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Sedation in elderly patient undergoing surgery with spinal anesthesia: propofol vs. midazolam

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ABSTRACT

It is widely known the need for a high quality sedation associated with local regional anesthesia in elderly patients' surgery. The aim of this study was to compare two sedation regimes: propofol and midazolam, associated to spinal anesthesia with isobaric 0.5% bupivacaine in lower abdominal surgery in elderly patients. After obtaining the informed consent, 60 patients aged between 65 and 82 years old (ASA I-III), scheduled for unilateral hernioplasty , under spinal anesthesia with isobaric bupivacaine 1,5 ml (0.5%), were randomized into two groups of 30 patients each: P group - patients received propofol 3mg/kg/body/hour in the first 10 minutes and then continuous infusion by injection of 1,8 mg/kg/body/hour, and group M–patients who have received midazolam 0,2mg/kg/body/hour in the first 10 minutes and then continuous infusion by injection of 0,15 mg/kg/body/hour. In order to achieve a similar level of sedation we used 0,1% midazolam infusion and 1% propofol. Intraoperative, the following have been monitored: heart rate and breath, mean arterial pressure, hemoglobin oxygen saturation. We have also recorded the sedation score (modified Wilson sedation scale), awakening times, patient satisfaction at 24 hours (satisfaction score according to Iowa University). The average score of sedation for group P was of 3,24 ± 0,23, compared to 2,64 ±0,42 in group M (p = 0.001). Both drugs reduce blood pressure, but not more than 20% of the initial value. There are no significant differences in the satisfaction score of the patient (p = 0,18). There was just one case of respiratory depression in group M with the decrease of SpO2 at 86%.Sedation with propofol associated with local regional anesthesia techniques in elderly patients seems to provide better conditions in terms of sedation score and lack of respiratory depression compared with the administration of midazolam. Recovery was significantly faster after sedation with propofol. The satisfaction score of the patient was similar in the two groups.

Keywords: propofol, midazolam, spinal anesthesia, elderly patients

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Introduction

Defining sedation as "a state of calm and tranquility" induced by medication known to have sedative effect, Johan Raeder has recently conducted a relevant analysis of various situations experienced by the patient and the physician to determine the optimal degree of sedation required for each patient, without being able to give the ideal recipe for sedation.

The need to associate a high quality, secure and fast elimination sedation, it is widely known for regional anesthesia. The way in which people have tried to achieve this goal has changed over the time, using different classes of drug.

In recent years, the use of propofol or midazolam for sedation has gained popularity, in combination with local regional anesthesia techniques and for diagnostic or therapeutic maneuvers. Despite the numerous advantages of these drugs (hemodynamic stability, rapid awakening, reduced incidence of postoperative nausea and vomiting) persists the disadvantage of respiratory depression, hypotension and/or bradycardia in their overdose.

The aim of this study was to see whether the administration of sedative doses of propofol, respectively of midazolam (iv.), both associated to spinal anesthesia with isobaric 0.5% bupivacaine in lower abdominal surgery in elderly patients: a) suppresses anxiety during surgery in elderly patients; b) determines changes in the hemodynamic behavior; c) depresses breathing changing pulse oximetry; d) there are differences in the level of sedation; e) there are differences in the awaking times and satisfaction in 24 hours.

Material and method

During the period February 1st, 2012 – September 1st, 2012 we have included 60 elderly patients proposed for surgery (unilateral hernioplasty), under spinal anesthesia with 1.5 ml 0,5% isobaric bupivacaine in a prospective randomized observational study approved by the Ethics Committee of the County Emergency Hospital Constanta.

The study was conducted in accordance with the principles of the Declaration of Helsinki.

The criteria for inclusion of patients in the study were: age over 65 years old; ASA I– III; scheduled abdominal surgery (unilateral hernioplasty); normal preoperative mental state, defined by the score ≥ 8 at the AMT adapted test (Abbreviated Mental Test - Table I); absence of contraindications for spinal anesthesia (clinical or laboratory), no allergy to egg, soya or lidocaine, absence of extreme malnutrition and cerebrovascular inefficiency.

*Table I. Abbreviated Mental Test (AMT) **

Age
Hour
Year
Hospital name
Hospital address
Recognition of two persons (eg doctor, nurse)
Date of birth
Year of commencement of World War
Name of the president
To count backwards from 20 to 1

** Patients were asked to answer these 10 questions. Each correct answer received one point.*

The day before surgery, during the pre-anesthetic consultation, patients were informed about the study protocol, they have filled in the sheet with psychological, pathological and personal data as well as the informed consent.

On the day of the surgery, patients were infused with 500 ml saline preoperative (8-10 ml/kg/body) and intraoperative with 250 ml saline (4 -5 ml/kg/body), followed by 250 ml colloidal solution of Voluven 6% (4 - 5 ml/kg/body).

