Oxycodone is superior to morphine for pain relief following peroral oesophageal myotomy: a prospective, randomized, controlled trial

Guohao Xie[1], Shuangyue Li[2,3], Min Zeng[1,3], Rui Zhou[1], Shengwen Song[1], Lihua Chu[1], Xiangming Fang[1]

[1]Department of Anaesthesiology, the First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China
[2]Department of Pain Management, Jiangwan Hospital, Shanghai, China
[3]Department of Anaesthesiology, Yinzhou Second Hospital, Ningbo, China

Videosurgery Miniinv 2022; 17 (4): 624–633
DOI: https://doi.org/10.5114/wiitm.2022.118544

Abstract

Introduction: *Patients underwent peroral endoscopic myotomy (POEM) for treating achalasia suffered with mild to moderate, sometimes even severe postoperative pain.*
Aim: *To evaluate the efficacy of oxycodone on postoperative analgesia of patients undergoing PEOM.*
Material and methods: *In this prospective, double-blinded, randomized, controlled trial, patients with achalasia were recruited and received 0.08 mg/kg oxycodone or morphine 15 min before the end of the POEM procedure. The short-form McGill questionnaire (SF-MPQ) was used to measure the postoperative pain at 0, 2, 6, 24, and 48 h after surgery, which included the visual analogue scale (VAS), the present pain intensity (PPI) scale, and the pain rating index (PRI).*
Results: *A total of 73 patients were included, of whom 36 received oxycodone, and 37 received morphine. Compared with morphine, patients received oxycodone were associated with lower VAS in the first 24 h postoperatively (1.64 ±0.76 vs. 2.14 ±1.23, p = 0.042) as well as PPI at 2 h (1.11 ±0.40 vs. 2.22 ±0.89, p < 0.001), 6 h (1.42 ±0.55 vs. 2.08 ±0.92, p < 0.001) and 24 h (1.06 ±0.23 vs. 1.30 ±0.46, p = 0.006). Patients who received oxycodone experienced lower sensory McGill pain score than those who received morphine at 2, 6, 24, and 48 h after surgery (p < 0.05). Significantly lowered affective McGill pain score was observed in the oxycodone group at 0, 2, and 24 h postoperatively. Regarding the PRI, the sum of both sensory and affective McGill pain scores, patients with oxycodone therapy were associated with better scores postoperatively.*
Conclusions: *Oxycodone appears to be superior to morphine in dealing with post-POEM pain, which has distinct visceral pain characteristics.*

Key words: *oxycodone, postoperative analgesia, short-form McGill questionnaire, peroral oesophageal myotomy, morphine.*

Introduction

Achalasia is caused by motor disorder of the lower oesophageal sphincter (LES), characterized by the incompetency of full relaxation of LES and stasis of food in the oesophagus [1]. The main clinical manifestations of the disease are dysphagia, reflux, weight loss, and post-sternum pain, which seriously affect the health and quality of life of patients.

Conventional treatments of achalasia include endoscopic botulinum injection, endoscopic balloon

Address for correspondence
Xiangming Fang, Department of Anaesthesiology, the First Affiliated Hospital, School of Medicine, Zhejiang University, Wenyi West Road 1367, Hangzhou City, Zhejiang Province, China, phone: +86 13857161019, e-mail: xmfang@zju.edu.cn

dilatation, and Heller operation under laparoscope, with either inaccurate effects or excessive trauma [1]. With the rapid development of endoscopic technology and related equipment, a more curative and less invasive procedure, peroral endoscopic myotomy (POEM), has become the main modality of treating achalasia in recent years. This procedure aims to decrease the tension of LES by endoscopic myotomy through the natural lumen from the mouth to the oesophagus [1].

Although POEM is described as a minimally invasive operation, mild to moderate acute pain is commonly observed in postoperative patients [2]. Moreover, Li *et al.* reported that the incidence of severe pain after POEM was as high as 10%, which affected the patients' rapid recovery and quality of life [3]. Post-POEM pain stems from the oesophagus and stomach and contains both somatic and visceral components. It involves not only the feeling of the location, intensity, and nature of pain (the sensory component of pain) but also the related unpleasant or disgusting emotional experience (the emotional component of pain) [4]. Post-POEM pain could affect the patient's eating, worsens the patient's mood, and increases postoperative complications and hospitalization time [5]. However, post-operative analgesia of POEM is not well investigated. The use of analgesic drugs reported in limited clinical observations includes opioids, nonsteroidal anti-inflammatory drugs, and paracetamols, which was mostly based on the experiences of clinicians in wards [2]. There is still a lack of related randomized controlled clinical trials.

