Efficacy appraisal of four regimens (granisetron, ketamine, dexmedetomidine, and lidocaine combined with fentanyl) for cystoscopy-associated sedation and analgesia and catheter-related bladder tolerance: a randomized clinical trial

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Abstract

The authors sought to quantify the clinical impacts of granisetron, ketamine, dexmedetomidine, and lidocaine combined with fentanyl, for procedural sedation and analgesia in cystoscopy and for bladder catheter tolerance. This double-blind trial recruited four stratified blocked randomized eligible groups of patients (n = 120) formerly identified as needing cystoscopy, each receiving one of the above four anesthetic agents. Dexmedetomidine-sedated subjects experienced less pain from 5 to 120 minutes after the beginning of procedure, and next the ketamine manifested a better pain relief experienced. Sedation score was found to be rather more satisfactory in the early-mentioned from 15 to 55 minutes and at 90 and 105 minutes after procedure. The mean opioid use was observed lower in the dexmedetomidine treated patients and next in the ketamine administered patients. Considering the findings emanating from the study and the lack of complications that need to be treated, dexmedetomidine and ketamine afforded superior pain relief, greater sedation, and less postoperative opioid use in patients undergoing cystoscopy, and thus, they could be suggested to be combined with fentanyl during outpatient cystoscopy.

Key words: analgesia; cystoscopy; dexmedetomidine; fentanyl; granisetron; ketamine; lidocaine; sedation

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Introduction

Cystoscopy is attracting growing attention as an invasive, diagnostic procedure on the genitourinary system, whereas being lengthy exploited for studying and treating diseases involving the tract.[1] This is underlined as an easy, effective approach to ensuring diagnosing and following up patients suffering hematuria, lower urinary tract symptoms, and bladder tumors, besides being available in outpatient clinics. Though the flexible cystoscopy is associated with less post-procedure pain, some patients perceive discomfort of passing the cystoscope into the bladder.[2] Cystoscopy may be appropriately used with various anesthesiological techniques, comprising spinal, general, or local anesthetic.[1]

The subjects' stress response can bring about poor wound healing and immune function depression, owing to which the necessity of the patient's pain management is quite evident.[3] Several anesthetics drugs used in the procedure can with certainty be contributed to minimize anxiety and pain and may have side effects for the patient with kidney problems. The drugs when combined with a balanced dose help enhance the therapeutic effects and reduce their overall side effects.[4,5] Intravenous (IV) sedation and analgesia have been accepted as a safe, cost-effective alternative to general or regional anesthesia.[6] Ketamine is a derivative of phencyclidine and, as an IV anesthetic, has analgesic and amnesic effects,[4,7,8] is further metabolized by hepatic microsomal enzymes, and is mostly metabolized in norketamine which possess only 20–30% of the potency of ketamine. Pharmacokinetics of ketamine is rapid onset, leading to a short half-life.[9] Dexmedetomidine (DEX) is an α2-adrenoceptor agonist, and, if infused, reduces heart rate (HR), systemic vascular resistance, while it lowers blood pressure. This helps to maintain hemodynamic stability and produces anesthetic and analgesic effects that lessen opioid requirements, their complications, and stress response while it improves the quality of recovery.[10,11] Its analgesic effects appear to be through activation of the α2 adrenergic receptor in the dorsal horn of the spinal cord and the inhibitory influence on substance P-release.[12] Similar studies that have examined the efficacy of DEX for sedation in patients undergoing cystoscopy, all acknowledge the effect in reducing pain.[10,13]

Another 5-hydroxytryptamine 3 receptor-specific antagonist is granisetron and its impact lasts longer and has a better function than ondansetron, whereas it is frequently used for preventing nausea and vomiting after chemotherapy.[14,15] Several studies have successfully reported this drug to prevent pain on IV injection of anesthetic drugs such as propofol that

can be painful on IV injection and additionally to function as an adjuvant in IV regional block.[15,16]

Modir et al.[14] cited that granisetron helps significantly relieve intra- and post-operative pain in forearm surgery. Likewise, Soltani-Mohammadi et al.[17] undertook a study aimed at the effect of systemic granisetron on cystoscopy and suggested that systemic granisetron does not affect the duration of sensory and motor block after spinal anesthesia with hyperbaric bupivacaine, while no IV granisetron-administered subject received any drug to reduce pain and nausea.

