Clinical Trial/Experimental Study

Medicine®

OPEN

Efficacy of oxycodone in intravenous patient-controlled analgesia with different infusion modes after laparoscopic radical surgery of cervical cancer a prospective, randomized, double-blind study

Yejing Zhu, PhD, Kangjie Xie, Master of Medical Science, Junbo Yuan, Master of Medical Science, Bin Gu, Master of Medical Science, Yanhong Lian, Bachelor of Medical Science, Huidan Zhou, Master of Medical Science*, Jun Fang, Bachelor of Medical Science*

Abstract

Backgroud: The aim of this study was to compare the analgesic and adverse effects of oxycodone with 3 different infusion modes on postoperative pain after laparoscopic radical surgery of cervical cancer.

Methods: Ninety patients undergoing laparoscopic radical surgery of cervical cancer were randomly divided into 3 groups: Group A (continuous infusion with 0.01 mg/kg/h and a bolus dose with 0.03 mg/kg), Group B (a bolus dose with 0.03 mg/kg) and Group C (PCA was administered as a time-scheduled decremental continuous infusion based on lean body mass). A blinded observer recorded Visual Analogue Scale (VAS), Ramsay sedation score (RSS), infused cumulative dose of oxycodone and side effects at 1, 6, 12, 24, and 48 hours postoperatively, and satisfaction during the postoperative 48 hours.

Results: There were significant differences in the VAS pain score when resting or coughing among 3 groups at 1, 6 and 48 hours postoperatively ($P < .05$). VAS was significantly higher in Group B than in Group A and C until postoperative 1, 6, and 48 hours ($P < .05$). There were significant differences in cumulative PCA dose among the 3 groups at 1 and 48 hours postoperatively ($P < .05$). Group C showed significantly less amount of cumulative PCA dose compared to other 2 groups at 1 hour, whereas cumulative PCA dose of Group A at 48 hours was significantly more than other 2 groups ($P < .05$). There were no significant differences in postoperative nausea and vomiting, FAS, muscle chilling score and RSS among 3 groups at 1, 6, 12, 24 and 48 hours postoperatively. In addition, there was no difference in overall satisfaction during 48 hours postoperatively among 3 groups.

Conclusions: Oxycodone provides significant analgesic effect in 3 different infusion modes over 48 hours after laparoscopic radical surgery of cervical cancer, and a time-scheduled decremental continuous infusion of oxycodone can become a better choice for patients after surgery of cervical cancer.

Abbreviations: ASA = American Society of Anesthesiologists, BMI = body mass index, FAS = functional activity score, MAP =mean arterial pressure, SpO2 = peripheral oxygen saturation, PCA = patient-controlled analgesia, VAS = visual analogue scale.

Keywords: laparoscopic radical surgery of cervical cancer, oxycodone, patient-controlled analgesia, postoperative pain

1. Introduction

Over the past few decades, the prevalence of laparoscopic radical surgery of cervical cancer has significant increased due to the better hemostatic control, improvement in surgical technique, and wider indications for early-stage cervical cancer.[1] However, severe under-treated postsurgical pain may delay mobilization, prolonged hospital stay, decrease patient satisfaction, require hospital re-admission and set the stage for chronic postsurgical pain syndromes.[2,3]

In recent decades, continuous or bolus infusions of different opioids have been widely used in patient-controlled analgesia (PCA) after many kinds of surgery.[4] However, an increase in analgesic-related side effects, such as respiratory depression, pruritus, hallucinations and post-operative nausea and vomiting (PONV) has also been reported. When oxycodone was introduced into clinical use, its highly effective analgesic and safety began to emerge. It is a semisynthetic opioid that may be an agonist of the central and peripheral κ as well as μ-opioid receptors. Many studies and trials demonstrate that oxycodone

Editor: Helen Gharaei.

This study was supported by the Natural Science Foundation of Zhejiang Province (LQ15H020001).

The authors have no conflicts of interest to disclose.

Department of Anesthesia, Cancer Hospital of the University Chinese Academy of Sciences, Hangzhou, Zhejiang Province, PR China.

* Correspondence: Huidan Zhou, Jun Fang, Department of Anesthesiology, Cancer Hospital of University of Chinese Academy of Science, No. 1 Banshan East Road, Hangzhou 310022, PR China (e-mail: zhdzxf@163.com, fangjun477@zjcc.org.cn).

