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Procedural Sedation and the Risk of Hypoxemia

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Abstract

Background: Today's hospital care shows an increase in therapeutic and diagnostic procedures performed outside the operating room under procedural sedation, rather than in the operating room. Yet, despite this shift in attitudes, there is evident paucity of studies examining the nature of the interventions performed under procedural sedation. The primary objective of this study was the identification of interventions performed under sedation outside the operating room, focusing on those associated with hypoxemia below SpO_2 90%.

Methods: From January the 1st 2011 up to December the 31st 2013, 2,328 diagnostic procedures in the outpatient setting of a general hospital were retrospectively analysed for hypoxemia with SpO_2 below 90% and below 85% for at least one minute and SpO_2 below 90% over 2 min. The assessed interventions were classified as endobronchial, in airway, and not in airway interventions. Absolute risk differences in desaturation among the three groups were calculated using the Wilson procedure.

Results: Endobronchial procedures were statistically significant associated with a higher prevalence of hypoxemia compared to the other two interventions. The absolute risk difference with the in-airway group and not-in-airway group was 20.2% (95%CI 13.0 to 27.9) and 21.3% (95% 14.0 to 29.2), respectively. The difference remained significant after correction for confounding by two established risk factors, BMI and ASA classification.

Conclusion: Endobronchial procedures were associated with significantly more frequent and longer periods of hypoxemia. Thus, it can be concluded that, during procedural sedation, the type of invasive procedure is an important factor in estimating the a priori risk of hypoxemia.

Keywords: Procedural sedation; Sedation; Hypoxemia; Risk factors; Diagnostic interventions; Therapeutic interventions

Background

In the last decade, procedural sedation and analgesia (PSA) has increased exponentially with the introduction of complex therapeutic and diagnostic procedures performed outside the operating room (OR). This development also exposes patients to significant co-morbidity risks. As the procedures are increasingly complex, invasive and last longer, they require extensive doses of hypnotics and sedatives.

The PSA in our hospital is being performed by specifically trained anaesthesia nurses and physician assistants (PA), under the indirect supervision of an anaesthesiologist. Since 2008, we have been required to respond to a growing demand for PSA. As a result, to date, we have performed approximately 1,500 PSAs per year for a very wide variety of procedures. Mostly invasive and applied to rather vulnerable patient categories. While there are several reasons for the growing demand, the main one stems from the introduction of new legislation in 2012, whereby the Dutch governmental Department of Health mandates that PSA is performed by specially trained medical personnel. The onus on value-based healthcare is the second reason, which has resulted in the growing number of procedures being performed in outpatient setting, rather than in the OR. The first reason probably makes the procedures safer, while the second can increase the adverse events during PSA.

Systematic reviews and large cohort studies that have been conducted to date yielded findings suggesting that PSA in the outpatient setting is safe, as very few complications occur [1-13]. However, a review of PSA procedures revealed that adverse effects and complications were more frequent and more severe in patients treated in an outpatient setting. One of the most commonly reported complications was hypoxemia with SpO_2 below 90% for more than 30 seconds [14,15]. In an extensive retrospective review encompassing 143,000 cases indicated that adverse events are associated with adult moderate PSA, whereby hypoxemia was found to be the most common complication [16]. Empirical evidence also suggested two general factors for the cause of hypoxemia during PSA, Body Mass Index (BMI) and the American Society of Anaesthesiologists classification (ASA) were the most important and is deemed independent from those pertinent to the field of general anaesthesia. However, many practitioners argue that they nonetheless contribute to the overall PSA risk. In contrast, the wide spectrum of innovative diagnostic and therapeutic interventions in the outpatient setting has not been assessed for these patient risks. One of the invasive procedures frequently performed in our hospital is endobronchial ultrasound (EBUS). In our clinical observation, EBUS was associated with longer periods of hypoxemia than procedures in the supraglottic airway and those not involving the airway, independently from the ASA

classification and patient's BMI. We thus hypothesized that, in addition to obesity and ASA classification, the site of intervention is an important predictor of hypoxemia during PSA. The goal of this retrospective database study was to identify specific PSA procedures associated with hypoxemia.

