

# Effects of Sedation and/or Sedation/Analgesic Drugs Administered during Central Venous Catheterization on the Level of End-tidal Carbon Dioxide Measured by Nasal Cannula in Our PICU

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## ABSTRACT

**Aims and objectives:** Sedatives and analgesics are commonly used in pediatric intensive care units during minor invasive procedures. Here, we aimed to measure the changes in end-tidal carbon dioxide (EtCO<sub>2</sub>) levels with different sedation/analgesic drug administrations (midazolam, ketamine, midazolam + ketamine/fentanyl) during central venous catheterization.

**Materials and methods:** This prospective study included 44 patients who needed sedation/analgesia for central venous catheterization. Patients were sedated with midazolam, ketamine, or midazolam + fentanyl/ketamine. End-tidal carbon dioxide values were measured before and after sedation–analgesia with nasal cannula and recorded from the capnograph. Oxygen saturation (SO<sub>2</sub>) was monitored by pulse oximetry. Whether respiratory depression occurred during the process was recorded.

**Results:** During the procedure, 15 (34%) patients were given 0.1 mg/kg dose of midazolam described as group I, 18 (41%) patients were given 1 mg/kg dose of ketamine only described as group II, and 11 (25%) patients who could not be effectively sedated with a single sedative–analgesic agent were given either 1 mg/kg dose of ketamine or 2 µg/kg dose of fentanyl together with 0.1 mg/kg dose of midazolam described as group III. According to our findings, hypoxia (54.5%) and hypercarbia (45.5%) were detected higher in group III but it was not statistically significant ( $p = 0.255$ ,  $p = 0.364$ ). Hypercarbia was detected in 29.5% patients, in 62% of these patients hypercarbia was accompanied by hypoxia, and 38% had only hypercarbia. When pre-sedation and post-sedation EtCO<sub>2</sub> values were compared, we detected a statistically significant difference in all groups.

**Conclusion:** We detected hypercarbia unaccompanied by hypoxemia in 38% patients. And we think that we have identified these patients early due to measurement of EtCO<sub>2</sub> by nasal cannula. This study demonstrated that EtCO<sub>2</sub> monitoring via nasal cannula is a feasible and practical way to follow ventilation during sedation/analgesia.

**Keywords:** Analgesia, Capnography, End-tidal carbon dioxide, Pediatric intensive care, Sedation.

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## INTRODUCTION

Sedatives and analgesics are commonly used in pediatric patients during minor invasive procedures to reduce pain and anxiety and provide ease of process.<sup>1</sup> All sedatives–analgesics have significant side effects, such as respiratory depression, bradycardia, and hypotension.<sup>2</sup> Monitoring of patients who were given sedatives–analgesics is critical both during and after the procedure.<sup>3</sup> Standard monitoring is performed with a pulse oximeter.<sup>4</sup> Capnography is the process of measuring carbon dioxide (CO<sub>2</sub>) partial pressure in the airway during respiration. End-tidal carbon dioxide (EtCO<sub>2</sub>) is the maximum value obtained at the end expiration. Capnograph is the device that shows CO<sub>2</sub> value against time or volume in graph.<sup>5</sup> Utilization of capnography has been increasing recently in many fields, particularly in procedural sedation analgesia in the emergency departments and pediatric intensive care units (PICU), and also in the evaluation of cardiopulmonary resuscitation events and ventilation monitoring in unconscious patients.<sup>6</sup> Two different types of measurements, namely mainstream and sidestream, are made with capnographs. In mainstream measurement method, a sensor is placed on the patient's airway and measurements are made directly; it is used commonly for the verification of intubation in intubated patients and for ventilation monitoring. In the sidestream measurement method, breath sample is taken

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from the respiration air with nasal cannula and measurement is made indirectly. Carbon dioxide measurement can be easily made with a nasal cannula when the patient is not intubated and breathing frequency and depth of the patient can be continuously monitored.<sup>7</sup> Decrease in breathing pattern or increase in EtCO<sub>2</sub> amount in the capnogram is interpreted as respiratory depression.<sup>8</sup>

It has been reported in previous studies that capnography is a tool that can be used safely in monitoring of the sedation–analgesia related side effects.<sup>1,3–5</sup>

The purpose of our study was to determine the effects of sedation–analgesia drugs administered during central venous catheterization performed in our tertiary care PICU on the EtCO<sub>2</sub> levels measured by nasal cannula and to determine the risk of inducing respiratory depression of different sedation–analgesia applications.