Oxycodone is one of the widely used clinical opioids in treating intraoperative and postoperative acute pain, with efficacy equivalent to that of morphine. Both basic and clinical studies have confirmed that, as an agonist of both μ- and κ-receptors with high affinity, oxycodone is more effective than other commonly used opioid drugs (e.g. morphine and sufentanil) in relieving visceral pain, e.g. in smooth muscle organs like the stomach and oesophagus [6, 7].

Aim

We performed this randomized controlled clinical trial and aimed to evaluate the efficacy of oxycodone for postoperative analgesia of patients undergoing PEOM compared to equivalent morphine. In this study, we adopted the simplified McGill Pain Scale (SF-MPQ), a widely accepted tool for describing and measuring pain, with good reliability, validity, and sensitivity, to assess the overall visual analogue scale (VAS) of post-POEM pain, the present pain intensity scale (PPI), as well as the sensory score, affective score, and total score of the pain rating index (PRI) [8].

Material and methods

Study design

This was a single-centre, prospective, double-blinded, randomized, controlled trial, comparing the analgesia effect for POEM in patients intraoperatively receiving oxycodone or morphine. The study protocol was approved by the Ethics Committee of the First Affiliated Hospital, College of Medicine, Zhejiang University (reference number: 2018-775) and was registered with China Clinical Trial Registry (http://www.chictr.org.cn/, registration number: ChiCTR1800017476). Informed, written consent was obtained from each patient. The authors have read the CONSORT 2010 Statement, and the manuscript was prepared and revised according to the CONSORT 2010 Statement.

Patients

A total of 80 POEM procedures performed from August 2018 to November 2019 in the Department of Endoscopy, the First Affiliated Hospital, School of Medicine, Zhejiang University were analysed in this trial. Patients with a diagnosis of achalasia and symptoms with an Eckardt score > 3, and scheduled for elective POEM, were screened for the present study [1]. Inclusion criteria were as follows: aged from 18 to 60 years, American Society of Anesthesiologists physical class (ASA) of I–II, and body mass index (BMI) of 16–28 kg/m^2. We excluded patients with oesophageal/gastric varices, active gastrointestinal malignancy, pregnancy, those allergic to oxycodone or morphine, and those unable to provide informed consent. Patients with intraoperative complications such as oesophageal perforation, subcutaneous emphysema, pneumothorax, pneumomediastinum, pneumoperitoneum, and pleural effusion, which would affect postoperative pain evaluation, were also excluded.

Randomization and blinding

Enrolled patients were randomized to receive either 0.08 mg/kg oxycodone (oxycodone group) or 0.08 mg/kg morphine (morphine group) for postoperative analgesia. Randomization was performed using a computer-generated randomization sequence (http://www.randomizer.org) by an investigator not involved in patient care or perioperative assessment. An anaesthesia nurse, not involved in the study, received sealed opaque envelops that contained the allocation results and then prepare oxycodone or morphine in identical 20-ml syringes according to the allocation.

An anaesthesiologist, blinded to group allocation and not involved in the patients' care, perioperative assessment, or data collection, gave 0.08 mg/kg oxycodone or morphine by intravenous injection 15 min before the end of the operation.

Patients' follow-up and data collection were conducted by another investigator who was also blinded to the group allocation.

Preparation for POEM

Patients were maintained on a clear liquid diet for 48 h prior to the procedure. Patients were kept nil per os (NPO) after midnight on the day of the POEM. Prophylactic intravenous antibiotics and proton pump inhibitor therapy were initiated on the day of the procedure and continued during the postoperative hospitalization. Anti-coagulation and/or anti-platelet therapy was managed according to the current American Society of Gastrointestinal Endoscopy (ASGE) guidelines [2].

Anaesthesia management and intraprocedural monitoring for POEM

All procedures were performed under general anaesthesia with endotracheal intubation and positive pressure ventilation in the Endoscopy Unit.

After arrival, electrocardiogram, non-invasive blood pressure, and pulse oxygen saturation were monitored. After positioning the patient in the left lateral position, 0.05 mg/kg midazolam was administered for mild sedation. And then the esophagogastroduodenoscopy (EGD) was performed under topical anaesthesia of lidocaine prophylactically to remove food or liquid in the enlarged oesophagus to minimize the risk of aspiration.

After EGD, general anaesthesia was induced with propofol 1.5–2 mg/kg, fentanyl 2.5 μg/kg, and cisatracurium 0.15 mg/kg when the total volume of administrated crystalloid reached to 4 ml/kg intravenously. Intravenous propofol and remifentanil were used to maintain the anaesthesia and keep the bispectral index between 40 and 60. Meanwhile, the tidal volume was set as 6–8 ml/kg after intubation, and the ventilation frequency was adjusted to maintain an end-tidal carbon dioxide tension of 35–40 mm Hg.

