Investigation of analgesic dose of nalbuphine combined with remifentanil after radical gastrectomy

YANG ZHANG[1*], RONGFANG ZHANG[1*] and NANNAN DING[2]

[1]Department of Anesthesiology, Xiangyang No. 1 People's Hospital, Hubei University of Medicine;
[2]Department of Pharmacy, Xiangyang Central Hospital Affiliated to Hubei University of Arts and Science, Xiangyang, Hubei 441000, P.R. China

Received June 21, 2018; Accepted May 28, 2019

DOI: 10.3892/etm.2019.7715

Abstract. Clinical analgesic effect of different doses of nalbuphine combined with remifentanil on postoperative gastric cancer patients was explored. One hundred cases of gastric cancer patients treated from December 2014 to December 2016 in the Xiangyang No. 1 People's Hospital were selected and separated into group A and group B. The dose in group A was 0.2 mg/kg of nalbuphine plus 0.2 μg/kg of remifentanil, and 0.3 mg/kg of nalbuphine plus 0.1 μg/kg of remifentanil in group B. Analgesia was performed by self-controlled intravenous injection. The Visual Analogue Scale (VAS) pain scores and the Brinell Comfort Score (BCS) at 2, 6, 12, 24 and 48 h after operation, and the incidence of adverse reactions were compared between the two groups. The VAS scores in group A were higher than those in group B, but the BCS scores in group A were lower (P<0.05). Postoperative patient-controlled intravenous analgesia (PCIA) press times in group A were lower than those in group B (P<0.05); the incidence of adverse reactions such as nausea and vomiting in group A was higher than that in group B (P<0.05). The analgesic effect of intravenous analgesia scheme of 0.3 mg/kg of nalbuphine and 0.1 μg/kg of remifentanil on gastric cancer patients after operation is better than that of 0.2 mg/kg of nalbuphine and 0.2 μg/kg of remifentanil, which reduces the incidence of adverse reactions, has greater security, and can be promoted.

Correspondence to: Dr Nannan Ding, Department of Pharmacy, Xiangyang Central Hospital Affiliated to Hubei University of Arts and Science, 136 Jingzhou Road, Xiangcheng, Xiangyang, Hubei 441000, P.R. China
E-mail: nnv2gr@163.com; dd1mol@163.com

*Contributed equally

Key words: nalbuphine, remifentanil, gastric cancer, visual analogue scale, Brinell comfort score

Introduction

Gastric cancer, a common malignancy, is mainly caused by unhealthy dietary habits. According to the latest statistics on the incidence and mortality of gastric cancer, it ranks second in malignancies worldwide (1). The incidence of gastric cancer in Vietnam and Philippines is highest (2) and it ranks first in gastrointestinal malignancies in the two countries. According to the recent statistics by the World Health Organization (3), the death toll of gastric cancer in 2015 (760,000) ranked fourth in cancer deaths over the world. In the past two years, the death toll tended to be flush with the second and the third, and the death is biased towards young age. Radical gastrectomy (4) refers to the complete removal of tumor, and then it may be cured, so radical gastrectomy is also called curative resection of gastric cancer. The primary sources of gastric cancer mainly include primary tumors, metastatic lymph nodes, and involve infiltrating tissues. The current surgical methods for radical gastrectomy include traditional laparotomy, laparoscope-assisted radical gastrectomy, full laparoscopic radical gastrectomy and robotic radical gastrectomy (5).

