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Safety of midazolam for sedation of HIV-positive patients undergoing colonoscopy

Elke S. Backman, Pharm.D.,

Department of Pharmacy, Massachusetts General Hospital, 55 Fruit Street, GRB-005, Boston, MA 02114, Tel: (617) 726-2503, Fax: (617) 726-7653

Virginia A. Triant, M.D., M.P.H.,

Infectious Disease Unit, Massachusetts General Hospital, Boston, MA

Jesse M. Ehrenfeld, M.D., M.P.H.,

Department of Anesthesiology, Vanderbilt University Medical Center, Nashville, TN

Zhigang Lu, M.D.,

Institute for Health Policy, Massachusetts General Hospital, Boston, MA

Paul Arpino, Pharm.D.,

Department of Pharmacy, Massachusetts General Hospital, Boston, MA

Elena Losina, Ph.D., and

Harvard University Center for AIDS Research, Harvard Medical School, Boston, MA

Rajesh T. Gandhi, M.D.

Infectious Disease Unit, Massachusetts General Hospital, 55 Fruit St, GRJ-504, Boston, MA, Tel: (617) 726-8403, Fax: 617-726-7653

Elke S. Backman: ebackman@partners.org; Rajesh T. Gandhi: rgandhi@partners.org

Summary

Concerns regarding possible interactions between midazolam and antiretroviral medicines have caused clinicians to use second-line sedatives, such as diazepam, instead. We demonstrated that patients who received midazolam during colonoscopy had similar clinical outcomes as those who received diazepam.

Background—Because of concerns regarding interactions between midazolam and antiretroviral therapy (ART), alternative sedatives are sometimes used during procedural sedation. Our objective was to compare outcomes in patients on ART who received intravenous (IV) midazolam versus IV diazepam, a second-line agent, during colonoscopy.

Methods—We conducted a retrospective analysis of adult HIV-infected patients who underwent colonoscopy over a 3.5-year period. Primary outcomes were sedation duration, nadir systolic blood pressure, nadir oxygen saturation, abnormal cardiac rhythm, and change in level of consciousness using a standardized scale. We calculated rates of adverse events according to

benzodiazepine use and identified risk factors for complications using univariate and multivariate analyses.

Results—We identified 136 patients for this analysis: 70 received midazolam-based sedation and 66 received a diazepam-based regimen. There were no significant differences between the two groups with respect to sedation duration (48 versus 45.7 minutes, $P = 0.68$), nadir systolic blood pressure (97 versus 101.6 mmHg, $P = 0.06$), nadir oxygen saturation (94.6 versus 94.8%, $P = 0.72$), or rate of abnormal cardiac rhythm (11.4 versus 19.7%, $P = 0.18$). More patients in the midazolam group experienced a depressed level of consciousness (91 versus 74%, $P = 0.0075$), but no patient required reversal of sedation or became unresponsive.

Conclusions—Although IV midazolam interacts with ART, we did not find evidence that patients who received this agent for procedural sedation had clinical outcomes statistically different from those who received diazepam. These findings should be confirmed in prospective studies or in a randomized controlled trial.

Keywords

Midazolam; HIV; antiretrovirals; colonoscopy; sedation

Introduction

There is limited information available to guide the use of sedatives in HIV-infected patients who are receiving antiretroviral therapy (ART). Midazolam is a first-line benzodiazepine sedative widely used in the United States as a sedative and anesthetic induction agent. However, product labeling of all protease inhibitors (PIs) and some non-nucleoside reverse transcriptase inhibitors (NNRTIs) includes strong warnings against the coadministration of these agents with midazolam due to expected inhibition of its metabolism. For a number of antiretroviral medications, including efavirenz, fosamprenavir, and nelfinavir, coadministration with IV midazolam is contraindicated [1-3].

