

An Evaluation of the Integrated Pulmonary Index (IPI) for the Detection of Respiratory Events in Propofol Sedated Patients Undergoing Upper Gastrointestinal Endoscopy

Vaessen HHB^{1*}, Knape JTA²

¹Department of Anaesthesiology, Intensive Care and Emergency Medicine, University Medical Centre Utrecht, Heidelberglaan, The Netherlands

²Division of Anaesthesiology, Intensive Care and Emergency Medicine, University Medical Centre Utrecht, Heidelberglaan, The Netherlands

*Corresponding author: H.H.B. (Paul) Vaessen, Department of Anaesthesiology, Intensive Care and Emergency Medicine, University Medical Centre Utrecht, Heidelberglaan 100, The Netherlands, Tel: +31 88 7559619; E-mail: H.H.B.Vaessen@umcutrecht.nl

Received date: April 09, 2016; Accepted date: June 06, 2016; Published date: June 13, 2016

Copyright: © 2016 Vaessen HHB, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Background: Monitoring of patients respiratory and ventilatory status during moderate-to-deep sedation in upper gastrointestinal (GI) endoscopic procedures may enable early recognition of altered respiratory patterns with potential danger for vital functions. The current standards of care for monitoring the ventilatory status during sedation are pulse oximetry and visual inspection of the breathing pattern. EtCO₂ monitoring is not routinely used. The Integrated Pulmonary Index (IPI) monitor is developed to detect specific patient's respiratory depression and changes status during sedation, by measuring the EtCO₂, respiratory rate, SpO₂ and pulse rate, displayed on a monitor. This monitor might provide an indication of the patient's overall ventilator status. The aim of this study was to explore the validity of the IPI index during PSA procedures and its application during upper GI endoscopy treatments, compared with our traditional current standards of monitoring care.

Methods: Twenty patients, scheduled for upper GI endoscopy procedures gave their informed consent. All patients were moderately to deeply sedate by trained sedation practitioners. Aside from standard monitoring, additionally the IPI was continuously measured, on a capnostream monitor. All data were analyzed and compared with the clinical status of the patient.

Results: All patients were moderate-to-deep sedated for upper GI endoscopy procedures. The mean age of the patients was 56 years. In 15/100 measure points, the IPI values (lower than 7) were not in agreement with the actual clinical state of the patient. The most common discrepancies, 9/100, were associated with an overshoot of the EtCO₂ value, due to leakage of CO₂, insufflated through the endoscope.

Conclusion: The IPI value as an early warning monitor of the ventilation in moderate-to-deep sedation procedures remains unclear and deserves further study. Its use in upper endoscopic gastrointestinal procedures where CO₂ insufflation is used by the endoscopist cannot be recommended.

Keywords: Procedural sedation and analgesia; Respiration and ventilation; Integrated pulmonary Index; Patient safety; Upper GI endoscopy

Introduction

Upper gastrointestinal (GI) endoscopic procedures are standard diagnostic tools for investigation and surveillance of diseases of the gastrointestinal tract. These endoscopic procedures are often uncomfortable for the patient. To relieve this discomfort, the use of sedative and analgesic drugs, is necessary during the procedure.

Over-sedation may lead to respiratory depression while under-sedation may cause discomfort for the patient [1]. Therefore, monitoring of vital functions and of the clinical effect of the sedation are essential requirements during these procedures. Guidelines [2,3] recommend continuous monitoring of the circulation, of respiratory function and ventilation during Procedural Sedation and Analgesia (PSA) procedures.

Monitoring of vital signs, which could recognize and detect early changes, which might deteriorate patient's respiratory function during sedation, is necessary. Pulse oximetry monitoring only provides information on oxygenation but gives no indication on the effectiveness of the ventilation [4].

Nowadays usually, end-tidal CO₂ (EtCO₂), Respiration Rate (RR), arterial oxygen saturation (SpO₂) and Pulse Rate (PR) are more or less standard during sedation procedures [5,6]. However, early indications of a potentially dangerous change in the ventilatory status may not always be shown by any of these parameters.

The validated [7] Integrated Pulmonary Index (IPI), a numerical value, based on an algorithm, integrates 4 parameters: EtCO₂, RR, SpO₂ and PR, in the form of a single index value ranging from 1 to 10 (Table 1) and displayed on a monitor.

This IPI could potentially recognize changes in patient's respiratory status during PSA early enough to allow an intervention by the sedation practitioner.