A total of 0.08 mg/kg oxycodone or morphine was administered intravenously 15 min before the end of the procedure for postoperative analgesia. Pyridostigmine 1 mg and tropisetron 5 mg were injected after the completion of the operation to reverse the muscle relaxation and prevent postoperative nausea and vomiting (PONV). The patient was then transferred to a post-anaesthesia care unit (PACU) and was extubated after verifying sufficient recovery of consciousness and spontaneous respiration.

POEM procedure

POEM was performed for achalasia types I to III, unresolved esophagogastric junction outflow obstruction, and/or spastic oesophageal disorders. A high-definition gastroscope (GIF 290, Olympus, Tokyo, Japan), fitted with a transparent cap (Olympus, Tokyo, Japan), was used. Insufflating carbon dioxide was used throughout the procedure. Submucosal tunnelling was established from 10 to 15 cm above to 2 cm below the esophagogastric junction using an ERBE Endocut Q 3:1:1 current with either a triangle-tip knife (Olympus Tokyo, Japan) or Hybridknife (ERBE, Germany). Selective myotomy was performed according to manometric findings and achalasia subclass. A Coagrasper (FD410-R, Olympus, Tokyo, Japan) was used for pre-emptive coagulation of large vessels or haemostasis when needed. After completion of myotomy, the mucosal incision was closed using through-the-scope clips.

Data collection

The primary outcome was the short-form McGill questionnaire (SF-MPQ), which consists of a visual analogue scale (VAS) in the first 24 h postoperatively, present pain intensity (PPI) scale, and pain rating index (PRI) at 0, 2, 6, 24, and 48 h after surgery. The Chinese version of the PRI scale includes 15 descriptors, of which 11 items are for the sensory McGill pain score and 4 are for the affective McGill pain score (Appendix 1). The time point of hours postop-

eratively was defined as the timing from extubation in PACU.

The secondary outcome was the patients' satisfaction for postoperative analgesia evaluated by a Likert scale with 5 degrees, consisting of "extremely", "very much", "moderately", "a little", and "not at all".

When a patient's VAS ≥ 4, 50 mg of flurbiprofen was injected intravenously for rescue analgesia. The number of patients requiring rescue analgesia was also collected.

Postoperative adverse effects related to opiates, like VAS for PONV, VAS for drowsiness, VAS for headache, VAS for itching, number of hypoxaemia (defined as SpO_2 < 94% with 3 l/min supplementary oxygen through nasal catheter), and number of urinating disturbances, were recorded.

Ethics

This study was approved by the Ethics Committee of the First Affiliated Hospital, College of Medicine, Zhejiang University (reference number: 2018-775), and written informed consent was obtained from all participants in the trial. The trial was registered with China Clinical Trial Registry (http://www.chictr.org.cn/, registration number: ChiCTR1800017476).

Statistical analysis

The sample size required was calculated choosing a difference of 2.7 in VAS as the minimum desired difference between the 2 groups according to the pilot study. Considering a 10% dropout per group, at least 32 patients per group were needed to detect a significant difference of 2.7 in VAS with a power of 0.9 at a level of $\alpha = 0.05$ (two-sided hypothesis).

Statistical analysis was performed using SPSS 20.0 software (IBM Corp., Armonk, NY, USA). Numerical data were presented as numbers (percentage). The Pearson χ^2 test was used to examine the significance of the association between 2 variables in a contingency table. Variables with a normal distribution were presented as mean ± standard deviation (SD) and compared using analysis of *t*-test. A *p*-value of 0.05 (two-sided) was considered statistically significant.

Results

The flow diagram for this trial is shown in Figure 1. A total of 80 patients assessed for eligibility were enrolled; 7 were exclude because of subcutaneous emphysema (*n* = 4), oesophageal perforation (*n* = 2), and converted to laparoscopic surgery (*n* = 1). Eventually, 73 patients completed the study. Patient and operation characteristics are detailed in Table I, with no significant differences between the oxycodone group and the morphine group.

Short-form McGill questionnaire

The comparison of VAS in 24 h postoperatively between the 2 groups is demonstrated in Figure 2.

