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Non-invasive carbon dioxide monitoring during moderate sedation at different oxygen flow rates in patients undergoing endoscopic retrograde cholangio-pancreatography

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ABSTRACT

Background: All patients receiving sedation to facilitate endoscopic procedures should have monitoring of cardiorespiratory parameters before, during, and after administration of sedation/analgesia. We evaluated the effects of different O_2 flow rates on the non-invasive CO_2 monitoring ($EtCO_2$) in adult patients that were breathing spontaneously under moderate sedation during ERCP.

Methods: This prospective randomized double-blind study was conducted on 120 patients assigned randomly to one of the three equal groups (n = 40) (Group I; 2 L/min oxygen flow rate, Group II; 4 L/min oxygen flow rate, and Group III; 6 L/min oxygen flow rate). Primary outcome was $EtCO_2$ at the end of procedure. Secondary outcomes included peripheral O_2 saturation, hemodynamics, time to recovery, total propofol dose, patients' satisfaction, sedation score, and complications.

Results: $EtCO_2$ increased significantly between the studied groups at pre-intervention, induction, 5, 10, 20, and 30 min but without any clinical significance (p-value ˂ 0.05). The HR changes were statistically significant at 10 and 20 min after induction of anesthesia. While SpO_2, MBP, and RR differences were statistically not significant between groups throughout the whole study periods (p-value >0.05). Arterial blood gas analysis showed PCO_2 was significantly different between the study groups but still within the normal range of readings, while pH and HCO_3 showed statistically insignificant differences between the three groups.

Conclusion: The study demonstrated that different O_2 flow rates did not affect the non-invasive $EtCO_2$ measurements by the Dual-Guard device during moderate sedation in patients undergoing ERCP. Non-invasive $EtCO_2$ monitoring can provide an early warning sign of hypoventilation during moderate sedation.

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1. Introduction

Sedation is a reduction in level of consciousness by many drugs. The clinical goals of sedation during gastrointestinal (GI) endoscopic procedures are to alleviate apprehension, ameliorate the examination findings, and minimize the patients' memories of the incident. Various analgesics and sedatives have been used to obtain the convenient levels of sedation for GI endoscopies. The recognition of the pharmacologic properties of sedative agents is essential for achieving the desirable levels of sedation [1].

Patients who are scheduled to receive sedation to ease the endoscopic steps should have cardiorespiratory parameters monitored throughout the period of sedative administration. Electronic monitoring may reveal early marks of patient distress and add to the ongoing clinical evaluation. Monitoring devices frequently used for patients subjected to endoscopic operations include single-lead continuous electrocardiographic (ECG) monitoring, pulse oximetry, and non-invasive blood pressure monitors [2,3]. Recently, due to the rise of propofol use to simplify endoscopies, less common monitoring equipment, including level of consciousness monitors and end-tidal carbon dioxide ($EtCO_2$), has been established. By changing the American Society of Anesthesiologists (ASA) guidelines, CO_2 monitoring for patients undergoing moderate or deep sedation is recommended, and thus familiarity with capnographic interpretation may be required [4].

Hypercapnia or respiratory depression may occur during deep sedation or through recovery from anesthesia. Hypoventilation usually shows desaturation in pulse oximetry monitoring as a delayed sign. Furthermore, administration of O_2 supplementation usually masks hypoventilation [5,6]. Hypoventilation may lead to hypoxemia in patient with spontaneous breathing under sedation. Subsequently, if the

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capnograph monitor is used, any increase in $EtCO_2$ during hypoventilation can alert the observing anesthetist to avoid hypoxemia [7]. Non-invasive measurement of CO_2 includes capnometry that lays out digital form only or capnography, which supports both digital and graphic forms [8].

In this study, we evaluated the effects of different O_2 flow rates on non-invasive CO_2 monitoring ($EtCO_2$) in patients breathing spontaneously under moderate sedation and scheduled for endoscopic retrograde cholangio-pancreatography (ERCP).

2. Materials

Study Eligibility: This prospective randomized controlled double-blind study was conducted at Assiut University Hospitals from June 2020 until December 2021 after approval from the Institutional Review Board, Faculty of Medicine, Assiut University, Egypt (IRB17101067) on 30 April 2020. Clinical trials registration at the clinicaltrials.gov (NCT04588272) on 1 June 2020 before the first patient enrollment and adhered to the declaration of Helsinki. A written informed consent from patients scheduled for elective ERCP under moderate sedation was obtained.

Randomization and Blinding: Patients were randomly allocated to three equal groups with the help of a computer-generated table of random numbers to receive the study protocol. The outcome measures were collected by an anesthesiologist and not included in giving the anesthetic technique. Neither the anesthesiologist collecting data nor the patients themselves were aware of group allocation to ensure blindness of the study. Patients could stop participation at any time without loss of medical service, and all endoscopic procedures were performed by the same operating team.