A previous study found that patients' psychology had a great impact on the success rate of the operation and the postoperative prognosis, and postoperative excessive pain had a strong negative impact on patient recovery (6), so the choice and dose of analgesics was crucial. Clinical studies have shown that remifentanil is a good postoperative tranquilizer (7-10). Due to its unique chemical structure - ester bond, remifentanil is easily hydrolyzed by non-specific cholinesterase in the body, and these hydrolyzed sites are mainly located in human tissues and plasma, so the elimination of remifentanil in the human body mainly relies on them rather than liver and kidney function. Therefore, remifentanil has the advantages of rapid onset of analgesia, strong analgesic effect, rapid drug effect, easy adjustment, no accumulation in the body and rapid elimination, which enables the patient to recover quickly after drug withdrawal. Nalbuphine also has superior advantages in anesthesia and analgesia (11,12), mainly due to the fact that it has a unique pharmacological property - antagonistic part of the μ-receptor that inhibits adverse reactions such as respiratory depression, nausea, cough, and drowsiness, which are caused by this receptor excitement. At present, it has not been studied or discussed by scholars to apply the combination of remifentanil and nalbuphine with

proper ratio in clinical analgesia. Therefore, this study mainly investigated the clinical analgesic effect of different doses of remifentanil combined with nalbuphine on postoperative gastric cancer patients, to improve postoperative analgesia regime.

Patients and methods

Patient data. One hundred cases of gastric cancer patients were treated from December 2014 to December 2016 in the Xiangyang No. 1 People's Hospital (Xiangyang, China), including 74 males and 26 females, aged from 40 to 68 years, with an average age of 51±6.22 years. The enrolled patients were divided into group A and B, with 50 cases in each group, according to the choice of patient postoperative analgesia regime. The regime in group A was 0.2 mg/kg of nalbuphine (Carbone Scientific Co., Ltd.) plus 0.2 μg/kg of remifentanil (Yaodu Jingwei Information Technology Co., Ltd., SFDA approval no.: H20143314); in group B it was 0.3 mg/kg of nalbuphine plus 0.1 μg/kg of remifentanil.

The basic clinical data of the patients were collected, including demographic data, operation time and vital signs. This study was approved by the Ethics Committee of the Xiangyang No. 1 People's Hospital. Patients who participated in this research had complete clinical data. The signed informed consents were obtained from the patients or the guardians.

Inclusion and exclusion criteria. Inclusion criteria (13,14): All enrolled patients met the requirements of the American Society of Anesthesiologists (ASA) (levels I-II); all gastric cancer patients admitted were confirmed as positive by clinical diagnosis; both enrolled patients and their family members were informed and agreed before treatment. Exclusion criteria: Patients who were allergic to analgesic drugs, who had a history of drug abuse, patients undergoing chemotherapy and radiotherapy one month before operation, patients unwilling to cooperate with the treatment or with disabilities, were excluded from the study.

Analgesic methods. After entering the operating room, patients' basic vital signs were measured. An intravenous channel was opened, oxygen was given, with ECG monitoring. Radical gastrectomy was performed in strict accordance with the relevant operating specifications throughout the entire process. All patients underwent postoperative analgesia using patient-controlled intravenous analgesia (PCIA). In group A, 0.2 μg/kg of remifentanil plus 0.2 mg/kg of nalbuphine plus 0.9% of sodium chloride solution were used to 100 ml for analgesia pump. In group B, 0.1 μg/kg of remifentanil plus 0.3 mg/kg of nalbuphine plus 0.9% of sodium chloride solution were used to 100 ml for analgesia pump. The background dose of the analgesic pump was 2 ml/h, the self-administered dose was 2 ml, and the locking time was 10 min.

