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A Pilot Evaluation of the Integrated Pulmonary Index (IPI) in Patients Undergoing Procedural Sedation: A Two-phase Observational Evaluation

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Abstract

Background: This study evaluated Integrated Pulmonary Index (IPI), a clinically validated algorithm combining $PetCO_2$, RR, SpO_2, and PR into a single value summarizing the adequacy of ventilation and oxygenation. ASA practice guidelines recommend continuous monitoring of these parameters during procedural sedation for early detection of respiratory compromise. Interpretation is routinely done by anesthesiologists but is challenging for other clinicians. IPI simplifies this process.

Methods: This was a two-phase observational evaluation of procedural sedation patients monitored with $PetCO_2$, RR, SpO_2 and PR (Capnostream20, Medtronic, Israel). In the first phase, IPI values were visible; in the second, the clinician was blinded to IPI. Clinician IPI evaluations were compared to algorithm-generated IPI.

Results: Good correlation and agreement between expert evaluation and actual IPI scores was found at both phases (ρ=0.98 for the first and 0.84 for the second, p-value for both <0.001; bias and standard were 0.04 ± 0.52 for the first and -0.01 ± 1.23 for the second).

Conclusion: IPI reliably interpreted respiratory status of patients undergoing procedural sedation or anesthesia in a clinical setting when compared to expert anesthesiologist evaluation and may simplify respiratory monitoring.

Trial registration: Not provided, was not required at time of enrollment (2010)

Introduction

In recent years, patient safety during procedural sedation has come under scrutiny and updated practice guidelines requiring continuous respiratory monitoring including capnography in patients undergoing moderate and deep sedation [1] have been published. Kurrek notes that capnography should no longer be considered a luxury but rather a necessity when providing deeper levels of sedation [2,3]. Capnography provides an early warning when a patient is at risk of respiratory compromise [4]. Adverse outcomes from sedation-related events continue to occur and recent guidelines published by the American Academy of Pediatrics call for enhanced respiratory monitoring, including capnography [5]. The most common issue judged to be associated with adverse sedation events is impaired respiration [6]. Most unwanted outcomes could have been prevented with earlier recognition of respiratory compromise and appropriate intervention.

The varying incidence of respiratory events amongst different sedation/anesthesia providers may reflect their expertise in respiratory event recognition and management: Anesthesiologists report fewer issues than pediatric intensivists or emergency medicine physicians [7,8]. This may be because not all healthcare professionals are equally trained in interpreting multiple continuous channels of capnography and oximetry data. Indeed, 'information overload' may lead to errors rather than being helpful [2] and research has shown that individuals have difficulty interpreting the overall significance of over three parameters concurrently [9,10]. Thus, a simple tool to follow the respiratory status of a monitored patient and help identify those at risk of respiratory compromise that may progress to respiratory insufficiency or beyond has potential to increase patient safety and be of use in determining need for intervention by non-anesthesiology physicians and nurses.

The Integrated Pulmonary Index™ (IPI: Medtronic, Israel) algorithm was developed and clinically validated [2] to provide a simple and accurate tool to help non-anesthesiologists identify and manage respiratory compromise. IPI is a mathematical model that integrates the values of End Tidal CO_2 ($PetCO_2$), respiratory rate (RR), oxygen saturation (SpO_2), and pulse rate (PR) in a single value. The index is calculated using the current values of these four parameters and their interactions, based on known clinical data and a clinical decision tree derived from expert opinions regarding the likelihood of different possible outcomes. The IPI scale ranges from 1 to 10: 1 for a patient requiring immediate intervention and 10 for a patient breathing normally. IPI is intended for both adult and pediatric patients. Four age groups (adult, 1-3 years, 3-6 years and 6-12 years) are defined to address different clinical ranges for respiratory parameters at different ages, particularly respiratory rate and pulse rate (Figure 1).

IPI	Patient Status
10	Normal
8-9	Within normal range
7	Close to normal range; requires attention
5-6	Requires attention and may require intervention
3-4	Requires intervention
1-2	Requires immediate intervention

Figure 1: IPI and associated patient status.

