



Propofol Requirements for Gastrointestinal Endoscopy in Patients Older than 75 Years Old Endoscopy sedation in Elderly with Propofol

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Abstract

Backgrounds and aims: There is literature on the safety of sedation with propofol in elderly patients. However, there are no clear guidelines regarding the dose of propofol to be used in these patients in which comorbidities can make them more fragile, making the standard dose/kg of weight excessive to achieve a safe sedation. The aims of this study were to establish the difference in dose of propofol in patients ≥ 75 years compared with < 75 years and to evaluate the safety of propofol administered by non-anesthesiologist in this group of patients.

Keywords: Elderly patients; Endoscopist; Propofol; Sedation

Abbreviations: NAAP: Non-Anesthesiologist Administered Propofol; ASA: American Society of Anesthesiologists; BMI: Body Mass Index; EGD: Esophagogastroduodenoscopies

Introduction

Gastrointestinal endoscopies are invasive, unpleasant, and sometimes painful procedures. For this reason, sedation is essential to reduce the anxiety, pain, and also to increase their efficacy. Propofol is considered the best single sedation agent for endoscopy [1], mainly because of its favorable pharmacokinetics profile that make it a safe and effective drug compared with traditionally endoscopic sedation drugs [2,3]. Propofol (2-6 diisopropylphenol) is a hypnotic drug with minimal analgesic properties. It is highly lipophilic, and thus can rapidly cross the blood-brain barrier resulting in an early onset of action (30-40 seconds). The depth of sedation increases in a dose-dependent manner, but his

short half-life (4 minutes) regardless of the length or depth of the sedation favors a prompt recovery (10 to 20 minutes after discontinuation) with a pleasing awakening, providing an outstanding comfort for the patients. With regard to side effects, it can induce a dose-dependent decrease in conscience, blood pressure and heart rate, and that's why its use is recommended under close supervision by trained healthcare personnel and using adequate surveillance with at least pulse O_2 saturation, heart and respiratory rate and blood pressure monitoring. To date, no pharmacological antagonist has been developed [4,5]. Propofol is contraindicated in patients allergic to propofol, and in patients at risk of bronchoaspiration or with low ejection fraction.

Sedation in gastrointestinal endoscopy performed by a specially trained nurse, guided by the endoscopist, is increasingly common in the European countries and it's known as NAAP (non-anesthesiologist administered propofol) [6]. It is important that the endoscopist have an appropriate management of sedation with careful training and knowledge about how propofol behaves in different settings or sort of patients. Of note, the European population has a high prevalence of elderly patients. Considering this issue, it is mandatory to have precise information about the dosage needed to achieve a safe sedation level in aged patients in which comorbidities will make them more fragile than the young ones. There are numerous published studies supporting the efficacy and safety of this technique, showing a rate of complications equal to, or lower than traditional sedation, in which propofol is administered during endoscopic procedures based on the weight, age and clinical status of the patient. There is literature on the safety of sedation with propofol in elderly patients in which lower doses are recommended [7,8]. However, there is lack of clear published data regarding the dose of propofol to be used in this group of patients in whom the dose per kg of weight may be excessive to reach a safe level of sedation [9,10]. We performed a prospective study to establish the dose of propofol in patients ≥ 75 years compared with patients < 75 years and to evaluate the safety of propofol when is administered by non-anesthesiologist in this population.

Material and Methods

The study protocol was previously approved by the local Committee for Human Studies. Between June 2012 and March 2014, all endoscopic procedures and safety data were prospectively recorded at the endoscopy unit of a university hospital. To homogenize both groups, only diagnostic procedures were included. Patients < 18 years, therapeutic procedures not sedated by endoscopist, incomplete procedures due to reasons not related with sedation, and patients with upper and lower endoscopies performed on the same day were excluded.

Prior to the procedure, a history of risk factors was taken from all patients leading to a risk stratification based on the criteria of the American Society of Anesthesiologists (ASA). Demographical and clinical data recorded from all patients were age, gender, weight, height, type of endoscopic intervention performed, clinical indication, complications related to sedation or to the endoscopic procedure, and dose of propofol. Oxygen was continuously administered on a

routine basis through a nasal probe at 2L/min. Heart rate and blood oxygen saturation levels were continuously monitored. Blood pressure was recorded before, during and after the procedure. All physicians and endoscopy nurses were specially certified for the administration and management of possible risks associated with the use of propofol.

To reduce variability and determine whether the differences between the dose of propofol in both groups were only related to age, all patients ≥ 75 years were matched on a 1:1 basis with the < 75 years group in terms of weight, body mass index (BMI) and endoscopic procedure. All esophagogastroduodenoscopies (EGDs) and colonoscopies received an initial dose of propofol 0.5-1 mg/kg. Colonoscopies also received a fixed dose of 50 mcg of fentanyl. Subsequently, boluses of 10-20 mg propofol were administered to maintain an adequate level of sedation. Mild adverse events were defined as those not requiring the interruption of the procedure: a transitory drop in peripheral oxygen saturation below 90%, decreases in the mean arterial pressure of more than 25% and decreases in the heart rate of more than 20%. Mild adverse events resolved spontaneously or with simple maneuvers (chin-lift maneuver, volume expansion, atropine administration). Severe adverse events were defined as those that required interruption of the procedure (the need for intervention with positioning of a tracheal tube, cardiac arrest or death). A statistical analysis was performed with the SPSS v20.0 program. Results are reported as frequencies or means \pm SD plus 95% confidence interval of the mean.