Methods

Study design

In this retrospective database study, we compared hypoxemia, defined as SpO_2 below 90% and below 85% for at least 1 min and SpO_2 below 90% over 2 min among three groups requiring PSA performed in the outpatient setting. The three types of diagnostic procedures consisted of Endobronchial procedures (EB), which included endobronchial ultrasound and bronchoscopy; In Airway procedures (IA), comprising gastroscopy, endo-ultrasound and endoscopic retrograde cholangiopancreatography (ERCP); and Not In Airway procedures (NIA), namely colonoscopy, urological, orthopaedic and gynaecological procedures.

After approval from the local medical ethics committee, we identified the records of patients that had been referred for PSA for diagnostic procedures in the outpatient setting of the OLVG hospital, a 550 bed general hospital. Data has been collected from January the 1st 2011 to December the 31st 2013. These records were assessed against the inclusion criteria, which required all patients to be adults (>18 years) and receiving PSA. Records of patient with initial SpO_2 below 90% were excluded from further analysis. The collected patient data included vital parameters, and patient characteristics, e.g. ASA classification, and procedure type. In the cases were parameters were registered incorrectly records were inspected manually and excluded from the study if necessary. For the patients undergoing two procedures during the same session the most invasive procedure was used in analysis.

PSA was conducted in accordance with the prevailing protocols. Briefly, the physical condition, including ASA classification and BMI were assessed before the start of the procedure. Patients received a 22 gauge intravenous catheter, pulse-oximeter, non-invasive intermittent blood pressure measurement, and a 3-channel ECG (Philips Medizin System e® 2008). All patients received oxygen support (100%, 3 L/min). Accuracy of measurements are confirmed by regularly checking the plethysmography. PSA was performed using propofol (Diprivan®, AstraZeneca) and alfentanil (Rapifen®, Jansen-Cilag bv). The total amounts administered were registered in the database via automated syringe pumps (Green Stream Argus 600 SY-P®, Swiss) connected to a data monitoring program, while boluses and other supporting medication were entered manually. The duration of the procedure was defined as the time between starting and ending measurements. PSA was provided by anaesthetic nurses and physician assistants with at least 5 years working experience in the OR. In the case of an adverse event, the anaesthesiologist was consulted.

Primary and secondary outcomes

Hypoxemia was defined as a SpO_2<90% for at least one minute. In addition, we also assessed patients in whom hypoxemia lasted more than two minutes, as well as those with severe hypoxemia (SpO_2<85%) for one minute or longer. The following variables were compared across the PSA groups (i.e., EB, IA and NIA groups): age, sex, ASA classification, procedure duration, BMI and the total amount of propofol in mg/kg/min.

Statistical analyses

Patients were divided into three groups according to the type of diagnostic procedure for which procedural sedation was initiated. Categorical data were presented in numbers, and percentages and continuous data with mean and standard deviation or median and interquartile range, where applicable. To explore differences in patient characteristics among the three groups, Kruskal-Wallis test was used to compare continuous variables depending on the distribution. Differences in the distribution of nominal variables among the three groups were explored using Chi-squared test.

To analyze desaturation in relation to the diagnostic procedure, the absolute risk differences (ARD) among the three groups were calculated with 95% confidence interval using Wilson's procedure. To explore for confounding in the relation between desaturation and the type of diagnostic procedure, logistic regression analysis was preformed. The statistical analysis was performed via SPSS software package, version 18.0 (SPSS Inc., Chicago, IL). In all analyses, p-values less than 0.05 were considered statistically significant.

Results

Patient characteristics are presented in Table 1. As previously noted, the cohort comprised of 2,328 patients and was divided into three groups, based on intervention type. Analyses revealed that 165 (7.1%) patients underwent an endobronchial procedure (EB), 1,382 (59.4%) underwent an in-airway procedure (IA) and the remaining 781 (33.5%) patients underwent a not in-airway procedure (NIA). The distribution of median BMI and the proportion of patients classified ASA II did not show statistically significant differences among the three groups.

