Original Article Ann Med Res 2023;30(1):52–57

Current issue list available at AnnMedRes

Annals of Medical Research

journal page: www.annalsmedres.org

Role of capnography in safe sedation of vitrectomy patients

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ARTICLE INFO

Keywords:
Vitrectomy
Capnography
Sedation
End-tidal carbon dioxide
$EtCO_2$

Received: Aug 09, 2022
Accepted: Nov 30, 2022
Available Online: 21.01.2023

DOI:
10.5455/annalsmedres.2022.08.240

Abstract

Aim: To evaluate the efficiency of the capnography monitoring added to routine monitoring of oxygen desaturation, hypoxemia, and other vital parameters.

Materials and Methods: 100 adult patients who had elective vitrectomy under sedation were included in this study. Patients were divided into "experiment"(capnography added to routine monitoring) and "control"(capnography not added to routine monitoring) groups. Hypoxemia, desaturation, tachycardia, bradycardia, and additional maneuvers for the airway were compared. Increase and decrease in end-tidal carbon dioxide ($EtCO_2$) levels, hypoxemia, desaturation, Integrated Pulmonary Index (IPI) levels requiring attention (5-7), and intervention (1-4) were determined in the experiment group, and frequencies of them were assessed.

Results: Desaturation and bradycardia rates and counts in the experiment group were significantly lower than the control group. No significant difference was seen between groups in terms of hypoxemia, tachycardia, and additional maneuvers. 76%(38/50) of experiment group patients had decrease in $EtCO_2$, 10%(5/50) increase in $EtCO_2$, 38%(19/50) apnea, 52%(26/50) IPI levels requiring attention, 14%(7/50) IPI levels requiring intervention.

Conclusion: With the addition of capnography to routine monitoring of sedated vitrectomy patients, oxygen desaturation and bradycardia can be less likely to occur, and with instant follow-up of the $EtCO_2$, apnea, and IPI levels, respiratory depression can be recognized before oxygen desaturation develops.

Introduction

In vitrectomy operations, analgesic and sedative drugs are used to reduce the pain that may occur during the induction of local anesthesia and at other stages of the operation. Serious complications such as airway obstruction, aspiration, respiratory depression (hypoxemia and apnea), and hemodynamic instability may develop in patients under sedation and analgesia. Standard parameters for essential monitoring may fail to reflect hypoxemia and apnea instantly [1].

Capnography is a non-invasive monitoring method that measures the amount of carbon dioxide in exhaled air ($EtCO_2$) and mirrors conditions such as apnea and hypoventilation much earlier than other monitoring methods. The waveform created by instant measurement of $EtCO_2$ momentarily reflects conditions such as hypoventilation, hyperventilation, bronchospasm, or apnea [2, 3].

There are no studies on the superiority or contribution of capnography to standard monitoring in patients undergoing vitrectomy under sedation in the literature.

We aimed to investigate the effect of capnography monitoring, which was performed in addition to standard monitoring, on desaturation, hypoxemia, and other standard monitoring parameters in sedated vitrectomy patients.

Materials and Methods

This study was approved by Bursa Uludağ University Faculty of Medicine Clinical Research Ethics Committee (decision number: 2017-12/1).

Study population

The study included 100 patients over 18 years of age, who underwent elective vitrectomy between July 20, 2017, and July 2, 2018, who had an American Society of Anaesthesiologists (ASA) score of 1-3, who were neither pregnant nor suspected of pregnancy, who approved the informed consent form and were not allergic to sedative agents. Patients who were under 18 years of age, who had an ASA

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score of 4 and above, who were pregnant or suspected to be pregnant, who had signs of a difficult airway, and patients with obstructive and restrictive lung disease, as well as emergency cases, were excluded from the study. Patients were divided into two groups of 50 people using the sealed envelope method. Patients who were subjected to capnography monitoring were regarded as the "Experimental Group" and patients who did not undergo capnography monitoring were defined as the "Control Group" (Figure 1).

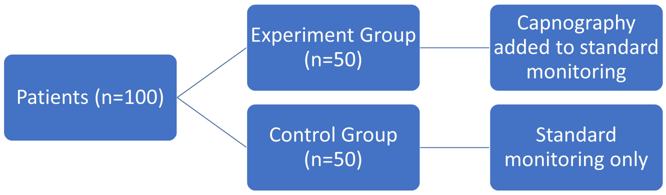

Figure 1. Flow chart of patient grouping.

Anesthesia protocol

All patients fasted for at least 6 hours before the operation. Premedication was not performed as it was thought to potentially affect hemodynamic responses, postoperative recovery, and the degree of sedation during and after the operation.

