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ORIGINAL ARTICLE

Efficacy and Safety of a Continuous Wound Catheter in Open Abdominal Partial Hepatectomy

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Key words: continuous wound catheter; postoperative pain; partial hepatectomy

Objective To investigate the efficacy and safety of continuous local anesthetic wound infiltration following open abdominal partial hepatectomy.

Methods We performed a prospective, non-randomized, concurrent and controlled study. Patients undergoing open abdominal partial hepatectomy, according to their willingness, accepted one of the following managements for the postoperative pain: continuous wound catheter (CWC) infiltration, patient-controlled epidural analgesia (PCEA), patient-controlled intravenous analgesia of morphine (PCIAM), and patient-controlled intravenous analgesia of sufentanil (PCIAS). The primary outcome was postoperative visual analogue scale (VAS) scores at rest and on movement. Secondary outcomes included consumption of rescue medication, side effects, and complications associated with postoperative pain management.

Results From August 2013 to December 2013, 80 patients were allocated to receive CWC ($n=10$), PCEA ($n=22$), PCIAM ($n=29$), or PCIAS ($n=19$). After adjusting for age, sex, body mass index, percentage of resected liver, operation time, and Amsterdam Preoperative Anxiety and Information Scale, there was no significant difference in the VAS scores at rest or on movement between Group CWC and the other groups, namely PCEA, PCIAM, and PCIAS, at 4, 12, 48, and 72 hours postoperatively (all $P>0.05$). The need for rescue medication was not significantly different between Group CWC and the other three groups at 48 and 72 hours postoperatively (all $P>0.05$). There was no significant difference in the incidence of postoperative nausea and vomiting or anal exsufflation time between group CWC and the other three groups (all $P>0.05$). No severe adverse effects associated with continuous wound infiltration were observed during the study period.

Conclusions CWC has a comparable analgesic effect compared with traditional analgesia methods at most time points postoperatively. CWC is a safe alternative for the postoperative analgesic management of open liver surgery.

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ADEQUATE postoperative analgesia decreases the incidence of complications and in-hospital death, shortens hospital stay length, and lowers costs. Patients undergoing liver resection report moderate to severe pain after the surgical procedure.¹⁻³ Postoperative drug metabolism and hemostasis may be changed because of either preoperative liver dysfunction or abnormalities that develop postoperatively owing to liver resection. These situations make postoperative management of analgesia for liver surgery a unique challenge. Patient-controlled intravenous opioids are widely used to relieve the pain postoperatively. However, when used alone, high doses of intravenous opioids are required to treat movement-related pain after liver surgery. Unwanted opioid-related side effects, such as postoperative nausea and vomiting (PONV), sedation, and respiratory depression, can be manifested. Epidural analgesia used to be recommended for provision of analgesia following liver surgery. However, epidural analgesia is associated with serious complications including hypotension, bradycardia, dural puncture, and neurological deficits. Continuous wound infiltration of local anesthetic with an indwelling catheter placed directly by the surgeon at the target site may be an effective alternative in this patient group. Therefore, this prospective, non-randomized, concurrent, controlled study was carried out to examine the efficacy and safety of continuous wound catheter (CWC) infiltration following open abdominal partial hepatectomy.

PATIENTS AND METHODS

Enrollment and management of patients

From August 2013 to December 2013, patients who were scheduled for an open abdominal partial hepatectomy at Peking Union Medical College Hospital were prospectively enrolled in this study. Patients with an older age (>65 years), American Society of Anesthesiologists (ASA) classification ≥ 3 , or the inability to cooperate were excluded.

During the preoperative visit, baseline anxiety evaluations were carried out using the Amsterdam Preoperative Anxiety and Information Scale (APAIS).⁴ Benefits and risks associated with patient-controlled epidural analgesia (PCEA), patient-controlled intravenous analgesia (PCIA), and CWC infiltration were thoroughly explained to the patients. Patients' questions and concerns were all answered before choosing the treatment method they were willing to accept.

