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Klinik Araştırma

Postoperative effects of preoperative midazolam application in outpatient elective urological surgery

Günübirlik minör ürolojik cerrahi girişimlerde preoperatif midazolam uygulanmasının postoperatif etkileri

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ABSTRACT

Objective: Preoperative medication, involves the psychological and a pharmaceutical preparation of patients to surgical procedures. The postoperative effects of preoperative midazolam application were evaluated in this prospective, randomized, double-blind study in urologic day case surgery.
Methods: Sixty-four ASA I-II group male patients aged between 18-65 years undergoing daily urological surgery (varicocele, testicular sperm extraction, hydrocele) were included in the study. STAI test was performed in all patients before they brought to the operating room. Twenty minutes before the intervention, an anesthesiologist not included in the study administered 0.03 mg/kg midazolam to Group I, and saline solution to Group 2. During the postoperative period vital signs, the degree of sedation (Ramsay Sedation Score), postoperative pain scores (VAS 0-10), side effects (nausea, vomiting) of the patients were recorded. Home readiness criteria (PADSS ≥9) of the patients were also recorded. Between 4-6 hours postoperatively, STAI test was performed again on all patients.
Results: Groups were comparable with respect to demographic data and duration of surgery. Preoperative STAI values, postoperative Ramsay Sedation Scores were similar in both groups. Although postoperative STAI values were lower in Group 1, the difference did not reach statistical significance. Time for home readiness was shorte in Group I. Postoperative pain scores in Group II were significantly higher than Group I.
Conclusions: We concluded that in patients who underwent day case urologic interventions administration of 0.03 mg/kg iv midazolam can decrease pain scores without adversely effecting early postoperative recovery, and sedation scores, and shorten the time interval to home readiness criteria which may provide advantage in patients undergoing daily urological surgery.

Key words: Anxiety, premedication, postoperative pain

ÖZ

Amaç: Preoperatif medikasyon, cerrahi girişim öncesinde hastalara uygulanan psikolojik ve farmakolojik hazırlığı içerir. Prospektif, randomize, çift-kör çalışmamızda günübirlik ürolojik girişimlerde (varikosel, testiküler sperm ekstraksiyonu, hidrosel) preoperatif midazolam uygulanmasının postoperatif etkileri değerlendirildi.
Yöntem: Günübirlik ürolojik elektif cerrahi uygulanacak olan ASA I-II grubu 18-65 yaş arası toplam 64 gönüllü erkek hasta çalışmaya dâhil edildi. Operasyon salonuna alınmadan önce tüm hastalara STAI testi uygulandı. Çalışmada yer almayan bir anestezi hekimi tarafından cerrahi girişimden 20 dk. önce 1. Gruba 0,03 mg/kg midazolam iv, 2. Gruba ise serum fizyolojik iv uygulandı. Postoperatif dönemde olguların vital bulguları, sedasyon düzeyi (Ramsey Sedasyon Skoru), postoperatif ağrı skorları (VAS 0-10), yan etkiler (bulantı-kusma gibi) kaydedildi. Eve gönderilme kriterlerini karşılama (PADS ≥9) süreleri kaydedildi. Postoperatif 4.-6. saatler arasında tüm olgulara STAI testi yine uygulandı.
Bulgular: Gruplar demografik veriler, operasyon süreleri yönünden benzerdi. Her iki grupta preoperatif STAI değerleri ve postoperatif Ramsey Sedasyon Skoru değerleri benzerdi. Postoperatif STAI değerleri Grup 1'de daha düşük olmakla birlikte gruplar arası fark anlamlı düzeyde değildi. PADS ≥9 olma süreleri midazolam uygulanan Grup 1'de Grup 2'ye kıyasla anlamlı olarak kısa bulundu. Postoperatif ağrı skorları Grup 2'de Grup 1'e göreanlamlı yüksek bulundu.
Sonuç: Günübirlik ürolojik girişim geçiren olgularda 0,03 mg/kg midazolam iv uygulamasının erken derlenme ve sedasyon skorları üzerine olumsuz etki göstermeksizin ağrı skorlarını düşürebildiği ve eve gönderilme kriterlerini karşılama sürelerini kısaltarak günübirlik olgularda avantaj sağlayabileceği kanısına varıldı.

