Doi: 10.5152/TJAR.2019.37108

Original Article

Intensive Care

Turkish Journal of Anaesthesiology & Reanimation

The Effect of Sevoflurane and Dexmedetomidine on Pulmonary Mechanics in ICU Patients

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Cite this article as: Türktan M, Güleç E, Hatipoğlu Z, Ilgınel MT, Özcengiz D. The Effect of Sevoflurane and Dexmedetomidine on Pulmonary Mechanics in ICU Patients. Turk J Anaesthesiol Reanim 2019; 47(3): 206-12.

Abstract

Objective: In intensive care unit (ICU) patients, intravenous (iv) and volatile agents are used for sedation. The aim of the present study was to investigate the effects of dexmedetomidine and sevoflurane on pulmonary mechanics in ICU patients with pulmonary disorders.

Methods: After approval of the ethical committee and informed consent between the ages of 18-65 years were obtained, 30 patients with an American Society of Anesthesiologist status I-III, who were mechanically ventilated, who had pulmonary disorders and who needed sedation were included in the study. Exclusion criteria were severe hepatic, pulmonary and renal failures; pregnancy; convulsion and/or seizure history; haemodynamic instability and no indication for sedation. Patients were divided into two groups by randomised numbers generated by a computer. For sedation, 0.5%-1% sevoflurane (4-10 mL h^{-1}) was used by an Anaesthetic Conserving Device in Group S (n=15), and iv dexmedetomidine infusion (1 μg^{-1} kg^{-1} 10 min^{-1} loading and 0.2-0.7 μg^{-1} kg^{-1} h^{-1} maintenance) was performed in Group D (n=15). Arterial blood gas analysis, airway resistance, positive end-expiratory pressure (PEEP), frequency, tidal volume (TV), peak airway pressure (Ppeak), static pulmonary compliance and end-tidal CO_2 values were recorded at baseline, 1, 3, 6, 9, 12 and 24 h.

Results: Demographic data, airway resistance, PEEP, frequency, TV, Ppeak and static pulmonary compliance values were similar between the groups. $PaCO_2$ and end-tidal CO_2 values were higher in Group S than in Group D. Sedation and patient comfort scores were similar between the two groups.

Conclusion: Both sevoflurane and dexmedetomidine are suitable sedative agents in ICU patients with pulmonary diseases.

Keywords: AnaConDa, dexmedetomidine, sedation, sevoflurane

Introduction

In intensive care unit (ICU) patients, sedation can be applied to facilitate invasive procedures, increase patient comfort and reduce anxiety (1). Intravenous (iv) agents (e.g. propofol, benzodiazepine, remifentanil and dexmedetomidine) are commonly used for sedation in mechanically ventilated patients in the ICUs (2). Dexmedetomidine is generally preferred due to its minimal respiratory depression and analgesic properties.

Volatile anaesthetics are alternatives to iv drugs for sedation of ventilator-dependent patients, and they were applied via the Anaesthetic Conserving Device (AnaConDa). Sevoflurane may often be preferred as a volatile agent because it provides faster induction, faster recovery, dose-dependent sedation and stable haemodynamics (3-5). In addition, it can be helpful in mechanically ventilated, critically ill patients with pulmonary disease due to its bronchodilator effect (2, 5).

The aim of this pilot study was to investigate the effects of dexmedetomidine and sevoflurane on pulmonary mechanics and sedation in ICU patients with pulmonary disorders. Our hypothesis was that sevoflurane has a better effect on pulmonary mechanics than dexmedetomidine in this population. The primary outcomes were airway resistance and peak airway pressure (P_{peak}), and the secondary outcomes were sedation and patient comfort scores.

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Received: 06.03.2018 Accepted: 23.07.2018

Available Online Date: 18.01.2019

Methods

Study design

This prospective pilot study was performed in our nine-bed reanimation unit in Çukurova University School of Medicine between February 2015 and February 2016.