Inclusion/Exclusion Criteria: Adult Patients aged 20–60 years, of both sex, ASA physical status I–II, and scheduled for ERCP were included in the trial. Patient's refusal or patients with abnormal renal function test, history of chronic chest disease, history of systemic illness, i.e.,, hypertension and diabetes, or cardiac patients were excluded.

Patients: One hundred and twenty patients were enrolled in the study and were equally divided into three groups: Group I: 40 patients received moderate sedation and O_2 supply at the rate of 2 L/min. Group II: 40 patients received moderate sedation and O_2 supply at the rate of 4 L/min. Group III: 40 patients received moderate sedation and O_2 supply at the rate of 6 L/min.

Outcome measures: Primary outcome included measuring end-tidal carbon dioxide ($EtCO_2$) non-invasively by Dual-Guard device. Secondary outcomes included O_2 saturation, hemodynamic parameters, arterial blood gas analysis, time to recovery, total intravenous propofol dose, patients' satisfaction, sedation score, and any complications.

Anesthetic Technique and Data Collection: Preoperative assessment and evaluation of all patients participating in the study was done in the preoperative anesthesia clinic. Intraoperative monitoring (electrocardiogram, non-invasive blood pressure, peripheral oxygen saturation, $EtCO_2$) was connected, and the pre-induction values were reported. An intravenous cannula 18 G was inserted and secured in the dorsum of the non-dominant hand of each patient, and then intravenous fluids (NaCl 0.9%) was started at the calculated volume and rate. After 3 min of 100% pre-oxygenation, anesthesia was induced with propofol 1.5 mg/kg and lidocaine 1 mg/kg. Moderate sedation was maintained throughout the whole procedure with intermittent boluses of propofol (0.25 to 0.5 mg/kg) every 2 to 5 min.

Technique of non-invasive monitoring of $EtCO_2$ were done through Dual-Guard device (Dual-Guard™ Flexicare Medical Ltd) which incorporates an endoscopy bite block with oxygen delivery and CO_2 monitoring from both the mouth and nose simultaneously. Vital signs including heart rate, non-invasive blood pressure, peripheral oxygen saturation, and end-tidal CO_2 were recorded every 5 min throughout the procedure. At the end of procedure, patient was transferred to the recovery area where Ramsay sedation scale, 5-point Likert satisfaction scale, and postoperative adverse effects were assessed.

Ramsay sedation scale [9] (1 = Patient is anxious and agitated or restless, or both. 2 = Patient is co-operative, oriented, and tranquil. 3 = Patient responds to commands only. 4 = Patient exhibits brisk response to light glabellar tap or loud auditory stimulus. 5 = Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus. 6 = Patient exhibits no response). The 5-point Likert satisfaction scale [10]: strongly satisfied, satisfied, neutral, not satisfied, or strongly not satisfied.

Statistical Analysis:

Sample size was calculated based on previous studies [4–7] using the G*Power 3 software [11], with a study power of 80% and type I error of 5% ($\alpha = 0.05$ and $\beta = 80\%$) on two-tailed test, and the minimum required sample was 120 patients assigned randomly into one of the three equal groups (n = 40) (Group I; 2 L oxygen, Group II; 4 L oxygen and Group III; 6 L oxygen) to detect an effect size of 0.2 in the main recovery outcomes.

Statistical analysis: Data were verified, coded by the researcher and analyzed using IBM-SPSS 24.0 (IBM-SPSS Inc., Chicago, Illinois, USA) [12]. Descriptive statistics: means, standard deviations, and percentages were calculated. Test of significances: for continuous variables with more than two categories; ANOVA test was calculated to test the mean differences of the data that

follow normal distribution, and two-way repeated measure ANOVA (RM-ANOVA) test was calculated to test the mean differences of the data that follow normal distribution and had repeated measures. Post-hoc test with Bonferroni correction was used for partwise comparisons. A significant p-value was considered when it is ˂ 0.05.

3. Results

The current study was conducted on 120 adult patients who underwent ERCP. The CONSORT flow diagram illustrating these participants is shown in Figure 1.

All groups were comparable with no statistically significant differences (p-value >0.05) regarding the demographics (age, sex, and weight) and baseline characteristics. The duration of sedation was 42.40 ± 11.1 min in group I, 41.90 ± 12.4 min in group II, and 40.52 ± 11.1 min in group III, with a p-value of 0.754. The mean procedure time was 29.53 ± 8.9 min in group I, 29.23 ± 9.8 min in group II, and 28.15 ± 8.9 min in group III, with a p-value of 0.783 (Table 1).