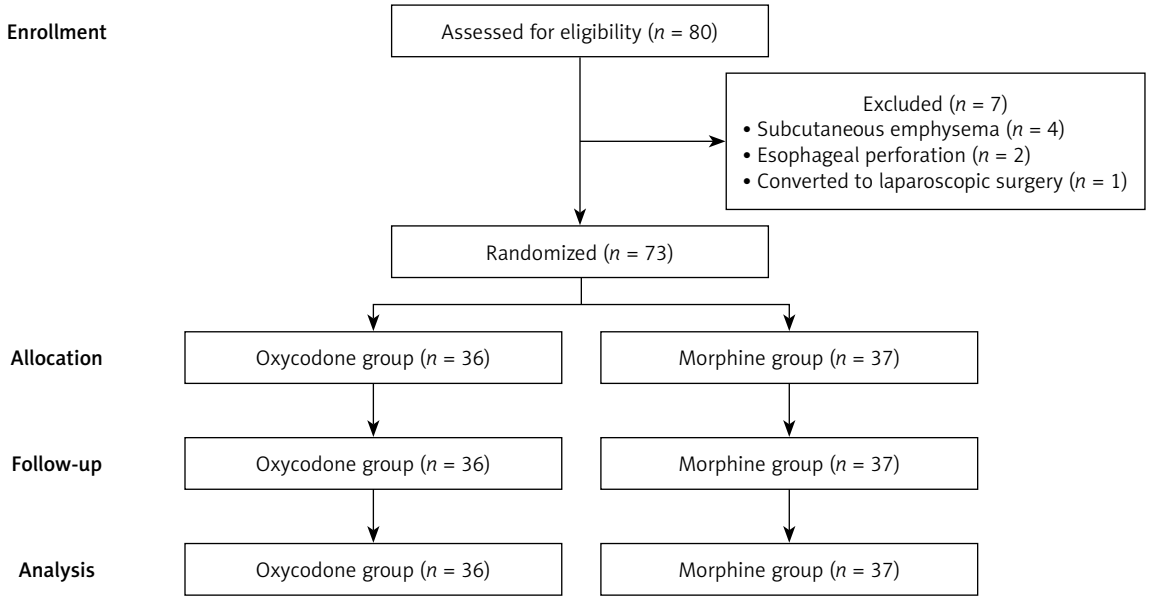

Figure 1. Patients' flow diagram

Table I. Patient characteristics

Variable	Oxycodone group	Morphine group	*P*-value
Number of patients (*n*)	36	37	
Age [years]	44.9 ±10.47	47.8 ±10.01	0.238
Gender (male)	15 (41.67)	13 (35.14)	0.634
BMI [kg/m^2]	22.37 ±3.39	23.01 ±3.59	0.446
ASA:			0.591
I	6 (16.67)	8 (21.62)	
II	30 (83.33)	29 (78.38)	
Preoperative thoracic pain or upper abdominal pain caused by achalasia:			
Number	5 (13.89)	6 (16.22)	0.980
VAS	0.25 ±0.69	0.27 ±0.69	0.901
Operation time [min]	82.78 ±64.19	72.68 ±61.55	0.495
Intraoperative bleeding [ml]	9.31 ±6.23	10.14 ±9.96	0.672
Intraoperative fentanyl consumption [μg]	235.03 ±45.38	243.11 ±39.54	0.421
Intraoperative remifentanil consumption [μg]	1480.56 ±894.69	1335.14 ±838.72	0.476
Intraoperative propofol consumption [mg]	651.36 ±325.08	598.43 ±304.72	0.475
Extubation time [min]	13.61 ±5.96	11.59 ±6.33	0.166
Total time in PACU [min]	27.61 ±9.51	28.68 ±10.35	0.649

Data are presented as mean ± standard deviation or number of patients (%). BMI – body mass index, ASA – American Society of Anesthesiologists, VAS – visual analogue scale, PACU – post-anaesthesia care unit.

Patients who received oxycodone therapy had lower VAS (1.64 ±0.76) than those who received morphine (2.14 ±1.23) (p = 0.042).

Compared with morphine treatment, oxycodone given intraoperatively was associated with lower PPI at 2 h (1.11 ±0.40 vs. 2.22 ±0.89, p < 0.001), 6 h (1.42 ±0.55 vs. 2.08 ±0.92, p < 0.001), and 24 h (1.06 ±0.23 vs. 1.30 ±0.46, p = 0.006) postoperatively (Figure 3).

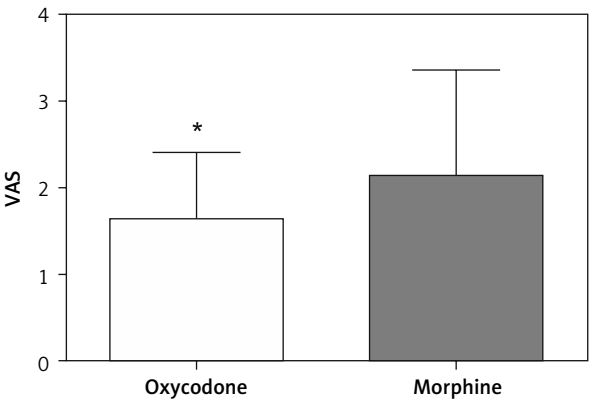

Figure 2. The comparison of VAS between the 2 groups in the first 24 h postoperatively. Patients who received oxycodone therapy had lower VAS than those who received morphine therapy

