Original Article

Deep sedation in GreenLight laser prostatectomy

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Abstract

Introduction: Evaluation of ketamine and propofol combination for the performance of photoselective vaporization of prostate (PVP).

Patients and Methods: Twenty-six patients undergoing PVP for benign prostatic hyperplasia were included in the study. Co-morbidities were present in 24 patients. Midazolam 2 mg intravenous was administered for the induction to anesthesia. Propofol (10 mg/ml) and ketamine (1 mg/ml) were administered with the use of two pumps. An initial bolus dose of 0.03 ml/kg of propofol and 5 mg of ketamine was administered intravenously. The anesthesia was maintained by continuous infusion of 0.01 ml/kg/min of propofol and 2 ml/min of ketamine. Fentanyl was administered when deemed necessary. The level of sedation, peri-operative parameters and side-effects were recorded.

Results: The average periods from the induction of anesthesia and intraoperative infusion were 12.38 ± 5.84 min and 59.5 ± 22.15 min, respectively. Average propofol and total ketamine dose were 85.5 ± 10.62 μg/kg/min and 144.9 ± 45.62 mg, respectively. The average dose of fentanyl administered was 29.81 ± 27.40 μcg. An average period between the end of the infusion and the discharge to the urology clinic was 34.62 ± 22.89 min. Ten patients experienced nausea and five eventually vomited. Hallucinations were observed in five cases while visual disturbances in two patients.

Conclusion: The combined use of ketamine and propofol for the performance of PVP proved to be an efficient method for anesthesia. The "deep sedation" provided by these drugs was not associated with significant side-effects. Moreover, the use of the above method is indicated in patients with significant co-morbidities that should undergo PVP.

Key Words: Ketamine, ketofol, laser prostatectomy, photoselective vaporization, propofol, prostate, sedation

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INTRODUCTION

Photoselective vaporization of prostate (PVP, GreenLight laser prostatectomy) represents a standard of care for benign prostatic hyperplasia (BPH). The recent establishment of the method provides benefits regarding intraoperative and postoperative course of patients.[1] Since the great majority of the patients

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is older than 50 years and has probably co-morbidities, the anesthetic care represents a challenge.

Recent evidence on anesthesia during transurethral and laser prostatectomy propose the use of deep sedation as an alternative to general or regional anesthesia.[1-3] Patient comfort and recovery have been reported to be improved in case of deep sedation.[2,4] Preliminary evidence suggested that ketamine may be a useful alternative to opiod adjuncts during propofol sedation.[5] Moreover, deep sedation with combination of ketamine and propofol has been effectively used in several emergency and routine procedures.[3,5,6] The combination of the above medication has the advantage of the efficient management of hemodynamic depression of propofol by the administration of ketamine that has sympathomimetic action.[2] Since the variable dosage of ketamine has not been studied adequately and the literature reports an opioid-sparing effect of ketamine without any clinically respiratory depression and low incidence of psychotomimetic effects,[2] we evaluated the use of the aforementioned combination in a population of patients undergoing PVP.

PATIENTS AND METHODS

Twenty-seven patients undergoing PVP for BPH were included in the study. Laser energy at 120 W was produced by a GreenLight HPS (AMS, Minnetonka, USA). Patients were classified according to American Anesthesiology Association (ASA). Patients of ASA I, II, and III were included in the investigation. Nevertheless, co-morbidities were present in 24 out of 26 patients [Table 1]. Patients with a history of drug or alcohol abuse, currently using sedative or analgesic drugs were not considered as candidates for the study. Written informed consent was obtained by all patients.