Lidocaine is an inexpensive, fast-acting local anesthetic[18] that works by blocking the sodium influx through nerve cell membrane and by binding to a specific receptor site in the entry of sodium channels,[19] and has adverse events, such as high blood pressure and HR, owing to sympathetic block.[9,20]

Besides, another study led by Altementt et al.[16] appraised the effect of IV lidocaine on the propofol requirements during anesthesia, reporting that IV lidocaine reduces the amount of propofol in general anesthesia. Fentanyl (FEN) is a highly potent synthetic opioid, 75–125 times stronger than morphine, used in different ways to produce analgesia and anesthesia. Preoperative administration of FEN can reduce postoperative opioid doses, as well as overall opioid intake. It possesses a more rapid onset of action, but a shorter half-life, when compared to morphine. The more rapid onset demonstrated a higher fat solubility which facilitates passage through the blood-brain barrier.[9] Considering that no trial has hitherto endeavored to fully compare our desired drugs and that former ones explored the efficacy of the drugs alone and produced different outcomes, while granisetron has not been studied for sedation of patients undergoing cystoscopy, the present trial was outlined to address the compared effects of granisetron, ketamine, DEX, and lidocaine combined with FEN on sedation and analgesia in cystoscopy and on catheter-related bladder tolerance.

Subjects and Methods

Study setting and patients

This prospective parallel double-blind trial enrolled 120 patients identified as requiring cystoscopy at Valiasr Hospital, Arak, Iran from October 2020 to April 2021. The written informed consent (**Additional file 1**) was obtained from all eligible patients based on inclusion and exclusion criteria. Sample size was calculated by MedCal software version 15.8 (MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org; 2015) and by considering power 80% and confidence interval 95% and the difference between sedation scores between groups according to our pervious study.[6] This study was approved with the ethics code of IR.ARAKMU.REC.1398.282 at January 5, 2020 (**Additional file 2**). Moreover, the study protocol was registered in Iranian Registry of Clinical Trials (No. IRCT20141209020258N138) on March 18, 2020 (**Figure 1**). This study follows the CONsolidated Standards Of Reporting Trials (CONSORT) statement for protocol reporting (**Additional file 3**).

Inclusion criteria: 18–65 years of age, patients of both sexes, American Society of Anesthesiologists I–II,[21,22] those undergoing cystoscopy, lack of drug sensitivity, no history of drug or other psychotropic substances and alcohol abuse, no history of psychological illness, no history of cardiovascular-hepatic and renal disease, a body mass index not greater than 36 kg/m^2, and no history of obstructive sleep apnea.

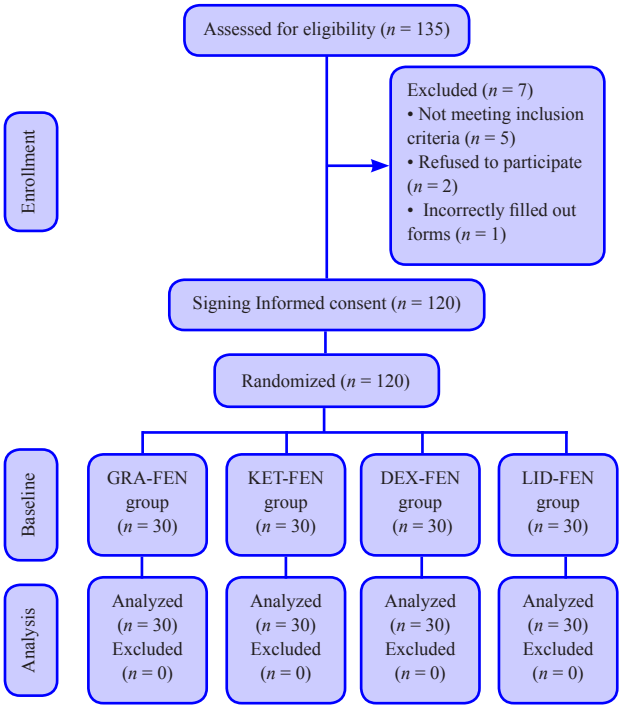

Figure 1: CONsolidated Standards Of Reporting Trials (CONSORT) diagram showing the flow of participants through each stage of a randomized trial.
Note: DEX: Dexmedetomidine; FEN: fentanyl; GRA: granisetron; KET: ketamine; LID: lidocaine.