Medicine (2019) 98:34(e16810)

Received: 31 January 2019 / Received in final form: 29 June 2019 / Accepted: 22 July 2019

http://dx.doi.org/10.1097/MD.0000000000016810

showed comparable effects for pain relief and lower incidence of side effects compared to classical opioids like morphine, fentanyl or alfentanil.[5–7] Nine percent of German hospitals use oxycodone for patient-controlled analgesia (PCA) following surgery.[8] Our group has confirmed that oxycodone showed surgery comparable effects with fentanyl in painless artificial abortion, and the incidence of intraoperative respiratory depression and hypoxemia is significantly lower than fentanyl.[9]

However, the administration of oxycodone at too high a dose to patients sensitive to opioids may cause serious side effects, such as respiratory depression, bradycardia, apnea, hypotension, circulatory collapse, and death. Therefore, the safe and recommended doses of oxycodone must be carefully determined. To the best of our knowledge, no comprehensive data exist regarding recommended doses of oxycodone in patients after laparoscopic radical surgery of cervical cancer.

In this prospectively, randomized, double-blind study, we compared the analgesic efficacy, adverse events, and patient satisfaction ratings of oxycodone with different infusion modes in patients experiencing moderate to severe pain after laparoscopic radical surgery of cervical cancer. We tried to explore the optimal dose and mode application of oxycodone.

2. Methods

2.1. 2.1 Subjects

This prospective study was conducted after receiving approval from the Human Research Ethics Board of Zhejiang Cancer Hospital, Hangzhou. A signed written informed consent document was obtained from each patient prior to participation. We collected patients in our institute from July 2016 to December 2017. One hundred patients were enrolled in our study who underwent laparoscopic radical surgery of cervical cancer and belonged to the American Society of Anesthesiologists (ASA) physical status class I or II. All female patients aged 18 to 65 years were included. Exclusion criteria were patients who had used preoperative acetaminophen or nonsteroidal anti-inflammatory drugs or opioids, patients who had a chronic pain, mental illness or existence of severe cardiovascular or cerebrovascular disease, patients who were allergic to opioids or other known drug, patients who had abnormal liver and kidney function, patients who were inappropriate candidates for PCA and patients who had communication disability.

2.2. Treatment

On the day before surgery, demographic and medical data, including the subject's age, body mass index (BMI) and history of diseases, were collected. The patients were not given any sedative, analgesic, antemetic or anti-itching drugs 24 hours before the operation. Meanwhile, all patients were instructed about the use of PCA system (Wireless analgesic pump, Renxian Medical, Jiangsu Province, China).

Subjects were randomly divided into 3 groups, by blinded researchers, according to a computer-generated simple randomization code, and all groups received intravenous PCA with 50 mg oxycodone (Oxycodone 10 mg/1 mL, Mundipharma, Limburg an der Lahn, Germany) and 95 ml 0.9% normal saline. Group A received oxycodone with continuous infusion of 0.01 mg/kg/h and 0.03 mg/kg bolus dose, Group B received oxycodone with 0.03 mg/kg bolus dose, and Group C was administered as a time-scheduled decremental continuous infusion based on lean body mass.[7] The rate of PCA, loading dose, and demand dose were calculated based on the lean body mass (LBM), which was calculated using Hume's formula :[10]

LBM(kg) = {0.29569 × weight (kg)}+ {0.41813 × height (cm)}− 43.2933.

Loading doses, demand doses, and background infusion rates were as follows:

Loading dose (mL) = LBM(kg) × 0.1 mL

Demand (bolus) dose (mL) = LBM(kg) × 0.04 mL.

Background infusion rate (BIR) is described as follows:

First 6 hours BIR after operation (mL/h)= LBM(kg) × 0.1 mL/h

6 to 24 hours BIR after operation (mL/h)= LBM(kg) × 0.02 mL/h

24 to 48 hours BIR after operation (mL/h)= LBM(kg) × 0.01 mL/h.

Both subjects and data collectors were blinded to group allocation except the attending anesthetist.

Anesthesia was standardized in all groups. The patients were transported to the operation room without preanesthetic medication. After entering the operating room, patients were monitored using standard monitoring devices. Penehyclidine hydrochloride was administrated before anesthesia induction. Anesthesia was induced by the intravenous injection of 2 mg/kg propofol, 0.5 μg/kg sufentanil and 0.8 mg/kg rocuronium bromide (Esmeron, Organon, Netherlands). Following endotracheal intubation, oxygen and air were supplied at a fraction of inspired oxygen (FiO_2) of 0.4. After tracheal intubation, anesthesia was maintained with infusion of propofol (4–8 mg/kg/h), remifentanil (0.05–0.4 μg/kg/min) and cisatracurium (1–2 mg/kg/min) according to clinical needs. Then 0.25 mg palonosetron was injected intravenously. Group A and B were administered with 0.05 mg/kg oxycodone as a loading dose 10 minutes before the end of the surgery. Group C was administered with a calculated loading dose of oxycodone as we mentioned. Neuromuscular blockade was reversed with 0.5 mg of atropine and 1 mg of neostigmine. After surgery, patients were extubated, provided their vital signs were within normal limits, and were transferred to the post anesthesia care unit.