Table 1: Patient demographic and history data

Number of patients	26
Age (years)	70.46 (44-84)
Weight (kg)	85.5 (73-108)
ASA physical status	I: 8, II: 13, III: 5
Co-morbidities (*n*)	
Cardiovascular	21
Hypertension	17
Myocardial infraction	4
Metabolic	16
Diabetes mellitus	4
Hypercholesterolemia	12
Pulmonary	7
Obstructive	5
Asthma	2
Anticoagulant agent	2
Antiplatelet agent	5

ASA: American Society of Anaesthesiologists

Baseline measurements were performed before the induction of anesthesia and included vital signs (blood pressure, pulse rate and oxymetry) as well as psychological evaluation of the patient by using the Mini-Mental State (MMS) test.[7] Patients who could not take the test (language barrier, refusal) or took >10 min to complete the test or scored <25 were excluded. Immediately before anesthesia administration, an intravenous (IV) line was established for the administration of fluids and medication. Midazolam 2 mg IV was administered to all patients for the induction to anesthesia. Standard monitoring was established in all cases. All patients received oxygen with the flow of 2 L/min by nasal prongs with CO_2 sampling port. Propofol and ketamine were administered in concentrations of 10 mg/ml and 1 mg/ml with the use of two pumps, respectively. An initial bolus dose of 0.03 ml/kg of propofol and 5 mg of ketamine was administered intravenously. Subsequently, continuous infusion of 0.01 ml/kg/min propofol and 2 ml/min ketamine was initiated.

The observer assessment of alertness/sedation (OAA/S) scale was used for the evaluation of the level of sedation.[8,9] Sedation level was reported as a maximum score of 5 representing alert status and minimum of 0 describing the unresponsive condition. The level of sedation was evaluated every 2 min. Infusion rate was adjusted to achieve a sedation level of 1 or 2 (OAA/S score) before starting the procedure. If the sedation level was not adequate 1 ml of bolus ketamine was administered, and the infusion rate was increased by 0.2 ml/min. At the beginning of the procedure, a dose of 25 μg of fentanyl was administered immediately after the insertion of the resectoscope if patient discomfort was evident. Intraoperative patient monitoring included blood pressure, pulse and respiratory rate as well as the level of sedation every 10 min. The infusion rate was adjusted intraoperatively to maintain sedation score of 1–2, normal blood pressure, heart and respiratory rate. If pain and discomfort of the patient were evident during the procedure the administration of additional 25 μg of fentanyl took place at the discretion of the anesthesiologist. Maneuvers such as chin lift and mask ventilation were used in case of decrease of SpO_2 below 90% or in the case of bradypnea (<8 breaths/min). In the latter cases, the infusion rate of propofol was decreased by 0.2 ml/min. The drug infusion was seized at the end of the procedure (urethral catheter placement). The surgeon assessed the intraoperative condition by a 3-point rating scale (score 1 = highly satisfactory, 2 = satisfactory and 3 = unsatisfactory).

Postoperative evaluation of the patient was performed according to the Aldrete scoring system.[9] A score ≥9 in the operating room allowed the transportation of the patient in the recovery department. Patient remained in the latter department until the patient was considered ready for discharge to the urology clinic. The time of discharge was decided when the patient had stable vital signs, was oriented, had no intractable nausea and vomiting as well as reported minimal pain. The recorded recovery time represented the period between the end of infusion and the decision of the attending physician for the discharge of the patient. The same methods for the baseline evaluation were also used for the postoperative assessment of the patient before discharge. Repeat MMS evaluation 30 min after surgery, and repeated at 60 min if the patient did not achieve presedation MMS scores at 30 min. Moreover, the patient was asked to recall the intraoperative experience and to report events such as pain, hallucinations, dreams, etc. Postoperative evaluation of the patient took place on the 1st postoperative day and included the rating of the overall patient satisfaction summarized in 4-points scoring scale. Score 1 = represented the maximum satisfaction, 2 = satisfaction, 3 = minimal satisfaction and 4 = dissatisfaction.

RESULTS

Sedation level was adequate in all cases when the aforementioned sedation scheme was used. The average period from the induction of anesthesia to the initiation of the procedure was 12.38 ± 5.84 min. The intraoperative infusion was necessary for an average period of 59.5 ± 22.15 min. Mean total infusion time including induction to anesthesia and intraoperative administration was 71.38 ± 22.41 min. Average propofol and total ketamine dose were 85.5 ± 10.62 μg/kg/min and 144.9 ± 45.62 mg, respectively. The average dose of fentanyl administered was 29.81 ± 27.40 μcg. Table 2 summarizes the results of the intraoperative and immediate postoperative recorded parameters.

