RESEARCH ARTICLE

Etomidate and Propofol: Which Would be Safe from the Hemodynamic Viewpoint in Colonoscopy Exams?

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Abstract

Justification
Most patients who undergo colonoscopy are over 55 years old, with comorbidities and who use cardio-depressant drugs. In addition, exam preparation includes the use of osmotic diuretics, causing osmotic diarrhea leading many patients to some degree of dehydration. Considering all these factors and knowing that the drug selected for sedation also acts by depressing the cardiovascular system, this study proposes to evaluate the action of two hypnotic drugs (etomidate and propofol) routinely used for sedation..

Methods
In two private clinics, 105 participants (18 to 90 years old), ASA I and ASA II (American Society of Anaesthesiologist score) were selected. Participants were divided into two groups: fentanyl 1 mcg / kg + midazolam 0.03 mg / kg + etomidate 0.3 mg / kg (n = 52) and fentanyl 1 mcg / kg + midazolam 0.03 mg / kg + propofol 2 mg / kg (n = 53). Participants were monitored with cardioscope, pulse oximeter and tensiometer. Blood pressure, heart rate and oxygen saturation parameters were observed before, during and after the exam.

Results
Most participants were ASA II (63%) and female (74%). In subjects who received propofol group significant reductions in the systolic ($p < 0.05$) and diastolic ($p < 0.05$) blood pressures and significantly increased heart rate ($p < 0.05$) compared to the group receiving etomidate. There was no difference in hemodynamic variation between male and female participants. There was no difference in satisfaction of endoscopists and patients regarding medications used for sedation.

Conclusion
The hypnotic drug etomidate was safer from the hemodynamic point of view for sedation in colonoscopy exams.

Keywords: Etomidate. Propofol, Colonoscopy Sedation

Introduction

Colonoscopy is an endoscopic examination performed for the purpose of diagnostic and therapeutic study of large bowel lesions. It has an average duration of 40 minutes and is indicated as a preventive test for colorectal cancer from 50 years of age[1]. The test is usually accompanied by discomfort and pain due to air insufflation in the intestine. Therefore, an anesthesiologist, in addition to sedation, should conduct cardiac and respiratory monitoring for the patient safety.

The anesthesiologist combines various medications to achieve synergism during the exam. Fentanyl, a morphine-derived opioid analgesic, is used with midazolam, benzodiazepine that produces hypnosis and retrograde amnesia.[2] Other hypnotics such as etomidate or propofol are added to the sedation regimen to provide greater satisfaction (absence of pain and recall of the exam) and patient safety.[3]

Propofol is a hypnotic agent that promotes practically immediate induction, has an ultrashort half-life with shorter recovery time.[4] It can be used in intermittent bolus or continuous infusion. Propofol, compared to all other hypnotic agents, promotes the lowest incidence of nausea and vomiting, and is therefore the drug of choice for outpatient procedures. Propofol decreases preload, peripheral vascular resistance with consequent vasodilation and hypotension, is negative inotropic, decreases respiratory rate, minute volume and tidal volume.[5]

Etomidate was introduced into clinical practice in 1972. It is a fast-acting, short-acting hypnotic agent with short half-life that causes lower respiratory depression than propofol.[8,9,10] Etomidate confers greater hemodynamic stability than others. Hypnotics in the Anesthesiologist's Therapeutic Arsenal.[6] Because it does not inhibit sympathetic tone and myocardial function, etomidate may be used in patients with bronchospasm or those who cannot have hypotension due to intracranial or coronary problems. [11,12,13]

Most patients undergoing colonoscopy examination are over 55 years of age with comorbidities. In fact, most use cardiodepressants.[19] In addition, the preparation of the examination includes the use of osmotic diuretics that can results in osmotic diarrhea in many patients. Considering all these factors and knowing that the hypnotic selected for sedation also acts by depressing the cardiovascular system, this study proposes to evaluate the action of two hypnotics (etomidate and propofol) routinely used for sedation.

Methods

This is an observational, prospective, open and longitudinal study conducted in two private clinics. Data were collected at the time of routine anesthetic sedation. Participants were monitored with pulse oximeter, tensiometer and received supplemental oxygen throughout the exam.