Midazolam is a rapid-acting drug with excellent amnestic properties. Significant interactions between midazolam and cytochrome P450 (CYP) 3A4 inhibitors have been described [4-6]. Although the interaction appears to be less pronounced with IV administration than with oral dosing [6-8], concern regarding coadministration of midazolam has led some clinicians to use general anesthesia during colonoscopy in HIV-infected patients on ART. However, general anesthesia is costly and has its own associated risks [9]. Other providers respond to the potential drug interaction by having patients stop their ART for one to two days before a planned procedure. This strategy is not likely to be effective because enzyme inhibition persists for several days after withdrawal of the antiretroviral medication. Furthermore, interrupting ART is not recommended from the perspective of HIV disease management [10]. Alternately, providers might choose to use a different sedative in HIV-infected patients undergoing a procedure.

Diazepam, a drug that utilizes multiple metabolic pathways and is a major substrate for CYP 2C19 as well as CYP 3A4, is less likely to interact with protease inhibitors [11-12]. However, midazolam is favored by most clinicians [13] because of its more rapid onset of

action, shorter half-life (1.5 versus 20 hours), ability to produce a profound anterograde amnesic effect [7, 14-15], and lower incidence of pain on injection or phlebitis compared to diazepam [7, 14-15].

We sought to evaluate the safety of IV midazolam by analyzing a large population of HIV-infected patients on ART who received procedural sedation for colonoscopy. Our objective was to compare clinical outcomes and identify risk factors for complications in patients who received midazolam versus diazepam.

Methods

Study Population

HIV-infected patients who were 18 years of age or older and who underwent outpatient colonoscopy between January 1, 2007 and June 30, 2010 were identified through the Research Patient Data Registry (RPDR), a clinical database which captures data from clinical and billing systems for the Partners Health-Care System (a large health-care network in Massachusetts which includes Massachusetts General Hospital and Brigham and Women's Hospital). Inclusion criteria were: 1) completion of colonoscopy with procedural sedation; 2) receipt of ART for a minimum of 4 weeks at the time of the colonoscopy; 3) receipt of midazolam- or diazepam-based sedation. We excluded patients who underwent a combined colonoscopy and esophagogastroduodenoscopy (EGD), were inpatients at the time of the colonoscopy, or had incomplete records (endoscopy flow charts or other medical records).

Data Collection

Gastrointestinal (GI) endoscopy procedure flow sheets were reviewed for each patient. Information documented on the endoscopy flow sheets included pre-procedure assessment, intra-procedural observations and measurements, and post-procedure report. Intra-procedural measurements included heart rate and rhythm, presence of an arrhythmia, blood pressure, oxygen saturation, respiratory rate, pain scale, airway status, skin perfusion, and level of consciousness. Measurements were taken continuously during the procedure and recovery period and recorded at 1-5 minute intervals. Selected physiologic parameters were assigned scores by the providers using a standardized institutional anesthesia scoring system (Figure 1). Dose-time relationships were used to evaluate the onset of hypotension or possible adverse events. Total sedative doses (mg/kg) were recorded to compare doses used in our HIV-infected population to standard doses used in otherwise healthy adults. Demographic data, past medical history, and medication data, including individual antiretroviral medications, were documented for each patient and confirmed via review of the electronic medical record.

Outcomes

Primary outcomes were sedation duration, nadir systolic blood pressure, nadir oxygen saturation, rate of abnormal cardiac rhythm, and change in level of consciousness. Level of consciousness was assessed using a standardized scale on which a score of 2 means awake and oriented, 1 means arousable or disoriented, and 0 means unresponsive (Figure 1).

Secondary outcomes included nadir and change from baseline respiratory rate and heart rate, airway status, quality of respirations, skin perfusion, systolic blood pressure change from baseline, pain score, procedure time, and total monitoring time required as documented in the post-procedure report. In addition to midazolam use, the following exposures were evaluated in terms of association with primary or secondary outcomes: coadministration of fentanyl or meperidine, chronic sedative use, and liver disease.

