Propofol sedation in Drug Induced Sedation Endoscopy without an anaesthesiologist – a study of safety and feasibility*

Eva Kirkegaard Kiær[1], Philip Tønnesen[2], Henrik Bredahl Sørensen[1], Niclas Rubek[1], Anne Hammering[3], Christine Møller[1], Anne Marie Hildebrandt[1], Poul Jørgen Jennum[1], Christian von Buchwald[1]

[1] Department of ORL, H&N Surgery and Audiology, Copenhagen University Hospital, Copenhagen, Denmark

[2] Danish Institute for Sleep Medicine, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark

[3] Department of Anesthesiology, Gentofte Hospital, Copenhagen, Denmark

Rhinology 57: 2, 125 - 131, 2019

https://doi.org/10.4193/Rhin18.066

***Received for publication:**

March 21, 2018

Accepted: August 20, 2018

Background: Propofol sedation in Drug Induced Sedation Endoscopy (DISE) of the upper airway of patients with obstructive sleep apnea (OSA) without the presence of anesthesiologist has not been done before. Propofol sedation is normally administered by an anesthesiologist. This is the first study of this new method.

Methodology: Based on the positive experience with Nurse-administered Propofol Sedation (NAPS) for endoscopic procedures in the departments of gastroenterology we wanted to test the set-up as method of propofol sedation for DISE procedures in our Otorhinolaryngology (ORL) department. The ORL specialists and staff nurses that carry out DISE procedures all underwent a formalized education in Nurse-administered Propofol Sedation before the study. We included 200 patients with severe snoring and / or obstructive sleep apnea. They were referred for DISE examination prior to possible targeted surgery based on the findings.

Results: In our study the aforementioned ORL team successfully cared out propofol sedation without the presence of an anesthesiologist. All examinations were carried out according to plan. There were no adverse events during the procedures or in the following observational period.

Conclusions: The NAPS method of sedation for DISE seems safe and feasible when performed by trained staff in a hospital setting

Key words: diagnostic techniques, respiratory system

Introduction

Nurse-administered Propofol Sedation /Non-Anesthesiologist Propofol Sedation (NAPS) was first introduced in 1998 in Oregon, USA, by John A. Walker and colleagues[(1)]. The protocol for NAPS was developed under the direction of an experienced anesthesiologist and has since then been used widespread during gastrointestinal endoscopy procedures. In the original NAPS regimen propofol is administered by a non-anesthetist nurse under the supervision of the surgeon performing the gastroenterological endoscopy[(2)]. It has been proven safe by more than 646,080 patients worldwide with very few adverse effects and safer than traditional sedation with benzodiazepines and opioids[(3)].

Obstructive Sleep Apnea (OSA) is characterized by periodic partial or complete obstruction of the upper airway during sleep. OSA is prevalent in an estimated 10-20 % of the adult population and symptomatic OSA (OSAS) is prevalent in an estimated 2-4% of adult male and 1-2% of the adult female population[(4)].

In 1991 Drug Induced Sedation Endoscopy (DISE) was introduced by Croft and Pringle[(5)]. It was developed as a means of investigating the upper airway of patients with OSA during simulated sleep prior to surgical intervention[(6)]. During sedation, the upper airway patency is examined with a fiber optic flexible scope introduced through the nasal cavity and advanced to the level of the endolarynx. Sedation is generally obtained by either propofol or midazolam or a combination of the two[(7)].

DISE was introduced in our Oto-rhino-laryngology (ORL) de-

partment in 2015. After a short period using midazolam as the sedative agent NAPS was introduced as the sedative regimen for the DISE-procedures. As propofol has advantages when compared to midazolam in inducing a sedation that best mimics natural sleep this was our drug of choice[8]. Propofol sedation normally requires the presence of an anesthetist whereas midazolam can be administered intravenously by nurses under the responsibility of the physician. Sedation in accordance with NAPS guidelines made propofol sedation without the presence of an anaesthesiologist possible.