Ethical concerns

The protocol for the present study is in accordance with the international guidelines concerning research in humans, and was approved by the Ethical Committee of the Universidade de Fortaleza, situated at Avenida Washington Soares 1321, Block M Room-30, *Diretoria de Pesquisa e Inovação Tecnológica* (Research and Technological Innovation Directorate), Brazil with the decision number 3.569.869.

Selection of participants

The subjects consisting of 105 individuals were distributed into two groups:

- Group 1 (n = 53) - were sedated with etomidate 0.3 mg/kg bolus followed by 0.05 mg / kg every 3 minutes in the first ten minutes of the procedure.
- Group 2 (n = 52) - were sedated with propofol 2 mg/kg bolus followed by 0.5 mg/kg every 3 minutes for the first ten minutes of the procedure.

All participants were sedated with 1 µg/kg fentanyl and 0.03 mg/kg midazolam and received supplemental oxygen (3 L/min)

The following data were collected:

- Sociodemographic data
- ASA score[14]
- Blood pressure before, during and after the examination.
- Heart rate before, during and after the examination.
- Oxygen saturation before, during and after the examination.
- Patient satisfaction (absence of memories of the moment of the examination)
- Endoscopist satisfaction (absence of participant movements that could impair the procedure and participants' memories of the examination)

Inclusion Criteria

Participants with ASAI and ASAII aged 18 to 90 years that marked their exams on an elective basis were included.

Exclusion Criteria

Participants with a history of hypersensitivity to any medication that was used in the anesthetic procedure and/or pregnant patients were excluded.

Statistical Analysis

Data were stored in a database built in Microsoft Excel computer program and then transferred to IBM SPSS version 23.0 software (IBM, USA). Qualitative variables were expressed as absolute count and frequencies represented by percentages. The frequency comparison of qualitative variables was performed by the chi-square test. All quantitative variables were tested for normal distribution using the Kolmogorov-Smirnov test. Normal data were then expressed as mean ± standard deviation. Student's t-test was used to compare means between "etomidate" and "propofol" groups.

In addition, paired analyzes were performed comparing hemodynamic parameters between 3 different periods (before, during and after hypnotic use) in each group. For this, ANOVA with repeated measures were used. For all tests, $p < 0.05$ was considered statistically significant.

Results

As can be seen in Table 1, 105 participants aged 18 to 90 years were included, the minority were male (n = 27; 26%), of these 52 received propofol and 53 received etomidate. 66 (63%) participants had ASA II physical status (mild systemic disease) and 39 (37%) were ASA I (healthy) status. No differences in gender-related hemodynamic variations were found.

Table 2 shows that during the use of hypnotics, the etomidate group had higher values ($p < 0.001$) of systolic and diastolic blood pressure during the examination, and the heart rate was lower ($p < 0.001$) than in the group that were sedated with propofol.

Table 1. General sample characteristics.

	Sample (n=105)
Age	58 ± 15,1
Hypnotics Used	
Etomidate	53 (51)
Propofol	52 (49)
Sex, Female	78 (74)
ASA score	
ASA I	39 (37)
ASA II	66 (63)
Hemodynamics before the examination	
SBP, mmHg	122.1 ± 19,0
DBP, mmHg	73.9 ± 12.1
HR, bpm	78.6 ± 9.4
Hemodynamics during hypnotic use	
SBP, mmHg	104.7 ± 22.5
DBP, mmHg	58 ± 13.4
HR, bpm	81.7 ± 9.5
Hemodynamics after hypnotic use	
SBP, mmHg	109.4 ± 19.6
DBP, mmHg	65.5 ± 13.3
HR, bpm	81.1 ± 8.8

Significant reduction in the values of systolic and diastolic blood pressure were observed in the participants sedated with propofol (Table 3) when compared to participants sedated with etomidate (Table 4). Moreover, in the participants who were sedated with propofol, a higher increase in the heart rate was observed as compared to participants sedated with etomidate reflecting the reaction of the cardiovascular system to propofol hypotension.

Table 2. Comparison of hemodynamic parameters before, during and after colonoscopy examination according to the hypnotic used.