IPI Index Range	Group	Patients Status
7-8-9-10	High	Normal range
4-5-6	Medium	Indicating that patient required attention
1-2-3	Low	Requires Immediate intervention
IPI: Integrated Pulmonary Index		

Table 1: The meaning of the IPI monitors readings.

Berkenstadt [8] used the IPI tool during colonoscopy and his results demonstrated a limited agreement between respiratory physiological parameters and the IPI. Following the example of his study, our aim was to investigate if an integrated IPI score could early recognize changes in the overall ventilatory status at ASA 1 and 2 patients [9] during upper GI endoscopy. Could this monitor reliably replace the traditional ventilatory monitoring during sedation using observation of the respiration, SpO₂, and EtCO₂, next to the ECG and pulse rate monitoring for safe moderate-to-deep sedation during upper GI endoscopic procedures? Therefore the IPI measurements were compared with a real time SpO₂, EtCO₂, PR, and RR monitor and in addition the NIBP and the Observer Assessment of Alertness/Sedation (OAA/S) score were measured in an observational pilot study with 20 patients.

Materials and Methods

Study population and design

Twenty patients were scheduled in this study for an upper GI endoscopy procedure with moderate-to-deep sedation between August 2014 and November 2014. Moderate-to-deep sedation was defined according to the Continuum of Depth of Sedation [10]. All patients underwent a medical pre-assessment in accordance with the hospital sedation screening protocol and following an informed consent for the propofol based sedation, the use of IPI measurements, and the upper GI endoscopic procedures, the Endoscopic Ultrasound Esophagogastroduodenoscopy (EUS) or the Endoscopic Retrograde Cholangio Pancreatography (ERCP). Patient variables were obtained including age, sex, body mass index (BMI) and the American Society of Anesthesiology classification (ASA) status. Exclusion criteria were: age <18 years, ASA physical-status class >2, allergy against soy, eggs, and non-fasting patient. Before the GI procedure, an intravenous (IV) infusion was initiated for fluid administration. Procedural sedation and anesthesia started with the IV administration of propofol (Lipuro 10mg/mL, B. Braun) 5 mg/kg/hr via infusion pump (Alaris Medical UK) and 200 µg of alfentanil (Janssen-Cilag) as a bolus. Additional intravenous boluses of 10 or 20 mg of propofol were titrated until the desired level of moderate-to-deep sedation (OAA/S sedation score of 4 or 3) was achieved, to allow the gastroenterologist to perform his upper GI endoscopy procedure. Therefore, a maximum of 4 litres CO₂ / minute was insufflate continuously through the endoscope for expansion of the oesophagus, stomach, and the duodenum allowing the endoscope to be passed through these areas. Our goal was to maintain a sedation level between moderate (patient responds to verbal or tactile stimulus) and deep (patient not aroused easily but responds to painful stimuli).

Monitoring

The vital signs of all patients were continuously observed and monitored (Qube Compact Monitor; Spacelabs Healthcare, Snoqualmie, Washington, USA), and all data were recorded every 5 minutes with AnStat, an anaesthesia information management system.

Heart activity was monitored with a three-lead ECG, and the arterial oxygen saturation with a pulse oximetry. NIBP measurements were taken at 5-minute intervals, and capnography readings (Smart CapnoLine Plus; Oridion Capnography, Needham, Massachusetts, USA) were continuously recorded. An additional monitor, (Capnostream 20, Oridion Medical 1987 Ltd., Jerusalem-Israel) was installed to calculate the Integrated Pulmonary Index (IPI) rate (by using a Microstream Smart BiteBloc - Oridion Capnography Inc., Needham, MA and a SpO₂ sensor). This monitor calculated the ventilatory status by measuring the EtCO₂, RR, SpO₂ and PR. Supplemental oxygen (2 l/min) was administered routinely by a nasal prong.

The IPI scores were divided to 3 groups: high IPI (score level 7–10) group indicating that the patient was in a normal range, medium IPI (score level 4–6) group indicating that the patient required attention and low IPI (score level 1–3) group indicating that the patient required immediate intervention. To assess the effectiveness of the IPI, all events with an IPI values <7 were identified, counted, and evaluated when it occurred for longer than one minute. These patients IPI value were compared with the traditional vital signs monitoring. The events were classified when a patient “required attention” or “required intervention” and when “no intervention” was recommended. “Required attention” events were defined as the SpO₂ was <92% and >88% and/or RR ≤ 8 and/or a 20% change in EtCO₂ from the baseline value for more than one minute. “Required intervention” events were defined when the SpO₂ ≤ 88% and/or loss of the EtCO₂ waveform for more than one minute. Procedural variables included the IPI rate, the OAA/S score [11] (Table 2) the doses of medications. A person who was not involved in the procedure registered the vital functions, SpO₂, EtCO₂, PR, and RR. The OAA/S sedation depth score was used to measure the level of alertness of the patients who are sedated [12] and recorded every 5 minutes throughout the procedure [13]. Data on each procedure were recorded for detailed evaluation and interpretation. These data were analyzed at 5 different moments: start of sedation (I), start of endoscopy (II), 15 minutes after start of the endoscopy (III), 30 minutes after the start of endoscopy (IV) and the end of the endoscopy (V).

