Journal of Hainan Medical University

http://www.hnykdxxb.com

Effect of oxycodone hydrochloride injection preemptive analgesia on serum inflammatory factors, neurotransmitter index and immune function in patients with laparoscopic cholecystectomy

Ting Liu, Yan−Bin Tang, Xuan−Dong Jia, Wen−Hua Wu, Da−Wei Yu✉, Mai−Tao Zhou

Department of Anesthesiology, The 101st Hospital of PLA, Jiangsu, Wuxi 214000, China

ARTICLE INFO

Article history:
Received 28 Aug 2017
Received in revised form 3 Sep 2017
Accepted 9 Sep 2017
Available online 14 Sep 2017

Keywords:
Laparoscopic cholecystectomy
Oxycodone hydrochloride injection
Inflammatory factor
Neurotransmitter
Immune function

ABSTRACT

Objective: To investigate the effect of oxycodone hydrochloride injection preemptive analgesia on serum inflammatory factors, neurotransmitter index and immune function in patients with laparoscopic cholecystectomy. **Methods:** According to random data table, 113 patients undergoing laparoscopic cholecystectomy were divided into control group (n=57) and observation group (n=56), patients in the control group were treated with sufentanil citrate injection analgesia, and the observation group patients were given oxycodone hydrochloride injection analgesia, level of serum inflammatory factors [tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6)], neurotransmitter index [5-hydroxy tryptamine (5-HT), P substance] and immune function index [$CD4^+$, $CD8^+$, $CD4^+/CD8^+$] of two groups between preoperative and postoperative 1d were compared. **Results:** There were no significant difference in level of TNF-α, IL-6, 5-HT, P substance, $CD4^+$, $CD8^+$ and $CD4^+/CD8^+$ between the two groups preoperative. Compared with the level of the same group preoperative, at postoperative 1 d level of TNF-α, IL-6, 5-HT, P substance, $CD8^+$were significantly increased, moreover level in the observation group were significantly lower compared with the control group, the difference was statistically significant; Postoperative 1 d, level of $CD4^+$, $CD4^+/CD8^+$ in the two groups were significantly lower than the preoperative level within the group, and the observation group was significantly higher than the control group. **Conclusion:** Oxycodone hydrochloride injection preemptive analgesia in laparoscopic cholecystectomy can effectively reduce serum inflammatory factors and neurotransmitter index release, improve immune function, has an important clinical value.

1. Introduction

Laparoscopic cholecystectomy was a common gallbladder operation in clinic, its trauma was small and amount of bleeding was small and recovery was fast. As a type of operation, it could cause pain and series of oxidative stress, hence affect clinical efficacy and recovery[1]. Patients always needed relieve pain by anaesthetic drug, the ideal analgesia could effectively reduce oxidative stress and complication after operation[2]. At present, analgesic drug in clinic after operation usually was opioid, oxycodone hydrochloride injection was a new opioid, with strong analgesia, widely used in post-operative analgesia[3,4]. This research was aimed to study serum inflammatory factors, neurotransmitter index and immune function and define its efficacy in preemptive analgesia.

2. Material and method

2.1. Clinical data

A total of 113 cases of patients with laparoscopic cholecystectomy who were admitted in our hospital from February 2016 to May 2017 were selected as subjects, divided into control group (n=57) and observation group (n=56) according to random table data. In control

✉Corresponding author: Da-Wei Yu, Department of Anesthesiology, The 101st Hospital of PLA, Jiangsu, Wuxi 214000, China.
Tel: 15190260869
E-mail: liuting3867@163.com.
Fund Project: General Project of Natural Science Fund of Jiangsu (Number: BK2015127).

group, 15 males, 42 females; aged from 31-57 year old; disease types: 52 cases of chronic cholecystitis, 5 cases of cholelithiasis. In observation group, 16 males, 40 females; aged from 30-56 year old; disease types: 50 cases of chronic cholecystitis, 6 cases of cholelithiasis. There was no difference in gender, age and disease types (P>0.05). This research was conformed to ethic committee and procedures was accorded with criteria and approved.

