Impact of Intravenous Dexmedetomidine on Postoperative Bowel Movement Recovery After Laparoscopic Nephrectomy: A Consort-Prospective, Randomized, Controlled Trial

shanshan huang
Shandong University Qilu Hospital
Fuxi Song
Second Hospital of Shandong University
Shuai Hu
Second Hospital of Shandong University
Shaozhong Yang
Shandong University Qilu Hospital
Shuqin Wang
Shandong University Qilu Hospital
Lianying Zhao
Shandong University Qilu Hospital
Qi Wu
shandong university qilu hospital
Xin Liu
Shandong University Qilu Hospital
Feng Qi (qifeng66321@sina.com)
Shandong University Qilu Hospital

Research article

Keywords: Dexmedetomidine, Bowel movement , Recovery, Flatus; Postoperative

Posted Date: January 22nd, 2021

DOI: https://doi.org/10.21203/rs.3.rs-152377/v1

Abstract

Background

Postoperative ileus is a frequent complication after surgery, especially abdominal surgery. Of the factors, sympathetic excitation is the primary factor for postoperative ileus. Sympathetic activation is always increased by the stress of surgery and postoperative pain. It was reported that dexmedetomidine (DEX) lessens pain and inhibits the sympathetic nerve by acting on the locus coeruleus. Therefore we designed our study to observe whether DEX promotes bowel movements in patients after laparoscopic nephrectomy.

Methods

One hundred and twenty patients undergoing laparoscopic nephrectomy were assigned into three groups, group C (normal saline infusion), group D1 (DEX 0.02 μg/kg/h), and group D2 (DEX 0.04 μg/kg/h). The primary outcome was to record the times of first flatus, defecation and eating after surgery. The secondary outcome was postoperative pain accessd by the numerical rating scale (NRS), concerning adverse effects, as well as the duration of the postoperative hospital stay.

Results

The times of first flatus, defecation and eating in groups D1 and D2 were shorter than those in group C ($P<0.01$). The NRS scores at 8 h and 24 h after surgery were obviously lower in groups D1 and D2 than in group C ($P<0.05$). There were no concerning adverse effects ($P>0.05$).

Conclusion

DEX in 0.04 μg/kg/h postoperative infusion facilitates bowel movements in patients undergoing laparoscopic nephrectomy.

Trial registration

This trial was registered in a Chinese Clinical Trial Registry (ChiCTR) center on December 23, 2015. The registered number was ChiCTR-IPR-15007628.

Background

Postoperative ileus (POI) is a common complication after abdominal operations, that manifests as a decrease in or stagnation of intestinal peristalsis and increased hospital stay [1]. POI occurs not only after abdominal surgery, but also after any other surgery that requires general anesthesia. Among the various factors, surgical trauma and direct intestinal operation are the most important elements for POI. General anesthesia, postoperative pain and the use of opioid drugs are also factors of POI [2, 3]. It is widely known that the nervous system plays an important role in regulating gastrointestinal motility.

Surgical stress and postoperative pain during the surgery can be transmitted to the nerve center, and activate the autonomic nervous system's sympathetic nerve. The activated sympathetic nerve affects the recovery of postoperative bowel movement and the secretion of gastrointestinal hormones and neurotransmitters (such as vasoactive intestinal peptide and nitric oxide), and bowel movement is slowed.

High sympathetic hyperactivity deserves the blame for all of these factors in common. Many methods are used, such as immediate feeding, early activity, never using blocking analgesia, and fluid restriction, but none of them can prevent POI completely [2 ~ 4].

Hence, an effective and noninvasive method is needed. DEX, as a highly selective α-2 adrenergic receptor agonist, has the effects of leep induction, sedation, and inhibition of sympathetic hyperactivity with little respiratory inhibition [5]. Based on these effects we hypothesized that DEX could promote postoperative bowel movement. Laparoscopic nephrectomy was chosen to investigate postoperative bowel movement recovery, thus avoiding gut damage.

Methods

Participants

This randomized, double-blinded, controlled trial was approved by the Institutional Medical Ethics Committee of Qilu Hospital of Shandong University, and it was also registered at chictr.org (ChiCTR-IPR-15007628), and consistent with the consort guidelines of the institution. We chose patients who were treated by laparoscopic nephrectomy with general anesthesia at Qilu Hospital and did not have exist the following conditions: body mass index (BMI) greater than 32 kg/m^2 or less than 18 kg/m^2; age older than 75 or younger than 18 years old; presence of bradycardia (basal heart rate (HR) less than 60 bpm) or other cardiac arrhythmia; presence of clinically significant dysfunction, including cardiovascular, renal, or hepatic diseases; previous history of chronic pain or long-term use of analgesics (at least > 3 months); or allery to the test drug. This trial was initiated in January 2016 and terminated in December 2017.