Statistical analysis

Descriptive analysis included means, percentages, medians, and ranges, as appropriate. Univariate analyses of associations between exposures and outcomes were performed using either Student's t test for continuous variables and the Wald χ^2 test or Fisher's exact test for categorical variables. Multivariate analyses were completed using logistic regression models. Covariates included in the analyses were concomitant CYP 3A4 inhibitors, chronic opioid use, chronic benzodiazepine use, liver disease, age, and gender. In a separate analysis, baseline information and outcomes were analyzed by four treatment groups: PI/midazolam; PI/diazepam; non-PI/midazolam; non-PI/diazepam. A P value < 0.05 was considered to be statistically significant.

Results

Patient Characteristics

We identified 344 HIV-infected patients receiving ART who were scheduled for a colonoscopy. Of this group, 208 were excluded for reasons listed in Figure 2. The final cohort consisted of 136 HIV-infected patients on ART who underwent outpatient colonoscopy with midazolam- or diazepam-based sedation (Figure 2).

Demographic characteristics in the midazolam and diazepam groups were similar (Table 1). The median CD4+ T cell count was 563 cells/ μ L and 85% had an undetectable HIV-1 RNA. A greater proportion of patients in the midazolam group had liver disease (mostly viral hepatitis) compared to the diazepam group (31% versus 17%, $P = 0.04$). Rates of alcohol, tobacco, and recreational drug use were similar in the two groups. The groups were similar with respect to physical characteristics, although there was a trend towards higher body mass index (BMI) in the midazolam group (28 versus 26 kg/m², $P = 0.05$). Baseline systolic blood pressure and concomitant medications were similar between the groups. Protease inhibitor-containing antiretroviral therapy was used by 53% of patients in the midazolam group and 61% of patients in the diazepam group ($P = 0.55$).

Procedural sedation

Of the 136 patients in the cohort, 70 (51%) received midazolam-based sedation and 66 (49%) received diazepam-based sedation. Colonoscopy procedures were performed by 34 different providers, 28 of whom used midazolam-based sedation in selected patients. The mean midazolam dose was 4.1 ± 1.2 mg (0.05 ± 0.02 mg/kg) with a mean initial bolus of 2 ± 0.2 mg. The mean diazepam dose was 7.7 ± 2.4 mg (0.10 ± 0.03 mg/kg) with a mean initial bolus of 3.4 ± 1.5 mg. Adjunctive sedatives were used in both groups of patients and were administered, for the most part, in incremental doses. Meperidine was given to 69 (99%) of

the patients who received midazolam-based sedation (mean total dose 79 mg meperidine), and to 57 (86%) of the patients who received diazepam-based sedation (mean total dose 89 mg meperidine). Fentanyl was given to 13 (19%) of the patients who received midazolam-based sedation (mean total dose 65 mcg fentanyl), and to 11 (17%) of the patients who received diazepam-based sedation (mean total dose 101 mcg fentanyl). One patient in the diazepam group received morphine 10 mg total as the adjunctive opioid.

Outcomes

There were no significant differences between the midazolam and diazepam groups with respect to duration of sedation (length of time consciousness score < 2; 48 versus 45.7 minutes, $P = 0.68$), nadir systolic blood pressure (97 versus 101.6 mmHg, $P = 0.06$), or nadir oxygen saturation (94.6 versus 94.8%, $P = 0.72$) (Table 2). The cardiac rhythm scores were similar between both groups with 8 patients in the midazolam group experiencing a newly abnormal cardiac rhythm versus 13 patients in the diazepam group ($P = 0.18$). No patient had a newly abnormal cardiac rhythm requiring treatment. Sinus bradycardia occurred in 6 patients (9%) in the midazolam group and 8 patients (12%) in the diazepam group. Other newly abnormal rhythms included premature ventricular contractions (1 patient in the midazolam group and 2 patients in the diazepam group) and sinus tachycardia (1 patient in the midazolam group and 2 patients in the diazepam group). No patient became unresponsive with a consciousness score of 0 at any time or required a reversal agent, but more patients in the midazolam group experienced a depressed level of consciousness, defined as a score of 1 (arousable or disoriented) at some point during the procedure (91.4 versus 74.2%, $P = 0.0075$).