Exclusion criteria: Dissatisfaction with participation in the study, allergy to treatment drugs, inadequate analgesia, and use of other anesthesia options to perform the procedure.

Intervention

Participants were randomly stratified into four groups using block randomization with randomly selected block sizes of 8. All subjects were NPO from the night before the procedure. They received 10 mL/kg of Ringer's lactate solution and 3–4 L/min of oxygen via the nasal cannula during cystoscopy while no other sedatives were used intraoperatively. There were 30 patients in each group as follows: The granisetron-FEN group (n = 30) receiving 3 mg granisetron (Caspian tamin Pharmaceutical Co., Rasht, Iran) plus 2 μg/kg FEN17; ketamine-FEN group (n = 30), 0.5 mg/kg ketamine (Rotexmedica Co., Hamburg, Germany) plus 2 μg/kg FEN10; DEX-FEN group (n = 30), 1 μg/kg DEX (Exir Pharmaceutical Co., Borujerd, Iran) plus 2 μg/kg FEN10; and lidocaine-FEN group (n = 30), 1.5 mg/kg lidocaine (Caspian tamin Pharmaceutical Co.) plus 2 μg/kg FEN16. At baseline, the dose of different drugs in each group was calculated and diluted to 10 mL with distilled water. They were slowly administered intravenously initially in each group for 10 minutes and then FEN, as a base drug, was given at the desired dose.

Measurements

We measured HR, oxygen saturation, and pain score with a visual analog scale,[23] provided on a 0–10 scale, with 0 and 10

being the respective lowest and highest levels of pain experienced by the subjects among whom the illiterate used the face model.[23] Sedation level was assessed by Ramsay sedation scale,[24,25] where 1 = Patient is anxious and agitated; 2 = Patient is tranquil, cooperative, and oriented; 3 = Patient is sedated and responds to commands only; 4 = Patient responds briskly to light and tactile stimuli; 5 = Patient responds sluggishly to the stimuli, and 6 = Patient does not respond. These data were recorded from baseline (before any intervention) to 120 minutes after intervention in all patients. The main primary outcome was pain score by stationary of hemodynamic parameters. Moreover, the secondary outcomes were Ramsay sedation score and percentage of opioid drug use patients in each group. Furthermore, the cystoscopy duration and post-anesthesia recovery score (Aldrete score)[26] were recorded and an Aldrete score > 8 was considered to be required for the discharge of the patient.

The urologist satisfaction[27] during cystoscopy was recorded at the procedure's end, as follows: zero means easy and full satisfaction; 1, moderate or partial satisfaction; and 2, difficult or dissatisfied with the cystoscopy procedure. When a visual analog scale > 4 was registered, 25 mg IV pethidine was given with each dose and the dose for opioid use was recorded. Needless to say, the data was measured by an intern who was unaware of grouping information, to ensure a double-blind study. The adjuvants were prepared for and administered to each group by an anesthesiologist, whereas the participants were unaware of the group in which they were allocated.

Statistical analysis

Data analysis was undertaken using SPSS version 20 (SPSS Inc., Chicago, IL, USA). The hemodynamic parameters, pain and Ramsay sedation scores among four groups were compared by one-way analysis of variance and Tukey's *post hoc* test. Repeated-measure analysis of variance was used to assess the trend of hemodynamic parameters during the time. Chi-square test was used to compare gender and other qualitative variables in different groups. A significant level lower than 0.05 was considered significant.