Randomization and masking

When the patients met the enrollment criteria, informed consent for participating in the trial was signed by them. Then, according to a computer-generated randomization table, they were randomly assigned to one of the three groups (group C, group D1 and group D2). On the day of surgery, the drugs and PCA were prepared by an anesthetist, who was blinded to the group assignment. Furthermore, the associated doctors and nurses were all blinded to the group assignment.

The process of anesthesia

Patients were premedicated with atropine 0.5 mg by intramuscular injection in the ward. Before anesthesia induction, each patient was monitored using electrocardiography, noninvasive blood pressure measurements, pulse oximetry saturation (SpO2), and end-tidal carbon dioxide (EtCO2) via an automated

system (Philips IntelliVue MP50; Philips Company, Beijing, China). HR, SpO2 and mean blood pressure (MBP) were monitored every 5 min.

After obtaining a baseline measurement of HR and MBP, groups D1 and D2 received 0.5 μg/kg DEX, and group C received 0.9% NS for 10 min. We used propofol, rocuronium and sufentanil for sequential induction. The laryngeal mask airway (LMA) was intubated after positive pressure mask ventilation for 5 min. An arterial cannula was required to monitor the invasive arterial blood pressure in the left radial artery. Anesthetic depth was monitored using a bispectral index (BIS) monitor, and sevoflurane was administered to maintain to keep the depth of anesthesia (BIS scores in the range of 40 to 60). Controlled ventilation was performed with 100% oxygen, and ETCO2 was maintained from 35 to 40 mm Hg. We inserted a temperature probe through the nasal cavity and keep the body temperature at 36 to 37 °C. We started to infuse the test drugs (groups D1 and D2 received the DEX infusion at rates of 0.2 μg/kg/h and 0.4 μg/kg/h respectively, while group C received saline instead of DEX) after the establishment of pneumoperitoneum and suspended them 30 min before the end of surgery. Rocuronium was administered intermittently to maintain a satisfactory muscle relaxation.

If more than a 20% fluctuation of in the baseline level was detected in MBP, vasoactive drugs (noradrenalin 5–10 μg or nitroglycerin 50–100 μg) were used to maintain hemodynamic stability. If the HR decreased to less than 45 beats/min, atropine 0.5 mg was applied. Conversely, if HR was greater than 100 beats/min, esmolol 0.5 mg/kg was administered to decrease the heart rate. When the laparoscope was withdrawn, palonosetron 0.25 mg was intravenously given to prevent postoperative nausea and vomiting (PONV). When spontaneous breathing appeared at the end of the surgery, neostigmine 0.04 mg/kg and atropine 0.02 mg/kg were administered to antagonize neuromuscular blockade before LMA extubation. If the SpO2 was above greater than 90% without oxygen for at least 5 min, patients could be sent back to the ward.

At the end of the surgery, a patient-controlled analgesia (PCA) pump was started (group C with sufentanil 0.02 μg/kg/h; group D1 with both sufentanil and DEX 0.02 μg/kg/h; group D2 with sufentanil 0.02 μg/kg/h and DEX 0.04 μg/kg/h). The PCA was programmed to deliver at a constant speed of 2 mL/h, and an additional dose of 0.5 ml could be administered with a lockout time of 10 min.

Regarding postoperative bowel movements, patients were given abdominal massage, miso soup, or both if the flatus time was more than 48 h. Intravenous nutrition was given if the flatus time was more than 72 h.

Outcomes

The primary outcome measures were the time of first flatus and defecation, and the duration of postoperative hospital stay. The secondary outcome measures were the postoperative pain scores, both at rest and during movement and concerning adverse effects.

HR, MBP, and SpO2 were collected at the following six time points: entering the OR (T0), 5 min after finishing the baseline text drug infusion (T1), 5 min after pneumoperitoneum establishment (T2), 1 h after

pneumoperitoneum establishment (T3), 2 h after pneumoperitoneum establishment (T4), and 5 min after extubation (T5). In addition, $ETCO_2$ was recorded from T1 to T4. Pain scores were assessed using NRS (0 = no pain to 10 = worst pain) at 1, 8, 24, and 48 h postoperatively.

Statistical analysis

Statistical analysis was performed using SPSS software, version 21.0 (SPSS Inc. Chicago, IL, USA). The Kolmogorov-Smirnov test was used to assess the distribution of the variables. Levene's test was used to compare the homogeneity of variance among the three groups. Normally distributed data are expressed as the mean and standard deviation, while data with a skewed distribution are expressed as the median and number (n). Percentages (%) were used to express the categorical data. Parameters such as age, operation time, anesthesia time, flatus and defecation time, MBP and HR among these groups were compared using 2-way analysis of variance (ANOVA). The Mann-Whitney test was used to evaluate the NRS among the three groups, and adverse reactions were analyzed using the χ^2 test. Multiple comparisons were performed using the LSD post-hoc test. P values < 0.05 were considered statistically significant.