Table 2 shows that the $EtCO_2$ differences between the studied groups were statistically significant at pre-intervention, induction time, 5, 10, 20, and 30 min after induction but without any clinical significance (P-value

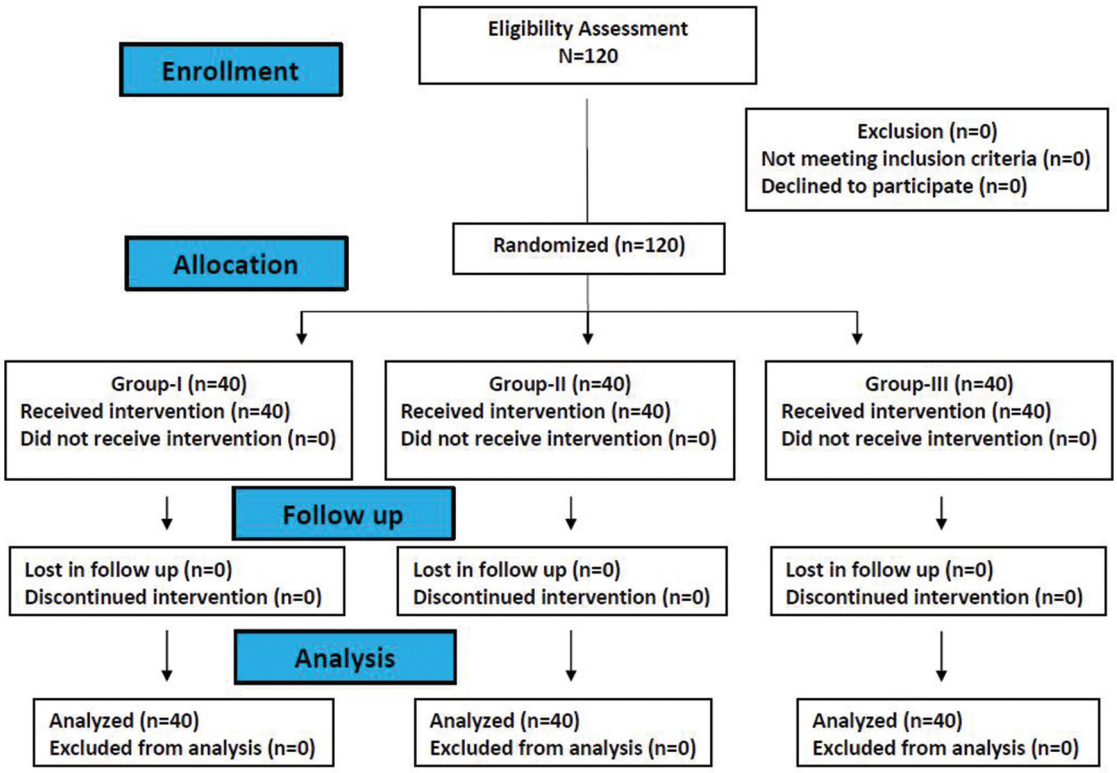

Figure 1. The CONSORT flow diagram of the study patients.

Table 1. Demographic and baseline characteristics between the studied groups.

	Group I (2 L) (n = 40)	Group II (4 L) (n = 40)	Group III (6 L) (n = 40)	P-value
Age/years	43.15 ± 13.5	47.95 ± 12.4	50.18 ± 13.9	0.059[a]
P-value[b]	1 vs. 2 = 0.110	2 vs. 3 = 0.457	1 vs. 3 = 0.020	
Sex				0.528[c]
• Female	24 (60%)	22 (55%)	19 (47.5%)	
• Male	16 (40%)	18 (45%)	21 (52.5%)	
Weight/kg	81.73 ± 7.5	82.57 ± 10.6	85.90 ± 6.9	0.072 [a]
P-value[b]	1 vs. 2 = 0.656	2 vs. 3 = 0.083	1 vs. 3 = 0.030	
Duration of Procedure/minutes				0.783[a]
• Mean ± SD	29.53 ± 8.9	29.23 ± 9.8	28.15 ± 8.9	
• Median (Range)	30 (20–45)	30 (20–47)	29.5 (20–46)	
P-value[b]	1 vs. 2 = 0.945	2 vs. 3 = 0.601	1 vs. 3 = 0.562	
Duration of Sedation/minutes				0.754[a]
• Mean ± SD	42.40 ± 11.1	41.90 ± 12.4	40.52 ± 11.1	
• Median (Range)	30 (20–45)	30 (20–45)	30 (20–45)	
P-value[b]	1 vs. 2 = 0.847	2 vs. 3 = 0.595	1 vs. 3 = 0.469	

Data were presented as mean ± SD, number of patients, or percentages.
P-value <0.05 was considered significant.
[a]ANOVA test, [b]Post-hoc test, [c]Chi-square test.

Table 2. End-tidal CO_2 differences between the studied groups.