Operation methods. All patients chose to have a supine position, and the position could be adjusted according to the needs of the operation. Laparoscopic radical surgery was performed with a five-hole approach. The surgeon made an incision about 2 cm below the navel. Trocar (10 mm) was inserted to establish the pneumoperitoneum. The pressure was controlled between 12 and 15 mmHg. The other four holes were punctured in the left, right upper abdomen, left and right abdomen. The left upper abdomen was set up as the main operating hole. After the first assistant pulled the membrane, the surgeon cut the membrane from the transverse colon with an ultrasonic scalpel, opened the membrane cavity, and separated and cut the gastroduodenal artery in the colonic liver region. Then the gastroenteric artery and vein were found near the posterior wall of the stomach, and the root of the artery and vein were clamped, and the distal part of the membrane was cut off and the sixth group of lymph nodes was removed. After the pancreatic envelope was separated, the left gastric artery and vein were exposed. The same method was used to clamp the left gastric artery and vein on the root, then the distal part was cut off, and the seventh and eighth groups of lymph nodes were removed completely. After hepatoduodenal ligament capsulotomy, the right gastric artery was exposed, and the distal end was cut off after root clamp, and the third and twelfth lymph nodes were removed. Finally, the lymph nodes in the spleen area were removed, the stomach was short-acting, the root of the vein was clamped and the distal end was cut, and the posterior gastric venous and venous and the ligaments around the stomach were cut off. The first and second sets of lymph nodes were removed and the cardia was freed. Total gastrectomy was performed, and the esophageal jejunum Roux-Y anastomosis or Bi-type anastomosis was performed. Grade I care was given after surgery, and conventional antibiotics were used. After the patient was ventilated, the fastening was released. All patients underwent the same surgical procedure and the number of lymph nodes removed was determined by the patient's condition at the time of surgery.

Methods of observation. The clinical experience of the patients in all groups at 2, 6, 12, 24 and 48 h after operation was observed and recorded using visual analogue scale (VAS) and Brinell comfort score (BCS) (15-18). The VAS scores range from 0 to 10 and the pain increases with the increase of the number. The BCS scores range from 1 to 4, and the comfort degree increases with the increase of the number. The effective PCIA press times and the effect of analgesic agents were observed and recorded for all patients within 20 h after operation; the incidence of adverse reactions during analgesia was observed and recorded, including cough, respiratory depression (breathing <8 times/min), drowsiness and pruritus.

Follow-up. The subjects in this group were followed up using ward round and other follow-up methods, and the analgesic methods and prognosis of patients were observed, and they were followed up for a maximum of 60 days. Analysis of the clinical analgesic effect of different doses of remifentanil combined with nalbuphine on postoperative gastric cancer patients was performed.

Statistical analysis. The data obtained from the records were statistically processed using the SPSS 20.0 statistical package (IBM Corp., Armonk, NY, USA). Measurement data were expressed in mean ± standard deviation (mean ± SD), and the comparison between two groups was tested by Student's t-test. Repeated measures analysis of variance was used for

Table I. Basic clinical data [mean ± SD or n/(%)].

Items	Group A	Group B	t/χ^2 value	P-value
Number	50	50		
Sex			0.208	0.648
Male	38 (76)	36 (72)		
Female	12 (24)	14 (28)		
Age distribution (years)	50.12±5.6	52.43±6.3	1.930	0.057
Systolic pressure before operation (mmHg)	137.02±6.10	134.69±5.89	1.943	0.055
Diastolic pressure before operation (mmHg)	81.34±9.36	79.6±8.66	0.937	0.351
Heart rate before operation (times/min)	76.51±10.35	77.27±9.52	0.382	0.703
Breathing before operation (times/min)	17.84±1.22	18.12±1.64	0.969	0.335
Operation time (min)	217.83±5.25	219.42±4.93	1.561	0.122
History of drinking	32 (64.00)	33 (66.00)	0.044	0.834
History of irregular diet	39 (78.00)	39 (78.00)	0.000	1.000
Tumor size			0.049	0.826
<4 cm	35 (70.00)	36 (72.00)		
≥4 cm	15 (30.00)	14 (28.00)		
Degree of tumor differentiation			0.220	0.896
High differentiation	2 (4.00)	3 (6.00)		
Middle differentiation	26 (52.00)	25 (50.00)		
Poor differentiation	22 (44.00)	22 (44.00)		
Tumor infiltration			0.539	0.970
T_1	14 (28.00)	13 (26.00)		
T_2	12 (24.00)	12 (24.00)		
T_3	19 (38.00)	20 (40.00)		
T_{4a}	3 (6.00)	4 (8.00)		
T_{4b}	2 (4.00)	1 (2.00)		
Number of lymph node metastases			1.450	0.996
N_0	21 (42.00)	18 (36.00)		
N_1	10 (20.00)	12 (24.00)		
N_2	11 (22.00)	13 (26.00)		
N_3	8 (16.00)	7 (14.00)		
Distant metastasis			0.502	0.919
M_0	47 (94.00)	48 (96.00)		
M_1	3 (6.00)	2 (4.00)		