Results

One hundred twenty-three patients were randomly distributed into three groups. Among the patients, two were eliminated due to conversion to open nephrectomy (one from group D1 and one from group D2). One was excluded after surgery because of incomplete clinical data (from group C) (Fig. 1). Patient characteristics were comparable among the three groups. The baseline characteristics and demographics of the patients were compared among the three groups (Table 1).

Table 1
Clinical Characteristics of Patients in Group C, D1 and D2

	Group C(n = 40)	Group D1(n = 40)	Group D2(n = 40)	P value
Sex, F/M, n	11/29	12/28	10/30	0.760
Age, years	51.05 ± 11.87	52.29 ± 10.18	51.93 ± 10.15	0.867
BMI, kg/m^2	26.24 ± 2.84	26.09 ± 1.46	25.83 ± 2.23	0.785
basic disease(hypertension /DM),n	11/6	11/5	15/5	0.789
ASA I /Ⅱ, n	10/30	7/33	6/34	0.484
Duration of anaesthesia, min	152.50 ± 63.63	149.67 ± 53.38	143.67 ± 57.63	0.836
Duration of surgery, min	134.00 ± 58.63	136.33 ± 53.22	128.83 ± 57.11	0.870
Dosage of sufentanil during surgery, ug	32.17 ± 8.06	30.81 ± 2.27	32.07 ± 3.66	0.533
Dosage of sufentanil after surgery (8 h), ml	16.40 ± 0.41	16.15 ± 0.41	16.27 ± 0.50	0.142
Dosage of sufentanil after surgery (24 h), ml	48.48 ± 0.63	48.23 ± 0.75	48.33 ± 0.66	0.344
Postoperative stay in hospital, d	8.60 ± 1.72	8.37 ± 1.33	8.41 ± 1.66	0.782

Variables presented as mean standard deviation SD or number of patients. None showed any statistical significance (P > 0.05). ASA = American Society of Anesthesiologists, BMI = Body Mass Index, DM = Diabetes Mellitus.

The first flatus time and the defecation time after surgery in group D1 (41.27 ± 8.72, 73.80 ± 19.19) and group D2 (39.41 ± 7.60, 72.50 ± 3.11) were significantly shorter than those in group C (51.31 ± 11.78, 92.80 ± 25.50) (P < 0.05, Table 2). The time to eat after surgery in groups D1 (42.95 ± 10.28) and D2 (44.93 ± 9.03) was shorter than that in group C (54.43 ± 11.51) (P < 0.05, Table 2).

Table 2
Bowel movement after Surgery in Group C, D1 and D2

	Group C (n = 40)	Group D1 (n = 40)	Group D2 (n = 40)	P valves (Pc and D1, Pc and D2, PD1 and D2)
Time to first flatus, h	51.31 ± 11.78	41.27 ± 8.72	39.41 ± 7.60	0.001*/ 0.001**/ 0.375
Time to defecation, h	92.80 ± 25.50	73.80 ± 19.19	72.5 ± 3.11	0.001*/ 0.001**/ 0.787
Time to eat, h	54.43 ± 11.51	42.95 ± 10.28	44.93 ± 9.03	0.001*/ 0.02**/ 0.487
Variables presented as mean ± SD				
*P value compared Group D1 with Group C, **P value compared Group D2 with Group C.				

MBP at T1 in groups D1 and D2 was significantly lower than in group C. MBP was lower than the baseline at T2, T3, T4, and T5 in group C, at T1, T4, and T5 in group D1, and at T1 and T4 in group D2 ($P < 0.05$, Table 3). HR at T1 in group D1 was significantly lower than in group C. HR was lower than baseline at T2, T3, T4, and T5 in group C, at T1, T2, T3, and T4 in group D1, and at T1, T2, T3, T4, and T5 in group D2 ($P < 0.05$, Table 3). The NRS score at rest or with movement at 8 h and 24 h after surgery was obviously lower in groups D1 and D2 than in group C ($P < 0.05$; Fig. 2).

Table 3
Vital signs in Group C, D1 and D2

	Time point	Group C(n = 40)	Group D1(n = 40)	Group D2(n = 40)	P value
MBP, mm Hg	T0	103.40 ± 11.90	99.47 ± 12.07	98.20 ± 10.89	0.153
	T1	101.33 ± 9.46	88.53 ± 13.81*#	87.03 ± 12.71*#	0.738
	T2	98.9 ± 10.55*	99.43 ± 11.78	96.77 ± 12.20	0.639
	T3	96.67 ± 10.16*	97.10 ± 8.53	96.07 ± 9.88	0.915
	T4	98.13 ± 7.96*	95.17 ± 11.04*	94.13 ± 9.71*	0.225
HR, bpm	T5	105.17 ± 14.33*	102.4 ± 14.72	100.6 ± 10.90	0.418
	T0	74.83 ± 11.53	71.53 ± 10.49	73.8 ± 9.46	0.473
	T1	74.23 ± 10.88	62.43 ± 10.56*#	64.77 ± 8.19*	0.087
	T2	65.30 ± 8.28*	60.23 ± 1.87*#	63.16 ± 7.22*	0.081
	T3	66.4 ± 11.66*	62.77 ± 8.81*	66.13 ± 7.75*	0.265
	T4	67.87 ± 10.86*	66.27 ± 11.16*	67.23 ± 10.61*	0.828
	T5	74.83 ± 9.24	74.43 ± 9.77	73.69 ± 8.65*	0.653