2.3. Assessment

Pain level, cumulative dose, sedation scale, adverse effects and satisfaction were evaluated and recorded at 1, 6, 12, 24, and 48 hours postoperatively. The level of pain was measured at movement by the visual analogue scale (VAS). Patients drew a point on a line, with scores ranging from 0 (no pain) to 10 (worst pain possible). The level of sedation was evaluated by the Ramsay score (RSS). A patient who was anxious and agitated, restless, or both had a score of 1; a patient cooperative, oriented, and tranquil a score of 2; a patient responsive to commands only a score of 3; a patient asleep with a brisk response to light glabellar tap or loud auditory stimulus a score of 4; a patient asleep with sluggish response to light glabellar tap or loud auditory stimulus a score of 5, and a patient asleep with no response to light glabellar tap or loud auditory stimulus a score of 6. For the level of nausea and vomiting, a score from 0 to 10 was given. A score of 0 was given if the patient had no nausea or vomiting, and a score of 10 was given if the patient had severe nausea and vomiting. Functional activity score (FAS) scores from 0 to 2 to evaluate functional activity. A score of 0 was given if the patient had no activity limitation, and a score of 2 was given if the patient had severe activity limitation. Severe activity limitation means the difficulty or need of assistance for basic activities everyone is expected to perform independently: washing, getting dressed,

feeding, getting in and out of bed, using the toilet.[11] Muscle chill was assessed by a score from 0 to 3. Zero represented no muscle chilling, whereas 1 meant face and neck muscle fibrillation. If more than 2 sets of muscles were chilled, the score was 2, and whole-muscle tremor with bed shaking scored 3. The patient's satisfaction with PCA during the 48 hours postoperatively was assessed according to the following scale: 1, very satisfactory; 2, satisfactory; 3, neutral; 4, unsatisfactory; 5, very unsatisfactory.

2.4. Statistical Analysis

We use SPSS 20.0 software for sample size analysis. A sample size of 30 in each group was determined to be required for a power of 0.90 and an a-value of 0.05. The primary end point was to compare the analgesic efficacy oxycodone with different infusion modes. Secondary outcomes were incidences of side-effects and patients' satisfaction. Categorical data were assessed with the χ^2 test. Normally distributed continuous variables were analyzed with one-way analysis of variance. Non-normally distributed data were further analyzed using the Mann–Whitney or Kruskal–Wallis H test. Lastly, P values $<.05$ were considered statistically significant.

3. Results

One hundred patients were assessed for eligibility. Six patients refused to participate, and 4 patients did not meet inclusion criteria in the study. Ninety patients were randomly divided into 3 groups. During the surgery, 5 patients required conversion to open surgery, and 2 patients suffered massive hemorrhage (>500 ml). Finally, 83 patients were studied per protocol for the planned preoperative and postoperative period (Fig. 1). Clinical characteristics and intraoperative data are shown in Table 1. There were no significant differences in age, weight, height, BMI and duration of surgery among subjects in Groups A, B, and C (Table 1).

As shown in Figure 2, there were significant differences in the VAS pain score when resting or coughing among 3 groups at 1, 6, and 48 hours postoperatively. Whatever resting or coughing, Group B had a higher VAS than Groups A and C at 1, 6 and 48 hours, ($P<.05$), whereas Groups A and C showed no significant differences. Five patients in Group B, 2 patients in Group A and 3 patients in Group C reported insufficient analgesia and requested additional analgesics, but the differences were not significant ($P=.91$).

The cumulative PCA doses were measured at 1, 6, 12, 24, and 48 hours after the operation. There were significant differences among 3 groups at 1 and 48 hours after surgery, and Group C showed significantly less amount of cumulative PCA dose compared to other 2 groups at 1 hour. Finally, cumulative dose of Group A at 48 hour was significantly more than other 2 groups ($P<.05$, Fig. 3), whereas Groups B and C showed no significant difference.