Results

The 120 patients in the DEX, ketamine, granisetron, and lidocaine groups, with 25–65 years, and a mean age of 43.40 ± 8.79 years, whereas 68 (57%) and 52 (43%) were male and female, respectively. No significant difference was seen in age, sex (**Table 1**), HR (**Figure 2**), or oxygen saturation (**Figure 3**) among the four groups ($P > 0.05$). HR was lower in the DEX group 15 minutes after the beginning of procedure ($P = 0.04$), while no statistically significant difference was seen in the rest of the time among them.

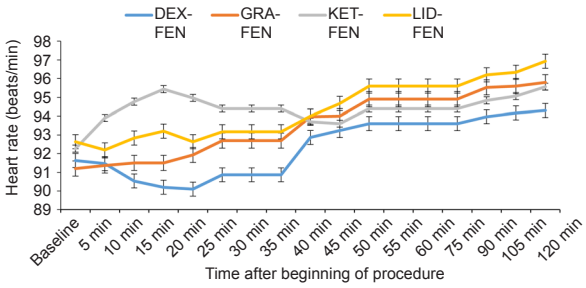

Figure 2: Trend of heart rate in the four groups.
Note: Data in age are expressed as mean and were analyzed by one-way analysis of variance followed by Tukey's *post hoc* test. DEX: Dexmedetomidine; FEN: fentanyl; GRA: granisetron; KET: ketamine; LID: lidocaine.

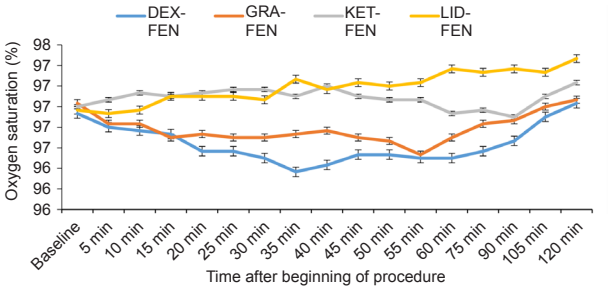

Figure 3: Trend of oxygen saturation in the four groups.
Note: Data in age are expressed as mean and were analyzed by one-way analysis of variance followed by Tukey's *post hoc* test. DEX: Dexmedetomidine; FEN: fentanyl; GRA: granisetron; KET: ketamine; LID: lidocaine.

As shown in **Table 2**, statistically significant differences were found in pain scores among the four groups ($P < 0.05$), whereas the DEX-FEN group experienced less pain from 5 to 120 minutes after the beginning of procedure and no difference was observed among them at 120 minutes after the beginning of procedure. Repeated-measure analysis of variance showed that the DEX-FEN group suffered less pain than the other groups ($P = 0.0001$).

As the results in **Table 3**, statistically significant differences were seen in sedation among the four groups from 15 to 55 minutes, and 90 and 105 minutes after the beginning of procedure ($P < 0.05$) during which sedation was greater in the DEX-FEN group. Repeated-measure analysis of variance showed a more satisfactory level of sedation in the DEX-FEN group ($P = 0.001$). In addition, according to **Table 4**, opioid use was lower in the DEX-FEN group than in other groups ($P = 0.006$). Moreover, the incidence of side effects was not different among the study groups.

As depicted in **Table 5**, cystoscopy duration, Aldrete score, and urologist satisfaction were not different among the four groups ($P > 0.05$).

Table 1: Age and sex distribution in the four groups

Variable	DEX-FEN (*n*=30)	GRA-FEN (*n*=30)	KET-FEN (*n*=30)	LID-FEN (*n*=30)	*P*-value
Age (yr)	41.46±8.98	42.43±7.47	42.43±7.47	48.26±7.53	> 0.05
Sex					> 0.05
Female	17(57)	16(53)	17(57)	17(57)	
Male	13(43)	14(47)	13(43)	13(43)	

Note: Data in age are expressed as mean±SD and were analyzed by one-way analysis of variance followed by Tukey's *post hoc* test. Data in sex are expressed as number (percentage), and were analyzed by Chi-square test. DEX: Dexmedetomidine; FEN: fentanyl; GRA: granisetron; KET: ketamine; LID: lidocaine.