$EtCO_2$ (mmHg)	Group I (2 L) (n = 40)	Group II (4 L) (n = 40)	Group III (6 L) (n = 40)	P-value
Pre-intervention	32.88 ± 2.6	33.93 ± 2.4	31.55 ± 2.3	< 0.001[a]
P-value[b]	1 vs. 2 = 0.058	2 vs. 3 < 0.001	1 vs. 3 = 0.017	
Induction	32.38 ± 2.1	34.58 ± 3.2	32.48 ± 2.7	< 0.001[a]
P-value[b]	1 vs. 2 < 0.001	2 vs. 3 = 0.001	1 vs. 3 = 0.896	
5-min	34.30 ± 2.1	36.78 ± 2.8	34.35 ± 2.8	< 0.001[a]
P-value[b]	1 vs. 2 < 0.001	2 vs. 3 = 0.001	1 vs. 3 = 0.941	
10-min	36.68 ± 2.2	38.95 ± 2.6	37.10 ± 3.1	< 0.001[a]
P-value[b]	1 vs. 2 < 0.001	2 vs. 3 = 0.002	1 vs. 3 = 0.496	
20-min	37.88 ± 3.1	40.28 ± 2.7	38.60 ± 2.4	= 0.001[a]
P-value[b]	1 vs. 2 < 0.001	2 vs. 3 = 0.007	1 vs. 3 = 0.240	
30-min.	37.88 ± 2.5	40.48 ± 3.1	39.24 ± 3.9	= 0.030[a]
P-value[b]	1 vs. 2 = 0.009	2 vs. 3 = 0.215	1 vs. 3 = 0.160	
45-min.	39.75 ± 1.9	39.90 ± 2.7	38.71 ± 2.8	= 0.691[a]
P-value[b]	1 vs. 2 = 0.903	2 vs. 3 = 0.357	1 vs. 3 = 0.442	
P-value[c]	= 0.034	= 0.001	= 0.047	= 0.391[#]

Data were presented as mean ± SD.
P-value <0.05 was considered significant.
[a]ANOVA, [b]Post-hoc, [c]Mean differences within group comparison.
#Two-way Repeated Measure ANOVA.

< 0.05). There were increases in $EtCO_2$ readings mostly after induction of sedation until the end of the procedure, which were statistically significant between periods in groups I, II, and III (p-values were 0.034, 0.001, and 0.047; respectively).

The HR changes between groups were statistically significant only at 10 and 20 min after induction of sedation without any clinical significance or adverse effects (p-value <0.05) (Figure 2). The MBP readings between the three study groups were statistically not significant throughout the whole study periods with p-values >0.05 (Figure 3).

The arterial blood gas evaluations were recorded between the studied groups both immediately after induction of sedation and upon recovery after the end of procedure. As regard PCO_2, there were statistically significant increases between the three study groups but still within the normal range of readings. While regarding pH and HCO_3, there were statistically insignificant differences between the three groups. All groups showed decrease in pH, increase in PCO_2, and slight decrease in HCO_3 values during recovery when compared to values after induction of sedation, with statistically significant differences and p-value <0.001 (Table 3).