Variables presented as mean ± SD, * P < 0.05 compared baseline, # P < 0.05 compared with group C.

Adverse effects had no statistically significant differences among the three groups (P > 0.05; Table 4).

Table 4
Adverse reactions after Surgery in Group C, D1 and D2

	Group C (n = 40)	GroupD1 (n = 40)	GroupD2 (n = 40)	P values
Abdominal massage/simo soup	5 (12.5%)	3 (7.5%)	2 (5%)	0.833
Intravenous nutrition	0 (0%)	0 (0%)	0 (0%)	1.000
Nausea and Vomiting	8 (20%)	7 (17.5%)	8 (20%)	0.937
Severe abdominal pain and distention	6(15%)	5 (12.5%)	4 (10%)	0.772
Drowsiness	1 (2.5%)	2 (5%)	4 (10%)	0.358
serious respiratory depression.	0 (0%)	0 (0%)	0 (0%)	1.000
Delirium	0 (0%)	0 (0%)	0 (0%)	1.000

Variables presented as number of patients, n(%)

Discussion

The perioperative use of 0.04ug/kg/h enhanced the recovery of postoperative bowel movement.

POI is a common complication after abdominal operations, and the clinical manifestations vary, including abdominal distension, nausea, vomiting, difficulty in defecation and prolonged feeding time. The causes of POI are complicated and involve many factors, including surgical trauma, activation of the inhibitory sympathetic reflex, and induction of local and systemic inflammatory mediators [2, 3].

First, the sympathetic nerve inhibits bowel movement by reducing the release of acetylcholine, and the vagus nerve stimulates bowel movement by inducing the release of acetylcholine. Nerve reflex regulation is an important physiological mechanism for postoperative control of bowel movement. Surgery, pain, gut damage and other factors, directly or indirectly activate the sympathetic nerve to inhibit postoperative bowel movement. As a highly selective α2-adrenoceptor agonist, DEX inhibits sympatholytic excitation, sedation and analgesia. It acts on α2-adrenoceptors in the central nervous system to reduce sympathetic tone [6]. Hence, after the use of DEX, the activated sympathetic nerve was downregulated, and the vagus nerve was relatively excited; as a result, bowel movements were facilitated.

Second, postoperative pain was relieved by perioperative use of DEX [7 ~ 9]. Although opioids are a priority for postoperative pain, they are unfavorable because they inhibit gastrointestinal motility and aggravating POI [10, 11]. In our study, laparoscopic surgery relieved postoperative pain compared with open surgery.. Although the total volumes of opioid drugs were not different among the three groups, postoperative pain with rest and movement was significantly relieved by the combined use of DEX. Effective pain relief contributed to alleviating POI by allowing for postoperative activities earlier.

Third, the influence of gut damage on POI was excluded by laparoscopic nephrectomy. Laparoscopic surgery can reduce surgical trauma and weaken the immune response compared with open surgery, reducing the time for flatulence and shorting the time to resume a soft diet after surgery and decreasing the length of the hospital stay [12 ~ 14]. Visualizing laparoscopic surgery and pneumoperitoneum induction can lead to sympathetic nerve activation [15, 16]. In addition, CO_2 pneumoperitoneum can induce hypercarbia, which can directly or indirectly stimulate the sympathetic nervous system and cause evaluated levels of catecholamine [15, 17]. Sympathetic stimulation could provide the main inhibitory force for intestinal peristalsis, while parasympathetic stimulation enhances gastrointestinal motility [18]. DEX, as a highly selective α-2 adrenergic receptor agonist, acts on α2-adrenoceptors in the central nervous system to reduce sympathetic tone and decrease the secretion of catecholamine [6]. It has also been proved to reduce the sympathetic effect caused sweating and abate blood pressure increased and catecholamine release caused by tremor [19]. DEX has been proved to attenuate sympathetic activation induced by pneumoperitoneum and surgical stress [20]. Hence, DEX could prompt postoperative bowel movement by weakening sympathetic activation. In our study the flatus times and defecation times were significantly shorter after the use of DEX. The outcomes were consistent with previous hypothesis. Between the groups D1 and D2, group D2 had shorter flatus and defecation times than group D1,

although the difference was insignificantly. For patients, one hour is still important. This study provides evidence for the relief of postoperative peristalsis in patients undergoing endoscopic surgery.