the comparison of different time points within the group. LSD test was the post hoc test. The enumeration data was expressed in percentage [n/(%)], and the comparison between the groups was tested by Chi-square test. P<0.05 was considered to indicate a statistically significant difference.

Results

Analysis of the basic clinical data of the two groups. The subjects included in this study were 100 gastric cancer patients who were divided into two groups, with 50 cases in each group. The t-test and Chi-square test were used for statistical analysis of the clinical data of the two groups. The results showed that there were no statistically significant differences between the two groups in main vital signs, proportion of male and female and medical history (P>0.05) (Table I). The two groups of patients were comparable. The proportion of patients who had a history of drinking and irregular diet, and the proportion of male patients were high patients.

Patients' VAS pain condition and BCS comfort scores. The VAS scores of patients were observed and recorded at 2, 6, 12, 24 and 48 h after operation. The VAS scores of patients were higher in group A than those in group B at each time point (P<0.05). Patients' comfort degree (BCS scores) was lower in group A than that in group B at each time point (P<0.05) (Table II).

PCIA press times and adverse reactions of patients. After observation and record, it was found that within 20 h after operation, the effective PCIA press times in group A (6.2±1.5 times) were lower than those in group B (13.8±2.5 times), and the

Table II. Comparison of VAS pain scores and BCS comfort scores between the two groups of patients at 2, 6, 12, 24 and 48 h (mean ± SD, scores).

	VAS scores				BCS scores			
Time (h)	Group A	Group B	t value	P-value	Group A	Group B	t value	P-value
2	5.08±0.75	3.02±0.25	18.430	<0.001	1.52±0.12[a]	2.85±0.12	55.420	<0.001
6	4.51±0.54[a]	3.05±0.15	18.420	<0.001	1.66±0.08[a]	3.05±0.16	54.940	<0.001
12	3.95±0.45[a]	2.68±0.13	19.170	<0.001	1.85±0.08[a]	2.95±0.23	31.940	<0.001
24	3.71±0.24[a]	2.45±0.14	31.090	<0.001	1.95±0.13[a]	2.98±0.45	15.500	<0.001
48	3.61±0.34[a]	2.45±0.14	22.310	<0.001	1.86±0.16[a]	2.96±0.45	16.290	<0.001
F value	77.110	153.200			108.900	2.596		
P-value	<0.001	<0.001			<0.001	0.037		

[a]P<0.05, compared with group B at the same time point.

Table III. Comparison of adverse reactions between the two groups [n (%)].

Items	Group A	Group B	χ^2 value	P-value
n	50	50		
Epigastric discomfort	15 (30.00)	6 (12.00)	0.012	0.911
Nausea, vomiting	11 (22.00)	3 (6.00)	5.316	0.021
Cough	10 (20.00)	2 (4.00)	6.061	0.014
Respiratory depression	17 (34.00)	5 (10.00)	8.392	0.004
Drowsiness	12 (24.00)	4 (8.00)	4.762	0.029
Pruritus	7 (14.00)	1 (2.00)	4.891	0.027
Total	26 (52.00)	12 (24.00)	8.319	0.004

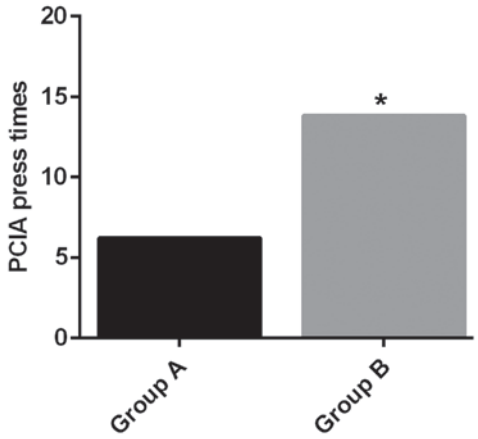

Figure 1. Comparison of PCIA press times between the two groups of patients. The postoperative effective PCIA press times in group A of patients were significantly lower than those in group B, and the difference was statistically significant (P<0.05). *P<0.05 at the same time point, compared with group A. PCIA, patient-controlled intravenous analgesia.

