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Research Article

Respiratory adverse events associated with deep propofol sedation during upper gastrointestinal procedures in children

William E Novotny[1]*, Khanh Nguyen[1], Folashade Jose[2], Dynita Haislip[3], Gregg A Grothmann[1] and Dmitry Tumin[1]

[1]Department of Pediatrics, Brody School of Medicine, 600 Moye Blvd, Greenville, NC 27834, USA

[2]Carolina Pediatric Gastroenterology, 100 Medical Park Drive, Suite 310, Concord, NC 28025, USA

[3]Vidant Medical Center, 2100 Stantonsburg Road, Pediatric Intensive Care Unit, Greenville, NC 27834, USA

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***Corresponding author:** William E Novotny, Department of Pediatrics, Brody School of Medicine, 600 Moye Blvd, Greenville, NC 27834, USA, Fax: 252-744-5759; E-mail: novotnyw@ecu.edu

ORCID: https://orcid.org/0000-0001-7010-0590

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Abstract

Background/Aims: Upper airway stimulation with endoscopes and pH-impedance probes during deep propofol sedation confers unknown risk for associated respiratory adverse airway events. This report quantifies frequencies of such events and airway rescue interventions associated with Esophagogastroduodenoscopies (EGD) and multi-channel intraluminal acid detection impedance probe (MIIP) placements.

Methods: This was a prospective observational study regarding occurrence of adverse respiratory events in 42 children undergoing propofol sedated EGDs and MIIP placements: Group 1. (n=21 EGDs), Group2 (n=21 EGDs before MIIP), Group 3. (n=21 during MIIP).

Results: All procedures were successfully completed using deep propofol sedation. Respiratory events were transient and associated with no morbidity or mortality. Nearly half of each group experienced a respiratory event. "Partial airway obstruction" during 42 EGDs occurred in 28.6% and responded to simple airway interventions. "Complete airway obstruction" occurred during 1/42 EGDs and 2/21 MIIPs. Throughout MIIP placement, endoscopic visualization of the glottis was maintained and unnecessary stimulation of the glottis was avoided; nonetheless, complete airway obstruction occurred in 2/21. Advanced airway rescue maneuvers were not required in either instance.

Conclusions: Respiratory adverse events commonly occurred during EGDs and MIIP placements. All events were successfully rescued by simple airway interventions.

Introduction

Deep sedation or general endotracheal anesthesia is typically employed to facilitate the performance of upper endoscopic procedures in children. Deep intravenous (IV) sedation is known to increase patient comfort, improve endoscopic performance and to increase endoscopist satisfaction [1]. When IV propofol is used during pediatric EGD to induce deep sedation, respiratory complications are known to occur [2]. In a retrospective analysis of EGD and colonoscopy performed in children with propofol, the prevalence of adverse events was 4.8%; these included "persistent desaturations" (1.5%), airway obstruction (1%), cough (0.9%), and laryngospasm (0.6%) [3]. Perioperative laryngospasm has been noted to be a more common adverse event in children than adults [4] and is more frequent during oral esophagoscopy (48.5/1000)

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than other non-endoscopic procedures (17.3/1000) [4]. It is not known whether insertion of a nasal-esophageal multi-channel intraluminal acid detection Impedance Probe (MIIP) after completion of an EGD utilizing deep sedation with propofol is associated with increased incidence of airway compromise, when compared to that occurring during EGDs. This study sought to determine whether the incidence of respiratory compromise was different in children undergoing an EGD vs. those having an MIIP placed.

