# Safety and efficacy of sedation/analgesia administered by the urologist for minimally invasive transurethral procedures

*A. Beri, N.J. Mabjeesh, M. Sofer, H. Matzkin, J. Chen, A. Greenstein*

## Abstract

**Aim:** To evaluate the safety and efficacy of sedation/analgesia administered solely by the treating urologist during minimally invasive transurethral procedures.

**Methods:** All patients who underwent minimally invasive transurethral procedures under sedation/analgesia delivered solely by the treating urologist were analyzed. They all received intravenous midazolam, and some also received ketamine according to the discretion of the urologist.

**Results:** The 77 study patients uneventfully underwent insertion of an internal ureteral stent (n=30), cystoscopy (n=26), cold cup biopsies of bladder tumors (n=19), and urethral dilations (n=2).

**Conclusion:** Sedation/analgesia administered solely by the treating urologist during minimally invasive transurethral procedures is safe and effective.

**Keywords: transurethral procedures, sedation, safety, efficacy.**

**Authors' address: Department of Urology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, affiliated to the Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel.**

**Corresponding Author: A. Greenstein, Department of Urology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel.** ***Email:*** **surge04@post.tau.ac.il.**

## Introduction

Minimally invasive transurethral procedures, such as cystoscopy, insertion of indwelling ureteral stents, bladder biopsies, and fulguration of superficial bladder tumors may be associated with pain and discomfort for patients. Performing them on an outpatient basis would have significant implications on conserving financial and workforce resources, but they must be tolerable [1]. The pain, restlessness and movements of the patient that may lead to complications and the necessity to abort the procedure can be resolved by providing sedation combined with analgesia/anesthesia, usually induced by an anesthesiologist. The aim of the present study was to evaluate the safety and efficacy of sedation/analgesia administered solely by the treating urologist to patients undergoing minimally invasive transurethral procedures.

## Materials and Methods

This study was approved by the Ethics Committee (Helsinki) of the Tel Aviv Sourasky Medical Center.

## Patients

Seventy-seven patients age between 18-85 years who were referred for bladder biopsy, insertion of indwelling ureteral catheters, or fulguration of small bladder tumors comprised the study group. They were classified according The American Society of Anesthesiologists (ASA) Physical Status system, and those with a score > 3 were excluded. They all received sedation/analgesia delivered by the treating urologist in our institution between 2014 and 2016.

## Qualifications of the Medical Staff

One urologist and one nurse assistant who both completed the Advanced Cardiovascular Life Support (ACLS) Provider Course and a one-day instructional course for providing analgesia and sedative medications as well as for evaluating patients before a procedure were in attendance. The ACLS course is designed for healthcare providers who either direct or participate in the management of cardiopulmonary arrest or other cardiovascular emergencies. Evaluation and monitoring of patients before and following the procedures was carried out by the urological nurse and by the urologist according to LEMON criteria (Look externally, Evaluate the 3-3-2 rule, Mallampati, Obstruction, Neck mobility) for assessing airway competence [2,3].

## Sedation/analgesia administration

All patients with ASA classification less than IV who underwent either bladder biopsy, insertion of an indwelling ureteral catheter, fulguration of small bladder tumors, or cystoscopy were evaluated by the urologist and the nurse. They received an explanation about the urological and the sedation/analgesia procedures and signed an informed consent for both sedation/analgesia and the urological intervention. They were instructed to arrive with an adult escort and to refrain from driving during the 24 hours following sedation/analgesia. Patients who were reluctant to undergo the procedure while awake or whose procedure was estimated to take more than 60 minutes were scheduled for a formal operating room session. These procedures usually take between 15 and 50 minutes in our hands.

An intravenous (IV) cannula was inserted by the urologist or the nurse in all complying patients, and sedation/analgesia were administrated by the urologist performing the transurethral procedure. All the patients received IV midazolam 3–5 mg, and the addition of ketamine dose was left to the discretion of the urologist and based on the scheduled urological procedure and the patient's tolerance. Both the midazolam and ketamine were administered until minor or moderate level of sedation was achieved. A minor level of sedation was defined when the patient was able to respond to instructions without cardiac and/or respiratory compromise but with mild mental and cognitive short-term decline. A moderate level of sedation was defined as the patient being awake but not responding to instructions, and depression of cardiac and/or respiratory reflexes without airway

or respiratory compromise [3]. A designated cardiopulmonary resuscitation (CPR) cart that included antidotes (e.g., flumazenil, a selective benzodiazepine receptor antagonist) was available in the room.