Table 2: Effects of granisetron (GRA), ketamine (KET), dexmedetomidine (DEX), and lidocaine (LID) combined with fentanyl (FEN) on visual analog scale (pain) of patients with cystoscopy and on catheter-related bladder tolerance

Time point	DEX-FEN	GRA-FEN	KET-FEN	LID-FEN	*P*-value
Baseline	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00	>0.05
After the beginning of procedure					
5 min	0.30±0.47	1.60±0.50	0.40±0.50	1.53±0.50	>0.001
10 min	0.466±0.51	2.60±0.50	1.13±0.34	2.50±0.51	>0.001
15 min	1.46±0.51	3.06±0.24	2.06±0.45	2.50±0.51	>0.001
20 min	1.46±0.51	2.6±0.50	1.13±0.34	2.50±0.51	>0.001
25 min	1.23±0.43	3.3±0.47	2.13±0.34	3.03±0.32	>0.001
30 min	1.23±0.43	3.43±0.50	2.13±0.34	3.13±0.43	>0.001
35 min	1.53±0.51	3.50±0.51	2.13±0.34	3.26±0.45	>0.001
40 min	2.06±0.25	3.5±0.51	2.13±0.34	3.26±0.449	>0.001
45 min	2.26±0.45	3.5±0.5	2.26±0.45	3.26±0.45	>0.001
50 min	2.26±0.45	3.5±0.51	2.40±0.50	3.26±0.45	>0.001
55 min	2.23±0.48	3.5±0.51	2.40±0.50	3.26±0.45	>0.001
60 min	2.43±0.50	3.66±0.48	2.40±0.50	3.50±0.51	>0.001
75 min	3.06±0.25	3.93±0.25	3.26±0.45	3.93±0.25	>0.001
90 min	3.46±0.51	3.96±0.18	3.70±0.47	3.93±0.25	>0.001
105 min	4.00±0.01	4.16±0.38	3.93±0.25	4.16±0.38	>0.001
120 min	4.06±0.25	4.30±0.41	4.20±0.34	4.20±0.41	0.419

Note: Data are expressed as mean ± SD and were analyzed by one-way or repeated-measure analysis of variance.

Table 3: Effects of granisetron (GRA), ketamine (KET), dexmedetomidine (DEX), and lidocaine (LID) combined with fentanyl (FEN) on Ramsay sedation score scale of patients with cystoscopy and on catheter-related bladder tolerance

Time point	DEX-FEN	GRA-FEN	KET-FEN	LID-FEN	*P*-value
Baseline	2.00±0.00	2.00±0.00	2.00±0.00	2.00±0.00	>0.05
After the beginning of procedure					
5 min	2.00±0.00	2.00±0.00	2.00±0.00	2.00±0.00	>0.05
10 min	2.00±0.00	2.00±0.00	2.00±0.00	2.00±0.00	>0.05
15 min	2.36±0.49	2.00±0.00	2.26±0.45	2.13±0.34	0.002
20 min	2.43±0.50	2.00±0.00	2.26±0.45	2.13±0.34	>0.001
25 min	2.50±0.51	2.00±0.00	2.26±0.45	2.13±0.34	>0.001
30 min	2.50±0.51	2.00±0.00	2.26±0.45	2.13±0.34	>0.001
35 min	2.50±0.51	2.00±0.00	2.26±0.45	2.13±0.34	>0.001
40 min	2.50±0.51	2.00±0.00	2.26±0.45	2.13±0.34	>0.001
45 min	2.50±0.51	2.00±0.00	2.26±0.45	2.00±0.00	>0.001
50 min	2.50±0.51	2.00±0.00	2.00±0.00	2.00±0.00	>0.001
55 min	2.00±0.00	2.00±0.00	2.00±0.00	2.00±0.00	>0.05
60 min	2.00±0.00	2.00±0.00	2.00±0.00	2.00±0.00	>0.05
75 min	2.00±0.00	2.00±0.00	2.00±0.00	2.00±0.00	>0.05
90 min	2.00±0.00	1.60±0.50	1.96±0.18	1.86±0.34	>0.001
105 min	2.00±0.00	1.60±0.50	1.96±0.18	1.83±0.38	>0.001
120 min	2.00±0.00	1.80±0.41	1.86±0.34	1.80±0.41	0.074

Note: Data are expressed as mean±SD and were analyzed by one-way or repeated-measure analysis of variance.