Main adverse events were reported in Table 2. The incidence of postoperative nausea and vomiting in Group A was higher than other 2 groups during the 48 hours postoperatively, but there were no differences among 3 groups at 1, 6, 12, 24, and 48 hours postoperatively. However, 1 patient experienced moderate vomiting and was administered metoclopramide 10 mg i.m in each of Group B and C, and 2 patients experienced severe vomiting and requested terminating PCA use in Group A. As shown in Table 2, there were no statistically significant differences in FAS and muscle chilling score among 3 groups at 1, 6, 12, 24, and 48 hours postoperatively. Otherwise, no one reported respiratory depression in 3 groups.

Sedation grade was expressed using the Ramsay score, and there were no differences among 3 groups at 1, 6, 12, 24, and 48 hours postoperatively (Fig. 4). In addition, there was no difference in overall satisfaction during the 48 hours postoperatively among 3 groups (Table 3).

4. Discussion

There are 2 important observations in our study. First, oxycodone provided significant analgesic effect in 3 different infusion modes over 48 hours after laparoscopic radical surgery of cervical cancer. Second, a time-scheduled decremental continuous infusion of oxycodone can become a better choice for patients after surgery of cervical cancer.

Cervical cancer is one of the leading causes of cancer and cancer-related deaths among women worldwide, with an estimated 527,600 new cases and 265,700 related deaths.[12] The standard treatment for women diagnosed with cervical cancer is radical hysterectomy and pelvic lymphadenectomy. Laparoscopic radical surgery of cervical cancer becomes a better choice due to less surgical trauma. But many female patients still describe their abdominal pain as "severe" or "extreme" after surgery. It means the visceral pain component is a large contributor to a patient's overall postoperative pain. Most opioid drugs are commonly used to treat pain by targeting μ-receptors. Regarding to specific features of visceral pain, the κ-opioid receptor plays an important role in the mediation of pain.[13] As we know, oxycodone is an agonist of selective μ-opioid receptor, and also binds to κ-opioid receptors in the brain as well.[14] Previous studies have shown that oxycodone has a good therapeutic effect on visceral pain and acute postoperative pain.[5,15,16] In our study, the VAS score of most patients was lower than four whatever resting or coughing, which was in line with previous studies.

However, the recommended doses of oxycodone after laparoscopic radical surgery of cervical cancer are yet to be established. We planned to evaluate the analgesic efficacy and tolerability of intravenous oxycodone with different infusion modes in patients after laparoscopic radical surgery of cervical cancer. It is thought that bolus dose infusion of PCA allows patients to self-administer small boluses of analgesic and provide better titration, whereas a background infusion of PCA can improve the level of analgesia and reduce breakthrough pain in the postoperative period.[17] Recent studies evaluating the effect of postoperative analgesia using the concomitant background infusion of oxycodone, still had not provided reliable adequate analgesia including PCA bolus and a background infusion. Meanwhile, a routine fixed-rate background infusion increases the analgesic dosage and the incidence of adverse respiratory events and postoperative nausea and vomiting (PONV) in the postoperative period, which was common and relatively long-lasting.[18,19] Kim et al reported that a time-scheduled decremental continuous infusion provided sufficient analgesic effect without increasing side effects.[20] Thus, we designed to compare 3 infusion modes to find an optimal infusion of oxycodone.

The analgesic effect was measured with VAS and patient satisfaction. VAS is a practical and familiar assessment of pain intensity during the management of postoperative pain. In our study, there were significant differences in the VAS when resting