Sedation without the presence of an anesthesiologist reduces costs as the procedure is performed entirely by the staff in the ORL department and does not require an operating theatre. Perioperative observation can be performed by staff nurses under the responsibility of the physician. Endoscopy performed under propofol sedation is faster and the patient recovers quickly when compared to i.e. midazolam thus reducing risks and costs for post-sedation observation.

To our knowledge this study is the first where NAPS has been used as the sedative regimen for DISE procedures. The purpose of the study was to evaluate the safety and feasibility of the NAPS regimen for DISE procedures in our ORL department.

Materials and methods

In this prospective feasibility study, we evaluated 200 patients with OSA or severe snoring that underwent DISE with propofol as the sedative agent. The sedation was administered according to NAPS guidelines by nurses under the supervision of the ORL specialist performing the DISE.

The primary end point was an evaluation of patient safety and the second end point was an evaluation of the feasibility to obtain a full evaluation of the four anatomical levels of upper airway collapse in accordance with the VOTE-classification (Velum-Oropharynx-Tongue base-Epiglottis classification)[9].

Two ORL specialists and two staff nurses from the ORL department at the Copenhagen University Hospital underwent the Danish NAPS education at the Copenhagen Academy for Medical Education and Simulation (CAMES). They all passed both the written examination and practical exam. The latter exam was specialty-specific and supervised by an anesthetist. All doctors and nurses had experience with DISE using midazolam as the sedative agent prior to the introduction of propofol. All procedures were performed by one of the two aforementioned specialists in cooperation with both of the staff nurses, with the possibility of prompt anesthetic backup if needed.

Patients were referred for surgical evaluation at the ORL department at Copenhagen University Hospital, Copenhagen, Denmark, from one of two sleep centers in the Capital Region of Denmark or private Ear-nose-and-throat-clinics. All were severe snorers or patients with obstructive sleep apnea and poor or no compliance to CPAP-treatment (Continuous Positive Airway Pressure treatment). Patients suspected for OSA all had a one-night polygraph i.e. a Cardio Respiratory Monitoring (CRM) done prior to the DISE-examination. As all patients referred for DISE had a wish for further evaluation prior to any surgery the findings in the CRM did not exclude any patients from proceeding with the DISE examination.

Table 1. In- and exclusion criteria for patients considered for DISE-examination in accordance with NAPS-guidelines.

Inclusion criteria	Exclusion criteria
Patients with OSA and / or severe snoring	BMI > 35
ASA class 1-2	Former thromboembolic disease
Age 18 years and above	Allergy towards soy, peanuts and eggs*
Patients able to give an informed consent	Severe liver disease

DISE examination: Drug Induced Sedation Endoscopy; NAPS: Nurse-administered Propofol Sedation; OSA: Obstructive Sleep Apnea; ASA-classification: the American Society of Anesthesiologists classification of comorbidity; BMI: Body Mass Index (weight in kilograms divided by height in meters squared). A measurement of body fat that applies to both adult men and women. * This would cause a risk of allergy towards propofol.

All patients underwent a thorough examination by an ORL specialist with experience in surgical treatment of OSA. This included a fiberscope examination from the nasal cavities to the endolarynx. This was to ensure an open passage through the nasal cavity and in order to exclude tumors or any abnormalities that would risk airway patency during sedation.

Patients that fit the inclusion criteria (Table 1) were offered at DISE-examination. The participating patients gave an informed consent. Patients that were ASA 3 (American Society of Anesthesiology classification of comorbidity) and above did not meet the inclusion criteria for NAPS, and by this were not considered for a DISE examination.

Prior to the DISE examination the patients were fasted for 2 hours for fluids and 6 hours for solids. The examinations were all carried out in an examination room in the ward at the ORL department Gentofte, Copenhagen University Hospital.