**P < 0.05 versus morphine group. VAS – visual analogue scale.*

Analyses of PRI including the sensory McGill Pain Score, affective McGill Pain Score, and the sum of both (PRI) are shown in Figure 4. Patients who received oxycodone experienced lower sensory McGill pain score than those who received morphine at 2 h (2.47 ±1.96 vs. 3.70 ±1.85, p = 0.007), 6 h (3.50 ±2.08 vs. 4.49 ±1.71, p = 0.030), 24 h (2.19 ±1.26 vs. 2.81 ±1.22, p = 0.037), and 48 h (1.22 ±0.90 vs. 1.70 ±0.85, p = 0.021) after surgery (Figure 4 A). There was also significantly lower affective McGill pain score in the oxycodone group than in the morphine group at 0 h (0.75 ±0.94 vs. 1.32 ±1.36, p = 0.039), 2 h (0.78 ±0.99 vs. 1.30 ±1.20, p = 0.047), and 24 h (0.44 ±0.61 vs. 0.84 ±0.87, p = 0.028) postoperatively (Figure 4 B). When referred to PRI, patients with oxycodone therapy were also associated with better score than those with morphine treatment at every follow-up time point (0 h: 2.17 ±2.18 vs. 3.38 ±2.53, p = 0.032; 2 h: 3.25 ±2.41 vs. 5.00 ±2.29, p = 0.002; 6 h: 4.61 ±2.60 vs. 5.76 ±2.02, p = 0.039; 24 h: 2.64

±1.50 vs. 3.65 ±1.59, p = 0.007; 48 h: 1.56 ±1.00 vs. 2.19 ±0.91, p = 0.006) (Figure 4 C).

Secondary outcomes

The rate of 'extremely' and 'very much' satisfaction degree was higher in patients receiving oxycodone intraoperatively (p = 0.047) (Table II). No statistically significant differences were seen in opiate-related complications and the number of patients requiring rescue analgesia, except VAS score for PONV, indicating that less PONV occurred in patients who received oxycodone (1.64 ±0.76 vs. 2.14 ±1.23, p = 0.042) (Table III).

Discussion

In this randomized, double-blind, controlled trial, intravenous oxycodone administered as a bolus of 0.08 mg/kg before the end of the POEM procedure showed a good analgesia effect post-operatively.

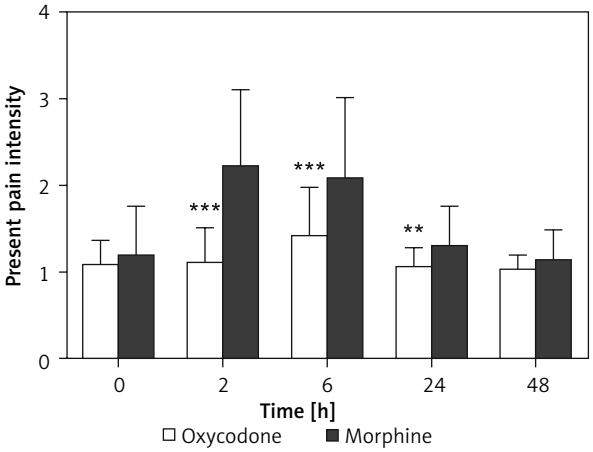

Figure 3. The comparison of PPI between the 2 groups at the 5 follow-up time points. PPIs were significantly lower in the oxycodone group than in the morphine group at 2, 6, and 24 h postoperatively

**P < 0.05 versus morphine group; **p < 0.01 versus morphine group; ***p < 0.001 versus morphine group. PPI – present pain intensity.*