When DEX was used as a bolus, the blood vessels contracted and hypertension could be seen in the first 1–3 min. It was seen but not recorded, and when used as an infusion drug, the central sympatholytic impact of DEX was the main effect [21, 22]. Developing bradycardia and hypotension (requiring treatment) were increased only when a loading dose and a maintenance dose of DEX > 0.07 μg/kg/h were given to critically ill patients. [23] HR and MBP were significantly lower after the loading dose of DEX without bradycardia and hypotension. DEX could decrease the plasma concentration and the release of catecholamine [6, 21, 24]. The infusion of DEX during anesthesia showed a medium decrease and fewer variations in MBP and HR [25, 26]. There was an insignificant difference among the three groups in HR and MBP, so the dose of DEX was safe for patients.

DEX, as a highly selective α-2 adrenergic receptor agonist, has the effects of leep induction, and sedation, with little respiratory inhibition [5, 27]. There were no significant differences in drowsiness, which is easily arousable, or severe respiratory depression, which was not consistent with its sedative effect to some extent [28, 29]. There were no significant differences PONV or postoperative delirium which was not consistent with the report of Song et al [30 ~ 32].

Some limitations exist in our study. First, before anesthesia induction, DEX was administered at a rate of 0.5 μg/kg for 10 minutes and then at a rate of 0.2 to 0.4 μg/kg/h during the operation. However, we were unable to determine the effect of plasma DEX concentrations on intraoperative hemodynamics because we did not measure the serum concentrations of DEX at any time point. Finally, laparoscopic nephrectomy was performed by two different surgical methods: transabdominal and retroperitoneal. Therefore, different surgical techniques might have had different effects on postoperative analgesia and the recovery of bowel movement.

Conclusions

DEX infusion at 0.04 ug/kg/h after surgery result in better, faster recovery of bowel movement and a better analgesic effect without additional adverse effects in patients after laparoscopic nephrectomy.

Abbreviations

DEX: Dexmedetomidine, POI: Postoperative ileus, BMI: Body mass index, HR: Heart rate, SpO2: Pulse oximetry saturation, EtCO2: End-tidal carbon dioxide, MBP: Mean blood pressure, LMA: Laryngeal mask airway, BIS: Bispectral index, PONV: Postoperative nausea and vomiting, PCA: Patient-controlled analgesia, NRS: Numerical rating scale, ASA: American Society of Anesthesiologists, DM: Diabetes mellitus, SRD: Serious respiratory depression.

Declarations

Ethics approval and consent to participate

The trial was authorized by the Institutional Medical Ethics Committee of Qilu Hospital of Shandong University on December 23, 2015 and it was conducted in accordance with the consort guidelines of the institution. It was also registered at chictr.org (ChiCTR-IPR-15007628). Informed consent was obtained from all of the participants.

Consent for publication

Not applicable

Availability of data and material

The datasets used in the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was funded in part by the National Natural Science Foundation of China (No. 81672250) and the Fundamental Research Funds of Shandong University. The funder played no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Authors' contributions

SH designed the study, collected, and analyzed the data and wrote the manuscript. FS helped to collect the data. SHu helped to collect the data. SY helped to collect, and analyze the data and revise the manuscript. SW helped to collect the data. LZ helped to collect the data. QW helped to collect the data. XL helped to collect the data. FQ designed, and conducted the study and revised the manuscript.

Acknowledgements

None.

References

1. Koscielny A, Kalff JC. T-helper cell type 1 memory cells and postoperative ileus in the entire gut. Curr Opin Gastroenterol. 2011;27(6):509–14.
2. Bragg D, El-Sharkawy AM, Psaltis E, Maxwell-Armstrong CA, Lobo DN. Postoperative ileus: Recent developments in pathophysiology and management. J Clin Nutr. 2015;34:367–76.