Lidocaine gel 2% was installed into the urethra of the male patients. Blood pressure was monitored with arm cuffs, continuous heart activity was monitored with ECG screen monitor and blood oxygen saturation was monitored with a pulse oximeter. Monitoring continued throughout and following the procedures, and the data were recorded by the nurse every five minutes during the procedure and every 15 minutes during the recovery period up to at least 30 minutes until the patient was discharged from the ambulatory urological suite by the treating urologist. A formal cardiopulmonary resuscitation cart was available in the room with antidotes such as Flumazenil which is a selective benzodiazepine receptor antagonist.

## Safety

Safety was defined as the absence of any of the following: a reason to provide CPR, an oxygen saturation <90%, an emergency call for anesthesia team, and hospitalization of the patient due to a complication attributed to the sedation/analgesia. The highest and the lowest blood pressure and heart rate measurements recorded during the procedure and throughout the recovery period were included in the analysis.

## Efficacy

Efficacy was defined as the uneventful completion of the planned urological procedures. Reasons for stopping the procedures due to failed sedation/analgesia, such as pain, patient movement, etc., were recorded.

## Clinical data collection

The compiled patient characteristics included age, sex, type of transurethral procedure and whether the procedure was performed in ambulatory or operating room settings. The documented procedure-related measures included the ASA score, the lowest and highest blood pressure and pulse rates, as well as the lowest oxygen saturation level during the sedation.

### Patient's Self-Report of Pain/Discomfort

Following the recovery period and before discharge home or to the ward, the patients were asked to grade their pain level during the procedure using a Likert visual analog scale (VAS) where 0 = no pain and 10 = unbearable pain.

### Statistics

Descriptive statistics of the study sample were used to summarize participant characteristics. ANOVA was used for comparison of two means between the two groups of sedation, i.e., midazolam alone and midazolam + ketamine. All tests were two-tailed, and statistical significance was defined as a p-level < 0.05.

## Results

Data of 77 patients (51 men and 26 women) undergoing urological transurethral procedures with sedation/analgesia were analyzed. Five patients received 3-4 mg midazolam and the remaining 72 received 5 mg midazolam. 28 patients also received ketamine with dose range 10-25 mg. Table 1 summarizes the clinical characteristics of all the study patients. Table 2 summarizes the procedure-related measurements, and Table 3 displays the results of the midazolam alone group (n =49) compared to those of the midazolam + ketamine group (n = 28).

None of the patients indicated that they wanted to stop the procedure, and only six reported that it had been painful (level 1 = 4 patients, level 2 = 1 and level 4 =1).

**Table 1** Procedures Suitable for Patient Controlled Sedation.

| Characteristic | Patients, n |
|---|---|
| Age (yr) | |
| Mean (SD) | 58.4 (17.1) |
| Median (IQR) | 61 (50–73) |
| Gender | |
| Males | 51 |
| Females | 26 |
| Transurethral procedure | |
| Bladder biopsy | 19 |
| Cystoscopy | 26 |
| DJ stent insertion or replacement | 30 |
| Endoscopic urethral dilation | 2 |
| Patient status | |
| Hospitalized | 30 |
| Ambulatory | 47 |

SD = standard deviation; IQR = interquartile range; DJ = double J.

**Table 2** Procedure-related measures (n = 77).

| Measure | Patients, n |
|---|---|
| ASA grading | |
| I | 58.4 (17.1) |
| II | 61 (50–73) |
| III | |
| Self-report pain score (0–10) (n=71) | |
| 1 | 4 |
| 2 | 1 |
| 4 | 1 |
| Highest blood pressure (mmHg) | |
| Mean (SD) | 152.4 (20.6) |
| Median (IQR) | 151 (140–168) |
| Lowest blood pressure (mmHg) | |
| Mean (SD) | 123.5 (18.5) |
| Median (IQR) | 124 (110–134) |
| Highest pulse (bpm) | |
| Mean (SD) | 82.7 (15) |
| Median (IQR) | 81 (72–91) |
| Lowest pulse (bpm) | |
| Mean (SD) | 67.7 (10.1) |
| Median (IQR) | 65 (60–74) |
| Lowest oxygen saturation (%) | |
| Mean (SD) | 94.2 (2) |
| Median (IQR) | 94 (93–96) |

SD = standard deviation; IQR = interquartile range.