Materials and methods

This was a prospective observational cohort study approved the Investigational Review Board at East Carolina School of Medicine conducted at a tertiary care medical center from November 2016 through February 2019. It conformed to the ethical standards of the Declaration of Helsinki. This study was reviewed and sanctioned by the Investigational Review Board of the biomedical division of East Carolina University IRB00000705. Patients were prospectively recruited on the day that the sedated gastrointestinal procedures were performed. Informed and signed consent/assent was obtained in each instance. A sample of 42 children ages 0-18 years who required sedated EGDs (n=21 in Group 1 and n= 21 in Group 2.) were studied. Group 2 children also underwent MIIP placement performed following performance of the EGD. The time interval needed for MIIP placement was separately analyzed for respiratory adverse events. This MIIP placement time interval is designated as "Group 3.". Data collection was incomplete for 3 children who were initially assigned to Group 2-Group 3. For this reason, three additional sequential children were recruited and enrolled who had both EGDs and MIIP placement performed to help avoid bias. Study enrollment was discontinued after a total of 42 patients were studied (n=21 Group1 and n=21 Groups 2-.Group 3.) where complete data had been collected. This "convenience sample" was chosen because different pediatric gastroenterologists began to perform the procedures being studied, and a different model of an esophageal MIIP had been purchased for insertion.

One experienced and practiced sedationist who had previous pediatric intensivist training, administered propofol, provided airway support during the procedures and recorded all complications and interventions that were encountered during the sedated procedure. Before each procedure was performed, data that might have predicted increase risk for respiratory compromise in the setting of sedation/anesthesia were collected. These included age, weight, body mass index, tonsil size, Mallampati score, ASA score, history of Gastroesophageal Reflux (GER), snoring, current URI/URI within the last 2 weeks, sinusitis, problems with previous sedation, problems with previous anesthesia, smoking status, presence of pre-procedure anxiety [5-14]. Before, during and after the sedation, heart rate, blood pressure, respiratory rate, pulse oximeter saturations and end-tidal carbon dioxide readings were monitored by the sedationist and recorded every every 5 minutes by the bedside nurse and more frequently as clinically indicated. Supplemental nasal canula oxygen at 3 liters/minute was routinely administered during all procedures. Data descriptive of patient respiratory compromise was recorded by the sedationist on data collection sheets immediately following completion of the procedure/s; these data included those listed in Tables 1-3.

Initial intravenous propofol boluses were administered at 1.5 mg/kg up to a maximum dose of 40 mg; simultaneously an infusion rate of 200 mcg/kg/minute was continued throughout the procedure. Further boluses were administered in addition to the propofol infusion rate to achieve minimal patient movement to pinch of the arm throughout the procedure(s). If during insertion of the endoscope or the MIIP the child's arm contracted, or the neck extended then up to an additional 1 mg/kg of propofol bolus was administered to a maximum of 25 mg. Once adequate sedation was accomplished, the EGD and/or placement of the MIIP was performed. If airway obstruction occurred that was not remediated by airway suctioning and repositioning, then additional propofol was administered. Intravenous glycopyrrolate (5 mcg/kg/IV up to 0.2 mg) was dosed prior to the 41 of 42 procedure(s) to reduce airway secretions. One of two experienced pediatric gastroenterologists performed all procedures in an outpatient endoscopy suite.

Endoscopies were performed using an Olympus 180 flexible endoscope (Olympus Corp, Tokyo, Japan). An esophageal 6.4 Fr MIIP (Medtronic Inc., Minneapolis MN) was placed after completion of the EGD in each child of Group 3. During passage of the MIIP, efforts were made to maintain a "continuous" endoscopic view of the glottis; where possible, tactile noxious stimuli to the glottis from the MIIP was avoided. If the endoscopic view of the glottis was only transiently maintained or incomplete, the view was scored as "partial". The MIIP was advanced far enough to have the distal tip of the probe positioned in the stomach. A second, proximal sensing site on the impedance sensor was estimated to be in appropriate position as demonstrated on a chest radiograph.

The primary Respiratory Adverse Events (RAE) outcome variables were the occurrence of pulse oximeter desaturation <90% for ≥30 seconds, use of bag mask ventilation and occurrence of airway obstruction. The "airway obstruction" was evidenced by the appearance of tracheal tugging. "Partial airway obstruction" was evidenced by grossly audible airway noise which remediated with repositioning and/or suctioning of the airway. "Complete airway obstruction" was recognized to be present if no airway noise accompanied breathing efforts and this condition was not remediated after these airway rescue interventions were performed. Other RAEs included use of blow by oxygen in addition to nasal cannula oxygen for decreasing pulse oximeter saturation in the range of >90%, suctioning of airway secretions or occurrence of coughing during the procedure. Airway assessment and intervention methods were identical in both groups. Until fully awakened each child was monitored by the sedationist the treatment room.