3. Venara A, Neunlist M, Slim K, Barbieux J, Colas PA, Hamy A, Meurette G. Postoperative ileus: Pathophysiology, incidence, and prevention. J Visc Surg. 2016;153(6):439–46.
4. Rohloff M, Cicic A, Christensen C, Maatman TK, Lindberg J, Maatman TJ. Reduction in postoperative ileus rates utilizing lower pressure pneumoperitoneum in robotic-assisted radical prostatectomy. J Robot Surg. 2019;13(5):671–4.
5. Carollo DS, Nossaman BD, Ramadhyani U. Dexmedetomidine: a review of clinical applications. Curr Opin Anaesthesiol. 2008;21:457–61.
6. Khan ZP, Ferguson CN, Jones RM. Alpha-2 and imidazoline receptor agomists. Their pharmacology and therapeutic role. Anaesthesia. 1999;54:146–65.
7. Chan AK, Cheung CW, Chong YK. Alpha-2 agonists in acute pain management. Expert Opin Pharmacother. 2010;11(17):2849–68.
8. Abdel Hamid MHE. Intravenous dexmedetomidine infusion compared with that of fentanyl in patients undergoing arthroscopic shoulder surgery under general anesthesia. Anesth Essays Res. 2017;11(4):1070–4.
9. Sharma R, Gupta R, Choudhary R, Singh Bajwa SJ. Postoperative analgesia with intravenous paracetamol and dexmedetomidine in laparoscopic cholecystectomy surgeries: a prospective randomized comparative study. Int J Appl Basic Med Res. 2017;7(4):218–22.
10. Ferraz AA, Cowles VE, Condon RE, Schulte WJ. Opioid and nonopioid analgesic drug effects on colon contractions in monkeys. Dig Dis Sci. 1995;40(7):1417–9.
11. De Winter BY, Boeckxstaens GE, De Man JG, Moreels TG, Herman AG, Pelckmans PA. Effects of mu- and kappa-opioid receptors on postoperative ileus in rats. Eur J Pharmacol. 1997;339(1):63–7.
12. Sundbom M, Hedberg J. Use of Laparoscopy in Gastrointestinal Surgery in Sweden 1998–2014: A Nationwide Study. Scand J Surg. 2017 Mar;106(1):34–9.
13. Lee MS, Lee JH, Park do J, Lee HJ, Kim HH, Yang HK. Comparison of short- and long-term outcome of laparoscopic-assisted total gastrectomy and open total gastrectomy in gastric cancer patients. Surg Endosc. 2013;27:2598–605.
14. Okhlom C, Goetze JP, Svendsen LB, Achiam MP. Inflammatory resonse in laparoscopic vs. open surgery for gastric cancer. Scand J Gastro-entrrol. 2014;49(9):1027–34.
15. Chen YQ, Xie YYZ, Xue YR, Wang B, Jin XJ. Effects of ultrasound-guided stellate ganglion block on autonomic nervous function during CO2-pneumoperitoneum: A randomized double-blind control trial. J Clin Anesth. 2016;32:255–61.
16. Rohloff M, Cicic A, Christensen C, Maatman TK, Lindberg J, Maatman TJ. Reduction in postoperative ileus rates utilizing lower pressure pneumoperitoneum in robotic-assisted radical prostatectomy. J Robot Surg. 2019;13(5):671–4.
17. Rasmussen JP, Dauchot PJ, DePalma RG, Sorensen B, Regula G, Anton AH, et al. Cardiac function and hypercarbia. Arch Surg. 1978;113:1196–200.

18. Dubois A, Weise VK, Kopin IJ. Postoperative ileus in the rat: physiopathology, etiology and treatment. Ann Surg. 1973;178:781–6.
19. Hogue CW Jr, Talke P, Stein PK, Richardson C, Domitrovich PP, Sessler DI. Autonomic nervous system responses during sedative infusions of dexmedetomidine. Anesthesiology. 2002;97(3):592–98.
20. Cho JS, Kim HI, Lee KY, An JY, Bai SJ, Cho JY, Yoo YC. Effect of Intraoperative Dexmedetomidine Infusion on Postoperative Bowel Movements in Patients Undergoing Laparoscopic Gastrectomy: A Prospective, Randomized, Placebo-Controlled Study. Medicine. 2015;94(24):e959. doi:10.1097/.MD0000000000000959.
21. Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colinco MD. The effects of increasing plasma concentrations of dexmedetomidine in humans. Anesthesiology 2000;93:382 – 94.
22. Hall JE, Uhrich TD, Ebert TJ. Sedative, analgesic and cognitive effects of clonidine infusions in humans. Br J Anaesth. 2001;86:5–11.
23. Tan JA, Ho KM. Use of dexmedetomidine as a sedative and analgesic agent in critically ill adult patients: a meta-analysis. Intensive Care Med. 2010;36:926–39.
24. Jalonen J, Hynynen M, Kuitunen A, Heikkilä H, Perttilä J, Salmenperä M, Valtonen M, Aantaa R, Kallio A. Dexmedetomidine as an anesthetic adjunct in coronary artery bypass grafting. Anesthesiology. 1997;86:331–45.
25. Venn RM, Grounds RM. Comparison between dexmedetomidine and propofol for sedation in the intensive care unit: patient and clinician perception. Br J Anaesth. 2001;87(5):684–90.
26. Kabukçu HK, Sahin, ·N. Temel Y,·Titiz TA. Hemodynamics in coronary artery bypass surgery: effects of intraoperative dexmedetomidine administration. Anaesthesist. 2011;60(5):427–31.
27. Gillian M, Keating. Dexmedetomidine. A Review of Its Use for Sedation.
28. in the Intensive Care Setting. Drugs. 2015;75(10):1119–30.
29. Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colinco MD. The effects of increasing plasma concentrations of dexmedetomidine in humans. Anesthesiology. 2000;93(2):382–94.
30. Szumita PM, Baroletti SA, Anger KE, Wechsler ME. Sedation and analgesia in the intensive care unit: evaluating the role of dexmedetomidine. Am J Health Syst Pharm. 2007;64(1):37–44.
31. Song Y, Shim JK, Song JW, Kim EK, Kwak YL. Dexmedetomidine added to an opioid-based analgesic regimen for the prevention of postoperative nausea and vomiting in highly susceptible patients: A randomised controlled trial. Eur J Anaesthesiol. 2016;33(2):75–83.
32. Su X, Meng ZT, Wu XH, Cui F, Li HL, Wang DX, Zhu X, Zhu SN, Maze M, Ma D. Dexmedetomidine for prevention of delirium in elderly patients after non-cardiac surgery: a randomised, double-blind, placebo-controlled trial. Lancet. 2016;388(10054):1893–902.
33. Riker RR, Shehabi Y, Bokesch PM, Ceraso D, Wisemandle W, Koura F, Whitten P, Margolis BD, Byrne DW, Ely EW, Rocha MG. Dexmedetomidine vs midazolam for sedation of critically ill patients: a randomized trial. Jama. 2009;301(5):489–99.