All patients were anesthetized in the same conditions: spinal anesthesia, needle 22 G, median approach, space L2 – L3, seated position, 1.5 ml isobaric bupivacaine solution 0,5%.

Patients included in the study were randomly distributed by the method of random number lists, into two groups as follows: group P (n= 30), patients who received sedation with propofol and group M (n = 30), patients who were administered midazolam for intraoperative sedation.

Previous studies have shown that the average infusion rate of 3.7 mg/kg/body/hour for propofol and 0.27 mg/kg/body/hour for midazolam provide similar levels, for a satisfactory sedation in the young patient.

Given the particularities in elderly patients and aiming to ensure quality sedation with minimal risks, we have reduces the administered doses, as follows:

-group P: patients have received propofol 3mg/kg/body/hour in the first 10 minutes and then continuous infusion on auto injector 1,8 mg/kg/body/hour,

-group M: patients have received midazolam 0.2mg/kg/body/hour in the first 10 minutes and then then continuous infusion on auto injector 0.15 mg/kg/body/hour.

In order to achieve a similar level of sedation, midazolam infusion of 0.1% and respectively propofol 1% has been used. We have started the injectomat infusion immediately after spinal anesthesia.

Intraoperative, the following were monitored: breathing rate, mean arterial pressure at 3 minutes, continuous heart rate (HR) as well as ECG (DII) and hemoglobin oxygen saturation (SpO2).

We have recorded the sedation score obtained on the modified Wilson sedation scale (Table II) subsequently measured at 5 and 10 minutes after the interruption of the sedative medication. We have recorded the time intervals needed for eyes opening and replay psycho-cognitive functions assessed by the patient's ability to open his/her eyes upon command and to correctly pronounce the date and place of birth.

The appearance of respiratory depression has been followed (decreased respiratory rate below 10 breaths/min or decrease of SpO2 below 90%).

Table II. Modified Wilson Sedation Scale

Score	Description
1	Fully awake and oriented
2	Eyes closed but rousable to command
3	Eyes closed but rousable to mild physical stimulation (earlobe tug)
4	Eyes closed but unrousable to mild physical Simulation

Evolution of hemodynamic was assessed by a very good, good and unsatisfactory score. (Table III).

Table III. Assessment of hemodynamic behavior intraoperative

Evolution of hemodynamics	Definition	Score
Unsatisfactory	MAP decreased by more than 25% of the preoperative value over 20 mg ephedrine 1% required	1 point
Good	MAP decreased by up to 25% of the preoperative value up to 20 mg ephedrine 1% required	2 points
Very good	MAP decreased by up to 20% of the preoperative value does not require ephedrine 1%	3 points

Anxiety, as state of physical and mental sickness, was estimated according to three categories of symptoms: movement disorders, autonomic disorders, vigilance disorders, evaluated before surgery, during surgery and after awakening for hypnosis.

Patient satisfaction was recorded in a questionnaire with eight questions of interest satisfaction (items) (satisfaction score after Iowa University, Table IV), which the patient was asked to complete at 24 hours post-surgery. Each item of the questionnaire has received a score from 1 to 6, and subsequently patient satisfaction score was calculated as the arithmetic average of the eight scores.

After the surgery, patients were supervised and monitored in terms of hemodynamic, cardiac and respiratory values for 24 hours, by trained personnel, noting in particular: incidence of nausea, vomiting, excessive sedation, respiratory depression.

Parametric variables, were expressed as the average ± DS (deviation standard) and for their comparison the t – Student test has been used. For non-parametric variables the Mann-Whitny test has been used. The values $p<0.05$ were considered significant.

Table IV. Satisfaction score after Iowa University

1. I threw up or felt like throwing up • Disagree very much+1 • Disagree moderately+2 • Disagree slightly+3 • Agree slightly+4 • Agree moderately+5 • Agree very much+6	1. I felt pain • Disagree very much+1 • Disagree moderately+2 • Disagree slightly+3 • Agree slightly+4 • Agree moderately+5 • Agree very much+6
2. I would want to have the same anesthetic again • Disagree very much+1 • Disagree moderately+2 • Disagree slightly+3 • Agree slightly+4 • Agree moderately+5 • Agree very much+6	2. I felt safe • Disagree very much+1 • Disagree moderately+2 • Disagree slightly+3 • Agree slightly+4 • Agree moderately+5 • Agree very much+6
3. I itched • Disagree very much+1 • Disagree moderately+2 • Disagree slightly+3 • Agree slightly+4 • Agree moderately+5 • Agree very much+6	3. I was too cold or hot • Disagree very much+1 • Disagree moderately+2 • Disagree slightly+3 • Agree slightly+4 • Agree moderately+5 • Agree very much+6
4. I felt relaxed • Disagree very much+1 • Disagree moderately+2 • Disagree slightly+3 • Agree slightly+4 • Agree moderately+5 • Agree very much+6	4. I was satisfied with my anesthetic care • Disagree very much+1 • Disagree moderately+2 • Disagree slightly+3 • Agree slightly+4 • Agree moderately+5 • Agree very much+6

Results

There are no significant differences between the demographic data of the two groups of study, being considered homogenous (Table V).