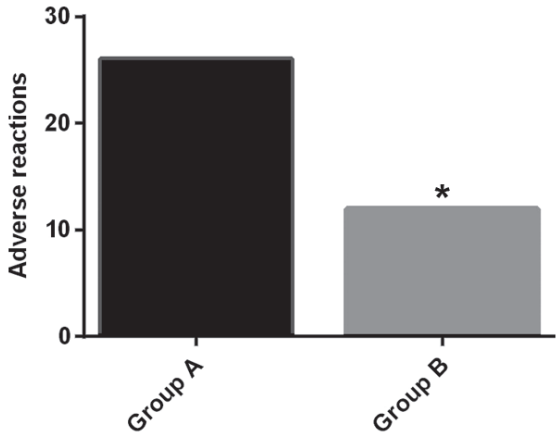

Figure 2. Comparison of adverse reactions between the two groups of patients. The incidence of adverse reactions such as nausea, vomiting and respiratory depression (breathing <8 times/min) in group A of patients was 26 (52.00%), higher than 12 (24.00%) of patients in group B, and the difference was statistically significant (P<0.05). *P<0.05, compared with group A.

difference was statistically significant (P<0.05) (Fig. 1); the incidence of adverse reactions such as nausea, vomiting and respiratory depression (breathing <8 times/min) in group A of patients was 52.00%, higher than 24.00% of patients in group B (P<0.05). The difference was not statistically significant in epigastric discomfort (P>0.05) (Table III and Fig. 2).

Discussion

Radical gastrectomy is an open surgery that severely damages the immune system. Under the influence of minimally invasive techniques, both the surgical method and the wound area have been optimized. However, it is still a hot topic how to effectively

relieve or eliminate acute pain of the patient caused by surgical trauma and minimize the incidence of side effects. Scientific statistics have proven that effective postoperative analgesia can accelerate postoperative recovery (19). First, it can effectively improve postoperative sleep quality of the patient. Moreover, it can reduce postoperative pain and encourage cough and expectoration. Finally, the complications caused by surgical trauma have also been improved. Rose and Kam (20) found that postoperative complications are mainly caused by the inhibition of the immune system, its mechanism of action is generally that the pituitary is excessively activated caused by the stimulation of postoperative excessive pain, thus releasing a large number of hormones that inhibit the immune system. In this study, remifentanil combined with nalbuphine was used for the postoperative stabilization of radical gastrectomy, and the effect of its dose on clinical analgesia was investigated.

Compared with conventional analgesic methods, PCIA can be administered by patients themselves to meet individual analgesic needs, and the titration of doses is more accurate, avoiding obvious fluctuations in blood drug concentration, thus achieving the greatest analgesic effect in the shortest time (21). The convenient administration of PCIA also makes the dosage individualized, and greatly reduces the workload of medical staff (22). Epidural anesthesia cannot ensure the anesthesia effect of patients because the dosage cannot be completely individualized. In the occurrence of certain emergencies such as insufficient depth of anesthesia, it is passive for the patient's anesthesia treatment, and when the anesthesia level is lower, it has a greater impact on blood pressure and other hemodynamic factors (23,24). Nerve block is also a common analgesic method, but the technical requirements for the operator are higher, the cost of anesthesia is more expensive, and when the operator is not experienced enough, a small error can cause nerve stimulation symptoms, even serious complications (25). As a result, in this study, we used PCIA to relieve postoperative pain.