**Table 3** Comparison between the midazolam alone group (n = 49) and the midazolam + ketamine group (n = 28).

| | Midazolam alone | Midazolam + ketamine | p value |
|---|---|---|---|
| Age (yr) mean ± SD | 59.1 ± 17.8 | 57.2 ± 15.9 | 0.647 |
| Gender (n) | | | 0.466 |
| Males | 31 | 20 | |
| Female | 18 | 8 | |
| Transurethral procedure (n) | | | 0.229 |
| Bladder biopsy | 9 | 10 | |
| Cystoscopy | 20 | 6 | |
| DJ stent insertion or replacement | 19 | 11 | |
| Endoscopic urethral dilation | 1 | 1 | |
| Patient's status (n) | | | 0.158 |
| Hospitalized | 27 | 20 | |
| Ambulatory | 22 | 8 | |
| ASA grading (n) | | | 0.261 |
| 1 | 17 | 14 | |
| 2 | 27 | 10 | |
| 3 | 5 | 4 | |
| Pain score (0–5) (n) | | | 0.122 |
| 0 | 45 | 26 | |
| 1 | 4 | 0 | |
| 2 | 0 | 1 | |
| 4 | 0 | 1 | |
| Highest blood pressure (mmHg) mean ± SD | 152.7 ± 21.2 | 151.8 ± 18.8 | 0.853 |
| Lowest blood pressure (mmHg) mean ± SD | 123.5 ± 18.8 | 123.4 ± 18.4 | 0.989 |
| Highest pulse (bpm) mean ± SD | 80.3 ± 15.1 | 87 ± 14.1 | 0.058 |
| Lowest pulse (bpm) mean ± SD | 67.5 ± 10.8 | 68.2 ± 8.8 | 0.762 |
| Lowest oxygen saturation (%) mean ± SD | 94.1 ± 2.1 | 94.4 ± 1.9 | 0.625 |

SD = standard deviation; DJ = double J; yr = year; *n* = number.

## Discussion

Minimally invasive transurethral procedures may be associated with pain and discomfort for patients, particularly among younger ones [4]. Due to patients' lack of understanding of the details of cystoscopy, the procedure is commonly considered as being associated with anxiety and pain. Some patients may therefore be reluctant to undergo the procedure due to the fear and concern about the pain associated with transurethral insertion of instruments. Pain is a physiologic response to tissue irritation, but a patient's reaction to pain is also emotional and related to any number of psychological influences, among them the level of pre-procedural anxiety and recall of an unpleasant experience associated with cystoscopy in the past. As a result, a patient's behavior during a transurethral procedure is essentially unpredictable. In colonoscopy, for example, it is common practice to administer sedation [5].

Intravenous sedation/analgesia is considered safe and a cost-effective alternative to other forms of anesthesia. Birch et al. reviewed 1020 endourologic cases involving the use of midazolam as a premedication combined with local anesthesia, before various urological procedures. They considered that the preference of 93% of patients over conventional general anesthesia was a testimony to its high degree of acceptability. They went on to suggest that it may eliminate the need for the nursing and anesthesia team along with anesthetic equipment and, as such, reduce the cost of selected urologic procedures [6]. Gastroenterologists routinely sedate their patients for endoscopic evaluations [3], and our experience is that urologists can safely and efficaciously administer sedative analgesia when needed without the presence of an anesthesiologist.

Ketamine has been in medical use for more than four decades due to its dissociative sedation and analgesics effects, and it is recommended for day care ambulatory short anesthesia [7]. Midazolam is a short-acting, water-soluble benzodiazepine, with anxiolytic properties and limited cardiovascular effects that allows for speedy recovery, without post-procedural sequelae, such as nausea and vomiting [2]. The benefits of combining midazolam and ketamine make it especially attractive for children undergoing various procedures [8].