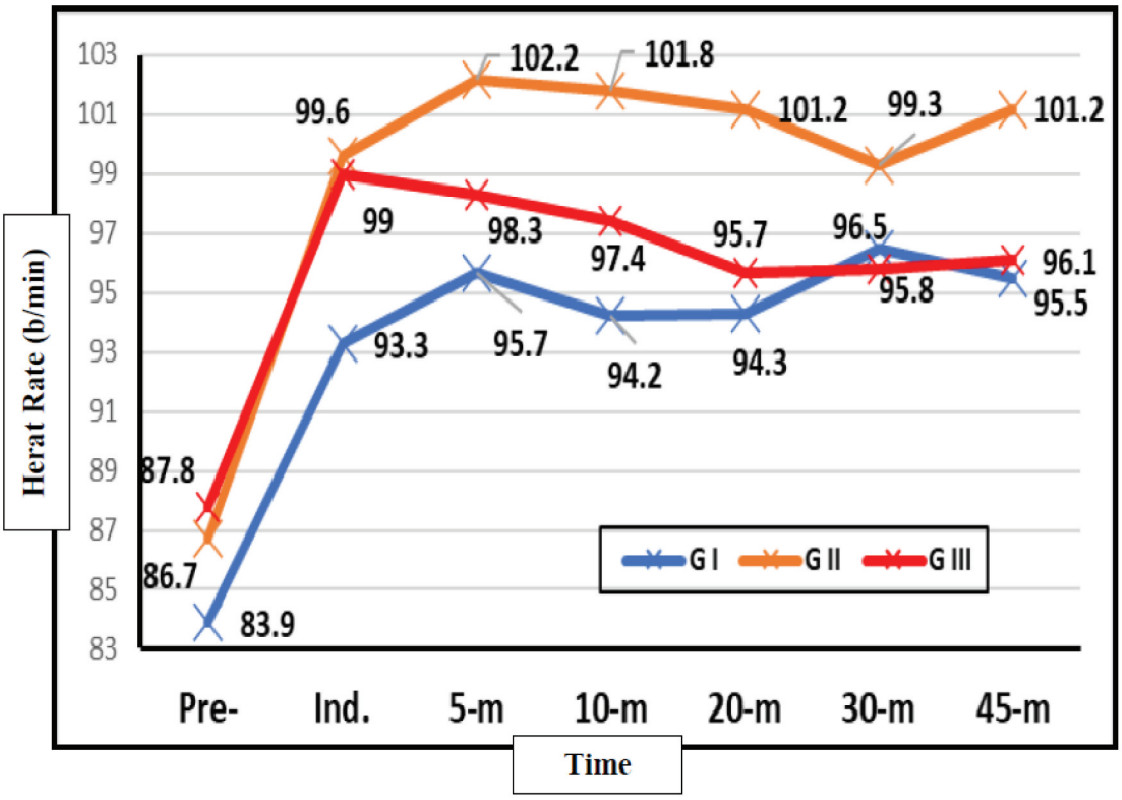

Figure 2. Differences in mean HR over time between the studied sample.

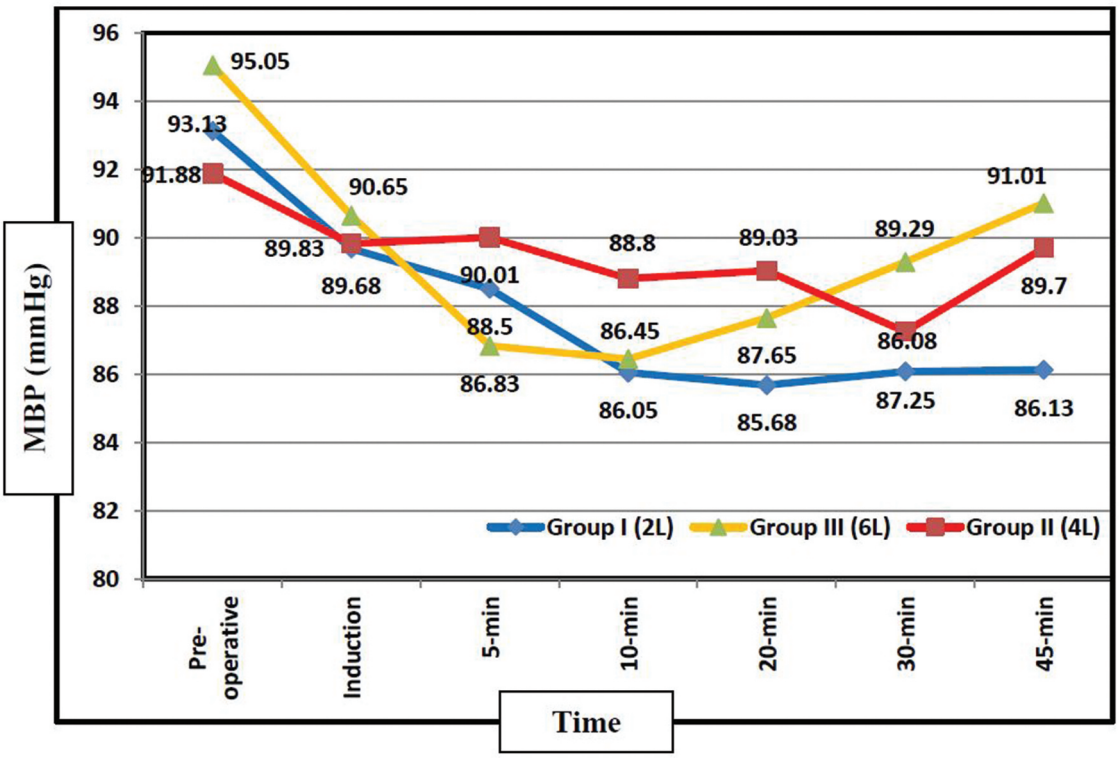

Figure 3. Differences in mean MBP over time between the studied sample.

Table 3. pH, $PaCO_2$, and HCO_3 differences between the studied groups.

	Group I (2 L) (n = 40)	Group II (4 L) (n = 40)	Group III (6 L) (n = 40)	P-value
		pH		
Pre-	7.40 ± 0.02	7.41 ± 0.02	7.40 ± 0.02	= 0.576[a]
P-value[b]	1 vs. 2 = 0.426	2 vs. 3 = 0.832	1 vs. 3 = 0.313	
Post-	7.35 ± 0.03	7.35 ± 0.03	7.35 ± 0.01	= 0.687[a]
P-value[b]	1 vs. 2 = 0.406	2 vs. 3 = 0.868	1 vs. 3 = 0.506	
P-value[c]	< 0.001	< 0.001	< 0.001	= 0.001[#]
		CO_2 (mmHg)		
Pre-	37.93 ± 3.2	38.50 ± 2.4	36.10 ± 2.3	< 0.001[a]
P-value[b]	1 vs. 2 = 0.345	2 vs. 3 < 0.001	1 vs. 3 = 0.003	
Post-	42.65 ± 3.1	44.73 ± 2.5	43.15 ± 3.1	= 0.005[a]
P-value[b]	1 vs. 2 = 0.002	2 vs. 3 = 0.018	1 vs. 3 = 0.484	
P-value[c]	< 0.001	< 0.001	< 0.001	< 0.001[#]
		HCO_3 (mEq/L)		
Pre-	22.58 ± 2.1	22.62 ± 1.5	23.14 ± 1.6	= 0.284[a]
P-value[b]	1 vs. 2 = 0.923	2 vs. 3 = 0.186	1 vs. 3 = 0.156	
Post-	22.31 ± 2.1	22.35 ± 1.5	22.78 ± 1.6	= 0.257[a]
P-value[b]	1 vs. 2 = 0.911	2 vs. 3 = 0.171	1 vs. 3 = 0.139	
P-value[c]	< 0.001	< 0.001	< 0.001	= 0.001[#]