Patient characteristics	Total cohort, 2328	Endobronchial 165 (7.1%)	In-airway 1382 (59.4%)	Not-in airway 781 (33.5%)	P-value
Age years (median, IQR)	59 (48-69)	62 (51-70)	61 (50-71)	54 (43-65)	<0.001
Male (N%)	1106 (47.5)	92 (55.8)	698 (50.5)	316 (40.5)	<0.001
Length cm (median, IQR)	172 (165-178)	171 (164-178)	171 (165-178)	172 (165-180)	0.067
Weight kg (median, IQR)	74 (63-84)	74 (62-83)	73 (64-83)	75 (63-85)	0.26
BMI (median, IQR)	24.0 (22-27.8)	24.0 (21.5-27.9)	24.0 (22.0-27.9)	24.5 (22.1-27.7)	0.9
ASA 1 (n%)	651 (28)	38 (23.0)	335 (24.2)	278 (35.6)	<0.001
ASA 2 (n%)	1258 (54)	82 (49.7	750 (54.3)	426 (54.5)	0.51
ASA 3 (n%)	387 (16.6)	44 (26.7)	271 (19.6)	72 (9.2)	<0.001
ASA 4 (n%)	32 (1.4)	1 (0.6)	26 (1.9)	5 (0.6)	0.04

Time procedure min. (median, IQR)	43 (30-61)	63 (52-78)	45 (32-61)	36 (26-51)	<0.001
Propofol mg/Kg/min (mean, SD)	0.08 (0.06-0.10)	0.08 (0.003)	0.09 (0.005)	0.09 (0.002)	<0.023

Table 1: Patient characteristics, differences are compared with Kruskall-Wallis test or Chi-square test depending on the variable and distribution. P value less than 0.05 is considered statistically significant.

All other patient characteristics showed statistically significant differences among the three groups. For example, patients in the NIA group were younger, whereby their median age was 8 and 7 years lower than that of the EB and the IA group, respectively (p=0.001). The proportion of male patients in the EB group was higher by 5% and 15% compared to the IA and the NIA group, respectively (p=0.001). In addition, significantly more patients in the EB group were classified as having higher ASA risk (7.1% vs. 17.5%, p=0.001), whereas those classified as lower ASA risk were asymmetrically distributed in the NIA group (11.4% vs. 12.6%, p=0.001). The proportion of patients classified as ASA IV in the IA group was higher by 1.3% compared to the EB and the NI group (p=0.04). The median duration of the EB procedure was 18 and 27 min longer compared to the IA and the NIA group, respectively (p=0.001). Finally, the total amount of propofol in mg/Kg/min was lower in the EB compared with the IA and NIA groups (p=0.023)

The primary and secondary outcomes are displayed in Table 2. As can be seen from the results, hypoxemia and severe hypoxemia occurred more frequently in the EB group compared to the other two intervention groups. The calculated absolute risk differences show that these results are statistically significant.

Outcome	Total cohort 2328	Endobronchial 165 (7.1%)	In-airway 1382 (59.4%)	Not-in airway 781 (33.5%)	Δ% (95%CI) EB vs IA	Δ% (95%CI) EB vs NIA	Δ% (95%CI) IA vs NIA
SpO_2<90% ≥ 1 min.**	373 (16.0)	58 (35.2)	207 (15.0)	108 (13.8)	20.2 (13.0 to 27.9)	21.3 (14.0 to 29.2)	1.2 (-2.0 to 4.1)
SpO_2<90% ≥ 2 min.**	194 (8.3)	35 (21.2)	112 (8.1)	47 (6.0)	13.1 (7.4 to 20.1)	15.2 (9.3 to 22.2)	2.0 (-0.2 to 4.2)
SpO_2<85% ≥ 1 min. **	145 (6.2)	24 (14.5)	82 (5.9)	39 (5.0)	8.6 (3.8 to 14.9)	9.6 (4.7 to 15.9)	0.9 (-1.1 to 2.8)

Table 2: Delta percentages for hypoxemia (SpO_2<90%) and severe hypoxemia (SpO_2<85%), calculation of 95% confidence interval for the difference between two independent proportions using the Wilson procedure without a correction for continuity.

Age and ASA class IV were detected as independent predictors of desaturation with odds ratios of respectively 1.008 (95% CI 1.001 to 1.015) and 2.24 (95% CI 1.137 to 5.154). Other characteristics, i.e., BMI and procedure duration, are not statistically significantly associated with hypoxemia in our data.