Figures

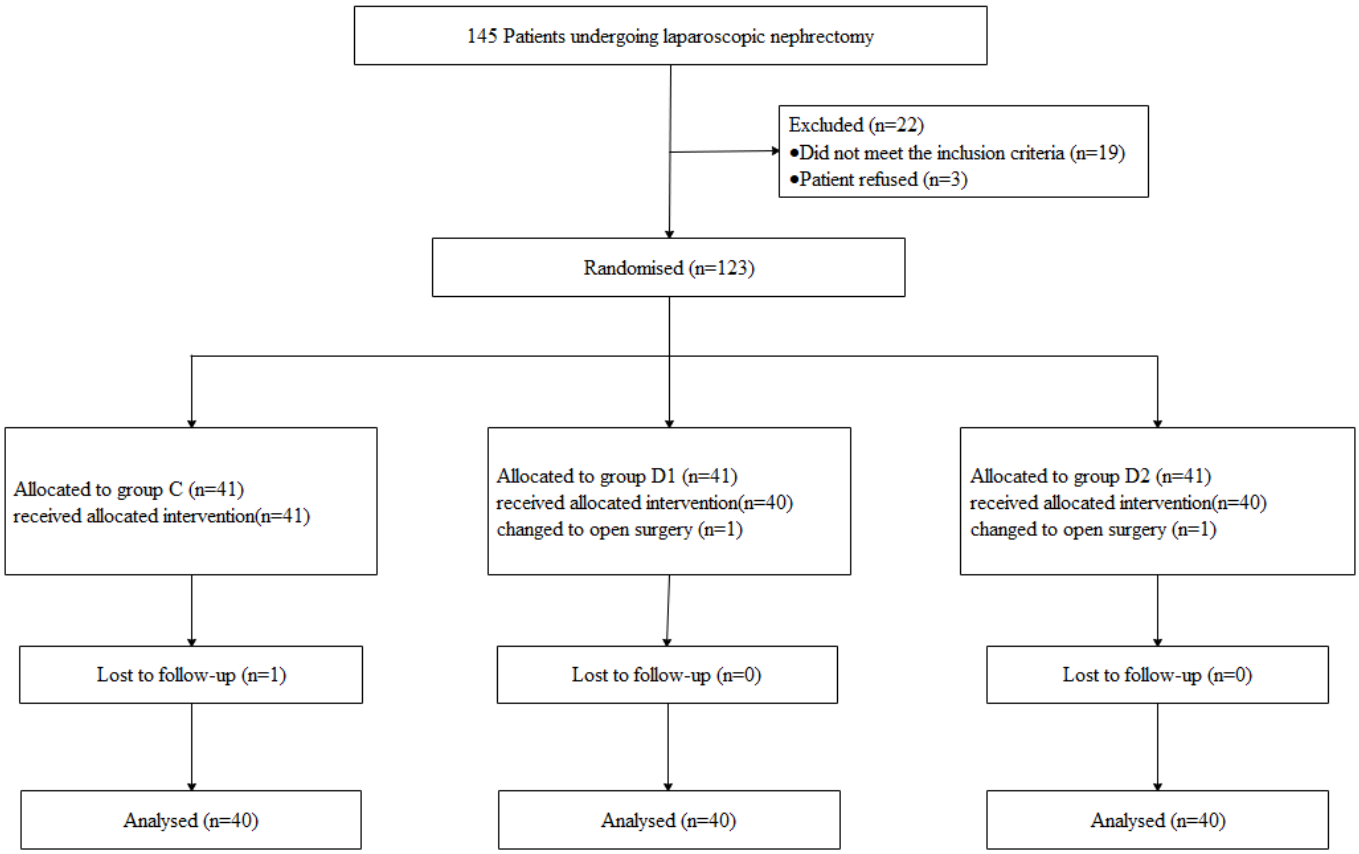

Figure 1

Patient enrolment flow diagram. This illustrates the flow of all patients screened, excluded, and randomized.

