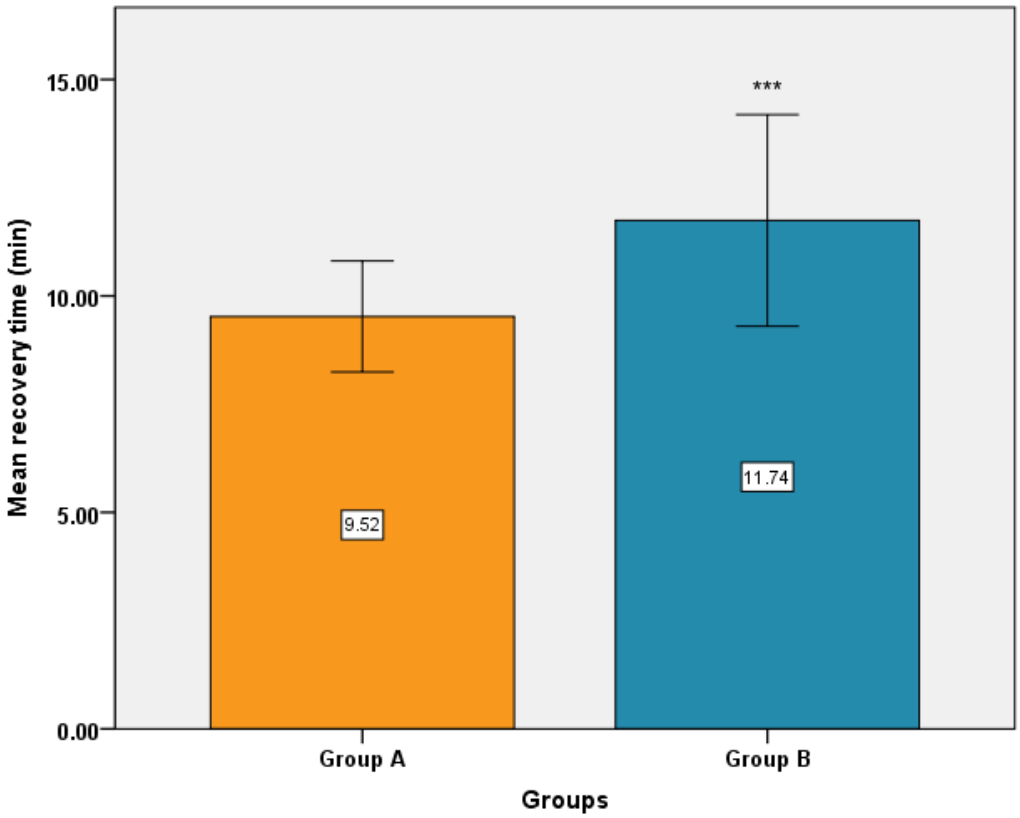

Figure 5: Comparison of recovery time

The average recovery time in group A was 9.52 ± 0.64 whereas in group B was 11.74 ± 1.22. On analysis, mean recovery time was significantly lower in Group A than Group B (p-value < 0.0001)

Discussion

Procedural sedation and analgesia (PSA) is required for relieving the anxiety and calming of patients during a wide variety of medical procedures. [21] The present study was conducted to evaluate the effect of EtCO2 on patient's safety in terms of CO2 retention and apneic events in propofol and fentanyl based sedation for short surgical procedures as compared to standard monitoring.