Patients

Çukurova University Ethical Committee (Date: 19.02.2015, 38/7) approved the study. Informed consent was obtained from the patient or patients' legal representative. Thirty patients between the ages of 18-65 years with an American Society of Anesthesiologist physical status I-III, who were mechanically ventilated, who had pulmonary disorder and who needed short-time sedation (<48 h) were included in the study. Exclusion criteria were severe hepatic, pulmonary and renal failure; pregnancy; convulsion and/or seizure history; hereditary malignant hyperthermia; haemodynamic instability (heart rate <50 beats min^{-1} and mean arterial pressure <60 mm Hg) and no indication for sedation.

Patients were randomly divided into two groups according to a computer-generated random number list. In Group S (n=15), 0.5%-1% sevoflurane (4-10 mL h^{-1}, average 5 mL h^{-1}) was used with an AnaConDa device (Sedana Medical AB, Uppsala, Sweden) for sedation, and iv dexmedetomidine infusion (1 μg^{-1} kg^{-1} 10 min^{-1} loading and 0.2-0.7 μg^{-1} kg^{-1} h^{-1} maintenance) was performed in Group D (n=15). During sedation, blood pressure, pulse oximetry and heart rate monitoring were performed continuously, and arterial blood gas analysis was examined every hour. Airway resistance (cm H_2O L^{-1} s^{-1}), positive end-expiratory pressure (PEEP, cm H_2O), frequency (breaths min^{-1}), tidal volume (TV, mL), P_{peak} (cm H_2O), compliance (mL cm H_2O) and end-tidal CO_2 (mmHg) values were obtained by a Drager Evita 4 ventilator and recorded at baseline, 1, 3, 6, 9, 12 and 24 h of sedation.

Assisted Spontaneous Breathing mode was preferred for patients with sufficient spontaneous ventilation, and Synchronized Intermittent Mandatory Ventilation mode was used in patients without spontaneous ventilation. Ventilation modes and the presence of respiratory depression were recorded. Respiratory depression was defined as 30% reduction of initial respiratory rate and oxygen saturation <90%.

Sedation and patient comfort assessment

Sedation was evaluated using a 7-point Riker Sedation Score (7=dangerous agitation, 6=very agitated, 5=agitated, 4=calm and cooperative, 3=sedated, 2=very sedated and 1=unarousable). Sevoflurane concentration and dexmedetomidine infusion rates were titrated to achieve a Riker sedation scale between 3 and 4. Patient comfort was evaluated as adaptation to mechanical ventilation using a 3-point scale (0=poor, 1=moderate and 2=excellent).

Anaesthetic conserving device

The AnaConDa is a modified heat-moisture exchanger containing a small vaporiser placed between the endotracheal tube and the Y-piece of the ventilator circuit (Figure 1). A syringe pump is needed for this application, and inhalation agents are administered by AnaConDa to the patients. The system has approximately 100 mL dead space, and this feature limits the use of the AnaConDa in paediatric intensive care. In adults, only sevoflurane and isoflurane can be applied via the system due to low vapour pressure. The TV must be at least 300 mL (appropriately 5-6 mL kg^{-1} body weight) to provide an effective inhalation agent concentration. On the other side, the system efficiency decreases in TVs >1000 mL (6). During expiration, 90% of the expired gas was absorbed by the carbon layer and recirculated to the next inspiratory period (7). It is single use for every patient, and the duration of use is 72-96 h.

Statistical analysis

All analyses were performed using the IBM Statistical Package for the Social Sciences Statistics (released 2011, IBM SPSS Statistics for Windows, version 20.0; IBM Corp., Armonk, NY, USA) statistical software package. Categori-