Table 4: Effects of granisetron (GRA), ketamine (KET), dexmedetomidine (DEX), and lidocaine (LID) combined with fentanyl (FEN) on frequency and percentage of drug use in patients with cystoscopy and on catheter-related bladder tolerance

Item	DEX-FEN	GRA-FEN	KET-FEN	LID-FEN	*P*-value
Opioid consumed	2(7)	11(37)	4(13)	11(37)	0.006
Adverse effect	0	3(10)	4(13)	5(17)	0.159

Note: Data are expressed as number (percentage) and were analyzed by Chi square test.

Table 5: Effects of granisetron (GRA), ketamine (KET), dexmedetomidine (DEX), and lidocaine (LID) combined with fentanyl (FEN) on cystoscopy duration, Alderet Score and satisfaction score of drug use in patients with cystoscopy and on catheter-related bladder tolerance

Item	DEX-FEN	GRA-FEN	KET-FEN	LID-FEN	*P*-value
Cystoscopy duration (min)	14.1±1.20	14.01±1.23	14.16±1.32	1.17±0.21	0.941
Alderet score	9.73±0.45	9.83±0.37	9.60±0.49	9.56±0.50	0.098
Urologist satisfaction score	0.35±0.21	1.33±0.34	0.45±0.12	0.10±0.02	0.165

Note: Data are expressed as mean±SD and were analyzed by one-way analysis of variance followed by Tukey's *post hoc* test.

Discussion

Our results showed that pain score was lower in the DEX group from 5 to 120 minutes after the beginning of procedure, while sedation was more satisfactory in the group from 15 to 55 minutes and at 90 and 105 minutes' post-baseline. The mean opioid use was lower in the group than in other groups. Overall, DEX was associated with superior pain relief, greater sedation, and less postoperative opioid use within 24 hours in patients undergoing cystoscopy. It contributes to maintaining hemodynamic stability, produces anesthetic and analgesic effects, reduces the need for opioids, their complications, and stress response, and improves the quality of recovery.[15,28] DEX analgesic effects can be through activation of the α2 adrenergic receptor in the dorsal horn of the spinal cord and the inhibitory influence on substance P-release.[12]

Modir et al.[6] undertook a study to assess the effect of DEX-ketamine and FEN-ketamine on sedation and analgesia for cystoscopy, reporting that the group receiving the first mixture relieved pain 30 minutes after cystoscopy and suggesting that the mixture may be used in patients undergoing cystoscopy. DEX-FEN mixture in our study had a better effect. Modir et al.[29] strived to address the pain reduction efficacy of granisetron, DEX, and lidocaine after etomidate injection. DEX has been more efficient than the others in reducing etomidate injection pain, while it had no adverse effect and the hemodynamic parameters were stable during anesthesia. Their study was consistent with our results.

Akça et al.[10] conducted a study comparing the prophylactic effects of ketamine and DEX on cystoscopy-related pain and suggested that the drugs are associated with similar pain relief and greater sedation in subjects, but DEX side effects are greater than those of ketamine. DEX in our study afforded superior pain relief, greater sedation, and less postoperative opioid use within 24 hours in patients undergoing cystoscopy. The reason for the difference can be attributed to the combined and comparable drugs in the two studies and the greater number of our samples.[10] Further, another study explored the effect of remifentanil combined with DEX in patients undergoing cystoscopy and reported that remifentanil and DEX can relieve pain in the cystoscopic procedure,[30] consistent with our findings.

Arpaki et al.[31] compared the sedation of remifentanil-DEX and remifentanil-midazolam mixtures in cystoscopy procedures, concluding that the first mixture produced faster sedation, less pain, and more superior satisfaction. The results of their study were in line with ours. Moreover, Li et al.[13] performed a trial to assess the effect of DEX on cystoscopic procedures in which HR increased at baseline in the normal saline group, while the sedation score and analgesic effects were better in the first group. Their study suggested that DEX is a safe, effective drug for cystoscopy13, consistent with our findings.