Regarding secondary objectives, there were no differences between the groups in mean lowest respiratory rate (15.8 versus 15.7 breaths per minute, $P = 0.63$). The diazepam group experienced a significantly greater change from baseline in respiratory rate, decreasing by 3.5 breaths per minute versus a decrease of 2.8 breaths per minute in the midazolam group ($P = 0.04$). The nadir heart rate (62 versus 64 beats per minute, $P = 0.9$) and the change in heart rate over the course of the procedure (17.6 versus 19.2 beats per minute, $P = 0.25$) were similar between the two groups. No patient experienced a score < 2 for airway status or quality of respirations. There was a trend towards a greater proportion of patients in the midazolam group than in the diazepam group with a skin perfusion score of 1 (pale, dusky, mottled or diaphoretic): 9% versus 2%, $P = 0.06$. There were no significant differences in the overall blood pressure score—which compares intra-procedure to pre-procedure blood pressure (Figure 1)—in the midazolam group compared to the diazepam group ($P = 0.38$). The time to nadir SBP following sedative administration was also similar between the two groups (44 minutes versus 47 minutes, $P = 0.46$). Peak pain scores were similar, with a mean of 1.5/10 for the midazolam group versus 1.35/10 for the diazepam group, with 10 being the worst pain ($P = 0.10$). Similar proportions of patients reported having no pain at all: 42 (60%) in the midazolam group versus 38 (58%) in the diazepam group. There was no difference between the groups in post-procedure monitoring time (98 versus 97 minutes, $P = 0.86$). There were no hospitalizations related to the procedure in either group.

We also compared outcomes in patients on PI-based ART versus non-PI-based ART. There were no significant differences between the group of patients who were on PIs and the group on non-PI regimens in terms of age, gender, liver disease, baseline SBP, concomitant CYP 3A4 inhibitors, chronic opioids, or chronic benzodiazepines. There were no significant differences between the four treatment groups (PI/midazolam; PI/diazepam; non-PI/midazolam; non-PI/diazepam) in the outcomes of lowest SBP, heart rate, nadir oxygen saturation, nadir respiratory rate, consciousness score < 2, sedation duration, or cardiac score < 2.

Multivariate Analysis

We performed multivariate analysis for four discrete outcomes – attainment of consciousness score < 2, sedation duration, nadir SBP, and cardiac rhythm score – adjusting for possible confounders based on clinical relevance and significance in univariate analysis. In adjusted analyses, we found that midazolam use (versus diazepam use) was significantly associated with a consciousness score < 2 (odds ratio = 3.80, 95% confidence interval 1.33; 10.88) (Table 3) but not with cardiac rhythm score, nadir SBP, or sedation duration (data not shown).

Discussion

As an increasing number of HIV-infected individuals achieve durable virologic suppression on ART, this group increasingly requires a variety of procedures requiring sedation, including colonoscopy, bronchoscopy, cardiac catheterization, and outpatient surgeries. Most endoscopic procedures are performed with the patient under moderate (“conscious”) sedation and analgesia, during which the patient is able to respond purposefully to verbal or tactile stimulation, and ventilator and cardiovascular function are maintained [16]. In the United States, more than 98% of all endoscopies are performed under some form of sedation [13]. Adequate sedation can both facilitate successful completion of the procedure and increase patient tolerability by decreasing anxiety and pain. However, the decision to undergo the procedure itself or the choice of sedation is often affected by concerns over potential drug interactions between sedatives and antiretroviral medications, particularly protease inhibitors.