The aim of our study was to evaluate the performance of the IPI in a clinical setting on adult and pediatric patients undergoing procedural sedation or anesthesia and to assess the utility of the algorithm.

Methods

Study design

The study was designed as a two-phase observational cohort study with the aim of evaluating correlation and agreement between the algorithm IPI and clinician estimated IPI (ceIPI). CeIPI was assessed by an anesthesiologist heading a dedicated procedural sedation service at the Hebrew University medical center and an experienced sedation nurse. Patients who were summoned for planned procedures were enrolled consecutively during the study in 2010. The study was approved by the hospital's ethics committee. Patients were monitored using the Capnostream20 monitor (Medtronic, Israel), alongside a Smart CapnoLine Microstream CO_2 sampling line (Medtronic, Israel) delivering supplemental oxygen up to 5 L/min (non-intubated) and a FilterLine Microstream CO_2 sampling line (Medtronic, Israel) (intubated).

Figure 2: Capnostream 20.

Phase one was not blinded, with the algorithm IPI alongside the four continuously monitored parameters ($PetCO_2$, RR, SpO_2 and PR) visible to the clinician. The clinician assessed the accuracy of the algorithm IPI value at 5-minute intervals based on the four continuously monitored parameters and their clinical assessment. In phase two, the clinician was blinded to the algorithm IPI value and used their clinical judgement and the four continuously monitored parameters to determine a ceIPI at 5-minute intervals. All monitored parameters were continuously recorded (Figure 2).

The sample size was intended to demonstrate the performance of the algorithm on a convenience sample of patients undergoing a variety of procedures under sedation and anesthesia, representing the typical patients cared for at the medical center.

Study population

Pediatric and adult patients undergoing moderate or deep procedural sedation or anesthesia in a clinical setting, monitored by a capnograph and pulse oximeter for at least 15 minutes during the procedure, were eligible for inclusion in the study. All patients provided informed consent. Patients <1 year, pregnant or lactating patients, and patients with an ASA classification of III-IV were excluded. The patient's age group was inputted to meet the algorithm IPI data entry requirements (1-3 years, 3-6 years, 6-12 years, and adult). No other selection criteria were applied, and the enrolled patients represented a typical sample of the patients at a hospital-based service.

Data analysis

Data were considered valid if at least 3 IPI pairs (algorithm IPI and ceIPI) were available per case. Cases that did not include at least 3 IPI pairs were not used. We evaluated the correlation of algorithm IPI and ceIPI using linear regression analysis and assessed the agreement between these measurements (bias [mean difference] and precision [standard deviation of the differences]) using the Bland–Altman technique for multiple observations [11].

Level of significance was set at $P<0.05$. Matlab software was employed for the analysis (Matlab version 8.5.0.197613 R2015a, Natick, MA: The MathWorks, Inc., 2003).

Results

Phase 1 included 56 valid cases from 72 enrolled patients. Of the 16 invalid cases, one dropped out early due to sedation failure, 13 cases had data recording issues, and two cases were identified as ASA 3 or 4 status. Valid cases included adults (N=12) and pediatrics, with a range of sedation agents used, including Propofol, Ketamine, Midazolam, Chloral hydrate, and Sevoflurane/N20/Isoflurane. Depth of sedation ranged from moderate sedation to anesthesia.

The 56 valid cases provided a total of 539 paired measurements (median=8, min-max: 3-25 per case). The average duration of the cases was 50 ± 29 min. The average value of algorithm IPI was 6.97(2.7), and the average value of the Ce IPI was 6.93(2.7).

Phase 2 consisted of 30 cases during which the clinician was blinded to the algorithm IPI during the entire case. There were no case exclusions and patients included adults (N=9) and pediatrics. Sedation agents included Propofol, Ketamine, Chloral hydrate, Triclonam, and Midazolam, and depth of sedation ranged from moderate sedation to anesthesia. The average duration of the cases was 40 ± 20 min. The 30