Data were presented as mean ± SD.
P-value <0.05 was considered significant.
[a]ANOVA test, [b]Post-hoc test, [c]Mean differences within group comparison.
[#]Two-way Repeated Measure ANOVA.
Pre-: Immediately after induction of sedation; Post-: at the end of procedure.

The SpO_2 differences between the study groups were statistically not significant throughout the whole study periods (p-value >0.05). Each group showed an inside-group significant increase in SpO_2 values after induction of sedation, which remained elevated till the end of the procedure with p-values of 0.011, 0.004, and 0.043 in groups I, II, and III, respectively (Table 4).

Time to recovery was 11.25 ± 2.1 min in group I, 11.63 ± 2.3 min in group II, and 11.62 ± 2.4 min in group III; with no statistically significant differences between all groups (p-value = 0.705). The total propofol dose was 475.00 ± 70.7 mg in group I, 487.50 ± 82.2 mg in group II, and 490.00 ± 84.1 mg in group III; with no statistically significant differences between groups (p-value = 0.664). The Ramsay sedation score was 2.20 ± 0.4 in group I, 2.33 ± 0.5 in group II, and 2.01 ± 0.5 in group III, also with no statistically significant differences between groups (p-value = 0.422). As regarding patients' satisfaction, there were no statistically significant differences between the three groups (p-value = 0.751). Group

Table 4. Oxygen saturation (SpO_2) differences between the studied groups.

$SpO_{2\%}$	Group I (2 L) (n = 40)	Group II (4 L) (n = 40)	Group III (6 L) (n = 40)	P-value
Pre-intervention	97.63 ± 0.7	97.85 ± 0.7	97.65 ± 0.7	= 0.306[a]
P-value[b]	1 vs. 2 = 0.161	2 vs. 3 = 0.213	1 vs. 3 = 0.876	
Induction	99.48 ± 0.6	99.73 ± 0.6	99.25 ± 0.6	= 0.222[a]
P-value[b]	1 vs. 2 = 0.255	2 vs. 3 = 0.569	1 vs. 3 = 0.089	
5-min	99.68 ± 0.6	99.53 ± 0.6	99.58 ± 0.6	= 0.558[a]
P-value[b]	1 vs. 2 = 0.290	2 vs. 3 = 0.224	1 vs. 3 = 0.480	
10-min	99.50 ± 0.7	99.73 ± 0.5	99.48 ± 0.6	= 0.137[a]
P-value[b]	1 vs. 2 = 0.103	2 vs. 3 = 0.071	1 vs. 3 = 0.856	
20-min	99.74 ± 0.5	99.75 ± 0.5	99.73 ± 0.5	= 0.975[a]
P-value[b]	1 vs. 2 = 0.956	2 vs. 3 = 0.829	1 vs. 3 = 0.873	
30-min.	99.79 ± 0.5	99.76 ± 0.4	99.67 ± 0.5	= 0.667[a]
P-value[b]	1 vs. 2 = 0.836	2 vs. 3 = 0.521	1 vs. 3 = 0.385	
45-min.	99.63 ± 0.5	99.90 ± 0.3	100.00 ± 0.0	= 0.122[a]
P-value[b]	1 vs. 2 = 0.117	2 vs. 3 = 0.574	1 vs. 3 = 0.054	
P-value[c]	= 0.011	= 0.004	= 0.043	= 0.395[#]

Data were presented as mean ± SD.
P-value <0.05 was considered significant.
[a]ANOVA test, [b]Post-hoc test, [c]Mean differences within group comparison.
[#]Two-way Repeated Measure ANOVA.

I showed 17 patients (47.5%) very satisfied, 19 patients (47.5%) satisfied, and 4 patients (10%) neutral. Group II showed 18 patients (45%) very satisfied, 17 patients (42.5%) satisfied, and 5 patients (12.5%) neutral. Group III showed 16 patients (40%) very satisfied, 16 patients (40%) satisfied, and 8 patients (20%) neutral (Table 5).