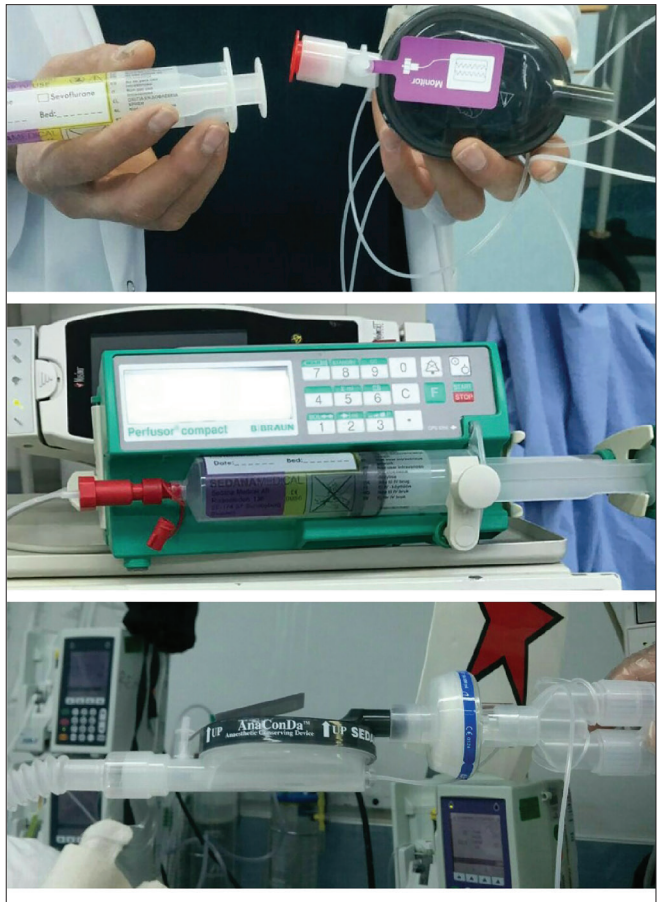

Figure 1. The Anaesthetic Conserving Device (AnaConDa). AnaConDa is a small vaporiser placed between the endotracheal tube and the Y-piece of the ventilatory circuit, and a syringe pump is needed for this application

cal variables were expressed as numbers and percentages, whereas continuous variables were expressed as mean and standard deviation and as median and minimum-maximum, where appropriate. Chi-square test was used for comparison of categorical variables between the groups. The normality of distribution for continuous variables was confirmed using the Kolmogorov-Smirnov test. For comparison of continuous variables between the two groups, the Student's t-test or Mann-Whitney U test was used depending on whether the statistical hypotheses were fulfilled or not. For evaluation of the change in the measurements obtained in the time interval, the Repeated Measurements Analysis was applied. A p value <0.05 was considered as statistically significant.

Results

Thirty patients were included, and all of them completed the study. Demographic data (gender, age, weight and length) and ventilation modes were similar between the groups (Table 1). There were no significant differences between the values of pulmonary mechanics including airway resistance, frequency, TV, P_{peak}, pulmonary compliance and PEEP values (Table 2). $PaCO_2$ and end-tidal CO_2 values were higher in Group S than in Group D (p=0.005, p=0.007, p=0.002, p=0.001, p=0.006, p=0.001 and p=0.001, respectively) (Table 3). The $PaCO_2$ levels gradually increased in the sevoflurane group during the study period (from 47.74±16.72 to 52.10±15.61), whereas it was more stable in the dexmedetomidine group (from 38.17±10.86 to 37.69±7.03). Patient comfort scores were similar between the two groups. Respiratory depression was not observed in both groups.

Discussion

In contrast to previous studies on AnaConDa, our study includes ICU patients with pulmonary disorders (e.g. multiple trauma, rib fracture, pneumothorax, pneumonia and chronic obstructive pulmonary disease (COPD)). As with bronchospasm, pulmonary complications with high airway pressure are more frequent in ICU patients, and our aim was to determine a suitable sedative agent for these patients. We found that sevoflurane and dexmedetomidine were suitable agents for sedation in ICU patients, and sevoflurane was not superior to dexmedetomidine in this patient population.