Score Level	Observation
5	Awake and responds reality to name spoken in normal tone
4	Lethargic responses to name in normal tone
3	Responds only after name is called loudly and/or repeatedly
2	Responds only after name is called loudly and mild shaking
1	Does not respond to mild pounding or shaking
OAA/S: Observers Assessment of Alertness Sedation scale	

Table 2: Observers Assessment of Alertness Sedation scale (OAA/S).

Statistical analysis

Statistical analysis was performed using SPSS version 21 software (SPSS INC, Chicago, IL). The incidence of each IPI value (low, medium and high) between the specified sedation moments was compared with the parameters SpO₂, EtCO₂, RR and PR and analysed by using the descriptive statistics tool.

Eight patients underwent a EUS procedure and twelve patients an ERCP treatment.

All patients were categorized according to the ASA classification system as ASA 2.

Descriptive statistics of IPI (low, medium and high) values and corresponding physiological parameters (EtCO₂, RR, SpO₂, PR and OAA/S,) are compared and presented in Table 3.

Results

This observational pilot study evaluated twenty patients (mean age 56; age group: 30-79, SD: 13.042 years) receiving PSA (propofol and alfentanil) for GI endoscopy procedures.

Measure moments	Parameters	N	Minimum	Maximum	Mean	Std. Deviation	N	Minimum	Maximum	Mean	Std. Deviation	N	Minimum	Maximum	Mean	Std. Deviation
(I) Start sedation	SpO ₂											20	93	100	97,7	1,976
	EtCO ₂											20	3,6	6,2	4,68	0,703
	Heart Rate											20	48	104	81,5	16,916
	Respiration rate											20	8	28	16,3	5,017
	IPI											20	7	10	9,1	1,071
	OAA/S											20	5	5	5	0,000
(II) Start endoscopy	SpO ₂						2	94	97	95,5	2,121	18	94	100	97,72	1,904
	EtCO ₂						2	4	4,8	4,4	0,566	18	3,2	5,6	4,48	0,681
	Heart Rate						2	70	100	85	21,21	18	44	100	77,44	14,01
	Respiration rate						2	6	8	7	1,414	18	7	26	17,28	5,039
	IPI						2				0	18	7	10	8,89	1132
	OAA/S						2	3	3	3	0	18	2		3,11	0,583
(III) 15 minutes after start endoscopy	SpO ₂	1	99	99	99		3	97	99	98	1	16	95	100	98	1,713
	EtCO ₂	1	9,9	9,9	9,9		3	3,9	13,6	10,2	5,462	16	3,5	7	5,113	0,961
	Heart Rate	1	88	88	88		3	81	96	89	7,55	16	48	110	76,5	16,685
	Respiration rate	1	20	20	20		3	8	26	14,33	10,116	16	11	32	18,38	4,924
	IPI	1	2	2	2		3		6	5,33	1155	16	7	10	9,13	1088
	OAA/S	1	3	3	3		3	3	4	3,33	0,577	16	2		2,81	0,655
(IV) 30 minutes after start endoscopy	SpO ₂	2	96	97	96,5	0,707	5	97	100	98,8	1,095	13	96	100	97,92	1,656
	EtCO ₂	2	10,3	13,9	12,1	2,545	5	4	12,8	7,5	3,489	13	3,4	7	4,777	0,938
	Heart Rate	2	86	95	90,5	6,364	5	67	92	82,8	10,33	13	55	108	76	14,83
	Respiration rate	2	5	16	10,5	7,778	5	8	27	18,6	7,127	13	14	31	19,31	4,571