No serious adverse effects were reported in the three study groups during the entire study observation periods.

4. Discussion

This study was conducted to detect the effect of different O_2 flow rates on non-invasive CO_2 monitoring in patients scheduled for ERCP under moderate sedation. The study results demonstrated that different O_2 flow rates through nasal route did not affect the non-invasive CO_2 measurements using the Dual-Guard device. To the best of our knowledge, this may be the first time to use this device for monitoring CO_2 non-invasively during ERCP at different O_2 flow rates, at least in our region.

$EtCO_2$ increased statistically after induction in all groups. The increase in $EtCO_2$ could be explained by the fact that patients in the prone position under sedation usually show hypoventilation. We also found that heart rate values slightly increased after induction of sedation in all study groups, while blood pressure values decreased after sedation induction but without any clinical risks. Changes in hemodynamic parameters could be explained by the fact that propofol is a peripheral vasodilator and cardio-depressant drug. We observed that the longer the duration of sedation and the higher the total intravenous propofol dose, the longer the recovery time required to the patients. All patients in our study had some degree of satisfaction, and no serious complications were recorded.

Yanagidate, established that a modified nasal cannula can afford continued $EtCO_2$ monitoring without determining oxygen distribution in 86 spontaneously breathing patients under sedation. Arterial blood

Table 5. Clinical data differences between the three studied groups.

	Group I (2 L) (n = 40)	Group II (4 L) (n = 40)	Group III (6 L) (n = 40)	P-value
Time to Recovery (min)				
• Mean ± SD	11.25 ± 2.1	11.63 ± 2.3	11.62 ± 2.4	= 0.705[a]
• Median (Range)	10 (10–15)	10 (10–15)	10 (10–15)	
P-value[b]	1 vs. 2 = 0.470	2 vs. 3 = 0.994	1 vs. 3 = 0.466	
Total Propofol Dose (mg)				
• Mean ± SD	475.00 ± 70.7	487.50 ± 82.2	490.00 ± 84.1	= 0.664[a]
• Median (Range)	500 (400–600)	500 (400–600)	500 (400–600)	
P-value[b]	1 vs. 2 = 0.482	2 vs. 3 = 0.888	1 vs. 3 = 0.399	
Ramsay Sedation Score				
• Mean ± SD	2.20 ± 0.4	2.33 ± 0.5	2.01 ± 0.5	= 0.422[a]
• Median (Range)	2 (2–3)	2 (2–3)	2 (2–3)	
P-value[b]	1 vs. 2 = 0.215	2 vs. 3 = 0.804	1 vs. 3 = 0.321	
Patients' Satisfaction				
• Very Satisfied	17 (42.5%)	18 (45%)	16 (40%)	
• Satisfied	19 (47.5%)	17 (42.5%)	16 (40%)	= 0.751[c]
• Neutral	4 (10%)	5 (12.5%)	8 (20%)	

Data were presented as mean ± SD, number of patients, or percentages.
P-value <0.05 was considered significant.
[a]ANOVA test, [b]Post-hoc test, [c]Chi-square test.

samples were obtained, while O_2 delivery was at flow rates of 0, 2, or 4 L/min, with/without clamping between the modified nasal cannula prongs. The $EtCO_2$ showed no waveforms when oxygen flow was greater than 2 L/min (without clamping between the prongs). While clamping, there was a considerable correlation (r = 0.83) between $EtCO_2$ and arterial CO_2 [13].

Our results are analogous with that Ebert, who concluded that nasal cannula (NC) designing could affect its capability to transmit O_2 and to accurately withdraw $EtCO_2$ samples at high fresh gas flows (FGFs). PaO_2 and $PaCO_2$ were measured in 11 volunteers utilizing arterial catheters. The O_2 FGF was set to 2, 4, or 6 L/min then data were recorded after stable recordings were achieved. The maneuvers were then repeated with the other three types of NCs. They complemented that the design in which O_2 is supplied out of one nasal prong and CO_2 is detected from the else prong, was considered to be most efficient and accurate for these goals [14].

Some investigators disclosed that the expanded monitoring with capnography revealed the precise evaluation of respiratory rate when compared to the reference standard of auscultation with pre-tracheal stethoscopes. Apnea and disordered respiration (ADR) existed in more than 50% of patients and proceeded most considerably by hypoxemia. They demonstrated that capnography was preferable to pulse oximetry and could act as the "early warning system" for an impending ventilation compromise [15].

Some authors were in agreement with the findings of our study. They reported that adding $EtCO_2$ monitors to standard monitoring during sedation with propofol could improve patients' safety through reducing the incidence of CO_2 retention, and thus the hypoxemia risk by early discrimination of apnea, and reducing the recovery time [16].