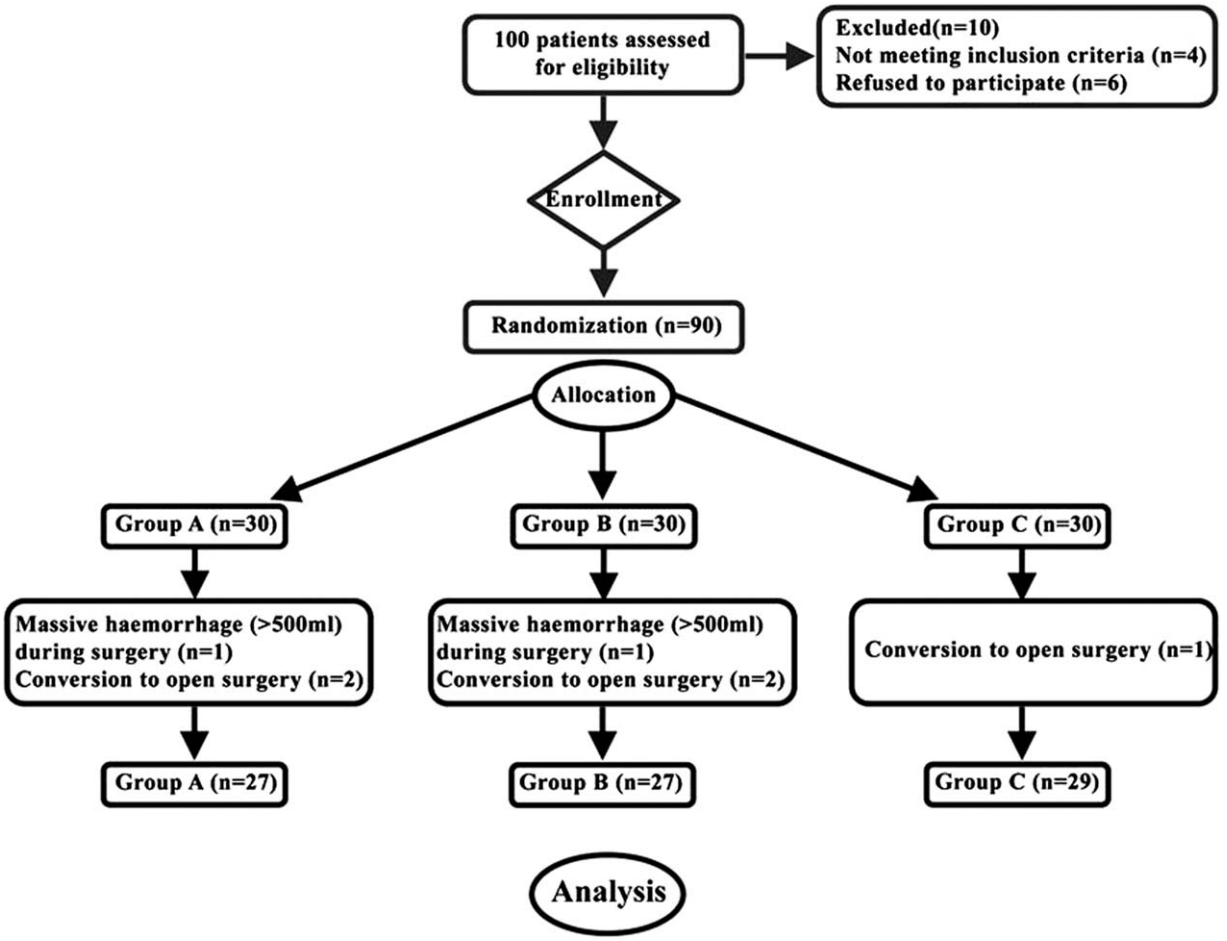

Figure 1. CONSORT flowchart.

or coughing among the 3 groups at 1, 6, and 48 hours postoperatively. Whatever resting or coughing, Group B had a higher VAS than Groups A and C at 1, 6, and 48 hours. and there were no differences between Group A and Group C at 1, 6, 12, 24, and 48 hours postoperatively. There was no statistically significant difference among 3 groups in terms of satisfaction 48 hours after the surgery. However, 2 patients in each group reported disappointment with the pain control. These results may indicate that although patients of Group B experienced a higher VAS, their overall satisfaction of 3 groups with the good analgesic effect presented almost similar ($P = .875$).

To be more specific, from the evaluation of VAS, our results seem to suggest that a background infusion of oxycodone, whatever a routine fixed-rate background infusion or a time-

Table 1

Clinical characteristics and intraoperative data.

	Group A	Group B	Group C	*P*
Age (yr)	49.4 ± 9.9	50.4 ± 10.3	49.8 ± 10.8	.886
Weight (kg)	56.70 ± 8.31	58.7 ± 7.97	56.81 ± 6.58	.571
Height (cm)	158.04 ± 5.21	156.59 ± 6.78	157.39 ± 5.58	.734
BMI (kg/m^2)	22.75 ± 3.40	23.94 ± 2.99	22.98 ± 2.83	.372
MAP (mmHg)	83.33 ± 7.03	82.22 ± 6.74	82.48 ± 6.88	.589
SpO2 (%)	99.51 ± 0.80	99.52 ± 1.05	99.48 ± 0.99	.919
BIS (mean)	47.93 ± 3.35	48.22 ± 3.78	47.07 ± 3.65	.638
Duration (min)				
Surgery	162.30 ± 18.99	158.15 ± 20.44	161.24 ± 19.77	.456
Anesthesia	207.07 ± 22.47	208.22 ± 25.16	210.66 ± 23.60	.647
Total propofol consumption (mg)	1182.37 ± 262.98	1221.64 ± 213.19	1196.46 ± 190.64	.875
Total remifentanil consumption (μg)	1885.64 ± 428.85	1853.68 ± 328.53	1833.00 ± 314.16	.979

The data expressed as mean ± standard deviation. There were no significant differences among 3 groups.
BMI = body mass index, BIS = bispectral index, MAP = mean arterial pressure, SpO2 = peripheral oxygen saturation.