	IPI	2	3	3	3	0	5		6	4,8	0,837	13	7	10	8,85	1214
	OAA/S	2	3	3	3	0	5	3	4	3,2	0,447	13	2		2,92	0,76
(V) End of endoscopy	SpO ₂						2	96	97	96,5	0,707	18	95	100	97,67	1,815
	EtCO ₂						2	8,5	10,5	9,5	1,414	18	3,5	6,6	4,9	0,924
	Heart Rate						2	60	100	80	28,28	18	56	108	82,17	14,03
	Respiration rate						2	12	24	18	8,485	18	8	30	18,94	4,783
	IPI						2		5	4,5	0,707	18	7	10	9	1,138
	OAA/S						2	3	3	3	0	18	2		3	0,594

SpO₂: Pulse oximetry; **EtCO₂:** End-tidal carbon dioxide; **IPI:** Integrated Pulmonary Index; **OAA/S:** Observation Assessment of Alertness/Sedation; **N:** Number of Patients; **Std. Deviation:** Standard Deviation

Table 3: The distribution of physiological parameters between different IPI values.

There were no different values between the IPI groups in terms of initial SpO₂ and PR. The event “no intervention” was documented for all patients when we started the sedation. Further, during the treatments, a total of 12 “required attention” events were documented. Of these 12 events, half were for an EtCO₂ increase of more than 20%, and in six measurement points no vital signs abnormalities were recorded. A total of 3 “required intervention” events were related to an

EtCO₂ increase \geq 20%. Assuming the IPI group reflected the true ventilatory events, the IPI value was not in agreement with the observations of the condition of our patient and the OAA/S score. The overall OAA/S score during all procedures are registered in Table 4. No ventilatory and circulatory interventions were necessary during any of the procedures.

OAAS Score	Start Sedation	Start Endoscopy	15 Min after start endoscopy	30 min after start endoscopy	End of the endoscopy	Overall score	OAA
OAAS 5	100% N = 20						20% N = 20
OAAS 4							
OAAS 3		100% N = 20	55.8% N = 11	70% N = 14	55% N = 11		56% N = 56
OAAS 2			45.2% N = 9	30% N = 6	45% N = 9		24% N = 24
OAAS 1							

OAAS: Observers Assessment of Alertness Sedation scale.

Table 4: The overall OAAS Score.

Discussion

Upper GI endoscopy treatments and procedures are often complex and time-consuming. Therefore these procedures are increasingly performed with controlled intravenous (IV) sedation to relieve the patient’s pain, anxiety [14], physical discomfort, and to improve the outcome of the examination. Controlled sedation and meticulous monitoring of patients undergoing upper gastrointestinal endoscopy is in particular important because the endoscopist and the sedation practitioner share the airway, which might compromise the airway and jeopardize spontaneous ventilation easily.

In almost any GI endoscopy procedures it is mandatory to insufflate some kind of gas into the gastrointestinal tract to secure good visualization. All endoscopes used for GI endoscopy are equipped with a gas insufflation unit. Traditionally room air was used in most cases to distend tissues but the use of CO₂ insufflation has become more and more popular [15,16], because it was suggested to be associated with a

reduction in procedure related pain experiences by the patient and decreased discomfort [17]. Compared with air insufflation, CO₂ insufflation during endoscopy procedures also reduced the volume of residual gas in the digestive tract, because it diffuses rapidly into the surrounding tissues [18]. In the Fernández et al. [19] study, where the insufflation of CO₂ instead of air during the endoscopy procedures was compared, the same favorable properties of CO₂ were observed. Maeda et al. [20], has shown in his study that CO₂ insufflation does not reduce abdominal distension and does not decrease pain scores. This in contrast with Allen [21], who described a low prevalence of pain during his procedures when room air was inflated in gastroscopy and colonoscopy procedures, while Lord and Riss [22] considered that air could be an acceptable alternative to the more expensive CO₂.

Propofol/opioid based sedation techniques are suitable to produce rapid and, when necessary, deep sedation, and its effects can be reversed within minutes. However, the line between moderate-to-deep

sedation is very narrow and the patient may easily drift into an unconscious state also in relation to rapid changes in pain sensation due to the procedure. During gastroscopy procedures which are often executed in dark or semi dark environments, observation of the ventilation may be difficult, especially when the patient is hypoventilating with minimal chest excursions. Airway obstruction or hypoventilation may be difficult to detect until hypoxia occurs as is indicated by pulse oximetry. The delayed identification of airway problems could lead to a delayed intervention causing serious morbidity [23,24]. Therefore continuous real time monitoring of the vital signs is required.