	Etomidate (n=53)	Propofol (n=52)	p
Age	58.1 ± 14.2	57.9 ± 16.2	0.938
Sex, Male	9 (17)	34 (65)	0.943
ASA score			
ASA I	17 (32)	22 (42)	0.311
ASA II	36 (68)	30 (58)	
Hemodynamics before the examination			
SBP, mmHg	125.3 ± 17.3	119 ± 20.3	0.091
DBP, mmHg	75.6 ± 12.8	72.1 ± 11.1	0.135
HR, bpm	77.3 ± 8.5	80 ± 10.2	0.135
Hemodynamics during hypnotic use			
SBP, mmHg	113.9 ± 21.1	95.3 ± 20	<0.001
DBP, mmHg	62.3 ± 10.5	53.5 ± 14.7	0.001
HR, bpm	78.3 ± 8.4	85.2 ± 9.4	<0.001
Hemodynamics after hypnotic use			
SBP, mmHg	116.2 ± 17.3	102.5 ± 19.5	<0.001
DBP, mmHg	67.9 ± 12.2	63 ± 14.1	0.057
HR, bpm	78.1 ± 8	84.2 ± 8.7	<0.001

Table 3. Comparison of hemodynamic parameters before, during and after colonoscopy examination using propofol.

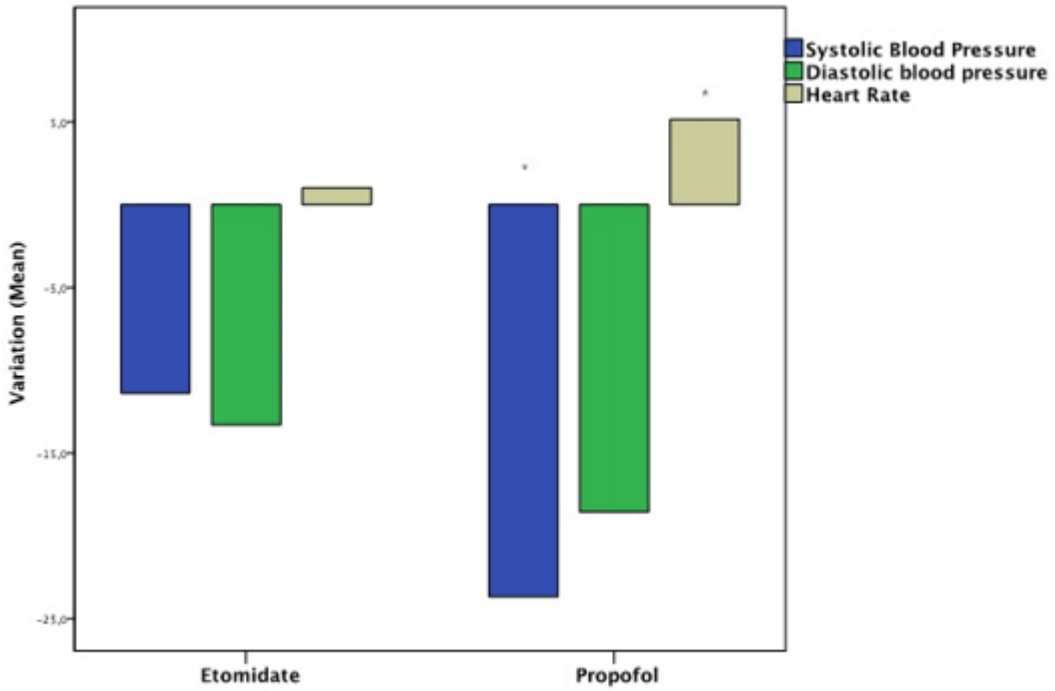
	Periods evaluated as regards propofol use			
	Before the use	**During the use**	**After the use**	**p**
Hemodynamic Parameters				
SBP, mmHg	118.98 ± 20.25	95.31 ± 19.97	102.46 ± 19.52	0.015[#]
DBP, mmHg	72.10 ± 11.12	53,54 ± 14.66	63.00 ± 14.08	0.001[#]
HR, bpm	80.00 ± 10.23	85.17 ± 9.42	84.23 ± 8.7	0.001*

Table 4. Comparison of hemodynamic parameters before, during and after colonoscopy examination using etomidate.

	Periods evaluated as regards Etomidate use			
	Before the use	**During the use**	**After the use**	**p**
Hemodynamic Parameters				
SBP, mmHg	125.25 ± 17.29	113.87 ± 21.06	116.23 ± 17.31	0.001*
DBP, mmHg	75.62 ± 12.82	62.32 ± 10.46	67.94 ± 12.2	0.001#
HR, bpm	77.25 ± 8.46	78.26 ± 8.39	78.13 ± 7.97	0.016*

Graph 1 shows the variations in systolic pressures, diastolic pressures and heart rate comparing the two groups, showing greater variation in hemodynamic parameters in the propofol-sedated participants compared to the etomidate-sedated participants. Demonstrating propofol action as an agent that decreases peripheral vascular resistance and its cardiodepressant action.