Future studies on long-term side effects and complications of these four regimes are warranted, as these outcomes were not assessed in this study.

Considering the findings emanating from the study and the lack of complication requiring treatment, DEX and then ketamine was associated with afforded superior pain relief, greater sedation, and less postoperative opioid use in patients undergoing cystoscopy and then could be suggested to be combined with FEN, while ultimately, the final choice does depend on both the patient physical condition and the anesthesiologist's preference.

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Author contributions
Study conceptualization: HM, RJ; data acquisition and analysis: AAH, KS; data interpretation: HM, RJ. All authors have read and approved the manuscript provided.

Conflicts of interest
There is no conflict of interest

Availability of data and materials
All data generated or analyzed during this study are included in this published article and its supplementary information files.

Additional files
***Additional file 1*:** Informed consent form (Persian).
***Additional file 2*:** Hospital Ethics Approval.
***Additional file 3*:** CONSORT checklist.

References

1. Wein AJ, Kavoussi LR, Partin AW, Peters CA. *Campbell-Walsh Urology*. Elsevier. 2015.
2. Gunendran T, Briggs RH, Wemyss-Holden GD, Neilson D. Does increasing hydrostatic pressure ("bag squeeze") during flexible cystoscopy improve patient comfort: a randomized, controlled study. *Urology*. 2008;72:255-258; discussion 258-259.
3. Allison SJ, Docherty PD, Pons D, Chase JG. Exposure to methoxyflurane: low-dose analgesia and occupational exposure. *Australas J Paramed*. 2020;17.