All the procedures performed on our study patients were accomplished as planned with no need for interruption due to complications. Specifically, none of the patients required CPR, the administration of an antidote, an emergency call for anesthesia team, or unscheduled hospitalization due to complications of the sedation/analgesia. Our results are in accordance with the results reported by Froehlich et al. in their study on patients undergoing colonoscopy [5]. They noted that the combination of low-dose midazolam and pethidine does not improve patient tolerance and pain perception during colonoscopy compared with either drug given alone, and concluded that the mode of sedation and analgesia should be based on the endoscopist's judgment. Hanno and Wein reported that the addition of meperidine does not augment significant analgesia or sedation to intravenous midazolam in men undergoing cystoscopy [9]. Contrary to our results, Kose et al reported their experience in 60 patients scheduled to outpatient transurethral procedures and were randomly assigned to receive midazolam-dexmedetomidine or ketamine-dexmedetomidine. Those authors concluded that while both combinations provided satisfactory sedation levels, the dexmedetomidine-ketamine combination provided better analgesia and hemodynamic stability, with less nausea and vomiting and shorter recovery time [10]. Similar to our results, the beneficial effects of combined ketamine and midazolam for transurethral procedures were reported by Attalah et al. in 1993 [11]. They conducted a double-blind study on 30 patients and concluded that ketamine produced satisfactory anesthesia and that the addition of midazolam did not change the cardiovascular parameters [11].

Our findings on the efficacy and safety of sedation/analgesia in our older patients were similar to those for our younger patients. Briggs et al. evaluated one hundred patients with a mean age of 78 years (range 59-97) and compared those under and over the age of 75 years and those with an ASA status of I and an ASA status of III or IV and concluded that elderly and medically unfit patients may be treated safely with no serious complications using sedation/analgesia [12].

The limitations of the present study are that our sample size is relatively small and the study was neither randomized nor blinded for patients and physicians. The choice of medication was made by the same team which administered the sedation/anesthesia, and no information on post-procedural analgesia requirement, if any, was available. We also did not have an untreated (no sedation) control group because we strongly believe that it is unethical to perform these procedures without some sedation/analgesia, although the level of pain experienced during diagnostic cystoscopy is reportedly low [4].

## Conclusions

Sedation/anesthesia using midazolam and ketamine administered solely by the urologist without the involvement of an anesthesia crew is safe and effective for minimally invasive transurethral procedures in an ambulatory setting.

## References


1. Aaronson DS, Walsh TJ, Smith JF, et al. Meta-analysis: does lidocaine gel before flexible cystoscopy provide pain relief? ***BJU International*** 2009;**104**:506-9; discussion 509–10.
2. Moran TC, Kaye AD, Mai AH, Bok LR. Sedation, analgesia, and local anesthesia: a review for general and interventional radiologists. ***Radiographics*** 2013;**33**:E47–60.
3. Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy. Lichtenstein DR, Jagannath S, Baron TH, et al. Sedation and anesthesia in GI endoscopy. ***Gastrointestinal Endoscopy*** 2008;**68**:815–26.
4. Greenstein A, Greenstein I, Senderovich S, Mabjeesh NJ. Is diagnostic cystoscopy painful? Analysis of 1,320 consecutive procedures. I***nternational Brazilian Journal of Urology*** 2014;**40**:533–8.
5. Froehlich F, Harris JK, Wlietlisbach V, et al. Current sedation and monitoring practice for colonoscopy: an International Observational Study (EPAGE). ***Endoscopy*** 2006;**38**:461–69.
6. Birch BR, Anson KM, Miller RA. Sedoanalgesia in urology: a safe, cost-effective alternative to general anaesthesia. A review of 1020 cases. ***British Journal of Urology*** 1990;**66**:342–50.
7. Kurdi MS, Theerth KA, Deva RS. Ketamine: current applications in anesthesia, pain, and critical care. ***Anesthesia Essays and Researches*** 2014;**8**:283–90.
8. Toft P, Romer U. Comparison of midazolam and diazepam to supplement total intravenous anaesthesia with ketamine for endoscopy. ***Canadian Journal of Anaesthesia*** 1987;**34**:466–9.
9. Hanno PM, Wein AJ. Anesthetic techniques for cystoscopy in men. ***Journal of Urology*** 1983;**130**:1070–2.
10. Kose EA, Honca M, Yılmaz E, Batislam E, Apan A. Comparison of effects of dexmedetomidine-ketamine and dexmedetomidine-midazolam combinations in transurethral procedures. ***Urology*** 2012;**79**:1214–9.
11. Attalah MM, Saied MM, Yahya R, Ibrahiem EH. Ketamine anesthesia for short transurethral urologic procedures. ***Middle East Journal of Anaesthesiology*** 1993;**12**:123–33.
12. Briggs TP, Anson KM, Jones A, Coker BJ, Miller RA. Urological day case surgery in elderly and medically unfit patients using sedoanalgesia: what are the limits? ***British Journal of Urology*** 1995;**75**:708–11.