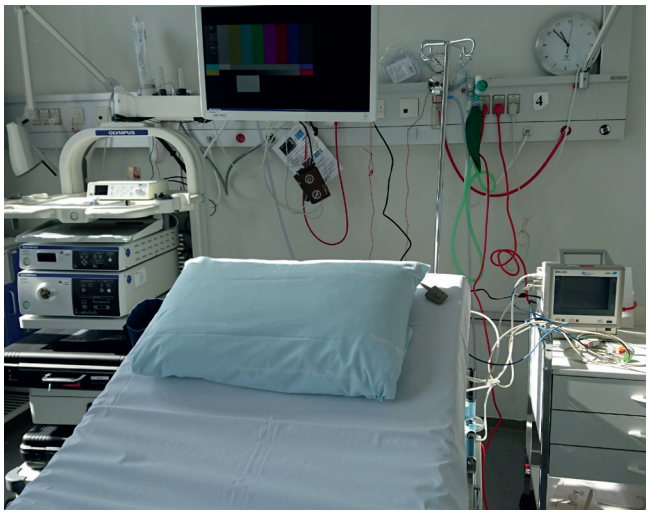

FIgure 1. The examination room for Drug Induced Sedation Endoscopy.

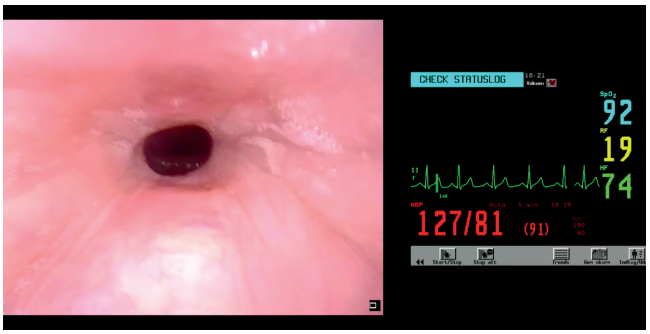

Figure 2. DISE-examination revealing concentric collapse at the level of the velum. the top of the epiglottis can be seen below. Simultaneously recorded vital signs are shown on the right.

In accordance with the NAPS-guidelines propofol 10 mg/mL was administered intravenously, via a cubital vein, in small incremental doses. The initial dose was 100 mg minus the age of the patient with a maximum dose of 60 mg. A saline infusion 9 g/L was administered intravenously (IV) at a rate of 500 mL/h. If sleep was not obtained after one-minute additional doses, of half the initial dose, was administered every 60 seconds until sleep with snoring and/or apnea was achieved. Transient upper limb movement with the introduction of the fiberscope through the nasal cavity was used to confirm that the level of sedation was not too deep. A maintenance dose of 10-20 mg of propofol was then administered every 60 seconds until the end of the examination. During the DISE-examination the aim was to administer the sedation in doses that would ensure that the number of breathing pauses and desaturations would correspond to the CRM, in order to best mimic the natural sleep. If maximum oxygen desaturation was reached the next dose would be reduced in order to prevent exaggerated desaturation. If the patient started swallowing, and the apneas stopped, this was taken as a sign of awakening and the higher maintenance dose of propofol was administered. Atropine, lidocaine and ephedrine were available in appropriate doses in the examination room to be administered in the case of bradycardia, coughing or hypotension respectively. Up to a 30 % change in blood pressure was accepted without intervention in accordance with NAPS guidelines. This was monitored by one of the two attending staff nurses under the responsibility of the ORL-specialist.

When the right level of sedation was achieved a fiberscope examination of the upper airway was performed with the patient in the supine position. An Olympus Flexible Video Endoscope (ENF-VH) was used for the examination. The monitor was connected to an Olympus split screen allowing the ENT specialist performing the DISE to overview both the endoscopy and the vital signs simultaneously (Figure 1). A small amount of gel was put on the tip of the fiberscope to facilitate the passage through the nasal cavity, but no local anesthesia or mucosal contractive agents were used, in order to maintain the natural environment and physiology of the upper airway in accordance with the European Position Paper on DISE[7]. The evaluation of upper airway obstruction in cases of OSA was made in accordance with the VOTE-classification. After primary evaluation of the upper airway an additional evaluation was performed with the mouth closed in order to evaluate any possible effect of a mandibular advancement device (MAD) in reducing snoring or obstruction.