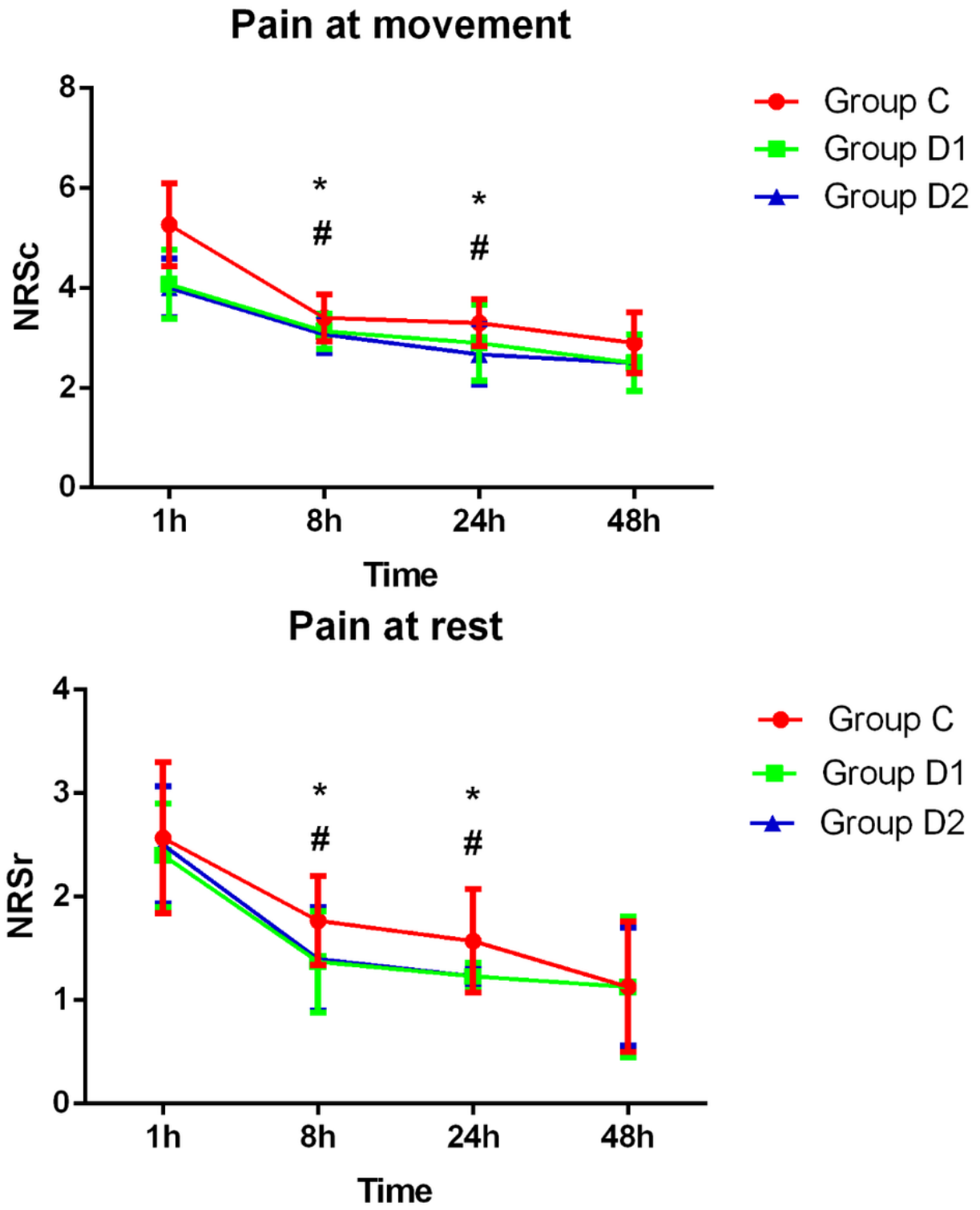

Figure 2

Pain scores (NRS) during 48 h after surgery in group C, D1 and D2. Variables presented as mean standard deviation. The NRS score of 8 h and 24 h were significantly lower in group D1 and D2 than group C at rest and at movement. (* meant P □ 0.05 compared group D1 with Group C, # meant P □ 0.05 compared group D2 with Group C).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- CONSORT2010Checklist.doc