In present study, we contrasted oxygen saturation amongst both groups at various time intervals. On analysis, the groups differed in mean oxygen saturation at time intervals of T10 to Tend (p-values < 0.05). Barnett et al., found that capnographic group had a slightly higher prevalence of identified desaturation (5 vs. 2.4%, p-value =0.04) compared with the standard monitoring group. [22] Klare et al., Friedrich-Rust et al., estimated baseline mean values of heart rate, systolic blood pressure and oxygen saturation in their study. According to them, all parameters were comparable at all the intervals. (All p-values > 0.05).[23,24] In present study, we appraised pH amongst both groups at various time intervals. On analysis, mean pH was significantly lower in group B than group A at 15 minutes and at the end of the study (both p-values < 0.0001). Similarly, Li et al., found that the pH was below 7.35 at 5 10, 20 and 30 min after starting sedation and at the end of the procedure in the standard monitoring group but within the normal range in the EtCO2 monitoring group. [12] This can be attributed to the high incidence of CO2 retention in patients who underwent standard monitoring. Inadvertent over sedation sometimes causes respiratory depression and oxygen desaturation, although sedation is necessary and recommended for short surgical procedures.[25] It is known that the SpO2 decline could be delayed by 45–60 seconds after an apnea episode.[26] Hence, the capnographic monitoring allows for the earlier detection of apnea episodes in patients undergoing short surgical procedures under fentanyl and propofol sedation, more real measurement values of carbon dioxide than pulse oximetry.[27]

In present study, EtCO2 was monitored only in group A. During the study, mean EtCO2 ranged from 34.65 ± 1.98 at baseline to 39.25 ± 3.27 at the end of the study with maximum mean value seen at T10 (45.50 ± 3.35). Similarly, mean PaCO2 was maximum at 15 minutes in group A (41.43 ± 2.04 mmHg) and group B (49.38 ± 3.15 mmHg) while it was minimum at baseline in both, group A (38.40 ± 2.24 mmHg) and group B (38.33 ± 2.43 mmHg). However, mean PaCO2 had statistically significant difference amongst both groups at 15 minutes and

at the end of the study (both p-values < 0.0001). EtCO2 monitoring has been shown to be the earliest indicator of airway compromise. In a study by Burton et al, abnormal EtCO2 findings were documented in 36 of the 60 patients (60%).[28] Li et al valued that PaCO2 was above 6 kPa at 5 10, 20 and 30 min after starting sedation (T2, T3, T4 and T5, respectively) and at the end of the procedure (T6) in the standard monitoring group but within the normal range in the EtCO2 monitoring group.[12] It was observed in the similar study by Li et al that the PaCO2- EtCO2 gradient was 0.62kPa, which was similar to what was observed in a previous study by Kasuya et al.[12,29] Physically, there is a difference of 0.27 to 0.67 kPa between EtCO2 and PaCO2.(30) EtCO2 values will always be lower than PaCO2 when these two parameters are measured simultaneously, as shown by Li et al.[12] Hence, when the value of EtCO2 is high, anesthetists should be more alert to the occurrence of CO retention.[12,30]

Most episodes of adverse events are not detected by visual assessment or pulse oximetry. Although pulse oximetry is the standard of care in respiratory and cardiovascular monitoring for patients undergoing deep sedation, it cannot accurately detect early hypoventilation.[31] EtCO2 monitoring has been shown to be the earliest indicator of airway compromise.[32] We figured out various outcomes like carbon dioxide retention, desaturation, apnea, airway intervention, hypotension, and bradycardia in our study.