All DISE patients were monitored in regards to peripheral blood pressure, ECG (Electro-Cardio-Gram), heart rate, oxygen saturation and respiratory frequency during the examination (Figure 2). In the examination room, there was equipment for respiratory support in the form of supplemental oxygen supply, pharyngeal tubes and the possibility for positive pressure ventilation if needed. There was also a possibility for quick anaesthesia back-up if needed.

Monitoring was continued by the nurses and ORL specialist until the patient was completely awake. No sooner than 30 minutes after the examination was the patient allowed to leave the hospital. As precautionary measure patients were instructed to be under adult supervision until the next day and were instructed not to drive in the same period.

The project was approved by the local Scientific Ethics Committees.

Statistsics

Descriptive data was obtained using Microsoft Office Excel and IBM SPSS.

Results

A total of 200 patients met the inclusion criteria. They were offe-

Table 2. Characteristics of the 200 patients in the study.

Patient characteristics	N=200
Female sex	17.5 % (35)
Male sex	82.5 % (165)
Snorers without OSA (AHI below 5)	7.8 % (15/192)
Patients with mild OSA (AHI 5.0-14.9)	34.4 % (66/192)
Patients with moderate OSA (AHI 15.0-29.9)	26.6 % (51/192)
Patients with severe OSA (AHI 30 and above)	31.3 % (60/192)
Median AHI (range 0-147)	19.0 (IQR 23.3)
Median BMI (range 19-35)	27.0 (IQR 5)
Mean age in years (range 20-76)	44.0 (SD 11.8)

Information on OSA severity was not available in 8 patients. OSA: Obstructive Sleep Apnea; AHI: Apnea-Hypopnea-Index (a sum of apneas and hypopneas per hour of sleep); IQR: Interquartile Range (the mid-spread); BMI: Body Mass Index (weight in kilograms divided by height in meters squared). A measurement of body fat that applies to both adult men and women. SD: Standard Sedation

red a DISE examination for further diagnostic evaluation and all patients accepted the offer. Patient characteristics are as shown in Table 2. They were mainly males (82.5%) with a mean age of 43.57 years (SD 11.8) and a median apnea-hypopnea index (AHI) of 19 (IQR 23.3) ranged between 0-147. The distribution of our patients regarding OSA severity is also shown in Table 2. We have insufficient data on AHI in 8 of the 200 patients. Thirty-three percent of the patients were ASA 1 and 67 % were ASA 2. The DISE was performed by one of two NAPS-trained ORL specialists between the 6th of May 2015 and the 29th of November 2017. During the NAPS-DISE procedure a mean total dose of 224 milligrams of propofol was administered (per DISE) (SD 60.7). Propofol was administered for a median period of 8 minutes (IQR 3). The lowest oxygen desaturation recorded during an examination was 62 %. The mean lowest oxygen desaturation level during the DISE-examinations was 81 % (SD 7.0). All oxygen desaturations dissolved spontaneously with the end of the obstructive event. The patients were only allowed to desaturate to the level of the habitual desaturations during apneic episodes as detected by the CRM.

All patients were discharged from the ward to their homes within one hour after the examination. None of the patients underwent surgery that day.

All had a follow up appointment within a few weeks after the DISE examination where the result of the DISE was discussed. No adverse effects after the DISE were reported by the patients.

No changes in blood pressure, heart rate or oxygen saturation requiring treatment were encountered in the study. Ephedrine, lidocaine and atropine were never used. There were no cases of laryngeal spasms and no need for forced ventilation. None of the known side effects to propofol were encountered[10].
All examinations were followed through and an assessment of obstruction level and pattern was successfully obtained according to plan in all cases. Information on the primary and secondary endpoints, i.e. safety and feasibility, was successfully obtained.

The department of anaesthesiology was contacted once. This was during the examination of a young, fit male who did not fall asleep on the small divided doses of propofol recommended by the NAPS guideline. After a total dose of 290 mgs he still was not at sleep and we discontinued propofol until he was completely awoken. A nurse anesthetist then gave him a higher initial dose (100 mgs) and higher second and third doses (60 mgs) of propofol and he fell asleep. The rest of the sedation was then carried out according to the guideline. As with the rest of the patients he experienced no adverse events after sedation. The total dose in the second examination was 310 mgs of propofol.

