High efficacy with deep nurse-administered propofol sedation for advanced gastroenterologic endoscopic procedures

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Background and study aims: Whereas data on moderate nurse-administered propofol sedation (NAPS) efficacy and safety for standard endoscopy is abundant, few reports on the use of deep sedation by endoscopy nurses during advanced endoscopy, such as Endoscopic Retrograde Cholangiopancreatography (ERCP) and Endoscopic Ultrasound (EUS) are available and potential benefits or hazards remain unclear. The aims of this study were to investigate the efficacy of intermittent deep sedation with propofol for a large cohort of advanced endoscopies and to provide data on the safety.

Patients and methods: All available data from patients sedated with intermittent deep NAPS for ERCP, EUS or double balloon enteroscopy (DBE, since the method was implemented in May 2007 through December 2012 were included for evaluation in a retrospective case-control design.

Results: Data from 1899 patients undergoing 1899 procedures were included for evaluation. All but one procedure were completed with intermittent deep NAPS. The mean propofol dose was 397 mg (SD: 232.4) and the infusion rate was 23.9 mg/kg. The frequency of hypoxia was 4.3% and 20 patients needed assisted ventilation (1.1%). Anesthesiologic support was requested eight times (0.4%). One patient was intubated due to suspected aspiration.

Conclusions: Intermittent deep NAPS for advanced endoscopies in selected patients provided an almost 100% success rate. However, the rate of hypoxia, hypotension and respiratory support was high compared with previously published data, but the method was still assessed as safe.

Introduction

Nurse-administered propofol sedation (NAPS) or non-anesthesiologist-administered propofol (NAAP) sedation is increasingly used for procedural sedation, particularly gastrointestinal endoscopy. Previously published large volume studies primarily evaluated the use of moderate NAPS for gastroscopies, sigmoidoscopies, and colonoscopies [1,2]. Evidence on NAPS efficacy and safety for advanced interventional endoscopy, such as endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound (EUS), is more limited [3,4] and even more so when deep sedation is applied. The increased focus on patient related quality and the development of advanced endoscopies such as ERCP, EUS, enteroscopies, and advanced colonoscopies has led to increased sedation requirements. The procedures are often longer than standard endoscopy and require a high degree of patient compliance in order to be successful [5]. Hence, either sedation or general anesthesia is almost always needed. The use of conscious sedation is sometimes insufficient during advanced endoscopy, especially upper endoscopy, and the use of deep sedation by non-anesthesia staff is debatable, particularly in the presence of considerable comorbidity [6,7]. Therefore, general anesthesia is commonly applied. The use of intermittent deep sedation could lead to a larger proportion of successfully completed advanced endoscopies without the need for general anesthesia. Administration by non-anesthesia staff would reduce the procedure costs and sedation would shorten time to induction, time to discharge, and put less stress on the vital functions of the patient than general anesthesia. Deep sedation with midazolam, alone or in combination with an opioid is impractical. In a high-output unit, the prolonged discharge time after deep sedation is often unacceptable and the risk of re-sedation after antidote administration is increased. Furthermore, the...
clinical effect of midazolam has a high degree of interpersonal variation [8].

With a short, context-sensitive half-life of 2 to 4 minutes, propofol administration can provide for periods of deep sedation with no risk of re-sedation and fast readiness for discharge [9]. With the increased sedation requirements, adverse events occur more frequently during advanced endoscopy [3,4] than during standard endoscopy [10,12] and likely even more so during deep sedation. From a safety perspective, adverse events should be minor and self-resolving or successfully handled by the endoscopy team without health consequences for the patient and the efficacy should be high to render deep sedation beneficial as compared to conscious sedation or general anesthesia. The aims of this study were to analyze the efficacy and safety of intermittent deep sedation with propofol in a large cohort of advanced endoscopies.

Patients and methods

Ethical approval was obtained from the Capital Region Ethics Committee No: H-4 – 2013 – 171 and the National Data protection agency No: HEH-2013–077. We used a retrospective case-control design, with cases being patients who developed an adverse event (dichotomous as 0 or 1) and the remainder serving as controls. All available data from patients sedated with NAPS for ERCP, EUS or double balloon enteroscopy (DBE) since the method was implemented in May 2007 through December 2012 were included for evaluation.

Patients

According to our guidelines, inclusion criteria for NAPS were age ≥16 years and ability to comply with 6 hours of fasting from solids and 2 hours of fasting from fluids. Patients were excluded if they were American Society of Anesthesiologists (ASA) class >2 (ASA class 3 patients in a stable condition were allowed); had a body mass index >35 kg/m²; were allergic to soy, eggs, or peanuts; or had a history of complicated anesthesia, potentially difficult airway (composite score of Mallampati score, atlanto-occipital ephedrine 5 mg), and was registered. In near adverse events, temporary increases in mean arterial pressure (MAP). Furthermore, arrhythmia was registered. In near adverse events, temporary increases in saline infusion to 2 L/h and oxygen flow to 5 L/min were administered as a precaution. Handling of adverse events was recorded as a dichotomous outcome (0 or 1) in case of administration of sedation during endoscopic stimulation and moderate or deep sedation in the absence of stimulation. If a patient's cardiopulmonary status was unstable, as expressed by a depression in vital parameters, the sedation was lifted one level.