## MATERIALS AND METHODS

Forty-four pediatric patients who were inserted central venous catheter and were administered sedation–analgesia, meanwhile in the PICU of Cukurova University Faculty of Medicine, between June 2018 and September 2018 were prospectively included in the study. Patients with severe systemic diseases, pulmonary, liver, or renal failure and patients with a history of allergic reaction to sedative–analgesics were excluded from the study. End-tidal carbon dioxide values were measured before and after sedation–analgesia with nasal cannula (Oridion, Capnostream) and were recorded from the capnograph. Patient oxygen saturation (SO<sub>2</sub>) was monitored by pulse oximetry. Whether respiratory depression occurred during the process was recorded. Respiratory depression was defined in two ways as hypercarbia and hypoxia. Hypercarbia was regarded as >10 mm Hg increase in the postsedation EtCO<sub>2</sub> level compared to pre sedation EtCO<sub>2</sub> level.<sup>9</sup> Hypoxia was considered as SO<sub>2</sub> being <92%.<sup>10</sup> Patients were sedated with midazolam (0.1 mg/kg dose) or ketamine (1 mg/kg) or midazolam + fentanyl (2 µg/kg) or ketamine (1 mg/kg). Central venous catheterization performed by pediatric intensive care fellows. Sedative–analgesia application changed to the clinical approach and experience of the fellow who inserted central venous catheter. The nasal cannula was well tolerated in all patients. The study was performed in accordance with the 1964 Declaration of Helsinki ethical criteria and was approved by Cukurova University School of Medicine, Clinical Study Ethics Committee. Written informed consent was obtained from the families of patients.

### Statistical Analysis

IBM SPSS Statistics version 20.0 package program was used in the statistical analysis. Categorical measurements were summarized in numbers and percentages, whereas numerical measurements were summarized as mean and standard deviation (median and minimum–maximum where necessary). Chi-square test statistic was used in the comparison of categorical measurements between the groups. Mann–Whitney U test was used while comparing numerical measurements with non-normal distribution between two groups. Statistical significance level was determined as 0.05 in all tests.

## RESULTS

A total of 44 patients were included in the study, and their mean age was 6.3 ± 5.4 years. Twenty-three (52%) of the patients were female. For the entire group, pre sedation EtCO<sub>2</sub> was 30.11 ± 5.75 mm Hg, and postsedation EtCO<sub>2</sub> was 35.55 ± 7.33 mm Hg. During the procedure, 15 (34%) patients were given 0.1 mg/kg dose of midazolam described as group I, 18 (41%) patients were given 1 mg/kg dose of ketamine only described as group II, and 11 (25%) patients who could not be effectively sedated with a single sedative–analgesic agent were given either 1 mg/kg dose of ketamine or

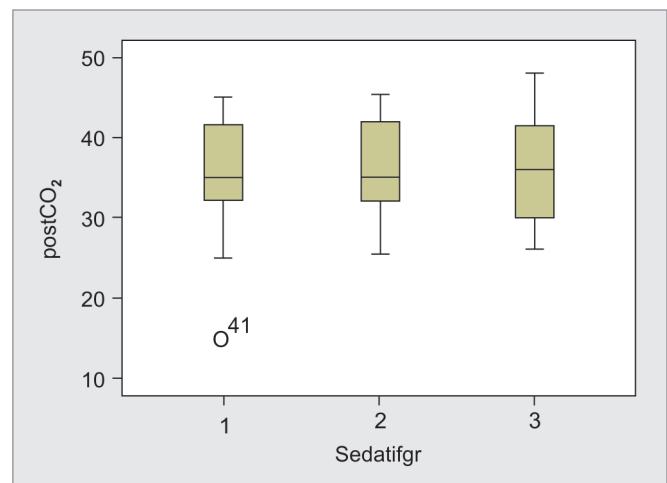
1 kg dose of fentanyl together with 0.1 mg/kg dose of midazolam described as group III. There was no significant difference between the three groups in terms of age, gender, body weight, pre sedation the EtCO<sub>2</sub>, and postsedation EtCO<sub>2</sub> values (Table 1). According to our findings, hypoxia (54.5%) and hypercarbia (45.5%) were detected higher in group III but it was not statistically significant ( $p = 0.255$ ,  $p = 0.364$ ). Hypercarbia was detected in 13 (29.5%) patients, in 8 (62%) of these patients hypercarbia was accompanied by hypoxia, and 5 (38%) had only hypercarbia. Postsedation EtCO<sub>2</sub> was 35 ± 8.1 mm Hg in group I, 35.8 ± 7.1 mm Hg in group II, and 35.7 ± 7.1 mm Hg in group III (Fig. 1). When pre sedation and postsedation EtCO<sub>2</sub> values were compared, a statistically significant difference was detected in all three groups and  $p$  values in each group were, respectively,  $p = 0.024$ ,  $p < 0.001$ , and  $p = 0.003$  (Fig. 2). A severe decrease in postsedation EtCO<sub>2</sub> levels was seen only in one patient in the midazolam group and the same patient was given tactile stimulation due to apnea development. None of the patients needed bag valve mask ventilation or intubation.