After obtaining informed consent, standard monitoring involving measurement of heart rate (HR), blood oxygen saturation (SpO_2), blood pressure (BP), and the 3-lead electrocardiography analysis was applied to all patients before sedation. In addition to standard monitoring, respiratory rate (RR), $EtCO_2$, and integrated pulmonary index (IPI) were non-invasively measured before sedation through a nasal cannula (FilterLine®) attached to the capnography device (Capnostream® 20p) for patients in the experimental group. Sedation and analgesia were performed in line with the routine sedation-analgesia protocol used by our department for vitrectomy cases. For analgesia, 50 µg of fentanyl was administered via the intravenous (IV) route. For the sedation agent, a 2 mg IV push of midazolam (Dormicum®; Roche) was administered. If necessary, titrated 0.5-1 mg midazolam and 25 µg fentanyl (Talinat®; Vem) were administered as a maintenance dose. The target sedation level was determined as level 3 (moderate sedation; appears asleep but responds to verbal stimuli) according to the Ramsay Sedation Scale (RSS). Following sedation, all patients received local anesthesia performed by an ophthalmologist using the retrobulbar technique. Subsequently, the operation was started.

During the operation, all patients were given 5 L/min oxygen through a nasal cannula. Throughout the operation, HR, SpO_2, BP, and 3-lead electrocardiography findings were monitored for all patients, and the RR, $EtCO_2$, and IPI levels were also monitored for patients in the experimental group. Capnography values were frequently evaluated for apnea, bronchospasm, and upper airway obstruction (UAO). In case that hypoventilation, hyperventilation, desaturation, hypoxemia, apnea, bronchospasm, or UAO developed during the operation, firstly, verbal and tactile stimulation (VTS) was given. If there was no response to those stimuli, a jaw-thrust maneuver (JTM) or head-tilt maneuver (HTM) was applied.

When the operation was completed, patients were taken to the recovery unit. In line with the routinely used recovery protocol, patients who had an Aldrete Score of 9 or higher were transferred to the clinic.

Data collection

Patient data, including age, gender, body weight, height, ASA class, and smoking history, was recorded before the operation, and the duration of anesthesia and duration of the procedure was recorded after the operation. Body mass index was calculated using patients' height and body weight measurements.

SpO_2, HR, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were recorded for all patients during sedation, at the 3rd, 6th, and 9th minutes after sedation and every 3 minutes till the end of the operation. Additionally, the RR, $EtCO_2$, and IPI scores were recorded for the experimental group patients during sedation, at the 3^{rd}, 6^{th}, and 9^{th} minutes after sedation, and every 3 minutes till the end of the operation. We also recorded the number of apnea, bronchospasm, and UAO episodes developing in the experimental group. The number of VTS, JTM and HTM procedures, duration of operation, and duration of anesthesia were recorded for all patients.

For all patients, the number of tachycardia, bradycardia, desaturation, and hypoxemia episodes was determined by evaluating the recorded SpO_2 and HR values. Tachycardia was defined as an HR higher than 100/min, and bradycardia was an HR less than 60/min. At least a 5% decrease according to the first measured SpO_2 value was defined as desaturation, and a SpO_2 value less than 90% was defined as hypoxemia.

The number of tachypnea, bradypnea, low $EtCO_2$, and high $EtCO_2$ episodes were determined by examining the $EtCO_2$ and RR values of the patients in the experimental group. Tachypnea was defined as a respiratory rate higher than 20/min and bradypnea as a RR lower than 10/min. An $EtCO_2$ value higher than 45 mmHg was defined as high $EtCO_2$, and lower than 35 mmHg was defined as low $EtCO_2$.

Examining the experimental group's IPI values, we determined the conditions that required attention and the conditions that required intervention [4]. An IPI score between 5 and 7 was defined as a condition requiring attention, between 1 and 4 as a condition requiring intervention.