Installation time of hypnosis (level 3 of sedation on the 4 steps Wilson scale) was late in the midazolam group, but without significant statistic differences (Table VI).

Table V.Patient demographic data and clinical characteristics

	Group M (midazolam) (n = 30)	Group P (propofol) (n = 30)	p
Age(yrs)	72,9±9,1	74,55±6,7	0,58
Weight (kg)	63,8±11,6	67,5±8,2	0,78
Height (cm)	163,4±14,1	167,4±15,8	0,11
Sex(M/F)	24/6	21/9	0,57
ASA class I/II/III	8/14/8	6/15/9	0,61

The data are presented as the mean ± SD or the number p > 0.05

Table VI. Installation time of hypnosis

	Group M (midazolam) (n = 30)	Group P (propofol) (n = 30)	p
Time (min.)	**9±3**	**7±2**	**0,058**

The data are presented as the mean ± SD , p > 0.05

During surgery, within the midazolam group, 26 patients were placed on level 3 of sedation and 4 patients on level 4, while in the group with propofol, 28 patients achieved level 3 of sedation and 2 patients level 4; 5 minutes after discontinuation of sedative medication in the propofol group, 25 patients were placed on level 2 on Wilson scale and 5 patients on level 3, while in the midazolam group, 19 patients remained on level 3 and for 11 patients sedation became superficial on level 2 Wilson scale. After 10 minutes, 16 patients sedated with midazolam reached level 1 and 12 patients level 2, while all the patients with propofol were on level 1 of sedation (Table VII, Figure 1.).

Table VII. Level of sedation on the 4 steps Wilson scale

Level of sedation	**Group M(midazolam) (n = 30)**			**Group P(propofol) (n = 30)**		
	During surgery	5 minutes after discontinuation of sedative medication	10minutes after discontinuation of sedative medication	During surgery	5 minutes after discontinuation of sedative medication	10 minutes after discontinuation of sedative medication
1.	-	-	16(53,3%)	-	-	30(100%)
2.	-	11(36,6%)	12(40%)	-	25(83,3%)	-
3.	26(86,6%)	19(63,3%)	2(6,6%)	28(93,3%)	5(16,6%)	-
4.	4(13,3%)	-	-	2(6,6%)	-	-

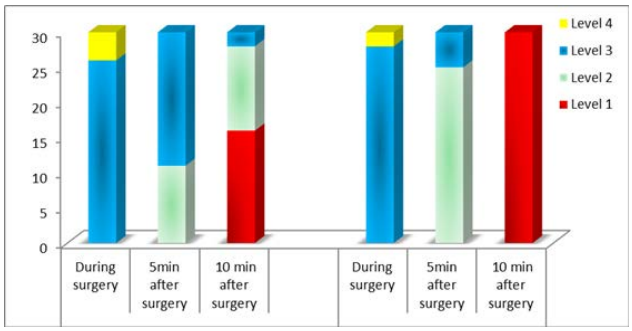

Figure 1 - Differences in the level of sedation on the Wilson scale

Recovery time of consciousness confirmed by eye opening and obtaining a coherent response on age, date and place of birth was significantly longer in the group of patients sedated with midazolam (Table VIII).

Table VIII. Recovery time of consciousness

	Group M (midazolam) (n = 30)	**Group P (propofol) (n = 30)**	**p**
eye opening (minute)	11±3	4±2	0,028
coherent response on age, date and place of birth (minute)	12±2	5±1	0,042

The data are presented as the mean ± SD p<0.05

Until sedative medication, all patients had one or more symptoms of anxiety suppressed by the administration of sedatives without significant differences between the two groups. Patients had a high degree of satisfaction regardless of the study group they had been part of. (Table IX).

Table IX. Patient satisfaction at 24 hours (satisfaction score according to Iowa University).

	Group M(midazolam) (n = 30)	**Group P (propofol) (n = 30)**
Fair/poor	-	-
Good	4	-
Excellent	26	30
Satisfaction score	3,24±0,23	2,64±0,42

Intra-surgically, hemodynamic was stable, the evolution of the patients enrolled in the study being assessed as very good. TAM decrease did not exceed 20% of the pre-anesthetic value, although it was more obvious in the case of sedation with midazolam (Table X).