In the past, volatile anaesthetics, especially halothane, had been suggested for reducing the incidence of bronchospasm

Table 1. Demographic data and ventilation modes of the groups

	Group S (n=15) (mean±SD or no. of patients)	Group D (n=15) (mean±SD or no. of patients)	p
Gender (male/female)	9/6	12/3	0.43
Age (year)	45.73±15.39	47.40±21.93	0.81
Weight (kg)	72.9±14.2	75.6±11.4	0.12
Height (cm)	162.6±5.3	161.7±5.5	0.20
Ventilation mode			
SIMV	12	14	0.68
ASB	3	1	
Admission diagnosis			
Multiple trauma	6	7	
• Rib fractures	4	5	
• Pulmonary contusion	1	3	
• Flail chest	2	3	
• Pneumothorax	2	1	
Pneumonia	2	3	
COPD	7	5	
Comorbidities			
None	5	6	
Hypertension	2	1	
Heart failure	4	3	
Diabetes mellitus	1	0	
Vasculopathy	2	1	
COPD	7	5	

Data are presented as mean±SD or number of patients. Statistical analysis included chi-square test and Student's t-test. SD: standard deviation; COPD: chronic obstructive pulmonary disease

Table 2. Pulmonary mechanics of the groups

	Group S (n=15) (mean±SD)	Group D (n=15) (mean±SD)	p
TV (mL)			
Baseline	461.00±42.22	481.67±36.92	0.16
1 h	472.50±30.29	475.93±45.50	0.84
3 h	448.33±42.32	469.53±43.59	0.37
6 h	461.67±27.86	481.67±36.92	0.24
9 h	472.50±30.29	475.93±45.50	0.84
12 h	448.33±43.33	469.53±43.59	0.37
24 h	466.67±20.65	479.67±39.48	0.45
Frequency (breaths min^{-1})			
Baseline	12.80±1.82	12.26±1.03	0.06
1 h	12.80±1.82	12.26±1.03	0.06
3 h	12.80±1.82	12.26±1.03	0.06
6 h	12.80±1.82	12.26±1.03	0.06
9 h	12.80±1.82	12.26±1.03	0.06
12 h	12.80±1.82	12.26±1.03	0.06
24 h	12.80±1.82	12.26±1.03	0.06
C (mL cm H_2O)			
Baseline	69.19±62.97	51.22±25.51	0.90
1 h	64.50±51.70	61.21±32.95	0.57
3 h	82.51±64.15	61.19±36.74	0.46
6 h	77.37±69.25	62.91±38.13	0.71
9 h	69.49±45.58	58.19±34.84	0.77
12 h	82.06±66.84	54.93±34.84	0.71
24 h	73.29±58.04	56.32±28.01	0.65
P_{peak} (cm H_2O)			
Baseline	25.40±6.80	23.13±4.59	0.29
1 h	24.33±7.84	24.87±5.09	0.83
3 h	24.53±6.97	25.40±4.95	0.69
6 h	23.33±6.29	23.80±4.68	0.82
9 h	23.73±7.14	24.40±4.44	0.76
12 h	22.87±6.19	24.07±4.76	0.56
24 h	22.33±5.11	24.47±4.53	0.24
R (cm H_2O L^{-1} s^{-1})			
Baseline	17.27±11.90	14.31±7.95	0.43
1 h	15.33±7.39	14.59±7.17	0.78
3 h	15.29±7.29	15.45±6.89	0.95
6 h	15.87±9.60	15.13±7.09	0.81
9 h	16.51±9.49	16.61±6.70	0.97
12 h	16.03±11.84	16.12±7.46	0.98
24 h	15.39±10.13	16.39±7.47	0.76
PEEP (cm H_2O)			
Baseline	6.05±1.99	6.25±2.49	0.81
1 h	6.07±2.28	6.11±2.65	0.96
3 h	6.15±2.35	6.17±2.71	0.98
6 h	6.22±2.29	6.12±2.60	0.91
9 h	6.09±2.31	6.05±2.53	0.94
12 h	6.07±2.33	6.45±3.02	0.70
24 h	5.69±2.33	6.19±2.49	0.57

Data are presented as mean±SD. Statistical analysis included Student's t-test. SD: standard deviation; TV: tidal volume; C: compliance; P_{peak}: peak airway pressure; R: airway resistance; PEEP: positive end-expiratory pressure.