This was a prospective descriptive study with no baseline complication rate related to positioning the MIIP established. Consequently, no *a priori* analysis was performed to power the study for detecting a predetermined difference among the study groups. Data analysis was initiated after all procedures had been completed. Patient characteristics were compared according to

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the occurrence of RAE using rank-sum tests for continuous data, and Chi-square tests for categorical data. Among children undergoing both EGD and MII probe placement, RAE incidence was compared between the 2 procedures using McNemar's test of paired proportions. Data analysis was performed in Stata/SE 15.1 (College Station, TX: StataCorp, LP), and P<0.05 was considered statistically significant.

Results

All procedures were successfully completed using deep propofol sedation. Neither cardiac arrest nor endotracheal intubation occurred. RAE's were transient, and none were associated with post-procedure morbidity. Twenty-one EGDs were conducted in each group (Group 1 and Groups 2) and 21 MIIP placements were performed 21 of 42 children (Group 3). Girls/boys were equally represented (12/21 with MIIP performed and 11/21 without MIIP performed). Average weights of children undergoing EGDs tallied 44.6 ±28.1 kg whereas those with an MIIP performed equaled 44.6 ± 18.5 kg. Average ages of these respective groups totaled 127.7 ±53.3 months and 126.9 ± 45.1 months. Blacks numbered 17/21 in group 1 and 12/21 in group 3 but this difference was not statistically significant.

No risk factors previously associated with occurrence of respiratory compromise in the setting of sedation/anesthesia (including prior history consistent with GER) were significantly associated with RAEs (Table 1). RAEs were noted in all groups in roughly half of the children enrolled: 9/21 patients undergoing EGD alone, 10/21 patients undergoing EGD before MIIP insertion, and 11/21 patients undergoing MIIP insertion after completion of EGD. Comparing patients undergoing EGD alone and those undergoing EGD followed by MIIP insertion, there was no statistically significant difference in the likelihood of RAE (Chi square p=0.162). Comparing EGD and MII probe insertion among patients who were undergoing both procedures, there was no statistically significant difference in the likelihood of RAE during each procedure (McNemar p=0.371).

Pre-procedure GER was clinically diagnosed in 16/21 of children in group 1 and 21/21 of children in group 2. Exclusion criteria included history of obstructive sleep apnea, Mallampati score of 4, tonsillar size of >75% of the distance between the tonsillar pillars, body mass index > 35, loose teeth that were not removed prior to procedure, prior complications with sedations/anesthesia, American Society of Anesthesiologists (ASA) score >3. Relative contraindications were wheezing not corrected by beta 2-agonist treatment or upper airway secretions not resolved by glycopyrrolate administration. Children/guardians were not assented/consented if they met exclusion criteria for the study. The number of children excluded by these criteria was not recorded.

Pulse oximeter desaturation to <90% for ≥30 seconds occurred during 4/42 EGDs (9.5%) and 5/21 MIIP placements (23.8%) (Tables 2,3). Bag-mask rescue therapy was utilized more frequently during MIIP placement 3/21 (14.3%) than during EGDs alone 1/42 (2.9%) (Tables 2,3). Central apnea was recorded in one child in Group 1. but in no child in Group 2 or Group 3. Partial airway obstruction was the most common

Table 1: The association of the occurrence of respiratory adverse events and study variables.