Table X. Evolution of clinical behavior during surgery

Parameters	**Grup M(midazolam) (n = 30)**	**Grup P(propofol) (n = 30)**
HR(bpm)	80,9 ±12,4	79,6± 13,5
TAM(mm Hg)	83 ±12,3	78,5±4 7,8
SpO2(%)	98 ±0,6	99,1± 0,7

The data are presented as the mean ± SD p>0.05

There was only one case of respiratory depression in group M, with desaturation up to 88% and slow breathing of 6 breaths/minute, when the patient was assisted breathing through the mask ventilation for 3 minutes, after which respiration became efficient and saturation returned to 99%. Administration of midazolam was reduced at 0.1 mg/ kg body/hour.

Discussions

Given the high incidence of associated diseases and reduced psychological resilience in the elderly, spinal anesthesia was preferred in geriatric surgery on the lower abdomen. Simpathicolysis and arterial hypotension can be reduced or avoided by using small doses of local anesthetic. The dose of bupivacaine recommended in specialized literature, 15-20 mg (3-4 ml solution 0.5 %) is too high for elderly patients.

Local anesthetic dose reduction has a beneficial effect on hemodynamic, but in the same time the quality and duration of sensory block is lost when it exceeds a certain lower limit of the amount on the quantity of anesthetic administered. In these circumstances, the association of intravenous sedative medication can bring more quality to the local regional anesthesia due to its sedative and anxiolytic effect.

In this study we have administered intravenously slow sedative doses of midazolam 0.15 mg/kg body/hour or propofol 1.8 mg/kg body/hour in elderly patients undergoing spinal anesthesia with 0.5% (7.5 mg) bupivacaine.

Slow infusion of midazolam and propofol as adjuncts for spinal anesthesia, proposed an excellent and easily controllable sedation. Within the interval of 13 – 15 minutes most patients have achieved level 3 of sedation: sleeping, as an immediate response to physical stimulation (slight tapping of the scalp) without significant difference in the two groups.

The incidence of side effects was slow. In both groups we have found a slight decrease in TAM that did not exceed by 20% the pre-anesthetic value. Also heart rate was dropped by more than 5-7 beats/minute.

The only difference between the two groups was the different recovery time of the consciousness state. The average time from discontinuous infusion and until the patient opened his/her eyes and gave information on the date of birth was significantly shorter in patients from the group sedated with propofol (3-4 minutes compared to 10-11 minutes).

In the group sedated with propofol awakening was quiet, prompt without residual sedation, compared to the group which received midazolam, where a mild sedation persisted for 30-60 minutes, sedation associated with amnesia.

In the specialized literature, both intravenous anesthetics were used as processing of regional anesthesia. Among benzodiazepine, midazolam is the most frequently used for intravenous sedation having a fast debut of the effect and a short elimination hart-life (2-4 hours). An important advantage of midazolam as adjunct to regional anesthesia is sedation associated with the effect of sedation and low incidence of side effects. However, being administered for long periods of time or in large doses than 2.5 mg/kg, midazolam delays the awakening of the patient.

Propofol has a pharmacokinetic profile characterized by a fast redistribution and high clearance which allows fast recovery from the sedative-hypnotic effects. Also, post-surgery side effects are rare, especially nausea and vomiting.

Many researchers have compared propofol to midazolam for the sedation during local and regional anesthesia. In the study drawn up by Wilson et al., 3.7 mg/kg body/hour propofol and 0.27 mg/kg body/hour midazolam have caused similar sedation levels during the subarachnoid anesthesia in young adults, but a significantly more rapid recovery after discontinuation of propofol. The titration of sedative infusion was easier with propofol, compared to midazolam and the risk of excessive sedation was reduced.

In our study we have not observed significant statistic differences between the two groups on the decrease of intra-anesthetic of TA.

Conclusions

In conclusion, the two intravenous anesthetics, midazolam (dose of 0.15 mg/kg body/hour) and propofol (1.8 mg/kg body/hour), when administered to elderly patients under spinal anesthesia with 7.5 mg bupivacaine 0.5%, have given comparable levels of sedation and they have presented cardiovascular

and respiratory stability. Propofol provided a pleasant awakening without residual sedation and superior patient recovery lucidity present after 3 -5 minutes prior discontinuous of administration.

Anxiety and unpleasant intraoperative sensations were absent, nausea and vomiting were absent, while post-surgery delirium (clinically manifested by psychomotor agitation, potentially self-traumatizing: fall out, plucking catheter, uprooting venous catheters) was not observed in any patient.

The novelty of our study is the significant reduction in the dosage of sedatives used in accordance with the characteristics of elderly patients, maintaining a balance between the expected benefits and potential risk of side effects. A correct hydration of elderly patients and their proper monitoring had a considerable contribution in obtaining these results.

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