Mean arterial pressure was observed to be decreased by 10–20 mm Hg in all cases in comparison to the baseline values. Heart rate remained similar to the baseline measurements in all cases. Bradypnea was never observed, while the need for additional maneuvers to support the airway was deemed necessary in seven patients as pulse oxymetry revealed values lower than 90% [Table 3].

An average period between the end of the infusion and the discharge to the urology clinic was 34.62 ± 22.89 min. During the period, after the end of the infusion and the hospitalization in the urology clinic, six patients experienced nausea while only two eventually vomited. Shivering was observed in six patients. Psychomimetic events such as hallucinations/dreams were observed in four cases while visual disturbances (nystagmus/double vision) were experienced by two patients. The majority of the side-effects were observed during the patient stay in the recovery facility. Only one patient experienced the event of hallucinations during the hospitalization in the Urology Department [Table 3].

Baseline results and postoperative psychological evaluation (MMS scores) of the patients is presented in Table 4. It should be noted that only two patients required additional performance of the MMS evaluation at 60 min. Surgeons satisfaction was deemed "highly satisfactory" in 22 cases while in the remaining of the cases was considered as "satisfactory." "Maximum satisfaction" was reported by 20 and "satisfaction" by the remaining patients.

DISCUSSION

Ketamine or S(+)-ketamine are drugs appropriate to achieve deep sedation for the performance of diagnostic and surgical procedures. Ketamine provides analgesia in combination to mild deactivation of consciousness.[10] The drug is associated with increased blood pressure and heart rate (sympathetic activation) in comparison to other anesthetic medication but the most important feature is the preservation of the respiratory activity. The favorable hemodynamic profile and bronchodilatory property of ketamine renders the drug suitable for patients with unstable cardiovascular and pulmonary

Table 2: Mean values intraoperative management and recovery times as well as mean medication dose

Time from initial drug bolus to surgery (min)	12.38±5.84
Intraoperative infusion (min)	59.5±22.15
Total infusion time (induction + surgery) (min)	71.38±22.41
Ketamine dose (mg)	144.9±45.62
Propofol dose (μg/kg/min)	85.5±10.62
Fentanyl dose (μcg)	29.81±27.40
Recovery time (min)	34.62±22.89

Table 3: Adverse events of the sedation medication

Adverse event	Number of patients (%)
Airway support	7 (26.9)
Nausea	6 (23)
Vomiting	2 (7)
Shivering	6 (23)
Hallucinations	4 (15.3)
Optical disturbances	2 (7)

Table 4: Preoperative and postoperative MMS scores

	Patients (*n*=26)			
	Preoperative	Postoperative 30 min	Postoperative 60 min	Difference
Orientation	10 (10,10)	10 (10,10)	10 (10,10)	No significance
Registration	3 (3,3)	3 (3,3)	3 (3,3)	
Attention	5 (5,5)	5 (5,5)	5 (5,5)	
Recall	3 (3,3)	3 (3,3)	3 (3,3)	
Language	9 (9,9)	9 (9,9)	9 (9,9)	
Total score	30 (30,30)	30 (30,30)	30 (30,30)	

Median values are presented (25th-75th percentage ranges). MMS: Mini-mental state diseases. The disassociative/psychomimetic reaction of ketamine represents a problem for its use as sole analgosedative drug. The use in combination with propofol minimizes the psychomimetic effects of ketamine.

The combined use of propofol and ketamine has been described for analgosedation during several diagnostic and surgical procedures as well as patients in Intensive Care Units with cardiopulmonary- and pulmonary-compromised adults and pediatric patients.[11-13] Moreover, the combination has proven to be effective for analgosedation in interventional radiology procedures and various minimally invasive procedures and could be considered as a tool in Emergency Department.[6,14] The combination of ketamine and propofol has been limited evaluated in urologic interventions despite the presence of evidence that these drugs may have a favorable effect. The comparison of analgosedation to local anesthesia (periprostatic infiltration) provided equal results in the case of PVP. In the latter investigation, drugs such as fentanyl, midazolam, and alfentanil were used.[1] Nevertheless, the use of the propofol - ketamine combination for the performance of PVP has not been reported yet and the efficiency of the method remains unclear.