Variable	Did not experience respiratory AE (N = 18)	Experienced respiratory AE (N = 23)	P[a]
	Median (IQR) or N (%)	Median (IQR) or N (%)	
Procedure			0.162
EGD only	11 (61%)	9 (39%)	
EGD and MII probe	7 (39%)	14 (61%)	
Age (months)	126 (97, 174)	123 (81, 150)	0.572
Weight (kg)	38 (23, 64)	47 (28, 51)	0.875
Tonsil size			0.095
Grade 1	5 (28%)	9 (39%)	
Grade 2	10 (56%)	11 (48%)	
Grade 3	3 (17%)	0	
Grade 4	0	3 (13%)	
Mallampati score			0.531
Grade 2	11 (61%)	10 (43%)	
Grade 3	5 (28%)	9 (39%)	
Grade 4	2 (11%)	4 (17%)	
ASA physical status			0.973
ASA I	11 (65%)	15 (65%)	
ASA II	6 (35%)	8 (35%)	
Gastroesophageal reflux	15 (83%)	20 (87%)	>0.999
Snoring	5 (28%)	10 (43%)	0.300
Upper respiratory infection	1 (6%)	2 (9%)	>0.999
Sinusitis	2 (11%)	1 (4%)	0.573
Pre-procedure anxiety	17 (94%)	21 (91%)	>0.999

AE: Adverse Event; ASA: American Society of Anesthesiologists; EGD: Esophagogastroduodenoscopy; IQR: Interquartile Range; MII: Multichannel Intraluminal Impedance

[a]P-value by rank-sum test for continuous data and Chi-square or Fisher's exact test for categorical data.

Table 2: RAEs recorded for propofol sedated children numbered in Group1. (numbered 1 through 21), Group 2. (numbered 22 through 42), Group 3. (numbered 22 through 42).

	Group 1. (total n=21)	Group 2. (total n=21)	Group 3. (total n=21)
Desat < 90% for ≥ 30 seconds	0	3	4
Bag mask ventilation	0	1	3
Partial airway obstruction +	5	7	3
Complete airway obstruction +	0	1	2
Blow by +	0	4	6
Suction of airway +	4	3	4
Patient coughing +	4	3	1

Table 3: Percentage of RAEs recorded in Groups 1+2 vs in Group 3.

	Groups 1+2	Group 3
Desat<90% for ≥30 seconds	3/42 or 7.1%	4/21 or 19.0%
Bag mask ventilation +	1/42 or 2.9%	3/21 or 14.3%
Partial airway obstruction +	12/42 or 28.6%	3/21 or 14.3%
Complete airway obstruction +	1/42 or 2.9%	2/21 or 9.5%
Blow by +	4/42 or 9.5%	6/21 or 28.6%
Suction of airway +	7/42 or 16.7%	4/21 or 19.0%
Patient coughing +	7/42 or 16.7%	1/21 or 0.5%

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RAE, occurring in 12/42 in Group 1+ Group 2 (28.6%) and 3/21 in Group 3 (14.3%) (Tables 2,3). Complete airway obstruction occurred only once (1/42) in Group 1 + Group 2 but twice (2/21) in Group 3.

Discussion

Despite delivery of supplemental nasal cannula oxygen, pulse oximeter desaturation below 90% occurred in 9.5% of EGDs and in a full 23.8% of MIIP placements. In a report of complications in 4662 pediatric EGDs primarily sedated with narcotics, benzodiazepines or ketamine, roughly 1.5% encountered hypoxemia [15]. In contrast, a smaller study reported oxygen desaturation to less than 90% during conscious sedation with narcotics and benzodiazepines in 68% of normal pediatric patients [16]. Biber more recently used primarily propofol sedation for a group of children undergoing wither EGD or colonoscopy. Pulse oximeter desaturation below 90% for greater than 30 seconds or below 80% for more than 3 minutes was estimated to occur in 1.5% of cases [17]. Our children had pulse oximeter readings below 90% for 30 seconds or longer in two categories: EGD's 7.1% and MIIP placement 19%. This over-representation of desaturations in our series may be attributed to initial deeper levels of propofol sedation or accumulation of propofol during the sedation. Bag mask ventilation was provided during 14.3% of MIIP placements but during fewer than 3% of EGDs. Initially propofol was bolused to prevent coughing, gagging, arching and withdrawal to arm pinch. Subsequent, infusion and boluses may have resulted in propofol accumulation and hypoventilation or upper airway obstruction may have resulted [17,18]. In doses used for sedation, propofol decreases tidal volume, minute ventilation, ventilator drive and protective airway responses [19,20]. Accepting lighter levels of sedation may have resulted in less hypoventilation. It was likely that higher levels of sedation were utilized during MIIP placement as evidenced by supplemental blow by oxygen being frequently instituted in 28.6% of the former (vs only 9.5% of EGDs) and coughing occurring in only 0.5% of MIIP placements (vs. more frequently in 16.7% of EGDs).