## DISCUSSION

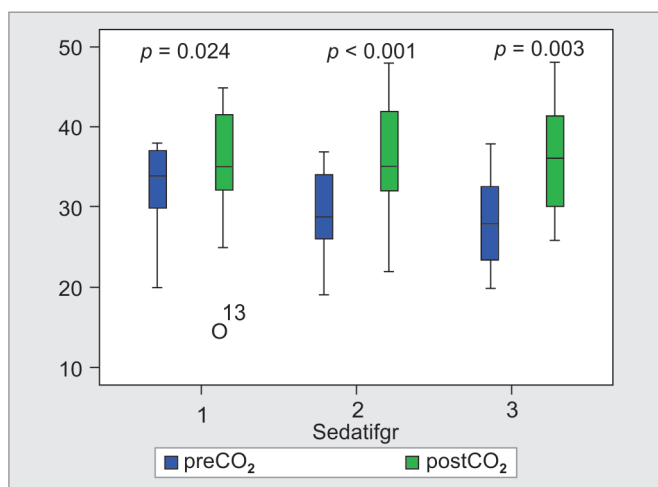
Capnometry is a routinely used noninvasive assessment technique that allows for the rapid and efficient monitoring of ventilation, circulation, and metabolism.<sup>11</sup> Sedation–analgesia is widely used during minor procedures which monitoring is crucial. American Academy of Pediatrics recommends the standard practice of monitoring EtCO<sub>2</sub> levels with capnography during deep sedation.<sup>12</sup>

**Table 1:** Comparison of pre sedation and postsedation EtCO<sub>2</sub> values and demographic characteristics of the groups

	Group I mean ± SD	Group II mean ± SD	Group III mean ± SD	<i>p</i> value
Age (years)	7.19 ± 5.59	6.45 ± 5.19	4.9 ± 5.78	0.54
Body weight (kg)	23.86 ± 18.13	20.36 ± 14.72	19.54 ± 18.95	0.61
Pre sedation EtCO <sub>2</sub> (mm Hg)	32.67 ± 5.3	29 ± 5.57	28.45 ± 6.12	0.07
Postsedation EtCO <sub>2</sub> (mm Hg)	35.07 ± 8.17	35.83 ± 7.14	35.73 ± 7.11	0.98



**Fig. 1:** Postsedation EtCO<sub>2</sub> values of the groups



**Fig. 2:** Comparison of presedation and postsedation EtCO<sub>2</sub> values for each group

Many studies have demonstrated that capnography is a reliable indicator and a useful diagnostic tool in identifying respiratory depression induced by sedation–analgesia.<sup>1,13</sup> Compared to the use of pulse oximetry, capnography identifies respiratory depression in the earlier period.<sup>12</sup> As we know, hypoxia is a relatively late finding compared to hypercarbia in respiratory depression.<sup>14</sup> Oxygen saturation can be measured within the normal range for several minutes even when respiratory depression occurs in patients who are receiving oxygen.<sup>14,15</sup> With capnograph, hypercarbia can be detected before hypoxia and it allows performing necessary interventions, such as withdrawing sedation, or giving stimulation to the patient.<sup>16</sup>