The dose in analgesic regime A was 0.2 mg/kg of nalbuphine plus 0.2 μg/kg of remifentanil and in the analgesic regime B it was 0.3 mg/kg of nalbuphine plus 0.1 μg/kg of remifentanil. The results of the study were as follows: The VAS scores in group A were higher than those in group B; the BCS scores in group A were lower than those in group B, and the difference was statistically significant ($P<0.05$), indicating that the postoperative discomfort and pain value in group A were overall higher than those in group B, that is, analgesic regime B was better. At the same time, related research (7) has also shown that the analgesic effect, drug efficacy duration and drug resistance to extensive surgical trauma have been improved when remifentanil at a dose of 0.1 μg/(kg·min) is used, which is consistent with this study. From a study on the pharmacological aspect of remifentanil (26), it was found that inhibitory G protein and excitatory G protein were conjugated to this type of drug at the time of analgesic effect, which increased body's sensitivity to pain. Therefore, the high-content remifentanil in group A also triggered more acute pain at the same time as high-efficiency analgesia, resulting in the comfort in group A being lower than that in group B, and the pain higher than that in group B.

This study also found that postoperative PCIA press times in group A of patients (6.2±1.5 times) were lower than those in group B (13.8±2.5 times) ($P<0.05$), and the incidence of adverse reactions such as nausea, vomiting and respiratory depression (breathing <8 times/min) in group A of patients was 52.00%, higher than 24.00% in group B ($P<0.05$). It further verifies this conclusion, indicating that high-content remifentanil has extended its drug resistance time, but it also increases the incidence frequency of adverse reactions. Compared to other studies of remifentanil combined with non-nalbuphine (27-29), under the same conditions as recording patient postoperative analgesia and the same setting of analgesic pump at the same time point, in this study, group B had lower VAS, higher BCS, and superior analgesic effect. It was proposed to be due to the optimal addition of remifentanil combined with nalbuphine in pharmacology (30). In terms of receptors, nalbuphine belongs to the κ-receptor but remifentanil belongs to the μ-receptor, and different receptors reduce receptor competition. In addition, nalbuphine contains antagonistic part of the μ-receptor, the excitement of which will cause adverse reactions, and the addition of remifentanil promotes the elimination of analgesic drugs. Therefore, the combination of remifentanil and nalbuphine optimizes the analgesic and anti-adverse reaction effects.

Due to limitations such as small experimental sample size and limited experimental conditions, this study can only preliminarily determine that the analgesic scheme of 0.3 mg/kg of nalbuphine plus 0.1 of μg/kg remifentanil is safer and more effective than that of 0.2 mg/kg of nalbuphine plus 0.2 μg/kg of remifentanil.

The intravenous analgesia scheme of 0.1 μg/kg of remifentanil plus 0.3 mg/kg of nalbuphine were superior to other schemes in analgesic effect, comfort and times of pressing, which reduces the incidence of adverse reactions. Low dose remifentanil combined with nalbuphine may have a higher security, and is worth further exploring.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

YZ conceived and designed the study. RZ collected and analyzed the data. YZ and RZ performed the experiments. ND was responsible for analgesia and follow-up. YZ, RZ and ND wrote the manuscript and revised it critically. All the authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Xiangyang No. 1 People's Hospital (Xiangyang, China).