Results

Between June 2012 and March 2014, 10,237 endoscopic procedures were performed. After exclusion criteria we analyzed a total of 6,121 diagnostic EGDs and colonoscopies. There were 439 diagnostic EGDs and 307 diagnostic colonoscopies performed in patients ≥ 75 years. The mean age was 81 ± 4 . When compared with patients < 75 years, there were significant differences between groups in mean propofol dose, and mild adverse events. No serious adverse events occurred. Patients ≥ 75 years required significantly less propofol than patients < 75 years, (72.99 ± 37.4 mg) vs. (120.54 ± 41.8 mg for EGDs) ($p < 0.001$) and (80.59 ± 34 mg) vs. (129.12 ± 55.9 mg) ($p < 0.001$) for colonoscopies (39.4% less in EGDs and 37.5% in colonoscopies). Table 1 shows the demographics, endoscopic procedures, propofol dose and adverse events in both groups.

Table 1: Demographic, endoscopic procedures, propofol dose and adverse events in both groups Data are presented as mean \pm SD (range: 95% CI of the mean).

Characteristic	≥ 75 years	< 75 years
Age	81 \pm 4	51.3 \pm 13
Weight	68.5 \pm 12,4	68.5 \pm 12,4
ASA I/II/III (%)	17.3/70.3/12.4	62.8/34.9/2.3
EGD n	439	439
Colonoscopy n (%)	307	307
Propofol dose EGD Colonoscopy	73 \pm 37.4 80.6 \pm 34	120.5 \pm 41.8** 129.1 \pm 55.9**
Adverse events (%) Mild: Desaturation/Bradycardia Severe	2.6/0.3 0	0.8/0.3* 0

Abbreviations: ASA: American Society of Anaesthesiology; EGD: Esophagogastroduodenoscopy

*P < .005; **P < .001

Discussion

Our study is a prospective investigation about sedation in elderly patients undergoing gastrointestinal endoscopy, which confirms what other studies demonstrate: this population requires less propofol to reach an adequate level of sedation [8,11,12]. We selected the mentioned "75 years old" as cut point age, considering that doing so we would be able to identify a group of patients in which comorbidities might be present, it is representative of our specific population with a high life expectancy and easily reproducible. Indeed we found another study in which the same cut point age was used for a similar analysis [13].

We also estimate how much less propofol they need when compared with younger patients. To our knowledge there is only one study, performed by Heuss, et al. [7], where the difference in the dose of propofol was estimated. In their prospective study, patients older than 85 years old required 60-65% less propofol than younger. Compared with this study, our investigation provides remarkable information regarding the dose of propofol used, in a very strictly selected population, where therapeutic procedures were excluded to avoid the risk of biases. Our study clearly reflects the dose of propofol needed by the patients as per their age, and not per the duration of the procedure or the need of therapeutically intervention. Moreover, our patients were matched according their BMI on a 1:1 basis to have a clear picture of what was happening with the dose of propofol we were using. We strongly believe this study provides valuable information for

all endoscopists practicing NAAP, but especially for young fellows who begin to administer propofol as their preferred method of sedation for endoscopic procedures.

We also reassure that propofol administered by endoscopists and trained nurses are a safe technique in elderly patients, who are more susceptible to serious adverse reactions. In our study only mild adverse events occurred. There were more cases of oxygen desaturation in the elder group, 15 were resolved by chin extension maneuver and only 3 required ventilation mask. Endoscopic procedures are becoming more frequent in the geriatric population. Numerous published studies demonstrate that endoscopic procedures and sedation with propofol are safe in elderly patients, so advanced age should not be a contraindication [14-17]. In our study, no serious adverse events occurred, neither with the sedation nor with the technique. Pre-procedure assessment and monitoring should be similar for elderly and younger patients, with particular attention to cardiopulmonary status, comorbidities and the use of medication that could affect sedation. Sedative agents should be administered with greater caution in elderly, considering the increased response to sedatives in this population. A variety of physiologic processes contribute to the increase in sensitivity and sedation risk in geriatric patients. The age-related increase in lipid fraction of body mass yields an expansion of the distribution volume for pharmacologic agents that are highly lipid soluble. In conjunction with reduced hepatic and renal clearance mechanisms, this can prolong recovery for elderly patients after sedation. A

complex interplay among heightened central nervous system sensitivity and alterations in drug receptors, volumes of distribution, and inter compartmental transfer contributes to the reduced dose requirements of all standard sedative agents. Rapid or excessive dosing contributes more to the cardiopulmonary adverse events of sedation than dose itself [18,19].

Recently, the American Society for Gastrointestinal Endoscopy [20] published a guideline about modifications in endoscopic practice procedures in elderly. They recommend the administration of fewer agents at a slower rate and with lower initial and cumulative doses. Doses based solely on milligram per kilogram of body weight may produce profound respiratory depression and hypotension. Propofol has a narrower margin of safety in elderly patients, but has been shown to be safe when used in elderly patients with continuous monitoring. It is clear that elderly patients need less propofol than younger patients. But how much less? This study demonstrates that patients ≥ 75 years globally require almost 40% less propofol than patients < 75 years to achieve a safe sedation. These results support the use of a lower dose of propofol in the elderly, and also demonstrate that sedation administered by non-anesthesiologists is safe in this population.

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