On the day of surgery, patients were managed with a standard general anesthesia protocol. Induction was carried out with propofol 1.5-2.0 mg/kg intravenously, fentanyl 2-3 μ g/kg, and rocuronium 1 mg/kg. Sevoflurane with

a target minimum alveolar concentration of 1.3 was administered for maintenance of anesthesia. For the prevention of PONV, dexamethasone 5 mg was administered intravenously at the start of surgery; ondansetron 4 mg was administered intravenously 30 minutes before the end of surgery. All the operations of liver resection were performed by the same surgical team, through a right subcostal incision extending upwards to the midline.

Postoperative pain management

In the CWC group, the ON-Q Pain Relief System (I-Flow Corp., Lake Forest, CA, USA) was used for postoperative pain management. This device consists of an elastomeric pump that holds 300 ml of 0.4% lidocaine and allows continuous infusion of local anesthetic to nearby tissues for 72 hours. At the end of the surgical procedure, wound catheters were placed between the transversus abdominis and rectus abdominis under direct vision by the surgeon.

In the PCEA group, before induction of anesthesia, patients received mid-thoracic epidural catheter insertion at T9-10. Infusion of 0.2% ropivacaine at 4 ml/h with a bolus of 4 ml and a lockout time of 15 minutes was provided.

In the PCIA group, at the end of surgery, PCIA pump infusion with either morphine 0.25 mg/ml or sufentanil 0.6 mcg/ml was started at 4 ml/h, with a bolus of 4 ml and a lockout time of 15 minutes. The choice of sufentanil or morphine was made by the anesthesiologist in charge of the patient.

Data collection

Baseline demographic information including sex, age, and body mass index were extracted from electronic records.

Intraoperative data including duration of anesthesia, operation time, and the percentage of resected liver were all recorded.

Patients were checked up at 4, 12, 48, and 72 hours postoperatively. Pain at rest and on movement was evaluated using visual analogue scale (VAS) scores. Rescue medication was indicated with a VAS score greater than 6. The time and amount of rescue medication provided was recorded. The incidence of PONV was recorded. PONV was evaluated on a numerical rating scale (NRS) of 1 to 3 (1=vomiting or feeling extremely nauseous; 2=no vomiting, but feeling moderately nauseous; and 3=no feeling of nausea or feeling mildly nauseous). Anal exsufflation time after surgery was noted. Adverse effects associated with CWC infiltration were recorded. Patients' platelet (PLT) level, prothrombin time (PT), activated partial thromboplastin time (APTT), and international normalized ratio were monitored daily for 1 week after surgery.

Statistical analysis

Normally distributed continuous variables were expressed as mean $\pm$ SD, and were compared using analysis of variance (ANOVA). Non-normally distributed continuous variables were expressed as median (interquartile range) with the exception of VAS score. VAS was expressed as mean $\pm$ SD for clinical purpose. All non-normally distributed continuous variables were compared using Kruskal and Wallis method. Categorical variables were expressed as frequency (%), and were compared using Chi-square analysis or Fisher exact tests, as appropriate. To ensure enough patients were allocated into each group, minimum sample size was calculated with a power of 0.8 ($\beta=0.2$) and a type I error rate of 2.5%. Statistical analysis was performed using SPSS version 21.0. $P<0.05$ was considered statistically significant.

RESULTS

Baseline information

From August 2013 to December 2013, 84 patients were scheduled to undergo abdominal partial hepatectomy at

our hospital. Four patients were excluded because of older age ($n=2$) and high grade of ASA classification ($n=2$). Among the included 80 patients, 22 consented to receive epidural analgesia, 29 consented to receive PCIA with morphine, 19 consented to receive PCIA with sufentanil, and 10 consented to receive CWC analgesia.

Baseline analysis showed that patients in each group were well matched in age ($F=0.79$, $P>0.05$), BMI ($\chi^2=1.58$, $P>0.05$), percentage of resected liver ($\chi^2=2.54$, $P>0.05$), surgical time ($F=0.42$, $P>0.05$), and APAIS score ($F=0.83$, $P>0.05$) (Table 1).