Patients who participated in this research had complete clinical data. The signed informed consents were obtained from the patients or the guardians.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Siegel RL, Miller KD and Jemal A: Cancer statistics, 2018. CA Cancer J Clin 68: 7-30, 2018.
2. Global Burden of Disease Cancer Collaboration, Fitzmaurice C, Allen C, Barber RM, Barregard L, Bhutta ZA, Brenner H, Dicker DJ, Chimed-Orchir O, Dandona R, Dandona L, *et al*: Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 32 cancer groups, 1990 to 2015: A systematic analysis for the global burden of disease study. JAMA Oncol 3: 524-548, 2017.
3. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D and Bray F: Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 136: E359-E386, 2015.
4. Xiao H, Xiao Y, Quan H, Liu W, Pan S and Ouyang Y: Intra-abdominal infection after radical gastrectomy for gastric cancer: Incidence, pathogens, risk factors and outcomes. Int J Surg 48: 195-200, 2017.
5. Bencivenga M, Verlato G, Han DS, Marrelli D, Roviello F, Yang HK and de Manzoni G; Italian Research Group for Gastric Cancer (GIRCG): Validation of two prognostic models for recurrence and survival after radical gastrectomy for gastric cancer. Br J Surg 104: 1235-1243, 2017.
6. Stessel B, Theunissen M, Marcus MA, Joosten EA, van Kuijk SMJ, Fiddelers AAA, Peters ML, Hoofwijk DMN, Buhre WFFA and Gramke HF: Prevalence and predictors of patient nonadherence to pharmacological acute pain therapy at home after day surgery: A prospective cohort study. Pain Pract 18: 194-204, 2018.
7. Daccache G, Caspersen E, Pegoix M, Monthé-Sagan K, Berger L, Fletcher D and Hanouz JL: A targeted remifentanil administration protocol based on the analgesia nociception index during vascular surgery. Anaesth Crit Care Pain Med 36: 229-232, 2017.
8. Eagleman SL, Drover CM, Drover DR, Ouellette NT and MacIver MB: Remifentanil and nitrous oxide anesthesia produces a unique pattern of EEG activity during loss and recovery of response. Front Hum Neurosci 12: 173, 2018.
9. Maguire DR and France C: Impact of delta-9-tetrahydrocannabinol on the reinforcing effects of remifentanil in rhesus monkeys responding under a food/drug choice procedure. FASEB J 31 (Suppl 1): lb591, 2017.
10. Eleveld DJ, Proost JH, Vereecke H, Absalom AR, Olofsen E, Vuyk J and Struys MMRF: An allometric model of remifentanil pharmacokinetics and pharmacodynamics. Anesthesiology 126: 1005-1018, 2017.
11. Cornelissen JC, Obeng S, Rice KC, Zhang Y, Negus SS and Banks ML: Application of receptor theory to the design and use of fixed-proportion mu-opioid agonist and antagonist mixtures in rhesus monkeys. J Pharmacol Exp Ther 365: 37-47, 2018.
12. Günther T, Dasgupta P, Mann A, Miess E, Kliewer A, Fritzwanker S, Steinborn R and Schulz S: Targeting multiple opioid receptors - improved analgesics with reduced side effects. Br J Pharmacol 175: 2857-2868, 2018.
13. Apfelbaum JL, Horlocker TT, Agarkar M, Connis RT, Hebl JR, Nickinovich DG, Palmer CM, Rathmell JP, Rosenquist RW and Wu CL; American Society of Anesthesiologists Committee on Standards and Practice Parameters: Practice guidelines for the prevention, detection, and management of respiratory depression associated with neuraxialn opioid administration: An updated report by the American Society of Anesthesiologists Task Force on Neuraxial Opioids and the American Society of Regional Anesthesia and Pain Medicine. Obstet Anesthes Dig 37: 11, 2017.
14. Cao X, Yumul R, Elvir Lazo OL, Friedman J, Durra O, Zhang X and White PF: A novel visual facial anxiety scale for assessing preoperative anxiety. PLoS One 12: e0171233, 2017.
15. Price DD, McGrath PA, Rafii A and Buckingham B: The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. Pain 17: 45-56, 1983.