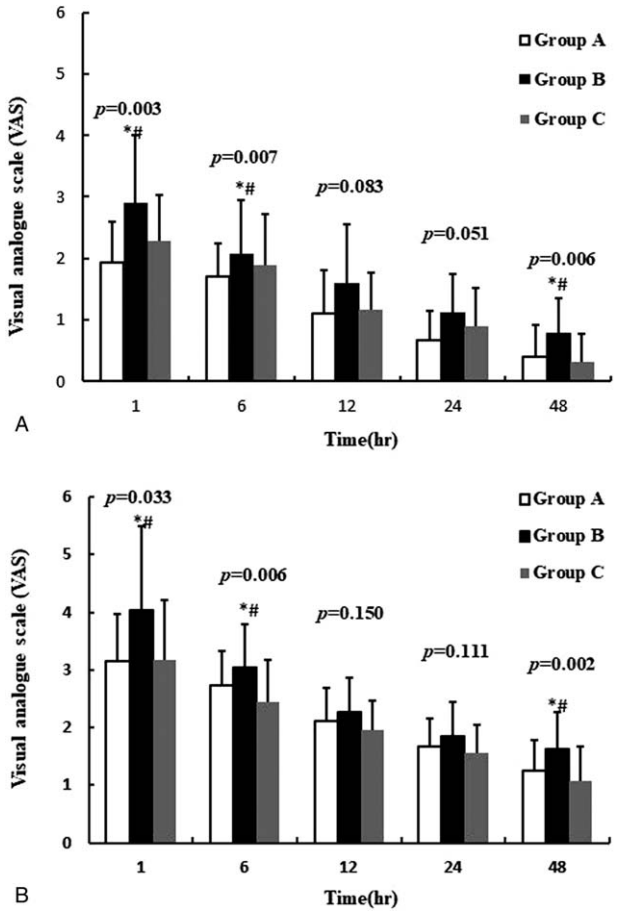

Figure 2. Visual analogue scales (VAS) of pain during resting (A) and coughing (B) at 1, 6, 12, 24, and 48 hours after the surgery. Means and standard deviation (SD) are shown. There were significant differences in the VAS pain score when resting or coughing among 3 groups at 1, 6, and 48 hours postoperatively ($P < .05$). Compared with Group A, * $P < .05$. Compared with Group C, $^{\#}P < .05$. VAS = visual analogue scale.

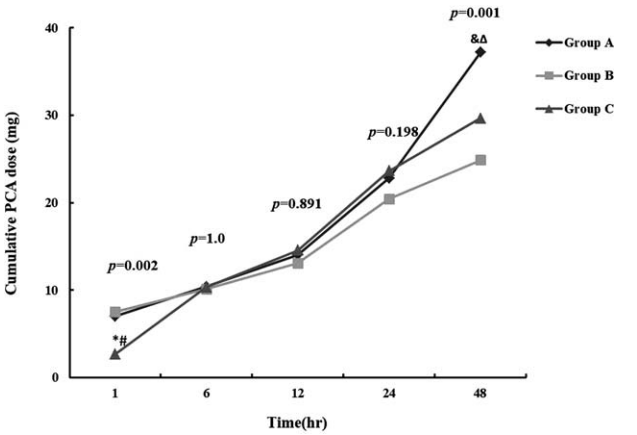

Figure 3. Cumulative patient-controlled analgesia dose measured between 1 and 48 hours after the operation. Means and standard deviation are shown. There were significant differences among 3 groups at 1 and 48 hours postoperatively ($P < .05$). Compared with Group A at 1 hour, * $P < .05$. Compared with Group B at 1 hour, $^{\#}P < .05$. Compared with Group B at 48 hour, $^{\&}P < .05$. Compared with Group C at 48 hours, $^{\Delta}P < .05$. PCA = patient-controlled analgesia.

scheduled decremental continuous infusion, could be more efficient compared with bolus infusion of PCA in postoperative pain control. Even so, we need to consider the cumulative doses of oxycodone in 3 groups. We found that Group C showed significantly less amount of cumulative dose compared to other 2 groups at 1 hour and cumulative dose of Group A at 48 hours was significantly more than other 2 groups finally. The pain management during postoperative initial phase is critical. Most patients complained of acute pain at 1 hour after the operation. Severe acute pain may lead to chronic pain. These results implies that pure bolus infusion mode by patient-controlled does not reduce dosages of oxycodone and also does not acquire lower VAS during postoperative initial phase. Meanwhile, compared with a routine fixed-rate background infusion mode, a time-scheduled decremental continuous infusion mode provides

Table 2

Postoperative adverse events during 48 hours.