cases provided a total of 283 paired measurements (median=9, min-max: 3-29 per case). The average value of the algorithm IPI was 8.25 ± 2.2 and the average ceIPI was 8.26 ± 2.2.
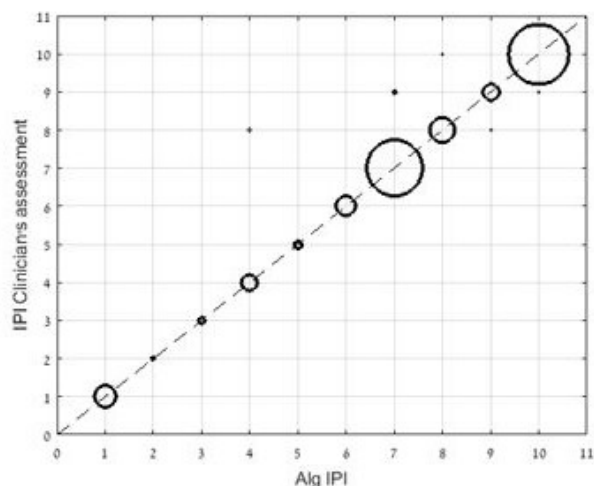

Figure 3: Scatter plot of IPI values as assessed by expert anesthesiologist and calculated by the algorithm for the non-blinded data (the circle's size is proportional to the number of samples). R=0.98 (p<<0.001).
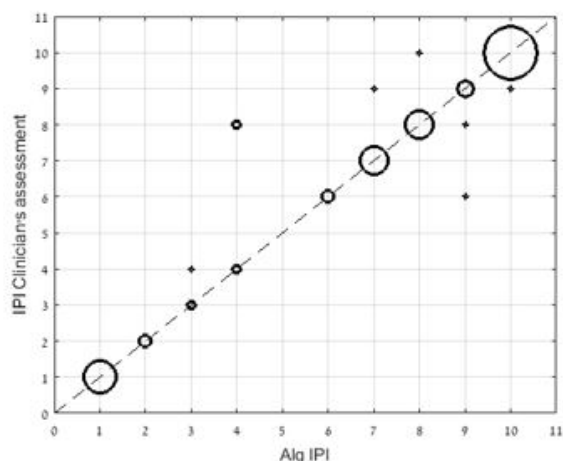

Figure 4: Scatter plot of the first value per case of IPI as assessed by expert anesthesiologist and calculated by the algorithm for the non-blinded data (the circle's size is proportional to the number of samples). R=0.96 (p<<0.001).

The level of agreement between the algorithm IPI and ceIPI was good, with a bias of -0.04 ± 0.52 for the non-blinded data in phase I (p=0.002) and -0.01 ± 1.23 for the blinded data in phase II (p<0.001). Per patient analysis was performed in addition to data point analysis to correct for potential patient bias. Significant, positive correlation was found for all data points (ρ=0.98; p<0.001) and the first data point per

case (ρ=0.96; p<0.001) in phase I (Figure 3). In phase II, the correlation value was lower but still positive and significant, being ρ=0.84 (p<0.001) for all data points and ρ=0.90 (p<0.001) for the first data point per case (Figures 4-8).
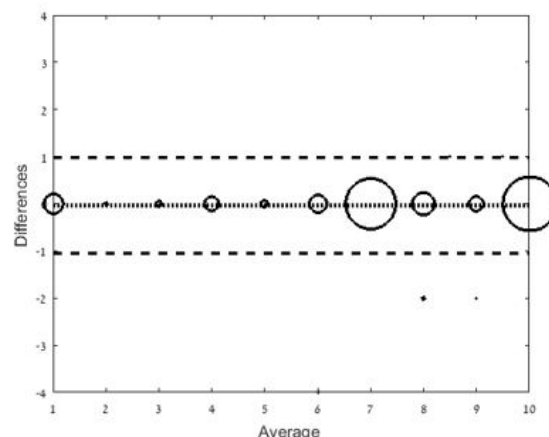