2.2. Selection criteria

Inclusion criteria: (1) Accorded with diagnostic criteria of chronic cholecystitis and cholelithiasis[5]; (2) Anesthetic risk grade was Ⅰ-Ⅱ grade; (3) Cardiac function grade was Ⅰ-Ⅱ grade; (4) Accorded with clinical indication of gall bladder surgery; (5) With complete clinical data, willing to participate in treatment.

Exclusion criteria: (1) allergic to anesthetic drug; (2) except for chronic cholecystitis and cholelithiasis, combined with other hepatic and gall disease; (3) combined with hypertension, hematopoietic disease, mental disease and severe cardiopulmonary disease; (4) took analgesic drug and immunoregulation agent, (5) with incomplete clinical data or unwilling to accept treatment.

2.3. Treatment method

Patients of both groups did not use any analgesic drugs, absolute diet, assured venous channel unhindered after in operation room, real-time monitoring of ECG, blood pressure, degree of blood oxygen saturation and partial pressure of carbon dioxide at respiratory terminal and other indexes. Until vital signs of patients were stable, open venous pathway, intravenous drip of sodium lactate Ringer′s injection (Shandong Qidu pharmaceutical Co, Ltd, approved number: H20023278, specification: 500 mL), 8-10 mL/(kg • h). Anesthesia induction: both of groups were given intravenous drip of sufentanil citrate injection (Yichang Renfu pharmaceutical Co, Ltd, approved number: H20054172, specification: 50 μg), 0.2-0.25 μg/kg, finished in 2-10 min; propofol injection (Li Mengxin, Xian Libang pharmaceutical Co, Ltd, approved number: H20123318, specification 10 mL: 100 mg * 5 tubes) 1.5-2.0 mg/kg; midazolam injection (Jiangsu Enhua pharmaceutical Co, Ltd, approved number: H10980025, specification 1 mL: 5 mg, 0.05-0.075 mg/kg), 0.05-0.075 mg/kg; Cisatracurium Besilate for Injection (Jiangsu Dongyang pharmaceutical Co,Ltd, approved number: H20060926, specification 10 mg), dissolved in 5 mL of sterile water for injection, 0.2 mg/kg; subsequently trachea cannula and connected with ventilator for mechanical ventilation: basis parameter: respiratory rate 10-12 times/min, respiratory quotient: 1:2, respiratory tidal volume 8-10 mL/kg. Selected propofol 0.8-1.0 mg/(kg min) and remifentanil 1-3 μg/(kg • h) (Yichang Renfu pharmaceutical Co, Ltd, approved number: H20030197, specification:1 mg), cisatracurium Besilate 2-4 μg/(kg • min) for maintenance of respiration. After gallbladder stripping, control group was given 5 μg/kg of sufentanil citrate injection for intravenous drip, observation group was given oxycodone hydrochloride injection (produced by NAPP pharmaceutical Co, Ltd, approved number: J20130166, specification: 2 mL: 20 mg), 0.1 mg/kg, given time was more than 2 min, all patients backed recover room after tube drawing in operation room.

2.4. Observation indexes

Extracted fasting periphery venous blood of patients before operation and 1 d of post-operation to observe respectively inflammatory factors [tumor necrosis factor-α (TNF-α),interleukin-6 (IL-6)], neurotransmitter [5-hydroxy tryptamine (5-HT), P substance] and immune function index [$CD4^+$, $CD8^+$, $CD4^+/CD8^+$]. TNF-α, IL-6 was measured by ELISA, kits were provided from Shanghai Sangon bio-engineering Co. Ltd; 5-hydroxy tryptamine (5-HT), P substance was measured by radioimmunoassay, kits were from Shanghai Shenmian Biotech Co, Ltd, NO detection used nitric reductases method; America Beckman Coulter flow cytometry was used to detect $CD3^+$, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$,operation was strict with kits introduction.

2.5. Statistcal analysis

Statistical Software SPSS 17.0 was used for all data processing and analyzing, inflammatory factors, neurotransmitter and immune function indexes were conformed to normal distribution and represented by Mean ± SD, t-test was applied to comparison of intra-group before and after treatment and inter-block after treatment, P<0.05 indicated the difference was statistical significant.