Langhan et al.<sup>17</sup> in their study in which they used nasal capnography monitoring during the invasive procedures which required sedation–analgesia in the pediatric emergency department have suggested that capnography is a superior means of detecting all kinds of hypoventilation. In the United States, noninvasive capnography monitoring was used in children receiving sedation–analgesia during 174 endoscopies carried out on 163 pediatric patients and it was suggested that capnography detected alveolar hypoventilation in the early periods in sedations administered during invasive procedures and that it was effective in early detection and prevention of hypoxemia.<sup>18</sup> In a neonatal study reported from Israel, nasal EtCO<sub>2</sub> were measured in 20 preterm, and 39 term infants in the prone and supine positions and it was demonstrated that measurements can be made in both positions and the measurements are consistent with each other.<sup>19</sup> In another study from Taiwan, 34 newborns followed up for respiratory distress were monitored with nasal capnography and a significant correlation between EtCO<sub>2</sub> and partial CO<sub>2</sub> in arterial blood gases was reported and the importance of the method was emphasized.<sup>20</sup> In the study by Flanagan and Tobias,<sup>21</sup> EtCO<sub>2</sub> measurements were made with nasal cannula in spontaneous breathing and it was determined that hypoventilation was characterized by an increase in the EtCO<sub>2</sub> levels. They reported that hypoxia was a later finding in the respiratory depression compared to hypercarbia. Yildizdas et al.<sup>22</sup> have detected hypoxia and hypercarbia in 3.2% of the patients, while hypercarbia was detected in 16.6% of the patients. According to this result, they emphasized the use of capnography during sedation–analgesia by saying that they could have identified

respiratory depression in only 4 of these 21 patients if they had been using only pulse oximetry monitoring. In our study, we detected hypercarbia unaccompanied by hypoxemia in five (38%) patients. And we think that we would have identified these patients later if we also were using only the pulse oximetry monitoring.

Similar to our study, Hart et al.<sup>23</sup> detected 20% respiratory depression in the fentanyl group, and 23% in the midazolam + fentanyl group. Tobias<sup>24</sup> reported 6% hypoxia in their where they used midazolam + ketamine. McQuillen and Steele<sup>1</sup> divided patients into groups of midazolam, midazolam + ketamine, and midazolam + fentanyl; and they reported the highest increase in the EtCO<sub>2</sub> levels in group III. We divided patients into three groups in our study as midazolam, ketamine, midazolam + ketamine/fentanyl groups, as well. We detected hypoxia and hypercarbia higher in the group III, even though it was statistically insignificant. Statistically significant differences were detected in all three groups when presedation and postsedation EtCO<sub>2</sub> values were compared. A severe decrease in postsedation EtCO<sub>2</sub> levels was seen only in one patient in the midazolam group and the same patient required to be given tactile stimulation due to apnea development. None of our patients required bag valve mask ventilation or intubation.

Reinhold and Graichen<sup>25</sup> did not detect EtCO<sub>2</sub> increase in the group given propofol for magnetic resonance imaging. Hertzog et al.<sup>26</sup> detected respiratory depression at the rate of 30% in the group given propofol during cardioversion. Yildizdas et al.<sup>22</sup> detected increase in EtCO<sub>2</sub> levels and hypoventilation, particularly in the group given propofol and reported that they consider that propofol might not be the first choice for short-term procedures. Based on the results of this study previously performed in our unit, we do not often prefer the use propofol for minor procedures in our clinical practices. Therefore, our study does not have the propofol group.

The main limitation of our study is the low number of patients. Also, the fact that bispectral index monitoring or sedation–analgesia scale measurement was not performed on our patients is another limitation.

In conclusion, we all know the incidence of subclinical respiratory depression in patients undergoing sedation–analgesia is greater than expected. In the present study, we detected hypercarbia unaccompanied by hypoxemia in 38% patients. And we think that we have identified these patients in the early period due to measurement of EtCO<sub>2</sub> by nasal cannula in addition to standard pulse oximetry monitoring. End-tidal carbon dioxide monitoring with nasal cannula is a useful monitoring tool for assessing sedation or sedation–analgesia during ventilation in pediatric patients. While further studies with larger groups of patients are necessary to evaluate the efficacy of capnography, we think that capnography will improve the quality of care of children during sedation and that it is crucial for the early detection of respiratory depression and for the necessary interventions to be made.

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