Propofol administration

Propofol was administered as intermittent bolus monotherapy by a dedicated endoscopy nurse, using the same guidelines as for standard endoscopies. Sufficient sedation for gag-free introduction of the endoscope was achieved with a dose of 100 mg minus the patient's age in years, but no more than 60 mg (hence, an 80-year-old would receive 20 mg). Additional doses of half the initial dose could be administered every 45 – 60 seconds until the patient was unresponsive to verbal and light tactile stimulation, as assessed by the team together. Maintenance of sedation was achieved with intermittent doses of 10 – 20 mg if the patient showed signs of discomfort, sound or movement, or every 1 to 2 minutes if the patient was a sleep with stable cardiopulmonary status. The dedicated nurse continuously monitored the patient's vital parameters on the monitor and the depth and frequency of respiration by assessing movement of the thorax and the air flow over the nose and mouth in the palm of a hand.

Adverse events

All patients were monitored with pulse oximetry, blood pressure (BP) taken every five minutes, and electrocardiography. Saline infusion (500 mL/hr) and supplemental oxygen (3 L/min) flow on a nasal cannula were administered to all patients and initiated a minimum of 3 minutes prior to sedation. Adverse events were oxygen saturation (SAT%) <92%, measured with pulse oximetry or a drop in BP from baseline of more than 50 mmHg systolic or 30% in mean arterial pressure (MAP). Furthermore, arrhythmia was registered. In near adverse events, temporary increases in saline infusion to 2 L/h and oxygen flow to 5 L/min were administered as a precaution. Handling of adverse events was recorded as a dichotomous outcome (0 or 1) in case of administration of ephedrine 5 – 10 mg, airway manipulation (oral- or nasal airway and suction) and mask ventilation.

Data items and statistical analysis

Sedation was considered efficient when the procedure was completed, regardless of findings. Sedation was considered inefficient when the procedure was incomplete or disrupted due to pain, movement or a sedation-related adverse event. Other than adverse events and handling, baseline demographics recorded were recorded sex, age, ASA class, procedure type, duration of sedation (available for the last 1200 procedures), and total propofol dose. Unsuccessful procedures and procedures that required anesthesiologic assistance also were recorded. Statistics were computed using IBM SPSS™ version 19. Binary logic regression was used to compare demographic risk factors and propofol administration in cases and controls. A P value <0.05 was considered significant.

Results

Data from 1899 patients undergoing 1899 procedures were included for evaluation. All but one procedure were completed with intermittent deep NAPS. One ERCP was disrupted and anesthesiologic expertise was summoned (0.05% of total). The mean

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The target state of motionless, unalert, and unaware were achieved for the full duration of all procedures and allowed for 99.95% of the procedures to be completed successfully, so the efficacy of sedation was good. The level of sedation was only registered prior to the procedure and before admission to the recovery room, but to avoid gagging, movement or cough, deep sedation is necessary for at least some part of EUS, DBE and ERCP and definitely achievable with a mean infusion rate of 23.9 mg/min propofol, hence the term “intermittent deep sedation.” In a previously published study [13] of patients undergoing standard endoscopic procedures (sigmoidoscopy, colonoscopy, and esophagogastroduodenoscopy) who were sedated with the same regimen by the same nurses, the average propofol consumption was 331.6 mg and the infusion rate 20.9 mg/min, both significantly lower than that required for advanced endoscopy. The higher propofol consumption during ERCP and EUS is confirmed by a number of authors reporting on mean propofol consumption between 78 mg and 277 mg during colonoscopy [9] as compared with 106−388 mg (Outlier low 51 mg and high 519 mg) (397 mg in the current study) for an advanced endoscopic population [3] or studies targeting deep sedation during endoscopy [6, 7, 14−18]. Adding to the higher propofol dose, the patients were older and more were ASA class 3 as compared with patients undergoing standard endoscopy, and therefore likely to be more responsive to propofol [13, 19, 20].