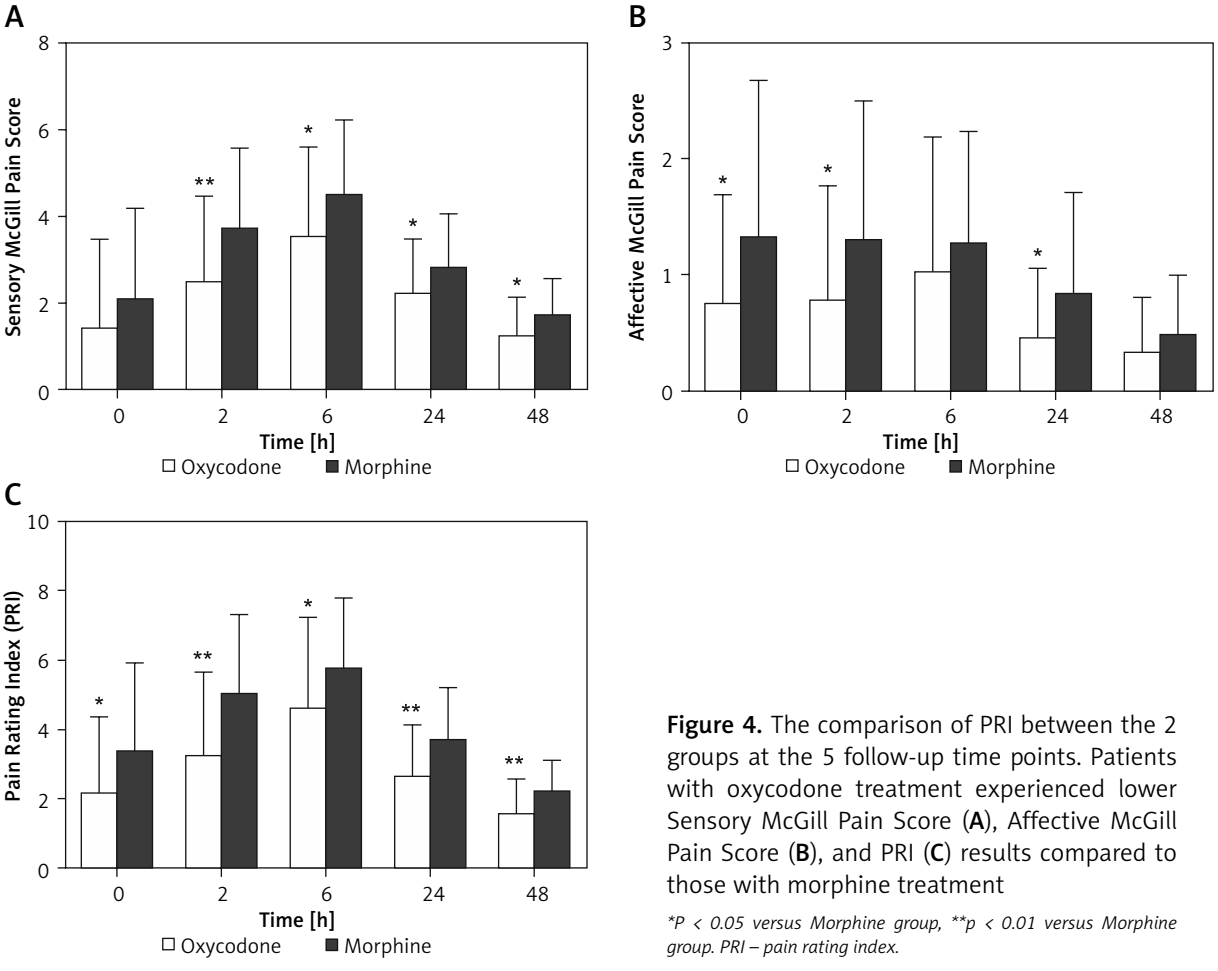

Figure 4. The comparison of PRI between the 2 groups at the 5 follow-up time points. Patients with oxycodone treatment experienced lower Sensory McGill Pain Score (**A**), Affective McGill Pain Score (**B**), and PRI (**C**) results compared to those with morphine treatment

**P < 0.05 versus Morphine group, **p < 0.01 versus Morphine group. PRI – pain rating index.*

Table II. Patients' satisfaction degree for postoperative analgesia

Variable	Oxycodone group	Morphine group	*P*-value
Number of patients (*n*)	36	37	0.047
Extremely	4 (11.11%)	1 (2.70%)	
Very much	25 (69.44%)	19 (51.35%)	
Moderately	7 (19.44%)	14 (37.84%)	
A little	0 (0%)	3 (8.11%)	
Not at all	0 (0%)	0 (0%)	

Data are presented as number of patients (%).

Table III. Opiate-related complications and rescue analgesia

Variable	Oxycodone group	Morphine group	*P*-value
Number of patients (*n*)	36	39	
VAS-score for PONV	1.64 ±0.76	2.14 ±1.23	0.042
VAS-score for drowsiness	1.06 ±0.63	0.81 ±0.78	0.144
VAS-score for headache	1.25 ±0.87	1.08 ±0.68	0.360
VAS-score for itching	0.31 ±0.75	0.22 ±0.71	0.603
SpO_2 < 94% (*n*)	2 (5.56%)	2 (5.71%)	0.978
Urinating disturbances (*n*)	4 (11.11%)	5 (13.51%)	0.755
Rescue analgesia (*n*)	2 (5.56%)	2 (5.71%)	0.978

Data are presented as mean ± standard deviation or number of patients (%). VAS – visual analogue scale.

Compared with intravenous morphine, oxycodone administration had better performances in SF-MPQ scores and overall satisfaction. To our knowledge, this is the first randomized controlled trial focussing on post-POEM analgesia.

It is well established that POEM is safe, feasible, and effective for achalasia treatment [9]. But mild to moderate acute pain is commonly observed in postoperative patients [2]. Pain of the oesophagus after POEM may be induced by mechanical, chemical, and thermal stimuli, ischaemia, and inflammation. The vagus nerve, afferent fibres of thoracic spinal cords, and the enteric nervous system are involved in the pain sensory and conduction process [10]. Pain of the oesophagus has a strong characteristic of visceral pain, which is difficult to locate and is accompanied by unpleasant emotional activities and visceral reaction [11]. Oxycodone is a dual-acting opioid μ-/κ-receptor agonist. Compared with classic μ-receptor agonists like morphine, it can effectively control both the somatic pain via μ-receptor and the visceral pain via κ-receptor in these patients [12, 13]. Therefore, oxycodone has advantages in analgesia after gastrointestinal surgeries. The present study has also confirmed this in endoscopic patients who received POEM procedure.