Table 3. Arterial blood gas analysis and end-tidal CO_2 values of the groups

	Group S (n=15) (mean±SD)	Group D (n=15) (mean±SD)	p
pH			
Baseline	7.42±0.06	7.41±0.07	0.85
1 h	7.41±0.07	7.41±0.06	0.86
3 h	7.41±0.05	7.42±0.05	0.63
6 h	7.40±0.05	7.41±0.04	0.48
9 h	7.41±0.06	7.41±0.05	0.97
12 h	7.39±0.09	7.42±0.03	0.29
24 h	7.41±0.07	7.42±0.04	0.67
p	0.63	0.86	
PaO_2 (mmHg)			
Baseline	82.68±19.00	84.13±21.38	0.85
1 h	91.47±23.19	81.21±15.42	0.16
3 h	89.09±19.59	81.37±14.83	0.23
6 h	93.07±36.78	83.38±20.55	0.38
9 h	101.63±39.15	83.43±17.35	0.11
12 h	94.41±22.49	84.28±17.74	0.18
24 h	90.68±27.58	85.01±16.09	0.49
p	0.56	0.36	
$PaCO_2$ (mmHg)			
Baseline	47.74±16.72	38.17±10.86	0.07
1 h	48.92±18.13	37.18±7.21	0.03*
3 h	48.19±16.21	36.23±6.88	0.01*
6 h	49.21±13.20	35.67±5.66	0.002*
9 h	48.25±12.54	37.35±8.39	0.01*
12 h	50.87±13.30	37.93±7.66	0.003*
24 h	52.10±15.61	37.69±7.03	0.004*
p	0.24	0.68	
End-tidal CO_2 (mmHg)			
Baseline	50.53±17.20	34.86±9.57	0.005*
1 h	48.73±16.24	34.40±8.67	0.007*
3 h	48.47±14.99	32.80±6.88	0.002*
6 h	48.13±14.53	32.73±7.54	0.001*
9 h	46.00±12.02	34.67±8.62	0.006*
12 h	46.87±9.41	35.00±7.43	0.001*
24 h	46.87±9.30	34.93±7.79	0.001*
p	0.45	0.13	

*p<0.05 compared with Group D. Data are presented as mean±SD. Statistical analysis included Student's t-test. SD: standard deviation.

due to endotracheal intubation (8). Recent studies support that sevoflurane may be a better option than the other volatile agents to reduce bronchospasm (9, 10). Therefore, it may be preferred for the prevention or treatment of bronchospasm in patients with pulmonary disorders. The other advantages of sevoflurane are rapid onset, low blood solubility, minimal cardioprotective effect and faster recovery (11, 12). Volta et al. (13) demonstrated that sevoflurane and isoflurane cause bronchodilation in patients with COPD undergoing thoracic surgery. Ruszkai et al. (14) performed sevoflurane therapy using the AnaConDa in a patient unresponsive to conventional treatment including bronchodilators, mucolytics, corticosteroids, antibiotics, fluid and oxygen management. They reported that sevoflurane application using the AnaConDa is a conceivable treatment in patients with refractory to conventional therapy of asthma.

Volatile anaesthetics have some cardioprotective and neuroprotective potentials due to ATP-dependent potassium channels, ryanodine receptors and G proteins (15). In addition, they especially act on the cerebral cortex and often smoothly on the recovery of consciousness (6). Posttraumatic stress dis-

order may be observed after iv sedation, but it is quite rare after volatile sedation (6). Especially sevoflurane, less change in haemodynamics is seen, and this effect is almost not observed in low concentrations (6). Chabanne et al. (16) demonstrated that AnaConDa increases work of breathing, but sevoflurane reduces this effect. The infusion rate of an inhalation agent is started at 5-10 mL h^{-1}, and acceptable sedation is provided with 2-5 mL h^{-1} for sevoflurane and 2-6 mL h^{-1} for isoflurane (7). In our study, we used sevoflurane 5 mL h^{-1} initial dose and approximately 4 mL h^{-1} (1-6 mL h^{-1}) maintenance dose, and the sedation score will be 3-4.