The screening of patients suited for intermittent deep sedation serves different purposes. A higher ASA classification and age are known to affect dose-response and assessment is necessary in order to adjust the propofol dose accordingly and thereby avoid an unpredictable course of sedation in patients with a possible reduced compensatory capacity [19, 20]. As described in a previous study [21], airway management during advanced upper endoscopy, particularly ERCP but probably also EUS, is still a matter of discussion. Depending on culture and local setup, in-hospital patients are often intubated or sedated by anesthesia personnel and out-of-hospital patients are increasingly sedated by gastroenterologists. In this study, only fasting patients were included and only non-obese (BMI ≤ 35) patients with a low comorbidity (ASA 1, 2, or stable class 3) were offered propofol. Causal analysis of the disrupted ERCP due to possible aspiration subsequently resulted in a review of the guideline so that pseudocyst drainage of a certain size required endotracheal intubation. The patient did not develop hypoxia or pneumonia. Furthermore, propofol was not given if patients presented a potentially difficult airway or difficult mask ventilation (DMV). Whereas the difficult airway is an exclusion criteria, screening for DMV is informally performed according to the OBSE criteria: Overweight (BMI 26 kg/m²), Beard, Edentulous, Snoring, Elderly (age older than 55 years) [22]. Although not necessarily excluded, patients at risk are observed closely and preferably examined in the lateral recumbent position to avoid obstruction of airways. In a previous study [22], the incidence of DMV was 5% in a mixed population. Utilizing an airway screening strategy in this study, the percentage was evidently lower, and no DMV has been encountered. The theoretical risk of DMV could possibly be reduced even further if the “OBSE” guideline was used as an exclusion criterion. To conclude on procedure safety, the incidence and severity of adverse events, the handling capability and the consequence should be assessed simultaneously. With this guideline, treatment is initiated before SAT% declines below 92%. Only three patients experienced concomitant SAT% < 88% and hypotension, all transient with a duration < 30 seconds and resolved with airway

### Discussion

The use of intermittent deep sedation provided a procedure success rate of nearly 100% in 1899 patients compliant with our NAPS criteria. However, intermittent deep sedation requires a relatively high propofol dose and leads to a higher frequency of sedation-related respiratory adverse events as compared with historical data, whereas the circulatory events rate seems less affected. Age and total propofol dose, but not ASA class, were associated with a higher frequency of adverse events.

| Table 1 Patient and procedure characteristics. |
|-----------------------------------------------|
| **EUS, ERCP, DBE**                            |
| **Patients, n**                               | 1899 |
| **Age, n**                                    | 1896 |
| **Mean (SD)**                                 | 62.5 (15.7) |
| **Range (years)**                             | 15 – 96 |
| **Sex, n**                                    | 1899 |
| **M (%)**                                     | 824 (43.4) |
| **F (%)**                                     | 1075 (56.6) |
| **ASA class, n**                              | 1882 |
| **I (%)**                                     | 455 (24.0) |
| **II (%)**                                    | 1158 (61.0) |
| **III (%)**                                   | 269 (14.2) |
| **Unknown (%)**                               | 17 (0.9) |
| **Total procedures**                          | 1899 |
| **EUS (%)**                                   | 1401 (73.8) |
| **ERCP (%)**                                  | 455 (24.0) |
| **DBE (%)**                                   | 43 (2.3) |
| **Sedation**                                  |     |
| **Propofol dose, n**                          | 1819 |
| **Mean (SD)**                                 | 397.0 mg (232.4) |
| **Median**                                    | 340 mg |
| **Sedation time, n**                          | 1194 |
| **Mean (SD)**                                 | 27.9 min (30.9) |
| **Median**                                    | 21.0 min |
| **Mg propofol/min, n**                        | 1193 |
| **Mean (SD)**                                 | 23.9 mg/min (25.8) |
| **Median**                                    | 16.5 mg/min |
| **Adverse events**                            |     |
| **Hypoxia < 92% SAT**                         | 81 (4.3) |
| **Hypotension**                               | 107 (5.6) |
| **Handling**                                  |     |
| **Assisted ventilation**                      | 20 (1.1) |
| **Airway manipulation**                       | 86 (4.5) |
| **Efedrin**                                   | 24 (1.3) |
| **Anesthesiologic assistance**                | 8 (0.4) |

N, patients with available data; SD, standard deviation; EUS, endoscopic ultrasound; ERCP, endoscopic retrograde cholangiopancreatography; DBE, double balloon enteroscopy
manipulation, increased oxygen and saline flow. None of these individuals required mask ventilation and no adverse event resulted in intubation or arrhythmia. In addition, all patients were expected to have some compensatory capacity. Mask ventilation resulted in intubation or arrhythmia. In addition, all patients were individuals required mask ventilation and no adverse event reported.

2 Logistic regression

1 Logistic regression

n, patients with available data; SD, standard deviation.

| Patients, n | 1818 | 81 (4.5) | 1792 | 107 (5.6) |
| Age, n | 1815 | 81 | 0.057 | 1789 | 107 |
| Mean (SD) | 62.3 (15.8) | 66.4 (11.9) | 62.2 (15.8) | 68.4 (13.0) | 0.001 |
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