Statistical analysis

A priori power analysis was performed based on the findings of the study conducted by Ishiwata et al [5]. Using the moderate effect size (d=0.46) sample size for each group was computed as n=50 per group, and a total of 100 participants was estimated for a power of 0.80 and alpha of 0.05. We used the descriptive statistics of mean, standard deviation, minimum, maximum, frequency, and ratio. The Kolmogorov-Smirnov test was used to measure the distribution of the variables. Independent quantitative data was analyzed using the independent sample t-test, and the Mann-Whitney U test. Dependent quantitative data were analyzed with the paired-sample t-test and the Wilcoxon test. Correlation analysis was performed with the Spearman correlation. α=0.05 was considered significant. The SPSS 22.0 program was used for the analyses. Descriptive statistics were applied to the parameters, including demographic data (age, gender, height, body weight, BMI, smoking history, and ASA score), anesthesia duration, duration of operation, hypoxemia, desaturation, tachycardia, bradycardia, VTS, JTM, and HTM in both experimental and control groups. Besides, descriptive statistics were employed for the parameters of high $EtCO_2$, low $EtCO_2$, tachypnea, bradypnea, and the IPI score of 5-7, the IPI score of 1-4, apnea, bronchospasm, and UAO in the experimental group. The two groups were compared regarding demographic data, anesthesia duration, and operation duration. The hypoxemia, desaturation, tachycardia, bradycardia, VTS, JTM, and HTM counts were compared between the two groups.

Results

In both groups, the percentage of genders, ASA scores, and smoking was calculated. No significant difference was detected between the groups regarding demographic data, anesthesia duration, and operation duration (p>0.05) (Table 1).

The counts of desaturation and bradycardia episodes were significantly lower in the experimental group than in the control group (p<0.001). No significant difference was detected between the two groups in the episode number of hypoxemia and tachycardia (p>0.05). There was no significant difference between the groups regarding the number of VTS, JTM, and HTM procedures applied (p>0.05) (Table 2).

The DBP, SBP, and HR values did not significantly differ

Table 1. Descriptive statistics of demographic data, anesthesia duration, and operation duration of the experimental and control groups.

	Control Group	Experimental Group
	Avg.±SD	Avg.±SD
Age	59.3±13	64±9.5
Height (cm)	165.9±9.3	164.7±10.1
Body weight (kg)	77.3±13.6	77.7±13.3
BMI	28.1±4.3	28.8±5.2
Duration of Anesthesia (min)	59±10.1	61.8±10.3
Duration of Operation (min)	55.5±10.3	58±10.8

		Control Group		Experimental Group	
		n	%	n	%
Gender	Female	21	42	22	44
	Male	29	58	28	56
ASA Score	I	12	24	9	18
	II	38	76	39	78
	III	0	0	2	4
Smoking	(-)	26	52	24	48
	(+)	24	48	26	52

The table indicates the average (Avg.) and standard deviation (SD) values for the parameters of age, height, weight, BMI, anesthesia duration and operation duration as well as a number of cases (n) and percentages (%)for gender, ASA score, and smoking.

Table 2. The rates of desaturation, tachycardia, bradycardia, and VTS and JTM episodes in the experimental and control groups.

	Number of Episodes	Control Group		Experimental Group	
		n	%	n	%
Desaturation*	0	32	64.0	46	92.0*
	1	15	30.0	3	6.0*
	2	3	6.0	1	2.0*
Tachycardia	0	44	88.0	46	92.0
	1	2	4.0	1	2.0
	2	0	0	1	2.0
	3	2	4.0	0	0
	11	0	0	1	2.0
	12	1	2.0	0	0
	19	1	2.0	0	0
	24	0	0	1	2.0
Bradycardia**	0	37	74.0	47	94.0**
	1	2	4.0	1	2.0**
	2	2	4.0	0	0**
	3	1	2.0	0	0**
	4	1	2.0	0	0**
	7	0	0	1	2.0**
	9	1	2.0	0	0**
	10	1	2.0	1	2.0**
	11	1	2.0	0	0**
	13	1	2.0	0	0**
	19	2	4.0	0	0**
	22	1	2.0	0	0**
VTS	0	32	64.0	28	56.0
	1	16	32.0	8	16.0
	2	1	2.0	7	14.0
	3	1	2.0	3	6.0
	4	0	0	3	6.0
	7	0	0	1	2.0
JTM	0	44	88.0	44	88.0
	1	6	12.0	5	10.0
	3	0	0	1	2.0
HTM	0	48	96.0	47	94.0
	1	2	4.0	3	6.0
Hypoxemia	0	49	98.0	48	96.0
	1	1	2.0	2	4.0

*: p<0.001 (compared to the control group), **: p<0.01 (compared to the control group), VTS: verbal-tactile stimulation, JTM: Jaw-Thrust maneuver, HTM: Head-Tilt maneuver, n: number of cases, %: Percentage. Chi-square test was employed. X^2:Chi-square test, m: Mann-Whitney u test.

Table 3. P values in the experimental and control groups that reflect the change of HR, SpO2, SBP, and DBP values after sedation according to pre-sedation.