Univariate logistic regression with hypoxemia with SpO_2<90% for at least one minute as dependent variable and the type of procedure as independent variable showed that the odds ratio of hypoxemia for patients undergoing EB was 3.378 (95%CI 2.313 to 4.933). Compared to patients undergoing NIA procedures as the reference group, there were no statistically significant differences in hypoxemia between the IA and the NIA group. Adjusted for age and ASA classification, the odds ratios of hypoxemia between patients undergoing IA and NIA procedures were 0.320 (95% CI) and 0.307 (95% CI) when compared to those in the EB group, as shown in Table 3.

Multivariate	Wald	Sig.	Exp (B)	95%CI for Exp (B)
Endobronchial	43.719	0	-	-
In-airway	40.062	0	0.32	0.224 to 0.455
Not-in-airway	36.61	0	0.307	0.210 to 0.450
Age	2.517	0.113	1.006	0.999 to 1.014
ASA 4	5.1	0.024	2.42	1.124 to 5.210

Table 3: Multivariate logistic regression analysis with hypoxemia SpO_2<90%>1 min as dependend variable and endobronchial procedures as reference category, R^2=0.020 (Cox & Snell R Square), 0.035 (Nagelkerke R Square) the amount of variation in the outcome variable that is accounted for by the model, model Chi Square 47.564 (4) p>0.001.

Discussion

In this retrospective database study, we have revealed that EB the type of diagnostic procedure acts as a predictor for hypoxemia and severe hypoxemia during procedural sedation. These findings are independent from the established patient-related risk factors, such as ASA classification and BMI.

In this study, age was also an independent predictor. This finding can be explained by the high percentage of young people undergoing mostly colonoscopy procedures in the NIA group. Such procedures are frequently performed on young adults with inflammatory bowel disease as well as in gynaecological procedures on young women. There can be several reasons behind the patients in the EB group being more prone to desaturation during the procedure. For example, it is well known that EB procedures compromise the airway patency by mechanic obstruction of the airway. Although IA procedures result in compromised access of the airway too, they are not accompanied by the extensive stimulation of the subglottic airway. EB procedures also tend to cause a very strong cough reflex that can result in less effective breathing. The other contributing factor could be the underlying pulmonic neoplasm in many of these patients. Although we excluded patients with an initial SpO_2 below 90%, patients with a lower FRC or a bronchus blocking tumour are prone to desaturation during PSA. Initially, we expected that the coughing reflex would be inhibited, as well as breathing frequency to be depressed, due to a higher dose of sedatives and analgesia.

The results, though, showed that the patient in the EB group received statistically significantly fewer sedatives compared to the other two groups (p=0.023). There can be several reasons for these findings. For example, the anaesthetic nurse or physician assistant administering sedation is maybe more inclined to use high doses of propofol with this vulnerable group of patients. Propofol reduces the respiratory rate and can cause apnoea, especially in combination with opioids. In this light, we recently started to give the ASA III/IV patients small doses of ketamine alongside propofol and alfentanil. However, further studies are needed in order to ascertain whether this protocol has any effect on hypoxemia prevalence during the EB procedures.

The findings yielded by our study prompt the question of whether the endobronchial procedure should be performed under general anaesthesia while the patient is intubated. We have discussed this with the performing pulmonologist and reached the conclusion that this procedure does pose a risk, as there is a chance of tube dislocation. Moreover, the likelihood of damaging the trachea is increased by the use of a breathing tube and the endobronchial scope at the same time. This implies that the relatively new EB procedures should be treated separately from the more conventional IA and NIA procedures. Alternative sedatives such as ketamine maybe an appropriate approach to circumvent hypoxemia [17].

Conclusion

In this retrospective cohort study exploring the predictors of hypoxemia during procedural sedation, endobronchial procedures were found to be an independent predictor of hypoxemia with a SpO_2<90% and a duration of more than one minute.

Conflicts of Interest

This study was supported by departmental funding. No other funding was received. The authors declare no conflicts of interest.

Author's Contributions

B Thiel, designed and conducted the study, analyzed the data, and wrote the manuscript. R. Kraima, helped design and conduct the study, analyze the data, and write the manuscript. S. Klok, has collected and verified the original study data. R. Schrier, helped design and conduct the study. M. Godfried, helped design and conduct the study, analyze the data, and write the manuscript, reviewed the analysis of the data and approved the final manuscript. All authors read and approved the final manuscript.

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