Anahtar kelimeler: Anksiyete, premedikasyon, postoperatif ağrı

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INTRODUCTION

Preoperative medication involves the psychological and a pharmaceutical preparation of patients for surgical procedures. With the appropriate premedication, preoperative anxiety of patients can be reduced, the need for intraoperative anesthesia can be decreased, and patient satisfaction can be increased [1-3]. Benzodiazepines are the most commonly used group of drugs for the premedication [4]. It was reported that premedication with midazolam provides sedation and preoperative anxiolysis without affecting the duration of being discharged from the hospital after surgery [5-7]. Richardson et al. [5] reported that 0.04 mg/kg intravenous midazolam premedication given to patients undergoing outpatient laparoscopic tubal sterilization 10 min before anesthesia did not affect the time for home readiness. In this prospective double-blind study we evaluated the postoperative effects of preoperative midazolam in patients undergoing outpatient urologic surgery.

METHODS

After the approval of Local Ethics Committee ASA I-II group aged between 18-65 years a total of 64 male volunteers undergoing outpatient elective urological surgery (varicocele, testicular sperm extraction, hydrocele) in between Aug-Dec, 2012, in Ege University Faculty of Medicine Department of Urology operating room, were included in the study and were randomly divided into two groups. Power 3.1 was used to determine the number of sample. The potency of the sample size was calculated by taking 0.5 was 40. Within the specified period, 64 patients were included in the study. The inclusion criteria were literacy in writing,and reading Turkish, absence of psychiatric and neurological disease, chronic alcohol use and psychiatric medication. Exclusion criteria were history of allergy to benzodiazepines, severe respiratory and liver failure, diagnosis of myasthenia gravis, BMI ≥30. State-Trait-Anxiety Inventory (STAI) was performed in all patients prior to bringing them to the operating room. Patients were informed about pain score VAS (Visual Analog Scale, where 0 = no pain and 10 = the most severe pain) to be evaluated after the operation. Preoperative vital signs, mean arterial pressure (MAP), heart rate (HR), respiratory rate (RR), O_2 saturation (SpO_2) of the patients were recorded. Five ml syringe of midazolam (1 mg/ml) or saline was prepared by an anesthesiologist not involved in the study. The investigator and the patient did not have information about the contents of the agent applied. Patients were divided into 2 groups according to the computerized randomization schedule Twenty minutes before the surgical procedure for sedation intravenous (iv) midazolam (0.03 mg/kg) was given to the Group 1, and, saline to the Group 2.

Patients, in both groups received a standard anesthesia. 0.5 mg atropine, 2-2.5 mg/kg propofol, 1 mg/kg remifentanil were used for induction of anesthesia and anesthesia was maintained with oropharyngeal laryngeal mask anesthesia (LMA) with infusion of 0.05-1 mg/kg/min remifentanil, 50% oxygen-50% air, with sevoflurane 1-2 percent. All the patients received paracetamol 1 gr/100 ml iv infusion at the end of the operation for not less than 20 min. 5 minutes before the end of surgery, LMAs were removed before laryngeal reflexes become active by terminating remifentanil infusion. Total amount of remifentanil was recorded at the end of the operation.

During the postoperative period, at every 15 minutes (as 0, 15, 30, 45, 60, 75, 90, 105, 120 min), vital signs (MAP, HR, RR, SpO_2), the degree of sedation (Ramsay Sedation Score), postoperative pain scores (VAS 0-10), side effects (nausea, vomiting) of the patients were recorded. Pain control was achieved by applying 75 mg diclofenac sodium if the postoperative pain VAS scores were 4 or more. Analgesic requirements and time to the first analgesic requirement of patients were recorded.

In both groups of patients in terms of recovery time, Aldrete ≥9 times, and meeting the criteria for being sent home (PADSS ≥9) were recorded. Between 4-6 hours postoperatively, STAI test was performed again, and patient satisfaction (very good, good, fair, poor) were recorded.

Statistical Methodology

Statistical evaluations were performed by Ege University, Department of Biostatistics. All measurements were expressed as mean±standard deviation. T-test for Demographic data (age, body weight, height), ASA physical status, type of surgery, anesthesia and surgery times, Aldrete ≥9 and PADSS ≥9 times, STAI, the need for intraoperative remifentanil; Mann-Whitney test for additional analgesic requirement and first analgesic requirement time; the Kolmogorov-Smirnov test for MAP, HR, SpO_2, RR, postoperative pain scores (VAS) and Ramsey Sedation Score, Chi-square test for patient satisfaction were used. P<0.05 was considered statistically significant.