Graph 1.



One hundred percent satisfaction was obtained from participants and endoscopists. Only one female participant had nausea and vomiting (main side effect of etomidate). Other participants did not show these symptoms until six hours after the exam.

Discussion

The present study evaluated whether hypnotic etomidate possesses safer hemodynamic option for sedation in colonoscopy examinations in adult subjects. Considering the age of the people who undergo this test (mostly over 60 years), there are comorbidities such as diabetes and high blood pressure.

Patients with these comorbidities use cardiodepressant and hypotensive drugs. Associated with these factors, the preparation for colonoscopy in most clinics is mannitol that causes osmotic diarrhea.[15] [16]

The combination of all these tends to cause the individual a state of dehydration that associated with the hemodynamic effects of anesthetic drugs may lead to cardiac, renal and/or neurological damage. [16]

In order to preserve patient safety and quick release after the examination, drugs that are proven to act with less intensity in the cardiovascular and respiratory system have been proposed to be used.

O diagnóstico de instabilidade hemodinâmica é feito levando em consideração a combinação de vários parâmetros; critérios clínicos e dados de monitorização. Sinais clínicos de falência circulatória primária levam à graus de gravidade cardiocirculatória que podem ser desde quadro de hipotensão arterial, ritmos cardíacos anormais, extremidades frias, cianose periférica, diminuição do débito urinário até os quadros clínicos de choque. (17) . Cada tipo de evento adverso hemodinâmico demanda seu respectivo tratamento que pode ser unicamente fluidoterapia, derivados do sangue, drogas vasoativas ou métodos mecânicos de otimização do estado cardiocirculatório (17). No caso das medicações anestésicas utilizadas em doses para sedação o que ocorre são eventos adversos na maioria das vezes reversíveis devido a metabolização desses medicamentos ou pela ação direta do anestesiologista com fluidoterapia não necessitando de drogas vasoativas (5).

It is known that the use of etomidate brings greater hemodynamic and respiratory stability.[17,18] Another aspect that can be evaluated is the financial aspect, since the greater hemodynamic and respiratory stability will require less medication to compensate for the clinical picture and less of supplemental oxygen.

In this study, it was observed that most participants were female (74%). This result is related to the fact that the request is usually made by gynecologists. Women have the habit of undergoing breast and cervical cancer screening tests annually and the request for colonoscopy as a colorectal cancer prevention from 50 years has become routine.[19]

The average age of participants was 58 years, 8 years older than the recommended colorectal cancer prevention routine, which is 50 years.[19] The major part (63%) of the participants were characterized as ASA II (patient with mild systemic disease). These participants had hypertension and diabetes as comorbidities. Although etomidate and propofol reduced systolic and diastolic blood pressure[7], it was found that propofol caused a

more intense reduction in the participants' systolic and diastolic blood pressure, reflecting the direct cardiodepressive action of propofol and its action in decreasing peripheral vascular resistance.

This reduction in blood pressure, depending on the patient's age and comorbidities, leads to unacceptable safety limits causing additional damage to the patient who will undergo a low complexity elective examination.[15,16]. Higher hemodynamic stability was observed in participants sedated with etomidate, without changes in heart rate compared to participants sedated with propofol group, who demonstrated increase in heart rate in response to lower blood pressure.

It is noteworthy that only one participant presented the main side effects of etomidate (nausea and vomiting). Hemodynamic safety is a priority over the effects that can be counteracted with antiemetics. Myoclonus, another side effect of etomidate, was not found in any of the participants sedated with etomidate. The use of fentanyl and midazolam may have prevented the onset of this symptom.

Conclusion

Etomidate is recommended to be used as a hypnotic in the sedation for colonoscopy examinatios, especially in elderly patients with comorbidities such as hypertension, diabetes, hypercholesterolemia, coronary artery disease and who use heart disease drugs, as this drug promotes greater hemodynamic stability.

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Conflict of interest

The authors have no conflicts of interest to declare.

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