In this retrospective analysis of adult HIV-infected patients on ART who underwent a colonoscopy, we assessed the safety of midazolam versus diazepam using multiple physiologic outcomes. We found that the patients in our cohort safely received midazolam-based sedation, with comparable hemodynamic, cardiac, and respiratory outcomes compared with patients who received diazepam. The duration of time patients experienced a depressed level of consciousness was similar between the two groups. Patients who received midazolam had a lower consciousness score than those who received diazepam, but no patient became unresponsive or required a reversal agent or hospitalization. There was a trend toward a lower nadir SBP in the midazolam group, which diminished after adjustment for differences in baseline SBP and chronic opioid use. Although in our study a greater proportion of patients in the diazepam group experienced an abnormal cardiac rhythm, the

difference was not significant in univariate analysis, nor was an association seen when we adjusted for age, gender, and antiretroviral regimen.

Concerns regarding the safety of midazolam use in HIV-infected patients on ART arise from the possibility of drug interactions resulting in increased levels of midazolam. Metabolism of midazolam is almost entirely dependent on hydroxylation by CYP 3A4. Based on expected interactions, product labeling of several antiretroviral medications originally stated that both oral and IV midazolam were contraindicated. However, more recent drug interaction studies have demonstrated the importance of gastrointestinal metabolism in the clearance of oral midazolam [4-6]. Protease inhibitor-mediated enzyme inhibition of CYP 3A4 enzymes in the intestinal wall is thought to contribute to the high serum levels of midazolam found following oral ingestion. The difference in effect of metabolic enzyme inhibitors on oral versus IV midazolam has been demonstrated in several pharmacokinetic studies [17-21]. Palkama and colleagues found that saquinavir increased the AUC of oral midazolam by more than five-fold but increased the AUC of IV midazolam by 2.4-fold [5]. Based on these data, IV midazolam might have less of an interaction with antiretroviral medications than oral midazolam. In recent years, the package inserts of several antiretroviral drugs (e.g. darunavir) have been updated and now indicate that IV midazolam can be administered, but only with close clinical monitoring; however, this recommendation has not been widely adopted in clinical practice.

Prior studies investigating the clinical impact of co-administration of midazolam and ART have yielded conflicting results. In a cohort of 143 ambulatory patients undergoing bronchoscopy and receiving midazolam (total doses ranged from 2-15 mg, average 7.5 mg), no patient suffered an adverse outcome or required intubation [24]. In contrast, there have been reports of prolonged sedation in patients who received concomitant antiretroviral medications and midazolam. A 1997 case report of a patient on a saquinavir-based regimen undergoing bone marrow biopsy reported prolonged sedation (30 minutes) requiring reversal [25]. Concomitant opioids or sedatives, if administered, were not reported. In a recently published study by Hsu et al, the authors retrospectively analyzed 241 HIV-positive inpatients who underwent bronchoscopy and received IV midazolam for procedural sedation. [26]. The incidence of prolonged sedation (>90 minutes) was 9.8% in patients receiving PIs compared with 1.58% in those not taking antiretroviral therapy. One possible reason for the difference between the findings of Hsu et al and our results is the fact that their cohort consisted of inpatients, in whom concomitant comorbidities may have predisposed patients to complications from sedation; indeed, 10% of the patients in the PI group had pre-existing respiratory distress or altered mental status prior to the procedure and 29% were diagnosed with PCP. By contrast, we examined only ambulatory patients and compared outcomes between patients on ART receiving IV midazolam to those receiving IV diazepam. It is important to acknowledge that the risks of IV midazolam may differ by procedure and the presence of medical co-morbidities.

The use of sedatives in the setting of antiretroviral medications, with support for cautious co-administration, has been broadly addressed in reviews and guidelines [27-29]. In addition, it has been demonstrated in a number of small studies that, with careful titration,

drugs such as fentanyl, meperidine, and midazolam, can be administered safely for short-term procedures in HIV-infected patients on ART [30-33].

In our institution, based on pharmacokinetic principles and available evidence, we generally do not empirically reduce the dose of midazolam for HIV-infected patients undergoing procedural sedation. Peak benzodiazepine concentrations after a single dose or multiple doses over a very short period of time (e.g. 20 minutes) are not affected by drug half-life or clearance. Furthermore, in the context of short-term use, the recovery time for benzodiazepines is mainly dependent on redistribution kinetics rather than half-life. Subsequent doses are administered as needed and titrated to effect.