3. Results

3.1. Comparison of inflammatory factors level of both groups

Results of TNF-α and IL-6 level of both groups was shown in Table1. Before operation, TNF-α and IL-6 in observation group and control group were no obvious difference (P>0.05). After 1d of operation, TNF-α and IL-6 level in control group and observation group (470.22±55.61) ng/L, (55.16±8.05) ng/L, (420.27±56.06) ng/L and (43.17±6.66) ng/L, which was significantly higher than intragroup before operation, moreover level in observation group was obviously lower than control group (P<0.05). As shown in Table 1.

Table 1.

Comparison of inflammatory factors level of both groups.

Group	n	Treatment time	TNF-α (ng/L)	IL-6 (ng/L)
Control group	57	Before operation	380.78±51.86	37.19±7.53
		After 1 d operation	470.22±55.61*	55.16±8.05*
Observation group	56	Before operation	379.72±51.71	36.94±7.58
		After 1 d operation	420.27±56.06*#	43.17±6.66*#

Note: Compared with before operation, *P<0.05; compared with control group after 1 d of operation, #P<0.05.

3.2. Comparison of neurotransmitter level of both groups

Results of 5-HT and P substance detection of both groups were shown in Table 2. Before operation, 5-HT and P substance of intergroup of both groups were no obvious difference (P>0.05). After 1d of operation, 5-HT and P substance in control group were (692.46±11.36) ng/mL and (213.14±16.62) ng/L, which was obviously higher than before treatment of intragroup, the difference was significantly different (P<0.05); both level in observation group were (611.31±11.37) ng/mL and (196.32±15.19) ng/L, which was obviously higher than before treatment of intragroup, moreover lower than control group dramatically (P<0.05). As shown in Table 2.

Table 2.

Comparison of neurotransmitter level of both groups.

Group	n	Treatment time	5-HT (ng/mL)	P substance (ng/L)
Control group	57	Before operation	455.91±10.52	186.63±20.42
		After 1 d operation	692.46±11.36*	213.14±16.62*
Observation group	56	Before operation	459.82±10.69	188.38±20.13
		After 1 d operation	611.31±11.37$^{*\#}$	196.32±15.19$^{*\#}$

Note: Compared with before operation, $^{*}P$<0.05; compared with control group after 1d of operation, $^{\#}P$<0.05.

3.3. Comparison of immune function level of both groups

Results of immune function indexes of both groups were shown in Table 3. $CD3^{+}$, $CD8^{+}$ and $CD4^{+}/CD8^{+}$ level of intragroup was no difference (P>0.05). Compared with before operation of intragroup, $CD4^{+}$ and $CD4^{+}/CD8^{+}$ level after 1 d of operation was decreased obviously, moreover (28.28±2.95)%, (1.07±0.12) in observation group was higher significantly than (23.55±2.42)%, (0.96±0.09), the difference was significant (P<0.05); after 1 d of operation, $CD8^{+}$ level of control group and observation group was (33.24±2.36)% and (31.23±2.29)%, which was higher than intragroup before operation, moreover lower than control group dramatically (P<0.05). As shown in Table 3.

4. Discussion

Patients with laparoscopic cholecystectomy usually have post-operation pain, mainly represented post-operative pain and visceral pain, more than half of patients had moderate pain in one day after operation, 23% of patients existed severe pain[6,7]. Pain was main reason of post-operation agitation, in clinic, always given patients with moderate and severe pain opioid drug by intramuscular injection, at present, widely used opioid receptor agonsit-antagonsit including sufentanil, dezocine et al[8,9]. Oxycodone hydrochloride injection was agonsits with double receptor (κ , μ), its mechanism was same with morphine, but its analgesic effect was 1-2 fold over morphine, with taking effect rapidly, and long action time[10,11]. Preemptive analgesia referred to enhance analgesic effect to reduce injury caused by pain and promote recovery of illness condition through analgesic treatment for patients of perioperative period[12]. In recent years, a lot of researches emphases on the safety evaluation and analgesic efficacy of oxycodone hydrochloride injection, however research about effect on serum biochemical indexes was little. Therefore, this research was aimed to explore effect of oxycodone hydrochloride injection on serum inflammatory factors, neurotransmitters and immune function.