Discussion

In our study, the training was based on the "gastroenterology NAPS guideline" and we found it suitable for the DISE procedures for OSA and snoring patients in our ORL clinic. The patients with OSA fell asleep within a few minutes and the maintenance doses of propofol were sufficient to keep the patients sedated, having breathing pauses and still "sleep" in accordance with their habitual sleep as recorded by the CRM. The patients with simple snoring or mild OSA also slept in accordance with their habitual sleep and did not have more apneas during sedation. This stresses our assumption that the patients were not overly sedated.

In the gastroenterology departments, where NAPS was first introduced, the presence of OSA is generally considered a relative contra-indication to NAPS for endoscopies.

Gastroenterologists, as opposed to ORL-specialists, are not trained in the potentially difficult upper airway management of these patients. Combining the ORL training with the fact that during DISE there is constant visual overview of upper airway patency will facilitate a prompt reaction to any unexpected decrease in patency.

In this first study of 200 patients NAPS with small incremental doses of propofol was successfully used as method of sedation for DISE. We encountered no inadvertent general anesthesia or problems with upper airway management. There was never need for the presence of an anesthesiologist for airway manage-

ment.

In 2011 Adler et al. studied the safety profile of NAPS for routine gastrointestinal endoscopic procedures in patients with OSA. They evaluated 215 patients divided into four groups: OSA patients undergoing endoscopy with NAPS, OSA patients undergoing endoscopy with benzodiazepines and narcotics, non-OSA patients undergoing endoscopy with NAPS, and non-OSA patients undergoing endoscopy with benzodiazepines and narcotics. They found no statistically significant difference in complication rates or overall outcomes in patients with OSA when compared to non-OSA patients when either NAPS or benzodiazepines was utilized, but faster procedures when sedation was accomplished by NAPS[11].

Jensen et al. performed a risk analysis in 2011 during the implementation phase of NAPS. They wanted to validate the structured training program during the implementation phase of NAPS. They studied 1764 patients and found NAPS for endoscopic procedures safe when performed by personnel properly trained in airway handling and sedation with propofol. They also found considerable advantages compared with conventional sedation for endoscopy[12].

In a following study in 2012 Jensen et al. made an analysis of propofol sedation for endoscopic pulmonary procedures when being carried out according to the "gastroenterological NAPS guideline". They found the guideline to be safe, but unsuited for pulmonary procedures[13].

Webb et al. as anesthesiologists question the safety of NAPS. They recognize the large international data supporting NAPS safety in gastrointestinal procedures but worry about uncritically applying these results to other specialties and procedures. A specialty-specific guidance and training, monitoring, following the guidelines closely and using small incremental boluses of propofol might enhance safety[14].

The use of small incremental doses of propofol ensures a low level of sedation and preserves a short half time. Before introducing NAPS for DISE the ORL specialists and staff nurses all completed the NAPS education at CAMES and a nurse anesthetist supervised the first 30 procedures and there is still a close cooperation with the colleagues at the department of anesthesiology.

The alternative to propofol is classic sedation with benzodiazepines which in larger studies have proven less effective as the use of these medications can be complicated by prolonged sedation, respiratory compromise, and the need for antagonists, which may in themselves have undesirable side effects(3).

Propofol serves as a quick-acting sedative with poor analgesic effect. This makes it favorable in comparison with benzodiazepines and narcotics in achieving a state of sedation that best mimics natural sleep.

Propofol has no antidote. The antidote is the short half time of 1.8 to 4.1 minutes[15]. The short half time favors a shorter sedation time and fast recovery times[16]. Sedation with propofol in accordance with NAPS guidelines would grant the benefits from propofol sedation but be no costlier than sedation with midazolam.

Koshy et al., among other things, studied patient satisfaction in 274 patients that were sedated with either propofol or midazolam for endoscopic gastrointestinal procedures and found that patients sedated by propofol were much more comfortable during the procedure than were those receiving midazolam[17].