Pulse oximetry and especially capnography may provide an early warning of respiratory depression during PSA in GI endoscopy intervention, to prevent hypoxemia. However, Van Loon et al. [25] showed in their study that capnography as a monitoring mode to prevent hypoxemia during elective non-anesthesiologist administered propofol sedation does not necessarily improve patient safety. New technical developments attempt to discover a methodology to integrate ventilation and oxygenation status in one device to assist, as an early warning device, if an intervention is required for the patients' safety.

In this study we evaluated the relevance of the IPI in patients undergoing upper gastrointestinal endoscopy under sedation. The IPI integrates four parameters, SpO₂, End-tidal CO₂, heart rate and respiratory rate into an algorithm to produce an online numerical value between 0 and 10. This IPI could potentially recognize changes in the patient's respiratory status at a very early moment. Garah [26] analyzed the effect of different medication dosages on the IPI during endoscopy in children even with higher ASA score patients. It is unclear, whether air or CO₂ during the endoscopy was used. In his study, lower IPI levels were registered due the presence of an anesthesiologist and the use of a higher dose of medication.

Berkenstadt showed in his study evaluating the IPI for the detection of respiratory events in sedated patients undergoing colonoscopy, a limited agreement between respiratory physiological parameters and the IPI. In our study we found 12/100 measure points indicating that the ventilation "required attention" and 3/100 measure points required "immediate intervention". The majority of "alarms" were associated with increases of the exhaled CO₂ concentration due to the insufflation of CO₂ gas by the endoscopist during upper GI endoscopy procedures. In the other "alarm" cases no association was found with data from the commonly used ventilator and circulatory parameters. Considering the inconsistency of the IPI data and based on the limited studies which have been carried out, we question whether the IPI can be developed further into a technique which will reliably inform the clinician that respiratory deterioration is at hand. A recent pilot study to test the hypothesis that the Oxygen Reserve Index would provide a clinically important warning of impending oxygen desaturation showed promising results in a selected group of patients and probably needs further exploration of its validity [27].

We conclude that the IPI has no additional value in monitoring patients under sedation for upper gastrointestinal endoscopy where CO₂ is used to dilate tissues by the endoscopist. Against the background of the results of our study, we recommend further study and to repeat our study in upper gastrointestinal endoscopy where room air, as insufflating gas, is used for tissue expansion, taking into account the uncertain effects of the insufflated gas on the pain experience of the patient. Although the value of capnography for detecting airway obstruction and/or hypoventilation is still a matter of debate we recommend the combination of pulse oximetry and

capnography as important monitors for evaluation of the ventilatory status of sedated patients next to personal observation of the patency of the airway, breathing movements and auscultation of the chest.

Conclusion

Although the Integrated Pulmonary Index as an integrated monitor of the ventilation has the potential to contribute to safety its use cannot be recommended in upper gastrointestinal endoscopy when CO₂ is used as insufflation gas. Its value in other situations related to sedation needs to be further investigated.

Acknowledgement

The authors like to thank Oridion Capnography Inc. Jerusalem, Israel, for lending us a capnostream monitor for this study.

References

- Schlag C, Wörner A, Wagenpfeil S, Kochs EF, Schmid RM, et al. (2013) Capnography improves detection of apnea during procedural sedation for percutaneous transhepatic cholangiodrainage. *Can J Gastroenterol* 27: 582-586.
- Dumonceau JM, Riphaut A, Aparicio JR, Beilenhoff U, Knape JT, et al. (2010) European Society of Gastrointestinal Endoscopy, European Society of Gastroenterology and Endoscopy Nurses and Associates, and the European Society of Anaesthesiology Guideline: Non-anesthesiologist administration of propofol for GI endoscopy. *Endoscopy* 42: 960-974.
- Lichtenstein DR, Jagannath S, Baron TH, Anderson MA, Banerjee S, et al. (2008) Sedation and anesthesia in GI endoscopy. *Gastrointest Endosc* 68: 815-826.
- Galvagno SM, Kodali BS (2009) Critical monitoring issues outside the operating room. *Anesthesiology Clin* 27: 141-156.
- Mehta PP, Kochhar G, Albeldawi M, Kirsh B, Rizk M, et al. (2016) Capnographic Monitoring in Routine EGD and Colonoscopy With Moderate Sedation: A Prospective, Randomized Controlled Trial. *Am J Gastroenterol* 111: 395-404.
- Vaessen HH, Knape JT (2016) Considerable Variability of Procedural Sedation and Analgesia Practices for Gastrointestinal Endoscopic Procedures in Europe. *Clin Endosc* 49: 47-55.
- Lightdale R, Fredette M, Atmadja M, Heard L, Jiang H. (2010) M1563: Pilot Study of the Smart Capnography Integrated Pulmonary Index™ in a pediatric gastroenterology procedure unit. *Gastrointest Endosc* 71: AB255.
- Berkenstadt H, Ben-Menachem E, Herman A, Dach R (2012) An evaluation of the Integrated Pulmonary Index (IPI) for the detection of respiratory events in sedated patients undergoing colonoscopy. *J Clin Monit Comput* 26: 177-181.
- <http://asahq.org/resources/clinical-information/asa-physical-status-classification-system>
- <http://asahq.org>
- Chernik DA, Gillings D, Laine H, Hendler J, Silver JM, et al. (1990) Validity and reliability of the observer's assessment of alertness/sedation scale: study with intravenous midazolam. *J Clin Psychopharmacol* 10: 244-251.
- (2002) Practice guidelines for sedation and analgesia by non-anesthesiologists. *Anesthesiology* 96: 1004-1017.
- Manyam SC, Gupta DK, Johnson KB, White JL, Pace NL, et al. (2007) When is a bispectral index of 60 too low?: Rational processed electroencephalographic targets are dependent on the sedative-opioid ratio. *Anesthesiology* 106: 472-483.
- Coté CJ, Wilson S (2008) Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures: an update. *Paediatr Anaesth* 18: 9-10.