		3rd min	6th min	9th min	12th min	15th min
HR	Experimental Group	0.851	0.940	0.924	0.853	0.277
	Control Group	0.650	0.279	0.114	0.533	0.743
SpO_2	Experimental Group	0.779	0.68	0.515	0.101	0.012
	Control Group	<0.001	0.012	0.009	<0.001	<0.001
SBP	Experimental Group	0.830	0.576	0.838	0.293	0.364
	Control Group	0.497	0.350	0.477	0.232	0.157
DBP	Experimental Group	0.126	0.092	0.630	0.479	0.427
	Control Group	0.479	0.647	0.447	0.741	0.350
		18th min	21st min	24th min	27th min	30th min
HR	Experimental Group	0.665	0.757	0.740	0.989	0.949
	Control Group	0.682	0.752	0.556	0.311	0.168
SpO_2	Experimental Group	<0.001	<0.001	<0.001	<0.001	<0.001
	Control Group	<0.001	<0.001	<0.001	<0.001	<0.001
SBP	Experimental Group	0.964	0.370	0.243	0.260	0.279
	Control Group	0.149	0.155	0.127	0.139	0.130
DBP	Experimental Group	0.418	0.392	0.498	0.252	0.359
	Control Group	0.332	0.267	0.416	0.295	0.340

The p values reflecting the significant decrease compared to the pre-sedation are indicated in red, and the p values reflecting a significant increase are indicated in green. HR: Heart rate; SpO_2: Peripheral oxygen saturation; SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

between the groups ($p>0.05$). The SpO_2 value measured at the 3rd minute was significantly higher in the experimental group than in the control group (97.2 ± 2.5 vs. 95 ± 2.6, $p < 0.001$). However, the SpO_2 values recorded at the other measurement times did not differ between the two groups ($p>0.05$).

We examined the change of the SpO_2, DBP, SBP, and HR values at the 3rd, 6th, 9th, 12th, 15th, 18th, 21st, 24th, 27th, and 30th minutes compared to pre-sedation (0th minute). In the control group, there was a significant decrease in the SpO_2 values measured at the 3rd and 6th minutes as compared to the pre-sedation ($p<0.05$), whereas there was a significant increase in the SpO_2 at the 9th and 12th minutes ($p<0.05$). In both experimental and control groups, the SpO_2 value significantly increased at the 15th, 18th, 21st, 24th, 27th, and 30th minutes as compared to the pre-sedation period ($p<0.05$). However, other parameters did not significantly change compared to the pre-sedation ($p>0.05$) (Table 3).

Among 50 people in the experimental group, low $EtCO_2$ was observed at least once in 76% (38/50), and high $EtCO_2$ was observed at least once in 10% (5/50). In 14% (7/50) of the patients, $EtCO_2$ was at normal levels throughout the operation. In 54% (27/50) of the patients, tachypnea developed at least once, and 44% (22/50) of the patients experienced bradypnea at least once. Conditions requiring attention based on the IPI scores were seen at least once in 52% (26/56) of the patients, and conditions requiring intervention at least once in 14% (7/50) of the patients. Also, 38% (19/50) of the patients experienced apnea at least once.

None of the patients experienced bronchospasm or UAO.

Discussion

In our study, there were fewer desaturation and bradycardia incidents in vitrectomy patients who received sedation and followed up with capnography than those who followed up using routine monitoring without capnography. Moreover, the SpO_2 values measured at the 3rd minute in the experimental group were significantly higher than those in the control group, and the 3rd and 6th minute SpO_2 values of the control group were significantly lower as compared to the pre-sedation values ($p < 0.05$). These results show that capnography monitoring provides benefits in terms of safe oxygenation and HR stability in sedated vitrectomy cases.

It has been reported in many studies that the occurrence of desaturation decreases with the use of capnography in interventional sedation [5,6]. However, it has been reported in some studies that adding capnography to standard monitoring did not contribute to the development of oxygen desaturation [7,8]. In the studies stating that capnography is not beneficial, desaturation was defined as a SpO_2 level of <90% or <92% [7,8]. These definitions do not conform to the definition of desaturation in our study; they rather conform to our definition of hypoxemia. We did not find a significant difference between the groups regarding the development of hypoxemia, which is a similar result. However, our patients did not breathe room air but were given oxygen through a nasal cannula. In the studies investigating the effect of capnography monitoring in procedural sedation on bradycardia, it has been stated that there was no decrease in bradycardia development by the addition of capnography [9,10]. However, in that study, bradycardia was defined as an HR below 50/min. In our study, on the other hand, bradycardia was described as an HR below 60/min [11]. It is observed that in the capnography studies performed on patients receiving interventional sedation and analgesia, low SpO_2 level has been defined differently and heterogeneously with the concepts such as desaturation, hypoxemia, mild desaturation, and severe desaturation [2, 6-8, 12, 13]. Similarly, there is no homogeneity in the definition of concepts such as bradycardia and hypotension, which causes a contradiction in the results related to the effectiveness of capnography [9-11]. These contradictions may be eliminated through meta-analyses involving a large number of studies with low deviation and prospective randomized controlled studies involving a large number of cases.