In a randomized, control trial Clark et al. studied neuropsychometric recovery, safety profile and patient tolerance in patients randomized to either propofol or midazolam sedation for flexible bronchoscopy. The sedation was administered by a non-anesthetist physician. Depth of sedation was monitored by the electro-encephalographic bispectral index (BIS). The study showed decreased recovery time and higher patient satisfaction in the propofol group as compared to traditional sedation techniques. The recovery time was reduced by more than half in the propofol group[18].

Sedation with propofol does not induce natural sleep. Propofol exerts its action on GABAA (Gamma-Aminobutyric Acid A) receptors and induces a state of delta activity which simulates deep NREM (non-Rapid Eye Movement) sleep. In accordance with this Rabelo et al found that propofol altered sleep macro architecture, but when comparing the AHI and mean saturations during natural sleep and under propofol sedation in two groups (OSA patients and normal controls without sleep apnea) they found that the aforementioned respiratory parameters remained unaffected in both groups, thus concluding that propofol is an effective drug for DISE based on its pharmacological characteristics, short half-time and low-rate side effects[8]. Dexmedetomidine is one of the newer drugs that show promise in better mimicking natural sleep, but it is costlier[19]. Propofol was our drug of choice as its usefulness and safety in DISE examinations is thoroughly tested.

The national guidelines for sedation vary between countries. In some countries the administration of certain sedative drugs requires the presence of an anaesthetist whereas others can be administered by physicians in general. This being the case for propofol in some countries, as for instance Germany, where the

administration requires the presence of an anaesthetist probably based on a concern for exaggerated sedation whereas the administration of benzodiazepines does not have this restriction. Newer German guidelines do allow for a modified version of NAPS for endoscopies in the departments of gastroenterology but the physician responsible for the sedation is still required to be experienced in intensive care medicine[20]. Different guidelines for sedation may affect the drug of choice for DISE in different countries. This study of safety and feasibility of NAPS in DISE may inspire and allow for propofol sedation by trained ORL specialists in other countries as well.

Only one patient did not fall asleep on the propofol doses recommended in the NAPS guideline. In regards to general anesthesia it is known that some patients require larger doses of propofol to induce and withstand sleep. This phenomenon is often related to anxious patients or patients used to a large alcohol intake. In the case of alcohol it is thought to be caused by enzyme induction or cross tolerance[21]. When this young man was given larger doses, he fell asleep and slept in accordance with his CRM. He admitted to being used to a large alcohol consumption.

This prospective study has certain limitations. The patients were not randomized and statistics on 200 patients can only show a tendency, but as above mentioned we found no adverse effects, severe or minimal. We recognize that very rare events need larger sample sizes to become evident.

Conclusion

Based on this first study addressing the safety and feasibility of Nurse-administered Propofol Sedation for Drug Induced Sedation Endoscopy, on patients with OSA and snoring, the procedure seems safe and feasible when performed by trained ORL specialists and staff nurses in a hospital setting. It is of great importance that guidelines are being followed and that the inclusion criteria are enforced to ensure safety.

Further prospective studies are warranted aiming also to evaluate the efficacy, cost-effectiveness and patient satisfaction profile of NAPS versus traditional sedation regimens for DISE.

Acknowledgements

Rene Kærgaard Jensen contributed with inclusion of patients for the study.

Olympus provided fiberoptic endoscopes and screens for the Drug Induced Sedation Endoscopies but did not support the study financially.

Authorship contribution

EKK: Study design, patient inclusion, data collection and analysis, Drug Induced Sedation Endoscopy (DISE) examinations and main author; PT: Study design, data analysis; HB: Study design; NR: Data collection; AH: DISE examinations, data collection; CM: DISE examinations, propofol sedation, data collection, AMH: DISE examinations, propofol sedation, data collection; PJJ: Study design, data analysis; CvB: Study design, data analysis.

Conflict of interest

We did not receive funding for this study and have no conflict of interest.