Postoperative analgesic effects of the four methods

There was no significant difference in VAS scores at rest between the CWC group and the groups of PCEA, PCIAM, and PCIAS at all postoperative time points (all $P>0.05$, Table 2).

Postoperative pain peaked within 24 hours after surgery, and began to decrease after 45 hours. There was no difference in VAS scores on movement in the CWC group compared with the groups of PCIAM, PCIAS, and PCEA at all postoperative time points (all $P>0.05$, Table 2).

Table 1. Comparisons of baseline characteristics of the four groups

Groups	<i>n</i>	Age [§] (yrs)	BMI(<i>n</i>)		Liver resection ratio(<i>n</i>)		Operation time [§] (min)	APAIS
			<25 kg/m ²	$\geq$ 25 kg/m ²	<5%	$\geq$ 5%		
CWC group	10	55 $\pm$ 10	8	2	5	5	184 $\pm$ 57	15 $\pm$ 4
PCEA group	22	51 $\pm$ 12	14	8	15	7	203 $\pm$ 66	14 $\pm$ 4
PCIAS group	19	48 $\pm$ 13	14	5	14	5	192 $\pm$ 76	15 $\pm$ 5
PCIAM group	29	51 $\pm$ 12	18	11	22	7	184 $\pm$ 56	16 $\pm$ 5
<i>P</i> value		0.50	0.66		0.47		0.74	0.48

§: Plus-minus values are means $\pm$ SD.

BMI: body mass index; CWC: continuous wound catheter; PCEA: patient-controlled epidural analgesia; PCIAS: patient-controlled intravenous analgesia with sufentanil; PCIAM: patient-controlled intravenous analgesia with morphine; APAIS: Amsterdam Pre-operative Anxiety and Information Scale.

Table 2. Comparisons of postoperative visual analogue scale scores between the CWC and the other three methods at rest and on movement[§]

Groups	<i>n</i>	At rest					On movement				
		4 hours	12 hours	24 hours	48 hours	72 hours	4 hours	12 hours	24 hours	48 hours	72 hours
CWC group	10	3.30 $\pm$ 1.06	3.30 $\pm$ 2.16	3.40 $\pm$ 2.27	1.60 $\pm$ 1.90	1.40 $\pm$ 1.71	4.60 $\pm$ 1.71	4.20 $\pm$ 2.20	5.00 $\pm$ 2.54	3.30 $\pm$ 2.26	3.60 $\pm$ 2.46*
PCEA group	22	2.32 $\pm$ 1.96	2.18 $\pm$ 1.84	1.95 $\pm$ 2.13*	1.09 $\pm$ 1.34*	1.23 $\pm$ 1.48	3.23 $\pm$ 2.07	3.32 $\pm$ 1.94	3.23 $\pm$ 2.14	2.36 $\pm$ 1.79	2.59 $\pm$ 1.37*
PCIAS group	19	3.14 $\pm$ 2.01	2.76 $\pm$ 1.95	1.86 $\pm$ 1.63	1.10 $\pm$ 1.38*	1.41 $\pm$ 1.48	4.31 $\pm$ 2.14	4.38 $\pm$ 1.64	3.45 $\pm$ 1.91	3.28 $\pm$ 1.77	3.55 $\pm$ 1.91
PCIAM group	29	2.44 $\pm$ 2.31*	2.61 $\pm$ 2.17	2.33 $\pm$ 1.81	1.67 $\pm$ 1.85	1.00 $\pm$ 1.62	3.76 $\pm$ 1.99	4.28 $\pm$ 2.14	3.83 $\pm$ 1.86	1.67 $\pm$ 1.85	2.82 $\pm$ 1.42
<i>P</i> value		0.21	0.50	0.24	0.69	0.71	0.19	0.23	0.13	0.23	0.20

§: Plus-minus values are means $\pm$ SD.

*Data show a non-normal distribution. For non-normal distribution, Kruskal and Wallis was used to compare the difference between groups; for normal distribution, one way ANOVA was used to analyze the difference between groups.