The SpO_2 values measured with 3-minute intervals indicate that patients undergoing routine monitoring without capnography have a tendency to develop oxygen desaturation in the first 6 minutes following sedation. When it comes to the significant increase in the SpO_2 values of both groups as of minute 15 compared to the pre-sedation SpO_2 values, we believe that it might be due to the stabilization of the oxygenation as of the 15^{th} minute.

Although there were fewer desaturation and bradycardia incidents in the experimental group than in the control group, the rate of patients who had at least once low $EtCO_2$ was 76% (38/50), and the rate of patients who had at least once high $EtCO_2$ was 10% (5/50). $EtCO_2$ abnormality was not seen in 14% (7/50) of the patients. In cases undergoing sedation, respiratory depression may manifest itself as high $EtCO_2$ accompanied by bradypnea or as low $EtCO_2$ induced by hypopnea [14]. Additionally, 54% (27/50) of the patients developed tachypnea at least once, and 44% (22/50) of the patients experienced bradypnea at least once. This study revealed that vitrectomy patients, who had moderate sedation, developed severe respiratory depression and respiratory irregularity, and that respiratory depression could be detected instantly by capnography monitoring, allowing immediate intervention before impairment of oxygenation and cardiac rhythm.

In our study, nearly half of the experiment group patients experienced apnea at least once. Ishiwata et al. suggested that in patients undergoing bronchoscopy under sedation, the rate of apnea detected by capnography was 59%, and a >4% decrease was observed in SpO_2 values following 42% of apnea episodes [15]. The expression "more than 4% decrease in SpO_2" is similar to our definition of "desaturation." In the light of these results, we think that apnea episodes occurring in patients monitored with capnography have the potential to result in desaturation. Klare et al. compared clinical evaluation and capnography for apnea detection in a study performed on sedated endoscopic retrograde cholangiopancreaticography patients [10]. Capnography detected apnea in 64.5% of patients, while clinical evaluation detected apnea in 6% of patients, and thus, capnography was found to be significantly superior to clinical evaluation regarding apnea detection ($p < 0.001$). Vargo et al. suggested that capnography could detect only 50% of apnea episodes, which could be determined by pulse oximetry in sedated patients undergoing gastrointestinal system (GIS) endoscopy; however, clinical evaluation could detect no episodes [16].

IPI is a mathematical algorithm based on the combination of the values of $EtCO_2$, RR, HR, and SpO_2. This algorithm gives IPI values, which reflect vital parameters, between 1 and 10 [4]. Riphaus et al. have compared capnography monitoring procedures with IPI and without IPI evaluation in patients sedated with midazolam and propofol for upper GIS endoscopy [17]. In the groups where IPI was employed, the rate of apnea was significantly lower. Kaur et al. have mentioned the role of IPI in the prediction of unsuccessful extubation [18]. Two definitions based on these values have been made: conditions requiring attention and requiring intervention [4]. However, no studies were made to investigate the efficiency of these situations. Considering patients' IPI scores in our research, above half of the patients in the experimental group at least once experienced a condition that required attention, and some of them at least once experienced a condition requiring intervention. We think that IPI is a sensitive monitoring tool for detecting vital parameter instabilities and may improve the efficiency of standard monitoring.

The main limitation of our study is that it is a single-center study with a limited number of patients. Conducting multicenter studies involving a greater number of patients may yield more objective results regarding the effectiveness of capnography in sedated vitrectomy cases.

Conclusion

In conclusion, the addition of capnography to standard monitoring in sedated vitrectomy cases decreases oxygen desaturation and bradycardia incidents. Slight respiratory depressions, such as $EtCO_2$ abnormalities and apnea, may develop in sedated vitrectomy patients, and they have a potential for desaturation. With capnography usage, these early deoxygenation findings can immediately be detected, and necessary airway intervention can be performed before desaturation develops.

Ethics approval

This study was approved by Bursa Uludağ University Faculty of Medicine Clinical Research Ethics Committee (decision number: 2017-12/1).

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