References

1. Walker JA, McIntyre RD, Schleinitz PF, et al. Nurse-administered propofol sedation without anesthesia specialists in 9152 endoscopic cases in an ambulatory surgery center. Am J Gastroenterol 2003; 98: 1744–50.
2. Rex DK, Overley C, Kinser K, et al. Safety of propofol administered by registered nurses with gastroenterologist supervision in 2000 endoscopic cases. Am J Gastroenterol 2002; 97: 1159–63.
3. Rex DK, Deenadayalu VP, Eid E, et al. Endoscopist-Directed Administration of Propofol: A Worldwide Safety Experience. Gastroenterology 2009; 137: 1229–37.
4. Sundaram S, Lim J, Lasserson TJ. Surgery for obstructive sleep apnoea in adults (Review). Cochrane Collab 2013; 4: 1–76.
5. Croft C, Pringle M. Sleep nasendoscopy: a technique of assessment in snoring and obstructive sleep apnoea. Clin Otolaryngol Allied Sci 1991; 16: 504–9.
6. Kotecha BT, Hannan SA, Khalil HMB, Georgalas C, Bailey P. Sleep nasendoscopy: a 10-year retrospective audit study. Eur Arch Otorhinolaryngol 2007; 264: 1361–7.
7. De Vito A, Carrasco Llatas M, Vanni A, et al. European position paper on drug-induced sedation endoscopy (DISE). Sleep Breath 2014; 18: 453–65.
8. Rabelo FAW, Küpper DS, Sander HH, Fernandes RMF, Valera FCP. Polysomnographic evaluation of propofol-induced sleep in patients with respiratory sleep disorders and controls. Laryngoscope 2013; 123: 2300–5.
9. Hohenhorst W, Ravesloot MJL, Kezirian EJ, De Vries N. Drug-induced sleep endoscopy in adults with sleep-disordered breathing: Technique and the VOTE Classification system. Oper Tech Otolaryngol - Head Neck Surg 2012; 23: 11–18.
10. Propofol use, interactions and side effects. Online guidelines from the Danish Farmacy Board 2018; https://pro.medicin.dk/Medicin/Praeparater/2825
11. Adler DG, Kawa C, Hilden K, Fang J. Nurse-administered propofol sedation is safe for patients with obstructive sleep apnea undergoing routine endoscopy: A pilot study. Dig Dis Sci 2011; 56: 2666–71.
12. Jensen JT, Vilmann P, Horsted T et al. Nurse-administered propofol sedation for endoscopy: a risk analysis during an implementation phase. Endoscopy Germany 2011; 43: 716–22.
13. Jensen JT, Banning AM, Clementsen P, et al. Nurse administered propofol sedation for pulmonary endoscopies requires a specific protocol. Dan Med J 2012; 59: 1-5.
14. Conway A. Is sedation by non-anaesthetists really safe? Br J Anaesth 2014; 112: 583–4.
15. Bryson HM, Fulton BR, Faulds D. Propofol. Drugs 1995; 50: 513–59.
16. Chen SC, Rex DK. Registered nurse-administered propofol sedation for endoscopy. Aliment Pharmacol Ther 2004; 19: 147–55.
17. Koshy G, Nair S, Norkus EP, Hertan HI, Pitchumoni CS. Propofol versus midazolam and meperidine for conscious sedation in gi endoscopy. Am J Gastroenterol 2000; 95: 1476–9.

18. Clark G, Licker M, Younossian AB, Soccal PM, Frey JG, Rochat T, et al. Titrated sedation with propofol or midazolam for flexible bronchoscopy: A randomised trial. Eur Respir J 2009; 34: 1277–83.
19. Cadth W. Dexmedetomidine for Sedation in the ICU or PICU: A Review of CostEffectiveness and Guidelines. 2014.
20. Str H. Update S3-guideline: "sedation for gastrointestinal Update S3-Leitlinie„ Sedierung in der gastrointestinalen 2016; 2014: 58–95.
21. Chapman R, Plaat F. Alcohol and anaesthesia. Crit Care Pain 2009; 9: 10–3.

Eva Kirkegaard Kiær
Department of ORL
H&N Surgery and Audiology
Copenhagen University Hospital
Copenhagen
Denmark

Tel: +45 35 45 66 35
E-mail:
eva.kirkegaard.kiaer.01@regionh.dk