Figure 5: Bland-Altman plot demonstrating the level of agreement between algorithmic IPI and clinician's assessment for the non-blinded data (the circle's size is proportional to the number of samples). Bias=-0.04, std=0.52 (p<<0.001).
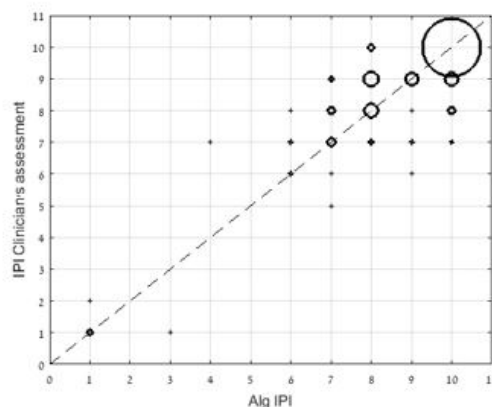

Figure 6: Scatter plot of IPI values as assessed by clinician and calculated by the algorithm for the blinded data (the circle's size is proportional to the number of samples).). R=0.84 (p<<0.001).
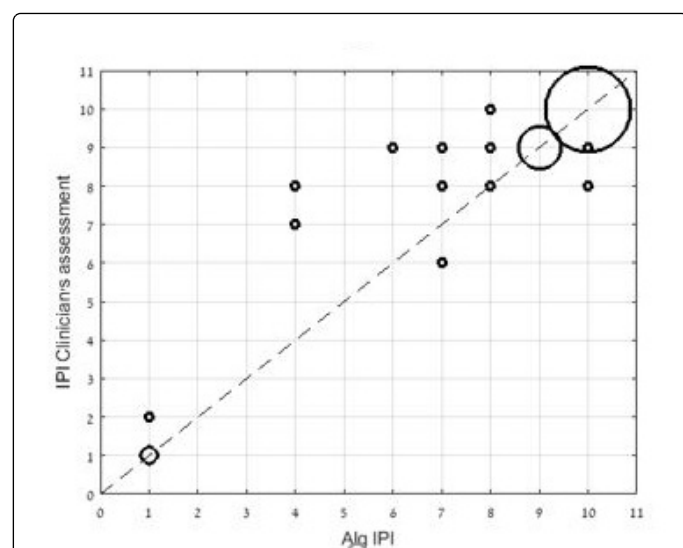
Figure 7: Scatter plot of the first value per case of IPI as assessed by expert anesthesiologist and calculated by the algorithm for the blinded data (the circle's size is proportional to the number of samples). R=0.90 (p<<0.001).
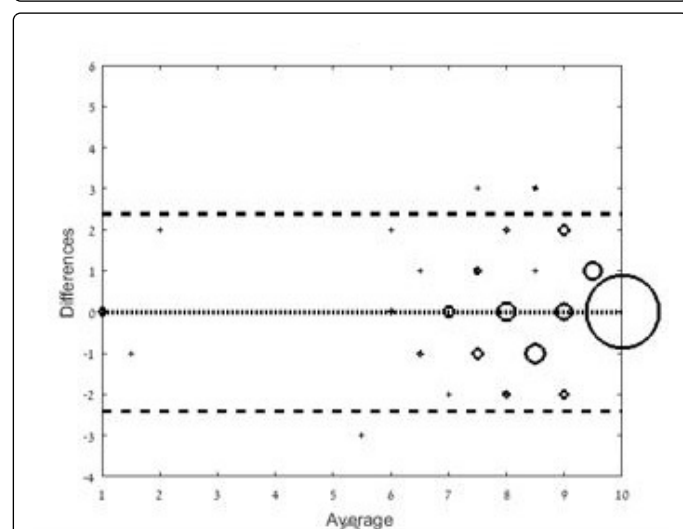

Figure 8: Bland-Altman plot demonstrating the level of agreement between algorithmic IPI and clinician's assessment for the blinded data (the circle's size is proportional to the number of samples). Bias=-0.01, std=1.23 (p<<0.001).

Discussion

The provision of sedation, once primarily performed by anesthesiologists, is now routinely implemented by other specialists [5]. Therefore, providing tools to simplify respiratory monitoring during sedation has the potential to improve patient outcomes.

This pilot study assessed the reliability of the IPI algorithm in actual clinical practice. In our study, expert clinicians attending the sedation provided real-time assessment of IPI. The study results demonstrate the reliability of the IPI algorithm used in a typical sedation service, as a tool that may simplify respiratory monitoring. High levels of agreement and correlation were demonstrated for both the non-blinded and blinded patients, indicating the clinical relevance of the IPI algorithm.