The AnaConDa is a recycle system, and one of the common concerns is the concentration of anaesthetic gas increase in the ICU, but it is kept within acceptable limits (<1 ppm) with waste removal systems (17, 18). This issue may be negligible because 90% of the expired gas was absorbed by the carbon layer and recirculated to the next inspiratory period. Closed circuit suction systems are recommended if tracheal aspiration is required to reduce the pollution of the ICU environment with volatile agents, and precisely for this reason, we used a closed-circuit suction system. Another concern is mild hypercapnia due to the dead space of the AnaConDa device (2, 7). Stresson et al. (19) observed that CO_2 retention develops within the first 30 min during the use of volatile anaesthetic with AnaConDa. The researchers have attributed hypercapnia development to the dead space in AnaConDa and 90% re-breathing of the CO_2 and volatile agent mixture. Clinically, the normal range of $PaCO_2$ is 35-45 mmHg, and we also observed significantly higher $PaCO_2$ levels in the sevoflurane group, and these values continued to increase over time. Here, a few points in this regard captured our attention; we performed the same mechanical ventilation settings in the sevoflurane and dexmedetomidine groups. This increase could be prevented by adjusting the respiratory frequency in the AnaConDa group. On the other hand, we did not observe any clinical differences between the two groups.

The iv agents used for sedation are midazolam, propofol, benzodiazepine, remifentanil and dexmedetomidine. Nowadays, dexmedetomidine is the most commonly used iv agent in ICU patients. Minimal respiratory depression and analgesic properties make dexmedetomidine unique compared with other sedative agents. Sackey et al. (3) used midazolam and isoflurane for sedation in the ICU, and they found shorter recovery time and time to extubation in the isoflurane group. In another study, Röhm et al. (20) used sevoflurane and propofol for short time sedation after cardiac surgery. They found that time to extubation and length of hospital stay are shorter with sevoflurane than with propofol; however, hospital costs were increased in the sevoflurane group. Mesnil et al. (21) demonstrated that sevoflurane decreases morphine consumption as well as the time to extubation compared with propofol and midazolam after long-term sedation. This result is related to the opioid sparing effect of sevoflurane via N-methyl-D-aspartate receptor antagonism (7, 17). In our study, we observed that patients receiving dexmedetomidine were highly stable.

Study limitations

There are some limitations in the present study. First, we did not evaluate blood sevoflurane and dexmedetomidine concentrations due to high costs. Second, the number of patients participating in the study (n=30) was insufficient. However, the number of patients requiring sedation in the ICUs within the period of the study was 30. Therefore, the study was presented as a preliminary study. Third, we did not measure the concentration of sevoflurane in the ICU because we did not have enough equipment to evaluate.

Conclusion

Both sevoflurane and dexmedetomidine are suitable sedative agents in ICU patients with pulmonary disorders. Although $PaCO_2$ and end-tidal CO_2 results are higher with sevoflurane, this result did not change the clinical condition of the patients. This problem can be prevented by setting the respiratory frequency higher in patients with AnaConDa. However, we need randomised, prospective and multicentre studies with larger sample sizes to compare the pulmonary effects of dexmedetomidine and sevoflurane in ICU patients.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Çukurova University School of Medicine (Date: 19.02.2015, 38/7).

Informed Consent: Written informed consent was obtained from the patient or patients' legal representative who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – D.Ö., M.T., E.G., Z.H., M.T.I.; Design – D.Ö., M.T., E.G., Z.H., M.T.I.; Supervision – D.Ö., M.T., E.G., Z.H., M.T.I.; Resources – M.T., Z.H., E.G.; Materials – M.T., Z.H., E.G., M.T.I.; Data Collection and/or Processing – M.T., M.T.I., E.G.; Analysis and/or Interpretation – M.T., E.G., Z.H., D.Ö.; Literature Search – M.T., E.G., M.T.I.; Writing Manuscript – M.T., E.G.; Critical Review – Z.H., D.Ö.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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