Limitations of this study include its retrospective design and the limited sample size. To address the possibility of confounding, we conducted a multivariable analysis adjusting for variables such as age, sex, liver disease, and concomitant medications including CYP 3A4 inhibitors. We also examined outcomes in four different subgroups—midazolam- and diazepam-based sedation with and without concomitant protease inhibitors—and could not detect an association between the treatment groups and any of the outcomes.

In conclusion, we demonstrated that patients who received IV midazolam for procedural sedation had similar clinical outcomes to those who received diazepam. Based on these findings, we conclude that the use of IV midazolam can be considered for HIV-infected patients on ART with close clinical monitoring. These findings should be confirmed in prospective studies or in a randomized controlled trial.

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Anesthesia Score Key		
Variable	Condition	Score
Airway	Clear airway	2
	Needs airway	1
	Guarded/trached	1
	Needs ETT	0
Respirations	Clear/BBS, Good TV	2
	Dyspnea or inadequate TV	1
	No spontaneous respirations	0
Skin perfusion	Pink/dry	2
	Pale, dusky, mottled	1
	Diaphoretic	1
	Cyanotic	0
Consciousness	Awake/oriented	2
	Arousable	1
	Disoriented	1
	Unresponsive	0
Blood pressure	SBP $\pm$ 20 mmHg PRE	2
	SBP $\pm$ 20-40 mmHg PRE	1
	SBP $\pm$ 40 mmHg PRE	0
Cardiac rhythm	Same as PRE	2
	Newly abnormal without treatment	1
	Newly abnormal requiring treatment	0

Note. GI, gastrointestinal; ETT, endotracheal tube; BBS, bilateral breath sounds; TV, tidal volume; SBP, systolic blood pressure; PRE, pre-procedure.

Figure 1. Institutional GI endoscopy anesthesia score key

EGD: esophagogastroduodenoscopy. ART: antiretroviral therapy.

Figure 2. Study Flow Diagram

Table 1
Baseline characteristics of HIV-infected patients who underwent outpatient colonoscopy receiving midazolam- or diazepam-based sedation

Characteristics	Midazolam (n = 70)	Diazepam (n = 66)	p-value
Age, mean $\pm$ SD	53 $\pm$ 7	54 $\pm$ 7	0.85
Male	56 (80)	56 (85)	0.46
Female	14 (20)	10 (15)	
Current alcohol use	29 (41)	32 (48)	0.41
Current tobacco use	18 (26)	16 (24)	0.84
Current illicit drug use	6 (9)	5 (8)	0.83
Height (inches)	68 $\pm$ 4	69 $\pm$ 3	0.59
Weight (lbs)	183 $\pm$ 45	174 $\pm$ 29	0.16
BMI	28 $\pm$ 6	26 $\pm$ 3	0.05
CD4+ count (cells/ μ L) $\pm$ SD	596 $\pm$ 298	592 $\pm$ 313	0.94
Undetectable HIV-1 RNA level	59 (84)	57 (86)	0.73
Liver disease	22 (31)	11 (17)	0.04
Baseline SBP mean $\pm$ SD	123 $\pm$ 15	126 $\pm$ 17	0.31
Concomitant CYP 3A4 inhibitors	3 (4)	2 (3)	0.70
Concomitant chronic opioids	7 (10)	6 (9)	0.86
Concomitant chronic benzodiazepines	11 (16)	12 (18)	0.70
ARV regimen:			
NNRTI-based	31 (44)	25 (38)	0.45
Efavirenz	22 (31)	25 (38)	
Nevirapine	6 (9)	0	
Etravirine	3 (4)	0	
NRTI only	2	0	0.17
PI-based	37 (53)	40 (61)	0.55
Atazanavir/ritonavir	21 (30)	18 (27)	
Darunavir/ritonavir	4 (6)	0	
Lopinavir/ritonavir	8 (11)	16 (24)	
Fosamprenavir/ritonavir	1 (1)	3 (5)	
Tipranavir/ritonavir	0	2 (3)	
Saquinavir/ritonavir	0	1 (2)	
Unboosted PI	4*	1**	