The current study was designed to evaluate the efficacy of ketamine - propofol for the performance of PVP and to investigate associated adverse events. The efficacy of the sedation scheme was proven to be adequate for the performance of the procedure. Patients reported to be satisfied by their experience. Moreover, operating surgeons concluded to the efficacy of the anesthetic method and the performance of surgery was not influenced by the anesthesia. Nevertheless, several adverse events associated with ketamine were observed. Ketamine has been related to psychotomimetic effects that are often referred as "emergence reactions."[2] Low doses of ketamine (up to 18 ± 7 μg/kg/min) provide analgesia while higher doses are related to clinically significant nausea and vomiting as well as psychotomimetic side-effects.[2] The combination with propofol significantly reduce psychotomimetic reactions.

The combination of ketamine and propofol is considered to counteract the cardiorespiratory depression that occurs by the solitary use of propofol. Thus, the patients receiving the combination of these drugs could be considered as more stable intraoperatively. An additional advantage of ketamine is its analgesic effect. The psychotomimetic effects of ketamine are reduced by the use of propofol. The combination of ketamine and propofol allows sedation to be achieved with lower total doses of each drug, minimizes the adverse event of each drug and improves recovery time profiles.[15]

Transurethral Resection of the Prostate (TURP) syndrome has not been observed in PVP and monitoring the neurologic status of the patient throughout the procedure by the anesthesiologist is not necessary. Thus, the preference of anesthesiologists to spinal anesthesia for TURP is unnecessary in the case of PVP.[16-18] Patients taking anticoagulants or have degenerative changes in the spine would have been more challenging candidates for spinal anesthesia and could be managed by deep sedation.[19] Moreover, spinal anesthesia can lead to urinary retention due to blockade of the parasympathetic fibers (S2–S4) that control detrusor contraction and bladder neck relaxation.[20] Urinary retention may delay discharge to home, and the significant advantage of PVP over TURP in terms of hospitalization may diminish. The reduction of the administered spinal dose or the use of short-acting local anesthetics may be reasonable. Nevertheless, incomplete spread or premature resolution of the regional anesthesia is a possibility. A proposed disadvantage of spinal anesthesia is that the patients do not maintain their sympathetic tone (unstable hemodynamics) and the risk of large intravascular volume shifts due to venous dilation are present. As a result, avoiding the spinal anesthesia would ultimately improve the anesthesia management of myocardial- and cardio-vascular-compromised patients.[4] Early evidence suggest that patients undergoing PVP have several choices for anesthesia. These patients could be managed by combined spinal epidural anesthesia while general anesthesia with use of inhaled or IV anesthetics could also be considered.[4,21]

A significant issue for deep sedation is the potential airway compromise and respiratory depression. Although these incidents are rare due to the aforementioned advantages of the combination of ketamine and propofol, five patients required airway support during the procedure. These patients were managed by chin lift and ventilation with the mask as the agents used are short-acting and their effect wears off within minutes. The latter advantage of the combination of ketamine and propofol facilitates the fast recovery of the patients and the fast tracking from surgery to recovery unit and urology clinic.[22]

The currently deep sedation method could also result in substantial cost savings for the institution. By avoiding spinal or general anesthesia, spinal insertion kits, endotracheal tubes, anesthesia circuits, and inhalational anesthetics are not necessary. The total time of the patient in the operating room is reduced with IV sedation. Another potential economical advantage of the technique is the decreased use of the Postanesthesia Care Unit (PACU), which results in "fast-tracking" of the patient to the urology clinic. The reduced monitoring period in PACU could represent potential cost savings to the institution. The above economical benefit has been also proposed by other investigators.[22]

CONCLUSION

The combined use of ketamine and propofol for the performance of PVP proved to be an efficient method for anesthesia. The "deep sedation" provided by these drugs was not associated with significant side-effects. Moreover, the use of the above method is indicated in patients with significant co-morbidities that should undergo PVP. Economical evaluation of the method would probably prove the cost-effectiveness of the ketamine-propofol deep sedation for PVP.

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Conflicts of interest
There are no conflicts of interest.

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