Propofol delivery and accumulation may have promoted dynamic collapse of the soft tissues above the larynx [21] with a resultant increase of airway resistance and reduction of gas flow. Partial airway obstruction was over twice as frequent during EGDs (28.6%) than during "endoscopically aided" MIIP placement (14.3%). During "endoscopically aided" MIIP, the presence of the tip of the endoscope situated immediately cephalad to the base of the tongue may have helped to stent this portion of the airway which is most prone to become narrowed during propofol anesthesia [22]. On the other hand, complete airway obstruction was scored in 9.5% of instances of MIIP placement but during only 2.9% of monitored EGDs. The goal of conducting "endoscopically aided MIIP placements" was to avoid unnecessary noxious tactile stimulation of the glottis by the tip of the MIIP. It was commonplace to intermittently lose view of the MIIP tip. The MIIP could have stimulated glottic spasm and complete airway obstruction. It was the unmeasured but unmistakable impressions of the sedationist and the endoscopists that "endoscopically aided MIIP placement" reduced markedly coughing and gagging when compared to "blind passage" of the MIIP during propofol sedation. The recognized association of complete airway obstruction during propofol-sedated MIIP placement must be weighed against the potential reduction of this risk in the awake child.

In this small study, no correlations were established between previously recognized risk factors for respiratory compromise and sedation. A larger study might have reproduced these previously demonstrated correlations or identified novel risk factors associated with RAE. The limitations of this pilot study were primarily due to the small number of participants enrolled in a single tertiary care children's medical center. Larger numbers of enrollees may have revealed significant differences between children with different risk factors. Furthermore, a single sedationist administered propofol and collected relevant data and only two pediatric gastroenterologists performed all of the procedures. These issues limit the ability to apply this experience to other institutions.

Conclusion

When carefully monitored for RAEs occurring during deep propofol sedation in children during EGDs and insertion of MIIPs are frequently reported. Non-sedated MIIP placements might be a preferable option compared to sedated MIIP placements to help avoid RAEs; more research is needed.

Conflicts of interests

There were no financial or personal conflicts of interest by any of the authors. The endoscopes utilized in this study were those routinely used throughout Vidant Health Care Center in Greenville, NC.

Author contributions

1] Conceptualization was accomplished by William Novotny, Khanh Nguyen, Folashade Jose, Dynita Haislip, Gregg Grothmann, Dmitry Tumin. 2] Data curation was primarily conducted by Khanh Nguyen. 3] Formal analysis – William Novotny, Khanh Nguyen, Dmitry Tumin, 4] Funding acquisition – none required, 5] investigation - William Novotny, Khanh Nguyen, Folashade Jose, Dynita Haislip, Gregg Grothmann, Dmitry Tumin, 6] methodology William Novotny, Khanh Nguyen, Folashade Jose, Dynita Haislip, Gregg Grothmann, Dmitry Tumin, 7] project administration William Novotny, Dmitry Tumin, Khanh Nguyen, 8] Resources – Folashade Jose, 9] Software Dmitry Tumin. 10] supervision Dmitry Tumin, William Novotny, 11] validation Dmitry Tumin, William Novotny, 12] visualization William Novotny, Dmitry Tumin, Writing original draft William Novotny, Khanh Nguyen, Folashade Jose, Dynita Haislip, Gregg Grothmann, Dmitry Tumin, 13] writing, review, editing - William Novotny, Khanh Nguyen, Folashade Jose, Dynita Haislip, Gregg Grothmann, Dmitry Tumin.

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