RESULTS

Patient's demographic data, ASA status, duration of anesthesia and surgery were similar in terms of the type of operation (Table 1).

Tablo 1. Groups' demographic data, ASA status, the type of operation, anesthesia and surgery durations (mean±SD).

	Group 1 (n=32)	Group 2 (n=32)
Age (years)	31.6±6.8	31.5±8.3
Weight (kg)	80±9.3	77±11.5
Height (cm)	177.4±7.4	175.3±7.7
ASA I-II	28/4	30/2
Duration of Anesthesia (min)	46.3±13.8	47.9±14.9
Duration of Operation (min)	34.3±12.4	35.2±13.6
TESE (n)	22	25
Varicoselectomi (n)	10	7

Blood pressure, heart rate, respiratory rate and O_2 saturation values were similar in both groups.

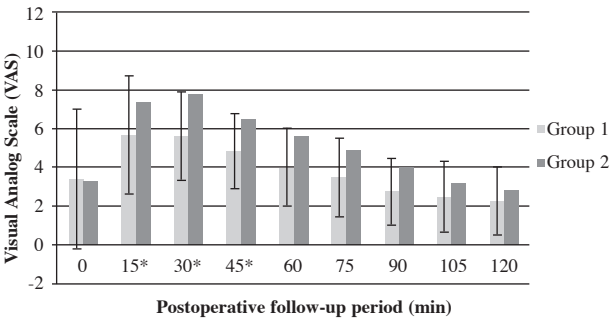
There was no difference between the two groups in terms of postoperative Ramsay Sedation Score values. Preoperative STAI values were similar in both groups. Although STAI values were lower in Group 1 in the postoperative assessment, the difference did not reach statistical significance (Table 2).

There was no significant difference between the groups in terms of intraoperative remifentanil dose (Table 2). When groups were compared in terms of postoperative pain scores, pain scores in Group 2 at postoperative 15-30-45 min were significantly higher than Group 1 (Figure 1). Although additional analgesic requirement in Group 2 was higher than Group 1, there was not significantly different between groups (Table 2). Groups were similar in terms of additional analgesic requirement (Table 2). There were no side effects in both two groups at the postoperative period.

Tablo 2. Study data (mean±SD).

		Group 1 (n=32)	Group 2 (n=32)	p
İntraoperative remifentanil dose (μg/kg/min)		0.142±0.045	0.148±0.086	0.2
STAI	Preoperative	39.4±9.5	38.8±9.1	0.59
	Postoperative	27.8±8.5	30.5±6.9	0.59
Patients who receive rescue analgesia (n)		21	30	0.37
Time to first analgesic need (min)		14.8±6.1	12.4±5.3	0.22
Aldrete ≥ 9 (min)		16.1±5.9	13±6.8	0.6
PADSS ≥ 9 (min)		145.4±51.9	174.2±48.9	0.026*
Patient satisfaction (excellent/good/moderate/bad)		14/16/2/0	8/16/8/0	0.34

*(*p<0.05)*



*(*p< 0.05)*

Figure 1. Postoperative pain scores (VAS) in Groups.

When groups were compared in terms of postoperative recovery, Aldrete ≥9 durations were similar in both two groups, but when home readiness was compared, PADSS ≥9 duration in Group 1 was significantly shorter (p<0,05) compared with Group 2 (Table 2). In comparison of both groups in terms of patient satisfaction, although patient satisfaction was very good in greater number of patients in Group 1, there was not significant difference between groups in terms of patient satisfaction.

DISCUSSION

In this study, we investigated the postoperative effects of preoperative midazolam application and observed that pain scores in early postoperative period were lower in the midazolam group than the control group and the criteria for being sent home is shorter. In the midazolam group, both Aldrete ≥9 time and Ramsay Sedation Scores were not different from the control group showing that 0.03 mg/kg intravenous dose of midazolam has not any negative effect on recovery parameters. In addition, use of midazolam did not cause prolongation of hospital stay. Lower levels of postoperative pain in the midazolam group resulted in shorter home readiness and provided an important advantage.