The SF-MPQ was first introduced by Mmezack *et al.* and validated in a great number of clinical studies on pain and analgesia [14–16]. It has 3 components, including the PPI, the PRI, and a VAS. The PRI contains the standard 15 word descriptors (11 sensory and 4 affective) with values of 0 (none) to 3 (severe). The sensory, affective, and total PRI score are derived from the sum of the intensity rank values of the 11 words chosen for sensory, the 4 words for affective, and all descriptors, respectively. In our study, the overall intensity of pain in the first 24 h postoperatively was assessed by the VAS. The results showed that, although intravenous morphine brought sufficient analgesia with a VAS of 2.14 ±1.23, patients who received intravenous oxycodone had lower VAS scores (1.64 ±0.76, $p < 0.05$). This is concomitant with Lenz *et al.*'s study, which found that the analgesic effect of oxycodone after hysterectomy was superior to that of morphine [17]. The PPI evaluated at predetermined time points represents the temporal dimension of post-POEM pain. It was found in our study that oxycodone performed

better than morphine in pain control at 2, 6, and 24 h after the procedure. Moreover, the PRI score was used to reflect the scope of post-POEM pain. It is known that pain after POEM could be caused by over-extension of the gastric wall, surgical injuries of the LES by cut and heat coagulation, inflammation of the surgical site, and local exposure to gastric acid. Hence, post-POEM pain is a complication of several miscellaneous uncomfortable sensations and relative emotional experiences. The present study found that patients in the oxycodone group had lower total PRI scores than those in the morphine group at 0, 2, 6, 24, and 48 h post-operatively, indicating that the oxycodone could not only better reduce the pain intensity but also suppress the scope of pain perception. Consistent with previous investigations, our study showed that oxycodone had more potent and comprehensive analgesic effects in patients who underwent POEM procedures when compared with morphine.

In the present study, it was observed that the oxycodone group had lower affective PRI score at 0 h when compared with the morphine group. However, oxycodone started to attenuate the sensory components of pain at the 2nd postoperative hour. This suggests the early emergence of visceral pain-related emotion and mood immediately after the POEM procedure, as well as oxycodone's rapid suppression of visceral through its peripheral κ-receptor agonist effect. This could also be explained in pharmacokinetic aspects [18, 19]. As for μ-receptors in the central nervous system, both oxycodone and morphine manifest two-compartment model pharmacokinetics characteristics. However, as for κ-receptor, oxycodone's pharmacokinetics characteristics are similar to the one-compartment model. Therefore, inhibition of the emotional components of pain by oxycodone emerged earlier than the suppression of the sensory components.

Although they have a strong analgesic effect, opioids have adverse reactions that cannot be ignored. We observed and recorded the common adverse reactions of opioids within 48 h after operation. We found that there was no significant difference in the incidence of drowsiness, dizziness, itching, and postoperative hypoxaemia and urinary retention between the oxycodone and morphine group, while the VAS score for nausea/vomiting was lower in the oxycodone group.

There were several limitations in our study. Firstly, all patients were followed up 48 h after the procedure, and chronic pain was not assessed [20]. Secondly, whether oxycodone or morphine could affect the inflammatory level after POEM was not evaluated, because serum mediators like IL-1β and TNF-α were not detected. Thirdly, although a single bolus of intravenous oxycodone showed sufficient analgesic effects, alternative methods of oxycodone administration for post-operative analgesia, such as patient-controlled analgesia, were not investigated in this study. Therefore, further multi-centred studies on post-POEM analgesia are still needed.

Conclusions

Intravenous oxycodone administered as a bolus of 0.08 mg/kg before the end of the POEM procedure could provide sufficient analgesia in the next 48 h. Oxycodone appeared to be superior to morphine in dealing with post-POEM pain, which has distinct visceral pain characteristics.

Acknowledgments

This work was supported by the National Key Research and Development Program of China (grant numbers 2018YFC2001904), Research on strategies for the prediction, prevention, and treatment of perioperative infection in elderly patients.

Guohao Xie and Shuangyue Li have contributed equally to this study.

Conflict of interest

The authors declare no conflict of interest.