Other researchers have evaluated the efficiency of $EtCO_2$ monitors to minimize the incidence of CO_2 retention during lumpectomy under sedation with sufentanil and propofol. Scheduled patients were allocated randomly to standard monitoring group or an experiential group using $EtCO_2$ monitoring. CO_2 retention was reported less frequently in the $EtCO_2$ monitoring group with p-value <0.0001. In the standard group, the pH was <7.35 and the mean P_aCO_2 was >45 mmHg [17].

Miner et al. (2002) noted that $EtCO_2$ monitoring during PS (procedural sedation) could reveal any respiratory depression. Respiratory depression was reported in 44.6% of adults subjected to procedural sedation in the emergency department. All incidents were detected by capnography. Respiratory depression was seen in 47.5%, 19%, 80%, and 66.6% of patients received methohexital, propofol, fentanyl, and etomidate, respectively. They concluded that $EtCO_2$ could improve safety during sedation by early detection of hypoventilation [18].

Quick reveal of apnea could be considered a safer monitoring to ventilation during procedural sedation due to the fast rise in $EtCO_2$ during apnea (with an average of 3–5 mmHg/min) and the later undesirable effects of hypercapnia on blood pressure and sedation. Moreover, the most significant importance of hypercapnia monitoring is the implied hypoventilation that drives the change, which ultimately leads to poor patients' oxygenation [19].

Deitch and others concluded that when using propofol for sedation, adding capnography to the standard monitoring decreased the incidence of hypoxia and raised the alert for any hypoxic event. They reported hypoxia in 25% of subjects during capnography monitoring but in 42% during blinded capnography. Capnography detected all states of hypoxia prior to its onset with the 60 seconds average time from capnographic detection of respiratory depression [20]. Another research covered 247 subjects who were evaluated for monitoring efficacy. From all hypoxemic incidents, 35% were recorded with absolute normal breathing. Hypoxemia occurred significantly in 69% of participants in the study blinded arm, compared to 46% of participants in the study open arm of monitoring [21].

A trial by Beitz included 760 participants. The intention-to-treat examination showed a significantly reduced the incidence of deoxygenation in the study arm used capnography when compared to the standard one (p-value <0.001). Also, the number of patients with reduced SaO_2 ≤85% or <90% were various significantly. No differences were reported as regards to rates of hypotension or bradycardia. The quality of sedation in both groups was the same [22].

Friedrich-Rust stated that in patients scheduled for colonoscopic procedures under sedation with propofol, capnography device decreased the prevalence of hypoxia. Patients were randomly assigned to standard monitoring plus capnography or standard monitoring only. The incidence of severe hypoxemia (SO_2 < 85%) and hypoxemia (SO_2 < 90%) were considerably decreased in patients with capnography device (18%) compared to standard monitoring (32%), with p-value of 0.00091 [23].

The results of our study are comparable with those of Tai et al., who established that measuring $EtCO_2$ by side-stream capnometry from a nasal cannula provided a non-invasive and valid $PaCO_2$ estimation in the non-intubated patients [24].

Mehta and colleagues found that using capnographic monitoring in routine GIT endoscopies did not decrease the incidence of hypoxia in patients subjected to moderate sedation using a combination of benzodiazepines and opioids. Patients were located to open or blinded

capnography alarm groups. The primary outcome was the occurrence of hypoxemia defined as reduced oxygen saturation to less than 90% for 10 seconds or more. No significant variations were observed regarding hypoxemia rates between both arms [25].

Klare et al., 2016 agreed with our results of hemodynamic parameters. Patients were divided into a control group (standard monitoring) or an interventional group (adding capnography). They observed no changes regarding bradycardia, hypotension, rates of hypoxemia, or quality of sedation when using propofol and midazolam for patients undergoing ERCP [26]. Gillham reported no attacks of decreased level of arterial blood oxygen ˂ 93% (while patients receiving O_2 at rate of 2 L/min through a nasal cannula) and no cases of hemodynamic instability in patients under sedation with propofol. They aimed to evaluate the effectiveness and safety of sedation in patients during ERCP [27].

Mazanikov et al., 2013 observed patients submitted to ERCP and received sedation with propofol as Patient-controlled sedation (PCS) or Target-controlled infusion (TCI). Less propofol consumption was recorded in PCS-group with a p-value of 0.002, and faster patients' recovery ($p = 0.035$). They reported no major complications from sedation techniques and no evidence of advantages of TCI over PCS [28].

Conclusion: Our study demonstrated that different O_2 flow rates did not affect the non-invasive $EtCO_2$ measurement by the Dual-Guard device during moderate sedation in patients undergoing ERCP and no serious adverse effects were reported. Non-invasive $EtCO_2$ monitoring may provide an early warning sign of hypoventilation during moderate sedation.

Limitations: One type of non-invasive CO_2 monitoring devices was used, and other devices could be tested to validate our findings. Correlation between $EtCO_2$ and arterial blood gas has not been performed, and this could be done to advocate the device accuracy. Further research may add to our idea regarding the optimal O_2 flow rate that could be used during procedural sedation.

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