Time	Observation indexes	Group A	Group B	Group C	*P*
1 hour	FAS	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	–
	Muscle chilling	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	–
	Nausea and vomiting	0.17 ± 0.32	0.15 ± 0.36	0.10 ± 0.41	.890
6 hours	FAS	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	–
	Muscle chilling	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	–
	Nausea and vomiting	0.15 ± 0.6	0.11 ± 0.32	0.10 ± 0.31	.918
12 hours	FAS	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	–
	Muscle chilling	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	–
	Nausea and vomiting	0.26 ± 0.94	0.07 ± 0.27	0.07 ± 0.26	.609
24 hours	FAS	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	–
	Muscle chilling	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	–
	Nausea and vomiting	0.19 ± 0.48	0.07 ± 0.27	0.07 ± 0.26	.385
48 hours	FAS	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	–
	Muscle chilling	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	–
	Nausea and vomiting	0.11 ± 0.32	0.07 ± 0.27	0.07 ± 0.26	.871

The data expressed as mean ± standard deviation. There were no significant differences among 3 groups.
FAS = functional activity score.

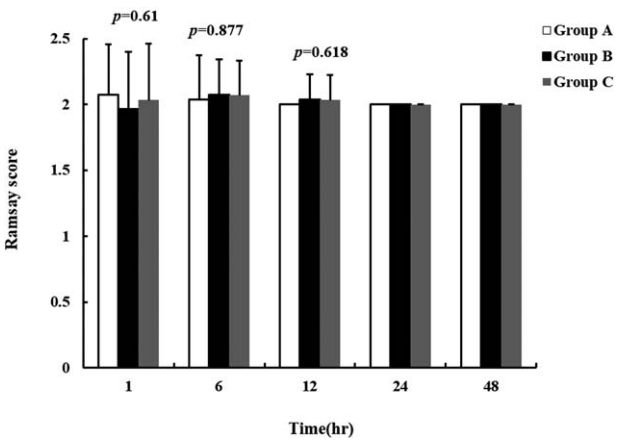

Figure 4. Ramsay score (RSS) of patients between 1 and 48 hours after the operation. Means and standard deviation (SD) are shown. There were no significant differences among 3 groups after surgery, RSS = Ramsay score.

Table 3

Satisfaction of patients at the postoperative 48 hours.

Satisfaction	Group A	Group B	Group C
Very satisfied	12 (44%)	9 (33%)	14 (48%)
Satisfied	10 (37%)	11 (40%)	11 (37%)
Neutral	3 (11%)	5 (18%)	2 (7.0%)
Dissatisfied	2 (7.4%)	2 (7.4%)	2 (6.9%)
Very dissatisfied	0 (0%)	0 (0%)	0 (0%)

Data are number of patients or %. There were no significant differences among 3 groups ($P = .875$).

similar analgesia and less dosages of oxycodone at 1 hour after the operation.

Many studies have shown that side effects of oxycodone include dizziness, nausea, vomiting, drowsiness, and fatigue.[18,19] Although there were no differences among 3 groups, the incidence of PONV in Group A was higher than other 2 groups during the 48 hours postoperatively. Two patients experienced severe vomiting and requested terminating PCA use in Group A and one patient experienced moderate vomiting and was administered metoclopramide 10 mg i.m in each of Group B and C. It means that the longer duration and larger dose administration of oxycodone in Group A induce more frequent nausea and vomiting. For the Ramsay sedation score, there was no significant difference among 3 groups, indicating that the sedative effect of oxycodone is similar in 3 groups, with the feature of increased drowsiness. Some studies showed that oxycodone produced significantly more dizziness and respiratory depression, but in our study, there were no statistically significant differences in FAS and muscle chilling score among 3 groups, and no one reported respiratory depression in 3 groups. We guess that the dose administration of oxycodone is lower than previous studies.

There were several limitations in present study. First, there were only 83 patients included in our analysis. Second, this study was performed at one center. A multi-center trial through investigate more various populations from different center would address more clinical outcome parameters in the future. Third, it was found that some factors are associated with postoperative pain in previous studies. Depression, anxiety, and poor functional stress are some examples of factors which have an association with acute postoperative pain. We would focus on these factors in our further extensive studies. However, despite the aforementioned limitations, we were able to demonstrate an effective analgesic effect of oxycodone with different infusion modes. We also show a time-scheduled decremental continuous infusion mode of oxycodone can be a new better choice of postoperative analgesia for patients after laparoscopic radical surgery of cervical cancer.