Operative trauma and pain stimulus prompted monocyte and macrophage produce largely and secrete inflammatory cytokine (TNF- α and IL-6 et al), as classic proinflammation factors, TNF- α and IL-6, its level change not only reflected degree of inflammatory stress, but related to pain at some extent[13,14]. Research pointed that TNF- α and IL-6 could promote sensitization of periphery tissue and central nervous system, thereby aggravated pain[15]. This research found that compared with before operation, TNF- α and IL-6 level of both groups after 1 d of operation was obviously increased, further demonstrated, operative trauma caused chronic inflammation, moreover, inflammatory factor level of patients were given oxycodone hydrochloride injection was higher than control group, it showed that oxycodone hydrochloride injection could inhibit inflammatory factor secretion after operation, it was better to postoperative recovery.

5-HT and P substance was main neurotransmitter that participated in pain information transmission, in gradual transmission of pain information, both affected and synergy[16]. neurotransmitter was an critical index reflected pain degree and stress reaction[17]. Related studies found that opioid could effectively inhibit release of 5-HT, P substance and acetyl choline, thereby relieved pain[18]. This research pointed out that transmitters level of both groups after 1d of operation was increased, revealing patients existed obvious pain after operation, body was in stress reaction, whereas transmitters level of patients were given oxycodone hydrochloride injection was higher than control group, it was accorded with previous reports[19,20]. Further revealed that compared with sufentanil, oxycodone

Table 3.

Comparison of immune function of both groups.

Group	n	Treatment time	$CD4^{+}$ (%)	$CD8^{+}$ (%)	$CD4^{+}/CD8^{+}$
Control group	57	Before operation	35.79±3.39	28.88±3.25	1.31±0.15
		After 1 d operation	23.55±2.42*	33.24±2.36*	0.96±0.09*
Observation group	56	Before operation	35.94±3.43	29.02±4.37	1.32±0.18
		After 1 d operation	28.28±2.95$^{*\#}$	31.23±2.29$^{*\#}$	1.07±0.12$^{*\#}$

Note: Compared with before operation, $^{*}P$<0.05; compared with control group after 1 d of operation, $^{\#}P$<0.05.

hydrochloride injection could inhibit more effectively release of P substance and other algogenic substance after operation, thereby hindered pain information transmission, analgesic effect was strong.

A lot of researches demonstrated that operative trauma was able to restrain immune function, immune dysfunction was main factors of operative complication[21,22]. $CD4^+$ T cell as adjuvant T cell of immune response and $CD8^+$ T cell was suppressor T cell that maintained immune balance, ratio of both reflected condition of immune regulation[23]. This research showed that $CD4^+/CD8^+$ level was decreased significantly after 1d of operation, revealing operative trauma decreased immune function, compared with sufentanil, after oxycodone hydrochloride injection, fluctuation of $CD4^+$, $CD8^+$, $CD4^+/CD8^+$ level was decreased, it showed that inhibition of immune function of oxycodone hydrochloride injection was milder, it was better to recovery.

In conclusion, preemptive analgesia by oxycodone hydrochloride injection for patients with laparoscopic cholecystectomy was better, it could effectively inhibit release of inflammatory factors, reduce neurotransmitter level, mild inhibition of immune function, it was better to recover immune function, with critical clinical significance.

Reference

[1] Deal SB, Stefanidis D, Brunt LM. Development of a multimedia tutorial to educate how to assess the critical view of safety in laparoscopic cholecystectomy using expert review and crowd-sourcing. *Am J Surg* 2017; **213**(5): 988-990.

[2] Cai Min. Change of microcirculation and pain related indexes of patients with laparoscopic cholecystectomy in preioperative period. *J Hainan Med Coll* 2015; **21**(7): 944-946.

[3] Wang N, Wang Y, Pang L. Effect of preemptive analgesia with intravenous oxycodone in the patients undergoing laparoscopic resection of ovarian tumor. *Pakistan J Med Sci* 2015; **31**(2): 300-303.

[4] Yadav G, Jain G, Samprathi A. Role of preemptive tapentadol in reduction of postoperative analgesic requirements after laparoscopic cholecystectomy. *J Anaesthesiol Clin Pharmacol* 2016; **32**(4): 492-496.

[5] Chinese Digestion Journal Edition Committee. Consensus and opinion of diagnosis and treatment of chronic cholecystitis, cholelithiasis (2014 Shanghai). *Gastroenterology* 2015; **20**(5): 292-296.