4. Lee KH, Lee SJ, Park JH, et al. Analgesia for spinal anesthesia positioning in elderly patients with proximal femoral fractures: Dexmedetomidine-ketamine versus dexmedetomidine-fentanyl. *Medicine (Baltimore)*. 2020;99:e20001.
5. Lee SH, Song YS, Park. YH. Utility and safety of midazolam anesthesia during cystoscopy. *Korean J Urol*. 2002;43:308-312.
6. Modir H, Moshiri E, Yazdi B, Kamalpour T, Goodarzi D, Mohammadbeigi A. Efficacy of dexmedetomidine-ketamine vs. fentanyl-ketamine on saturated oxygen, hemodynamic responses and sedation in cystoscopy: a doubleblinded randomized controlled clinical trial. *Med Gas Res*. 2020;10:91-95.
7. McVey JD, Tobias JD. Dexmedetomidine and ketamine for sedation during spinal anesthesia in children. *J Clin Anesth.* 2010;22:538-545.
8. Behdad S, Hajiesmaeili MR, Abbasi HR, Ayatollahi V, Khadiv Z, Sedaghat A. Analgesic effects of intravenous ketamine during spinal anesthesia in pregnant women undergone caesarean section; a randomized clinical trial. *Anesth Pain Med*. 2013;3:230-233.
9. Vuyk J, Sitsen E, Reekers M. Intravenous anesthetics. In: Miller R, Eriksson L, Fleisher L, Wiener-Kronish J, Cohen N, Young W, eds. *Miller's Anesthesia*: Saunders; 2014:858.
10. Akça B, Aydoğan-Eren E, Canbay Ö, et al. Comparison of efficacy of prophylactic ketamine and dexmedetomidine on postoperative bladder catheter-related discomfort. *Saudi Med J.* 2016;37:55-59.
11. Priyadarshini N, Rao WP, Anuradha A, JS V. A study of safety and efficacy of dexmedetomidine in cystoscopy. *Int J Health Clin Res.* 2020;3:104-109.
12. Janatmakan F, Nesioonpour S, Javaherforoosh Zadeh F, Teimouri A, Vaziri M. Comparing the effect of clonidine and dexmedetomidine on intraoperative bleeding in spine surgery. *Anesth Pain Med.* 2019;9:e83967.
13. Li XJ, Gan JH. Clinical study on application of dexmedetomidine for cystoscopy. *Zhongguo Yaofang.* 2013;24:1295-1296.
14. Modir H, Pazoki S, Khalili M, Salari H, Amani A. Comparison of analgesic effect of different doses of granisetron in combination with lidocaine for intravenous regional anesthesia. *Med J Mashhad Univ Med Sci*. 2016;59:9-16.
15. Modir H, Yazdi B, Moshiri E, Mohammadbeigi A, Afshari S. Efficacy of dexmedetomidine versus remifentanil to blunt the hemodynamic response to laryngoscopy and orotracheal intubation: a randomized clinical trial. *Med Gas Res*. 2018;8:85-90.
16. Altermatt FR, Bugedo DA, Delfino AE, et al. Evaluation of the effect of intravenous lidocaine on propofol requirements during total intravenous anaesthesia as measured by bispectral index. *Br J Anaesth*. 2012;108:979-983.
17. Soltani-Mohammadi S, Esmaeili S, Saliminia A. Effect of systemic granisetron in the clinical course of spinal anesthesia with hyperbaric bupivacaine for outpatient cystoscopy. *Acad J Surgery.* 2015;2:18-22.
18. Gooran S, Pourfakhr P, Bahrami S, et al. A randomized control trial comparing combined glandular lidocaine injection and intraurethral lidocaine gel with intraurethral lidocaine gel alone in cystoscopy and urethral dilatation. *Urol J.* 2017;14:4044-4047.
19. Forster C, Vanhaudenhuyse A, Gast P, et al. Intravenous infusion of lidocaine significantly reduces propofol dose for colonoscopy: a randomised placebo-controlled study. *Br J Anaesth*. 2018;121:1059-1064.
20. Kafle SK. Intrathecal meperidine for elective caesarean section: a comparison with lidocaine. *Can J Anaesth.* 1993;40:718-721.
21. Doyle DJ, Goyal A, Bansal P, Garmon EH. *American Society of Anesthesiologists Classification*. StatPearls. Treasure Island (FL): StatPearls Publishing; 2021.
22. Daabiss M. American Society of Anaesthesiologists physical status classification. *Indian J Anaesth.* 2011;55:111-115.
23. Delgado DA, Lambert BS, Boutris N, et al. Validation of digital Visual Analog Scale pain scoring with a traditional paper-based Visual Analog Scale in adults. *J Am Acad Orthop Surg Glob Res Rev.* 2018;2:e088.
24. Sessler CN, Grap MJ, Ramsay MA. Evaluating and monitoring analgesia and sedation in the intensive care unit. *Crit Care.* 2008;12 Suppl 3:S2.
25. De Jonghe B, Cook D, Appere-De-Vecchi C, Guyatt G, Meade M, Outin H. Using and understanding sedation scoring systems: a systematic review. *Intensive Care Med*. 2000;26:275-285.
26. Ead H. From Aldrete to PADSS: Reviewing discharge criteria after ambulatory surgery. *J Perianesth Nurs*. 2006;21:259-267.
27. Nixon R, Jaramillo F. Physician satisfaction scale: a proposed enhancement. *Clin Res Regul Aff.* 2003;20:447-455.
28. Saidie S, Modir H, Yazdi B, Moshiri E, Noori G, Mohammadbeigi A. The effect of dexmedetomidine on decrease of cough, hemodynamic parameters and Ramsay score versus lidocaine during general anesthesia: a randomized clinical trial. *Med Gas Res.* 2021;11:1-5.
29. Modir H, Moshiri E, Yazdi B, Kamali A, Soltani S. The pain reduction efficacy of granisetron, dexmedetomidine and lidocaine after etomidate injection for surgery under general anaesthesia. *Adv Hum Biol.* 2019;9:71-75.
30. Heo B, Kim M, Lee H, Park S, Jeong S. Optimal effect-site concentration of remifentanil when combined with dexmedetomidine in patients undergoing cystoscopy. *Korean J Anesthesiol.* 2014;66:39-43.
31. Arpaci AH, Bozkırlı F. Comparison of sedation effectiveness of remifentanil-dexmedetomidine and remifentanil-midazolam combinations and their effects on postoperative cognitive functions in cystoscopies: A randomized clinical trial. *J Res Med Sci.* 2013;18:107-114.

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