Vlymen van et al. [7] compared midazolam and diazepam for mammographic marking and breast biopsy. They reported that patient satisfaction was significantly higher in patients given benzodiazepines before mammographic marking and breast biopsy than the control group. Patients receiving premedication reported less discomfort during the interventions and significantly less frequently complained of discomfort during interventions. There was no difference between the groups in terms of duration for home readiness.

Shafer et al. [6] reported that the anxiety levels were lower with 5 mg midazolam given intramuscularly in out patient surgery. In a meta-analysis investigating the application of oral midazolam in children, it was shown that premedication with 0.5 mg/kg midazolam given 20-30 minutes before the surgery by the oral route reduced anxiety in children (separation anxiety and induction anxiety) and did not significantly prolong recovery time. In our study, we observed that 0.03 mg/kg iv doses of midazolam did not exert any negative effect on both sedation scores and early recovery, as well as meeting the criteria for being sent home.

Kain et al. [8] evaluated post-operative effects of the implementation of 5 mg im midazolam 30 min before surgery in patients undergoing general anesthesia for different surgical procedures in outpatient conditions. They found that patients given 5 mg im. midazolam had lower pain scores and needed less rescue analgesia during the first postoperative week. We also found that in patients undergoing minor urologic surgery 0.03 mg/kg midazolam given intravenously before surgery resulted lower postoperative pain scores and earlier home readiness compared with the control patients. Our results are in accordance with the results of the study by Kain et al. [9]. In an other study by the same authors (Kain et al), in patients undergoing abdominal hysterectomy who were given oral lorezepam the night before surgery and 5 mg midazolam im in the morning of surgery any significant difference in postoperative pain scores between the groups were not detected. However significant reduction in morphine consumption in patient controlled analgesia at the first four hours after surgery was detected in preoperatively sedated patients. The most important determinants of postoperative pain intensity are the type of surgical procedure and location of surgery. Therefore, the effect of preoperatively applied sedation on pain scores in major surgical procedures may not be apparent such as in minor surgery. Further researches are needed to present postoperative effects of preoperative sedation in different surgical procedures.

Conclusion Intravenous midazolam given at a dose of 0.03 mg/kg before surgery resulted in lower postoperative pain scores and earlier home readiness without affecting recovery in patients undergoing outpatient urologic surgery.

REFERENCES

1. Kayhan Z. Ameliyat öncesi değerlendirme ve hazırlık. In: Klinik Anestezi, 3. baskı, Logos Yayıncılık, İstanbul, 2004; 32-35.
2. Yang CY, Wong CS, Chang SY, Ho ST. İntrathecal ketamin reduces morphine requirements in patients with terminal cancer pain. *Can J Anaesth* 1996;43:379-383. http://dx.doi.org/10.1007/BF03011718
3. Leigh JM, Walker J, Janaganathan P. Effect of preoperative visit on anxiety. *Anaesthesiology* 1978;22:489-490.
4. Vlymen JM, White PF. Outpatient anesthesia. In: Miller's Anesthesia, 5th ed. Miller RD (eds), Churchill Livingstone, USA, 2000; 2213-2246.

5. Richardson MG, Wu CL, Hussain A. Midazolam premedication increases sedation but does not prolong discharge times after brief outpatient general anesthesia for laparoscopic tubal sterilization. *Anesth Analg* 1997;44:723-726.
6. Shafer A, White PF, Urquhart ML, Doze VA. Outpatient premedication: Use of midazolam and opioid analgesics. *Anesthesiology* 1989;71:495-501. http://dx.doi.org/10.1097/00000542-198910000-00004
7. Van Vlymen JM, Sa Rego MM, White PF. Can it improve outcome in patient undergoing breast biopsy procedures? *Anesthesiology* 1999;90:740-747. http://dx.doi.org/10.1097/00000542-199903000-00016
8. Kain Z, Sevarino F, Pincus S, Alexander GM, Wang SM, Ayoub C, Kosarussavadi B: Attenuation of the preoperative stress response with midazolam: effects on postoperative outcomes. *Anesthesiology* 2000;93:141-147. http://dx.doi.org/10.1097/00000542-200007000-00024
9. Kain ZN, Sevarino FB, Rinder C, Pincus S, Alexander GM, Ivy M. Preoperative anxiolysis and postoperative recovery in women undergoing abdominal hysterectomy. *Anesthesiology* 2001;94:415-422. http://dx.doi.org/10.1097/00000542-200103000-00009