Acknowledgments

We thank the individuals and their families who participated in this study.

Author contributions

Conceptualization: Jun Fang.
Data curation: Kangjie Xie, Yanhong Lian.
Investigation: Kangjie Xie.
Methodology: Junbo Yuan.
Resources: Bin Gu.
Project administration: Huidan Zhou.
Software: Jun Fang.
Writing – original draft: Yejing Zhu.
Writing – review & editing: Yejing Zhu.

References

[1] Laterza RM, Uccella S, Casarin J, et al. Recurrence of early stage cervical cancer after laparoscopic versus open radical surgery. Int J Gynecol Cancer 2016;26:547–52.
[2] Argoff CE. Recent management advances in acute postoperative pain. Pain Pract 2014;14:477–87.
[3] Daher M. Pain relief is a human right. Asian Pac J Cancer Prev 2010;11 (Suppl 1):97–101.
[4] Allen S, DeRoche A, Adams L, et al. Effect of epidural compared to patient-controlled intravenous analgesia on outcomes for patients undergoing liver resection for neoplastic disease. J Surg Oncol 2017; 115:402–6.
[5] Lenz H, Sandvik L, Qvigstad E, et al. A comparison of intravenous oxycodone and intravenous morphine in patient-controlled postoperative analgesia after laparoscopic hysterectomy. Anesth Analg 2009; 109:1279–83.
[6] 2014;Hwang BY, Kwon JY, Kim E, et al. Oxycodone vs. fentanyl patient-controlled analgesia after laparoscopic cholecystectomyJT Int J Med Sci. 11:658–62.
[7] Kwon YS, Jang JS, Lee NR, et al. A Comparison of oxycodone and alfentanil in intravenous patient-controlled analgesia with a time-scheduled decremental infusion after laparoscopic cholecystectomy. Pain Res Manag 2016;2016:7868152.
[8] Lassen CL, Link F, Lindenberg N, et al. Anesthesiological acute pain therapy in Germany: telephone-based survey. Der Anaesthesist 2013;62:355–64.
[9] Xie K, Zhang W, Fang W, et al. The analgesic efficacy of oxycodone hydrochloride versus fentanyl during outpatient artificial abortion operation: a randomized trial. Medicine 2017;96:e7376.
[10] Hume R. Prediction of lean body mass from height and weight. J Clin Pathol 1966;19:389–91.
[11] Berger N, Van Oyen H, Cambois E, et al. Assessing the validity of the Global Activity Limitation Indicator in fourteen European countries. BMC Med Res Methodol 2015;15:1.
[12] Torre LA, Islami F, Siegel RL, et al. Global Cancer in Women: Burden and Trends. Cancer Epidemiol Biomarkers Prev 2017;26:444–57.
[13] Staahl C, Christrup LL, Andersen SD, et al. A comparative study of oxycodone and morphine in a multi-modal, tissue-differentiated experimental pain model. Pain 2006;123:28–36.
[14] Ross FB, Smith MT. The intrinsic antinociceptive effects of oxycodone appear to be kappa-opioid receptor mediated. Pain 1997; 73:151–7.

[15] Staahl C, Dimcevski G, Andersen SD, et al. Differential effect of opioids in patients with chronic pancreatitis: an experimental pain study. Scand J Gastroenterol 2007;42:383–90.
[16] Koch S, Ahlburg P, Spangsberg N, et al. Oxycodone vs. fentanyl in the treatment of early post-operative pain after laparoscopic cholecystectomy: a randomised double-blind study. Acta Anaesthesiol Scand 2008;52:845–50.
[17] McCoy EP, Furness G, Wright PM. Patient-controlled analgesia with and without background infusion. Analgesia assessed using the demand: delivery ratio. Anaesthesia 1993;48:256–60.
[18] Kim NS, Kang KS, Yoo SH, et al. A comparison of oxycodone and fentanyl in intravenous patient-controlled analgesia after laparoscopic hysterectomy. Korean J Anesthesiol 2015;68:261–6.
[19] Park JH, Lee C, Shin Y, et al. Comparison of oxycodone and fentanyl for postoperative patient-controlled analgesia after laparoscopic gynecological surgery. Korean J Anesthesiol V 68 2015;153–8.
[20] Kim JY, Park SY, Chang HS, et al. The efficacy of the time-scheduled decremental continuous infusion of fentanyl for postoperative patient-controlled analgesia after total intravenous anesthesia. Korean J Anesthesiol 2013;65:544–51.