Characteristics	Midazolam (n = 70)	Diazepam (n = 66)	p-value
Raltegravir-based	0	1 (2)	0.30

Note: Data are no. (%) of patients, unless otherwise indicated. SD, standard deviation; BMI, body mass index; HIV, human immunodeficiency virus; SBP, systolic blood pressure; CYP, cytochrome P450; ARV, antiretroviral; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor. One patient in each group was on a double-PI-containing regimen.

* Two patients on unboosted atazanavir, two patients on nelfinavir.

** Nelfinavir

Table 2
Outcomes related to procedural sedation for endoscopy with midazolam-based versus diazepam-based sedation in HIV-infected patients on antiretroviral therapy

Variables	Midazolam (n = 70)	Diazepam (n = 66)	p-value
Anesthesia score			
Airway < 2	0	0	1.0
Respirations < 2	0	0	1.0
Skin perfusion			
Score = 2	64 (91)	65 (98)	0.06
Score = 1	6 (9)	1 (2)	
Consciousness			
Score = 2	6 (9)	17 (26)	0.0075
Score = 1	64 (91.4)	49 (74.2)	
Blood pressure			
Score = 2	15 (21)	17 (26)	0.38
Score = 1	45 (64.3)	35 (53)	
Score = 0	10 (14.3)	14 (21)	
Cardiac rhythm			
Score = 2	62 (89)	53 (80)	0.18
Score = 1	8 (11.4)	13 (19.7)	
Intra-procedural			
Lowest RR (breaths per min)	15.8	15.7	0.63
RR range ± SD, change from baseline (breaths per min)	2.8 ± 1.7	3.5 ± 2.2	0.04
Lowest HR (beats per min)	62	64	0.90
HR range ± SD, change from baseline (beats per min)	17.6 ± 6.2	19.2 ± 9.6	0.25
Lowest oxygen saturation (%)	94.6	94.8	0.72
Oxygen saturation range (%)	4.4±2.2	4.3±1.7	0.85
Lowest SBP ± SD (mmHg)	97 ± 13.9	101.6 ± 14.1	0.06
Highest SBP ± SD (mmHg)	134 ± 5	142 ± 18	0.01
Length of time consciousness score < 2 (min)	48 ± 28.6	45.7 ± 29.9	0.68
Pain scale (range 0-10, worst pain is 10)			
Score > 3	18 (26)	10 (15)	0.10
Score = 1-3	10 (14)	18 (27)	
Score = 0	42 (60)	38 (58)	

Variables	Midazolam (n = 70)	Diazepam (n = 66)	p-value
Procedure time (min)	21 ± 14	22 ± 15	0.76
Total time (min) including post-procedure monitoring	98 ± 31	97 ± 30	0.86

Note. RR, respiratory rate; SD, standard deviation; min, minutes; HR, heart rate; SBP, systolic blood pressure.

Table 3
Predictors of depressed consciousness in HIV-infected patients receiving midazolam- or diazepam-based procedural sedation*

Effect	Point Estimate	95% Wald Confidence Limits	P value
Midazolam (vs. diazepam)	3.804	1.330 10.878	0.01
NNRTI & OTHER (vs. PI)	0.921	0.342 2.484	0.87
Age	1.026	0.952 1.106	0.50
Female	1.609	0.405 6.392	0.50
Liver disease	0.879	0.246 3.138	0.84
Concomitant CYP 3A4 inhibitors	4.896	0.546 43.914	0.16
Chronic opioid use	<0.001	<0.001 >999.999	0.96
Chronic benzodiazepines	1.843	0.521 6.512	0.34

Note. MDZ, midazolam; DZP, diazepam; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; CYP, cytochrome P450.

* Depressed consciousness defined as consciousness score < 2.