Due to sample size limitations, it was not possible to perform sub-group analyses. A significant difference in average IPI values was noted between the non-blinded and blinded groups (6.97 vs. 8.25), p<0.01. Based on the high level of correlation between algorithm IPI and ceIPI in both phases, we conclude that this difference may be attributed to cohort differences between phase I and phase II, due to limitations in sample size.

All patients were attended by an expert anesthesiologist who participated in the development of the IPI algorithm. This may have in part influenced the high level of agreement between the ceIPI and the algorithm IPI values. It should be noted, however, that over 30 expert clinicians participated equally in development of the IPI and so the influence of one participant on the final IPI algorithm rules is not high.

There are four levels of sedation, often discussed as a continuum, defined by the American Society of Anesthesiologists: minimal sedation (anxiolysis), moderate sedation (conscious), deep sedation (unconscious) and general anesthesia [5]. Procedural sedation and analgesia, intended to provide a patient with a specific state of sedation, may lead to deeper state with unexpected ease and rapidity [1].

In a study by Cravero et al., anesthesiologists came in at third place as providers overseeing sedation of pediatric patients [12]. In 49,805 pediatric sedations, pediatric intensivists provided sedation in almost 49% of the cases, emergency medicine physicians in 36% and anesthesiologists in 10%. In this study, serious adverse events were rare; however minor (but potentially serious) adverse events occurred frequently: 1 in 65 propofol sedations. Cravero and colleagues [12] noted that 1 in 70 propofol sedations required airway and ventilation interventions, from a simple airway placement to tracheal intubation.

Cote et al. [5] identified several features associated with adverse sedation events and poor outcomes: inadequate resuscitation, medication errors, inadequate monitoring, and inadequate pre-sedation evaluation. The respiratory system was most often the first system affected. Cote's data suggest that poor outcomes occur when the sedating physician is not adequately vigilant during and after the procedure, and lacks the skills to manage respiratory depression. Another study showed that $PetCO_2$ abnormalities occur before oxygen desaturation or observed hypoventilation in patients with a critical respiratory event, especially with oxygen provision [8]. The Cravero study emphasized the need for monitoring of ventilation (such as $PetCO_2$) when propofol is administered for sedation, given the significant likelihood of airway obstruction or central apnea. In a study [13] conducted by the Pediatric Sedation Research Consortium evaluating the use of ketamine predominantly outside the operating room, an incidence of 1.77% of severe adverse events was noted in over 20,000 cases, indicating that pediatric sedation is not risk-free without propofol. Accordingly, the American Society of Anesthesiologists practice guidelines for sedation and analgesia by non-anesthesiologist's state that monitoring oxygenation by pulse oximetry is not a substitute for monitoring ventilatory function by capnography [1]. More recently, the American Academy of Pediatrics has issued guidelines requiring $PetCO_2$ monitoring during procedural sedation in children, based on recognition of the utility of continuous monitoring for the improvement of patient outcomes [5].

IPI includes all guideline-recommended respiratory parameters in a single value, allowing the sedation provider to recognize a potentially critical respiratory event and alert emergency assistance when required. Appropriate use of IPI could prevent the progress of respiratory compromise to respiratory failure and arrest. Further evaluations of IPI have been reported in both adult [14,15] and pediatric patients [16] with results and conclusions depending on the definitions of adverse events and alarm thresholds selected by the investigators. There is, though, general agreement in these studies that the IPI is of clinical relevance and could be of benefit to patient safety during sedation and anesthesia.

Conclusion

The present study demonstrates the reliability of the IPI in a mixed cohort of adult and pediatric patients. The IPI reliably interpreted the respiratory status of adult and pediatric patients undergoing procedural sedation in a clinical setting. The IPI is a useful tool for the simplification of respiratory monitoring. Sedation providers may benefit from using IPI when monitoring ventilation and oxygenation during procedural sedation.

Ethics Approval and Consent to Participate

The study was approved by the hospital Helsinki Committee and all patients provided informed consent.

Availability of Data and Material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests

Funding

Acknowledgements

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