[6] Pucher PH, Brunt LM, Fanelli RD. SAGES expert Delphi consensus: critical factors for safe surgical practice in laparoscopic cholecystectomy. *Surg Endoscopy* 2015; **29**(11): 3074-3085.

[7] Chen CB, Palazzo F, Doane SM. Increasing resident utilization and recognition of the critical view of safety during laparoscopic cholecystectomy: a pilot study from an academic medical center. *Surg Endoscopy* 2017; **31**(4): 1627-1635.

[8] Bhagat N, Yunus M, Karim HMR. Dexmedetomidine in attenuation of haemodynamic response and dose sparing effect on opioid and anaesthetic agents in patients undergoing laparoscopic cholecystectomy-a randomized study. *J Clin Diagn Res* 2016; **10**(11): UC01-UC05.

[9] Jiang Yandong, Zhao Sumin. Effect of remifentanil combined with propofol on stress reaction, blood gas index in patients with laparoscopic cholecystectomy. *J Hianan Med Coll* 2016; **22**(7): 677-679.

[10] Jokinen V, Lilius TO, Laitila J. Pregabalin enhances the antinociceptive effect of oxycodone and morphine in thermal models of nociception in the rat without any pharmacokinetic interactions. *Eur J Pain* 2016; **20**(2): 297-306.

[11] Yao Yueqin, Liu Yinghua, Fan Zhiyi. Clinical observation of oxycodone hydrochloride injection in acute pain of patients with lower abdominal operation revival period of full analgesia. *Chin New Med* 2017; **26**(6): 661-664.

[12] Tan Tan, Chen Wenjun. Efficacy comparison of parecoxib and flurbiprofen axetil in preemptive analgesia of hernia. *Pract Geriatr* 2016; **30**(6): 511-513.

[13] Zhu Y, Wang S, Wu H. Effect of perioperative parecoxib on postoperative pain and local inflammation factors PGE2 and IL-6 for total knee arthroplasty: a randomized, double-blind, placebo-controlled study. *Eur J Orthopaedic Surg Traumatol* 2014; **24**(3): 395-401.

[14] Beltran SR, Svoboda KKH, Kerns DG. Anti-inflammatory protein tumor necrosis factor- –stimulated protein 6 (tsg-6) promotes early gingival wound healing: an in vivo study. *J Periodontal* 2015; **86**(1): 62-71.

[15] Watt DG, Horgan PG, McMillan DC. Routine clinical markers of the magnitude of the systemic inflammatory response after elective operation: a systematic review. *Surgery* 2015; **157**(2): 362-380.

[16] Dawson A, Ghafouri B, Gerdle B. Effects of experimental tooth clenching on pain and intramuscular release of 5-HT and glutamate in patients with myofascial TMD. *Clin J Pain* 2015; **31**(8): 740-749.

[17] Lu Guohai. *Effect of different femoral nerve block on stress reaction and postoperative pain of total knee replacement*. Suzhou: Suzhou University; 2013.

[18] Banerjee J, John P, Arokya MS. Regulation of nonsmall-cell lung cancer stem cell like cells by neurotransmitters and opioid peptides. *Int J Cancer* 2015; **137**(12): 2815-2824.

[19] Zhang Jinfa, Liu Yuqin, Guo Chao. Analgesic effect and safety evaluation of oxycodone hydrochloride injection combined with dezocine in patients with laparoscopic cholecystectomy. *Chin Clin Pharmacol* 2016; **32**(15): 1384-1386.

[20] Liu Yanli. *Effect of oxycodone on P substance, 5HT and PCIA effect in patients with laparoscopic cholecystectomy*. Tangshan: North China University of Science and Technology; 2016.

[21] Meng XL, Qu Q. Effect of subcutaneous injection of lidocaine in zusanli (st 36) and jiaji (ex-b 2) regions on immune function in patients undergoing laparoscopic cholecystectomy. *Acupuncture Res* 2016; **41**(1): 74-79.

[22] Zhang LZ. Effect of laparoscopic cholecystectomy on the liver function and immune function. *J Hainan Med Univ* 2016; **22**(12): 63-66.

[23] Chopra SS, Haacke N, Meisel C. Postoperative immunosuppression after open and laparoscopic liver resection: assessment of cellular immune function and monocytic HLA-DR expression. *J Soc Laparoendoscopic Surg* 2013; **17**(4): 615-621.