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

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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 sedate 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.
GI endoscopic procedures, the Endoscopic Ultrasound (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) bolus of 10 or 20 mg of propofol were titrated until the desired level of moderate-to-deep sedation (OAA/S sedation score of 4–6) was achieved, to allow the gastroenterologist to perform his upper GI endoscopy procedure. Therefore, a maximum of 4 litres CO$_2$/ minute was insufflated 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 oximeter. NIBP measurements were taken at 5-minute intervals, and capnography readings (Smart CapnobLine 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 SpO$_2$ sensor). This monitor calculated the ventilatory status by measuring the EtCO$_2$, RR, SpO$_2$ 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 IPI patient values 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 SpO$_2$ was <92% and >88% and/or RR ≤ 8 and/or a 20% change in EtCO$_2$ from the baseline value for more than one minute. "Required intervention" events were defined when the SpO$_2$ ≤ 88% and/or loss of the EtCO$_2$ 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, SpO$_2$, EtCO$_2$, 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).

**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 monitors, 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 Systems, Needham, MA) and 200 μg of alfentanil (Janssen-Cilag) as a bolus. Additional intravenous bolus 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 CO$_2$/ minute was insufflated 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).

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**Table 1:** The meaning of the IPI monitors readings.

| 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

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

| 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 |
**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 SpO$_2$, EtCO$_2$, RR and PR and analysed by using the descriptive statistics tool.

**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.

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 (EtCO$_2$, RR, SpO$_2$, PR and OAA/S, ) are compared and presented in Table 3.

| Measure moments | Parameter | 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 |
| | Respiraion 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 |
| | EtCO$_2$ | 2 | 4 | 4.8 | 4.4 | 0.566 |
| | Heart Rate | 2 | 70 | 100 | 85 | 21.21 |
| | Respiraion rate | 2 | 6 | 8 | 7 | 1.414 |
| | IPI | 2 | 0 | 18 | 7 | 10 | 8.89 | 1132 |
| | OAA/S | 2 | 3 | 3 | 3 | 0 | 18 | 2 | 3.11 | 0.563 |
| (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 | 18 | 3.5 | 5 | 5.113 | 0.961 |
| | Heart Rate | 1 | 88 | 88 | 88 | 3 | 81 | 96 | 89 | 7.55 | 16 | 48 | 110 | 76.5 | 16.685 |
| | Respiraion rate | 1 | 20 | 20 | 20 | 3 | 8 | 26 | 14.33 | 10.116 | 18 | 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 |
| | Respiraion rate | 2 | 5 | 16 | 10.5 | 7.778 | 5 | 8 | 27 | 18.6 | 7.127 | 13 | 14 | 31 | 19.31 | 4.571 |
Suggestions made during the procedures can be documented as "required intervention". Of these 12 events, half were for an EtCO\textsubscript{2} increase of more than 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.

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

| OAAS Score | Start Sedation | Start Endoscopy | 15 Min after start endoscopy | 30 min after start endoscopy | End of the endoscopy | Overall score |
|------------|----------------|-----------------|-----------------------------|-----------------------------|---------------------|---------------|
| OAAS 5     | 100% N = 20    |                 |                             |                             |                     | 20% N = 20     |
| OAAS 4     | 100% N = 20    |                 |                             |                             |                     | 56% N = 56     |
| 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 CO\textsubscript{2} 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, CO\textsubscript{2} 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 CO\textsubscript{2} instead of air during the endoscopy procedures was compared, the same favorable properties of CO\textsubscript{2} were observed. Maeda et al. [20], has shown in his study that CO\textsubscript{2} 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 CO\textsubscript{2}.

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 and general anesthesia is often blurred. Therefore, it is necessary to monitor patients undergoing GI endoscopy properly for possible respiratory complications.
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 hypo-ventilating 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.

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