In present study, CO2 retention was observed in 2 subjects in group A whereas it was observed in 8 subjects in group B. On analysis, significantly greater proportion of patients in Group B than Group A had CO2 retention (p-value = 0.043). On comparison of patients with desaturation, in group A no subject suffered desaturation whereas desaturation occurred in 4 subjects in group B. On analysis, significantly greater proportion of patients in Group B than Group A had desaturation (p-value = 0.040). Majority cases in both the groups had no occurrence of any events like apnea (97.5% and 90% respectively), airway intervention (80% and 90% respectively), hypotensive episodes (100% and 97.5% respectively), and bradycardia (97.5% and 95% respectively). Regarding outcomes Campbell et al., valued no difference between the two groups in patients experiencing desaturation, although patients in the capnographic group were more likely than those in the standard monitoring group to require airway repositioning. Also, they couldn't establish any difference in the need for more aggressive airway intervention.[33] According to Klare et al., apnea was detected in 61.1% patients in the capnography arm and in 5.2% patients in the standard arm (p-value < 0.001). Severe hypoxemia was observed less frequently in the capnography arm compared with the standard arm. The incidence of increased oxygen supplementation was lower in the capnography arm compared with controls. There were no differences between incidence rates of bradycardia (p-value = 0.748) and hypotension (p-value = 0.103) between the two groups.[23] Similar to our results, Friedrich-Rust et al., found significant reduction in adverse events in patients undergoing colonoscopy with capnography. They showed a reduction in hypoxemia from 32 to 18% in the capnography group with the use of propofol for sedation.[24] Propofol is a hypnotic agent with different sedation characteristics compared with benzodiazepines or short acting opioids.(15) Propofol has a relatively narrow margin of safety, can rapidly cause apnea, airway obstruction, and hypotension, especially in older or hypovolemic patients, and there is no reversal agent for propofol.(16) In contrast, fentanyl tend to produce more gradual sedation, and, although they can cause apnea, it is less common at lower doses.[17] The properties of fentanyl and the immediate availability of reversal agents make this sedation inherently safe for younger, healthy patients.[18]

According to Li et al, CO2 retention occurred significantly less often in the EtCO2 monitoring group than in the standard monitoring group (10 vs. 87%; p-value < 0.0001). In their study, EtCO2 monitoring significantly decreased the incidence of retention of CO when compared with the standard monitoring method. This suggests that clinical observation and pulse oximetry are inadequate for assessment of ventilation parameters. Further, in the EtCO2 monitoring group, a total incidence of approximately 10 events within 30 min needing respiratory interventions was observed, whereas only approximately two respiratory interventions were required in the standard monitoring group. Hence, there were significantly more airway interventions and fewer episodes of apnea in the EtCO2 monitoring group, indicating that EtCO2 monitoring allowed earlier detection of hypoventilation.[12] This strongly supports the statement that early detection of apnea by means of capnography followed by immediate intervention to restore ventilation can prevent hypoxemia and reduce the incidence of Co2 retention.[25]

Barnett et al., appraised modestly significantly increased risk of O2 desaturation in the EtCO2 group (5.0 vs. 2.4%, p-value=0.04), overall sedation events (oxygen desaturation requiring intervention, procedure interruption due to hemodynamic or respiratory instability, problematic changes in blood pressure or hear rate) were similar in both groups. There were no cases of reversal agent usage or hospitalization for sedation-related issues in either cohort in their study.[22] An incidence of 33.3% for oxygen desaturation was evident in Deitch et al., while it was 9.1% in study by Langhan et

al.[34,35] In our study mean recovery time was 9.52 ± 0.64 minutes in group A and 11.74 ± 1.22 minutes in group B. On analysis, there was statistically significant difference between group B and group A (p-value < 0.0001). The recovery time was shorter when capnography was used (9.9 ± 1.4 vs. 11.4 ± 2.1 min; p-value = 0.048) in study by Li et al. Use of EtCo2 monitoring also shortened the recovery time, which may be attributed to the decreased incidence of Co2 retention.[12]

Conclusion

From this study we conclude that:

- There were more incidences of CO2 retention, apneic event in group B where the EtCO2 monitoring was not done as compared to group A with EtCO2 monitoring along with standard monitoring was done.
- The events like hypoventilation were early detectable in the group with EtCO2 monitoring and actions were taken as early as possible to restore the ventilation. Hence, the number of airway interventions such as chin lift, head tilt was more in this group.
- ABG analysis showed PaCO2 on higher side and pH on lower side in group without EtCO2 monitoring, indicating CO2 retention as compared to group with EtCO2 monitoring.
- The frequency of apnea was more in group without EtCO2 monitoring as compared to group with EtCO2 monitoring.
- The time required for the patients in the group with EtCO2 monitoring for recovery was less as compared to the patient in the group without EtCO2 monitoring.

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