References

1. Cappell MS, Stavropoulos SN, Friedel D. Updated systematic review of achalasia, with a focus on POEM therapy. Dig Dis Sci 2020; 65: 38-65.
2. Misra L, Fukami N, Nikolic K, et al. Peroral endoscopic myotomy: procedural complications and pain management for the perioperative clinician. Med Devices 2017; 10: 53-9.
3. Li QL, Chen WF, Zhou PH, et al. Peroral endoscopic myotomy for the treatment of achalasia: a clinical comparative study of endoscopic full-thickness and circular muscle myotomy. J Am Coll Surg 2013; 217: 442-51.
4. Ladabaum U, Minoshima S, Owyang C. Pathobiology of visceral pain: molecular mechanisms and therapeutic implications V. Central nervous system processing of somatic and visceral sensory signals. Am J Physiol 2000; 279: G1-G6.
5. Nabi Z, Reddy DN, Ramchandani M. Adverse events during and after peroral endoscopic myotomy: prevention, diagnosis, and management. Gastrointest Endosc 2018; 87: 4-17.

6. Chang SH, Maney KM, Phillips JP, et al. A comparison of the respiratory effects of oxycodone versus morphine: a randomised, double-blind, placebo-controlled investigation. Anaesthesia 2010; 65: 1007-12.
7. 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.
8. Melzack R. The short-form McGill Pain Questionnaire. Pain 1987; 30: 191-7.
9. Liu Q, Ruan W, Liu Z, et al. Effective factors of peroral endoscopic myotomy for treatment of achalasia. Videosurgery Miniinv 2022. doi:10.5114/wiitm.2022.114944.
10. Cervero F. Neurophysiology of gastrointestinal pain. Bailliere's Clin Gastroenterol 1988; 2: 183-99.
11. Shin S, Park CH, Kim HJ, et al. Patient satisfaction after endoscopic submucosal dissection under propofol-based sedation: a small premedication makes all the difference. Surg Endosc 2017; 31: 2636-44.
12. An Y, Zhao L, Wang T, et al. Preemptive oxycodone is superior to equal dose of sufentanil to reduce visceral pain and inflammatory markers after surgery: a randomized controlled trail. BMC Anesthesiol 2019; 19: 96.
13. Staahl C, Upton R, Foster DJ, et al. Pharmacokinetic-pharmacodynamic modeling of morphine and oxycodone concentrations and analgesic effect in a multimodal experimental pain model. J Clin Pharmacol 2008; 48: 619-31.
14. Wang JL, Zhang WJ, Gao M, et al. A cross-cultural adaptation and validation of the short-form McGill Pain Questionnaire-2: Chinese version in patients with chronic visceral pain. J Pain Res 2017; 10: 121-8.
15. Hasvik E, Haugen AJ, Haukeland-Parker S, et al. Cross-cultural Adaptation and Validation of the Norwegian Short-form McGill Pain Questionnaire-2 in Low Back-related Leg Pain. Spine 2019; 44: E774-81.
16. Wang J, Echevarria GC, Doan L, et al. Effects of a single subanaesthetic dose of ketamine on pain and mood after laparoscopic bariatric surgery: a randomised double-blind placebo controlled study. Eur J Anaesth 2019; 36: 16-24.
17. 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.
18. De Schepper HU, Cremonini F, Park MI, et al. Opioids and the gut: pharmacology and current clinical experience. Neurogastroenterol Motil 2004; 16: 383-94.
19. Riley J, Eisenberg E, Muller-Schwefe G, et al. Oxycodone: a review of its use in the management of pain. Curr Med Res Opin 2008; 24: 175-92.
20. Fletcher D, Martinez V. Opioid-induced hyperalgesia in patients after surgery: a systematic review and a meta-analysis. Br J Anaesth 2014; 112: 991-1004.

Received: 27.04.2022, **accepted:** 30.05.2022.

Appendix 1

PRI

	Sensory McGill pain	None	Mild	Moderate	Severe
1	Throbbing pain	0) ____	1) ____	2) ____	3) ____
2	Shooting pain	0) ____	1) ____	2) ____	3) ____
3	Stabbing pain	0) ____	1) ____	2) ____	3) ____
4	Sharping pain	0) ____	1) ____	2) ____	3) ____
5	Cramping pain	0) ____	1) ____	2) ____	3) ____
6	Gnawing pain	0) ____	1) ____	2) ____	3) ____
7	Hot-burning pain	0) ____	1) ____	2) ____	3) ____
8	Aching pain	0) ____	1) ____	2) ____	3) ____
9	Heavy pain	0) ____	1) ____	2) ____	3) ____
10	Tender	0) ____	1) ____	2) ____	3) ____
11	Splitting pain	0) ____	1) ____	2) ____	3) ____
	Affective McGill Pain				
12	Tiring-exhausting	0) ____	1) ____	2) ____	3) ____
13	Sickening	0) ____	1) ____	2) ____	3) ____
14	Fearful	0) ____	1) ____	2) ____	3) ____
15	Punishing-cruel	0) ____	1) ____	2) ____	3) ____