15. Domagk D, Bretthauer M, Lenz P, Aabakken L, Ullerich H, et al. (2007) Carbon dioxide insufflation improves intubation depth in double-balloon enteroscopy: a randomized, controlled, double-blind trial. *Endoscopy* 39: 1064-1067.
16. Bretthauer M, Lyngge AB, Thiis-Evensen E, Hoff G, Fausa O, et al. (2005) Carbon dioxide insufflation in colonoscopy: safe and effective in sedated patients. *Endoscopy* 37: 706-709.
17. Dellon ES, Hawk JS, Grimm IS, Shaheen NJ (2009) The use of carbon dioxide for insufflation during GI endoscopy: a systematic review. *Gastrointest Endosc* 69: 843-849.
18. Shi H, Chen S, Swar G, Wang Y, Ying M (2013) Carbon dioxide insufflation during endoscopic retrograde cholangiopancreatography: a review and meta-analysis. *Pancreas* 42: 1093-1100.
19. Fernández-Calderón M, Muñoz-Navas MÁ, Carrascosa-Gil J, Betés-Ibáñez MT, de-la-Riva S, et al. (2012) Carbon dioxide vs. air insufflation in ileo-colonoscopy and in gastroscopy plus ileo-colonoscopy: a comparative study. *Rev Esp Enferm Dig* 104: 237-241.
20. Maeda Y, Hirasawa D, Fujita N, Obana T, Sugawara T, et al. (2013) A prospective, randomized, double-blind, controlled trial on the efficacy of carbon dioxide insufflation in gastric endoscopic submucosal dissection. *Endoscopy* 45: 335-341.
21. Allen P, Shaw E, Jong A, Behrens H, Skinner I (2015) Severity and duration of pain after colonoscopy and gastroscopy: a cohort study. *J Clin Nurs* 24: 1895-903.
22. Lord AC, Riss S (2014) Is the type of insufflation a key issue in gastrointestinal endoscopy? *World J Gastroenterol* 20: 2193-2199.
23. Wang CY, Ling LC, Cardoso MS, Wong AK, Wong NW (2000) Hypoxia during upper gastrointestinal endoscopy with and without sedation and the effect of pre-oxygenation on oxygen saturation. *Anaesthesia* 55: 654-658.
24. Reed MW, O'Leary DP, Duncan JL, Majeed AW, Wright B, et al. (1993) Effects of sedation and supplemental oxygen during upper alimentary tract endoscopy. *Scand J Gastroenterol* 28: 319-322.
25. van Loon K, van Rheineck Leyssius AT, van Zaane B, Denteneer M, Kalkman CJ (2014) Capnography During Deep Sedation with Propofol by Nonanesthesiologists: A Randomized Controlled Trial. *Anesth Analg* 119: 49-55.
26. Garah J, Adiv OE, Rosen I, Shaoul R (2015) The value of Integrated Pulmonary Index (IPI) monitoring during endoscopies in children. *J Clin Monit Comput* 29: 773-778.
27. Szmuk P, Steiner JW, Olomu PN, Ploski RP, Sessler DI, et al. (2016) Oxygen Reserve Index: A Novel Noninvasive Measure of Oxygen Reserve-A Pilot Study. *Anesthesiology* 124: 779-784.