16. Yao ZY, Jia Z, Xie YH, Zhang LL, Zhang HS, Wu WQ, Zhang CK and Gan LJ: Analgesic effect of dezocine in different doses on elderly patients undergoing abdominal operation under general anesthesia and its influence on stress response to postoperative tracheal extubation. Eur Rev Med Pharmacol Sci 21: 5223-5229, 2017.
17. Cho JS, Lee MH, Kim SI, Park S, Park HS, Oh E, Lee JH and Koo BN: The Effects of perioperative anesthesia and analgesia on immune function in patients undergoing breast cancer resection: A prospective randomized study. Int J Med Sci 14: 970-976, 2018.
18. Sun HL, Dong YC, Wang CQ, Qian YN and Wang ZY: Effects of postoperative analgesia with the combination of tramadol and lornoxicam on serum inflammatory cytokines in patients with gastric cancer. Int J Clin Pharmacol Ther 52: 1023-1029, 2014.
19. McEvoy MD, Scott MJ, Gordon DB, Grant SA, Thacker JKM, Wu CL, Gan TJ, Mythen MG, Shaw AD and Miller TE; Perioperative Quality Initiative (POQI) I Workgroup: American Society for Enhanced Recovery (ASER) and Perioperative Quality Initiative (POQI) joint consensus statement on optimal analgesia within an enhanced recovery pathway for colorectal surgery: Part 1-from the preoperative period to PACU. Perioper Med (Lond) 6: 8, 2017.
20. Rose MA and Kam PC: Gabapentin: Pharmacology and its use in pain management. Anaesthesia 57: 451-462, 2002.
21. Viscusi ER, Grond S, Ding L, Danesi H, Jones JB and Sinatra RS: A comparison of opioid-related adverse events with fentanyl iontophoretic transdermal system versus morphine intravenous patient-controlled analgesia in acute postoperative pain. Pain Manag 6: 19-24, 2016.
22. Bijur PE, Mills AM, Chang AK, White D, Restivo A, Persaud S, Schechter CB, Gallagher EJ and Birnbaum AJ: Comparative effectiveness of patient-controlled analgesia for treating acute pain in the emergency department. Ann Emerg Med 70: 809-818. e2, 2017.
23. Loscovich A, Briskin A, Fadeev A, Grisaru-Granovsky S and Halpern S: Emergency cesarean section in a patient with Fontan circulation using an indwelling epidural catheter. J Clin Anesth 18: 631-634, 2006.
24. Yamada K, Abe Y, Satoh S, Yanagibashi Y, Hyakumachi T and Masuda T: Large increase in blood pressure after extubation and high body mass index elevate the risk of spinal epidural hematoma after spinal surgery. Spine 40: 1046-1052, 2015.
25. Britt T, Sturm R, Ricardi R and Labond V: Comparative evaluation of continuous intercostal nerve block or epidural analgesia on the rate of respiratory complications, intensive care unit, and hospital stay following traumatic rib fractures: A retrospective review. Local Reg Anesth 8: 79-84, 2015.
26. Sprenger C, Eichler IC, Eichler L, Zöllner C and Büchel C: Altered signaling in the descending pain-modulatory system after short-term infusion of the μ-opioid agonist remifentanil. J Neurosci 38: 2454-2470, 2018.
27. Ovari A, Bicker I, Machmueller S, Schuldt T, Sauer M, Soltesz S, Noeldge-Schomburg G, Mlynski R and Mencke T: Sevoflurane at 1.0 MAC together with remifentanil and propofol produces clinically acceptable intubation conditions at the vocal cords: A prospective randomized study. J Int Med Res 45: 1098-1108, 2017.
28. Wang HY, Ting CK, Liou JY, Chen KH, Tsou MY and Chang WK: A previously published propofol-remifentanil response surface model does not predict patient response well in video-assisted thoracic surgery. Medicine (Baltimore) 96: e6895, 2017.
29. de Hoogd S, Ahlers SJGM, van Dongen EP, van de Garde EMW, Daeter EJ, Dahan A, Tibboel D and Knibbe CAJ: Randomized controlled trial on the influence of intraoperative remifentanil versus fentanyl on acute and chronic pain after cardiac surgery. Pain Pract 18: 443-451, 2018.
30. Trescot AM, Datta S, Lee M and Hansen H: Opioid pharmacology. Pain Physician 11: 133-153, 2008.