Use of rescue medication, side effects, and complications

The incidence of patients who needed rescue medication in the CWC group was significantly higher than that of all the groups of PCIAM, PCIAS, and PCEA at 4 (60.0% vs. 5.7%), 12 (50.0% vs. 7.1%) and 24 hours (40.0% vs. 8.6%) after surgery ($P=0.01$); while at 48(20.0% vs. 11.4%) and 72 hours (20.0% vs. 12.8%) after surgery, no significant difference was found between them (all $P>0.05$).

There was no significant difference in the recovery time of gastrointestinal motility between the CWC group and the groups of PCEA, PCIAS, and PCIAM ($F=0.98$, $P>0.05$, Table 3). There was no significant difference in the incidence of severe and moderate PONV (NRS=1 and NRS=2) between the CWC group and the combined group of PCEA, PCIAS, and PCIAM at 4 (0 vs. 20%), 12 (20% vs. 30%), 24 (20% vs. 22%), 48 (10% vs. 14%), and 72 hours (0 vs. 8%) after surgery (all $P>0.05$). No patients in the CWC group or PCIAS group reported a NRS score of 1 at any time point. One patient reported a NRS score of 1 in the PCEA group at 4 hours

after surgery. Two patients in the PCIAM group reported a NRS score of 1 at 4 and 24 hours after surgery.

The PLT count decreased postoperatively, with the lowest count on the postoperative day 3 (Fig. 1). The percentages of patients with a platelet count $<80 \times 10^9/L$ on postoperative day 1, 2, 3-4, and 6-8 were 6.2% (5/80), 11.2% (9/80), 21.2% (17/80), and 6.2% (5/80), respectively.

There was a clear tendency of the PT/APTT elevation during the first 3 days after surgery (Fig. 2). The percentages of patients with an APTT value above the normal upper limit (31.8 seconds) on postoperative day 1, 2, 3-4, and 6-8 were 22.5% (18/80), 26.2% (21/80), 26.2% (21/80), and 15.0% (12/80), respectively. The percentages of patients with a PT value above the normal upper limit (12.6 seconds) on postoperative day 1, 2, 3-4, and 6-8 were 62.5% (50/80), 46.2% (37/80), 41.2% (33/80), and 30.0% (24/80), respectively.

There were no complications associated with CWC infiltration, including catheter-related complications, infection, catheter dislodgement, and systemic toxicity from local anesthetics.

Table 3. Number of patients restoring anal exhaust at the indicated postoperative time [n (%)]

Groups	n	4 hours	12 hours	24 hours	48 hours	72 hours
CWC	10	0	0	1(10.0)	4(40.0)	6(60.0)
PCEA	22	0	0	0	2(6.9)	17(58.6)
PCIAM	29	0	0	0	5(26.3)	13(68.4)
PCIAS	19	0	2(9.0)	3(13.6)	8(36.4)	16(72.7)

Figure 1. Postoperative evaluation of the platelet count ($n=80$). Data are shown as mean $\pm$ SD. pre=preoperative value.

Figure 2. Postoperative evaluation of prothrombin time/activated partial thromboplastin time (PT/APTT) ($n=80$). Data are shown as mean $\pm$ SD.

DISCUSSION

Uncontrolled postoperative pain has multiple detrimental effects. A change in postoperative drug metabolism and hemostasis results in more complicated postoperative analgesia for liver surgery. Adequate postoperative pain management, early mobilization, and early dietary intake, as part of the protocol of Enhanced Recovery after Surgery, have been advocated and shown to promote recovery in partial hepatectomy.⁵⁻⁶

A retrospective study showed that the analgesic effect of CWC infiltration is comparable to PCIA with less opioid consumption, less side effects, and a shorter length of hospital stay.^{3, 7} Several studies have shown the effectiveness of CWC in multiple surgical procedures.⁷⁻¹⁰ A meta-analysis demonstrated multiple potential benefits of CWCs, including the decrease of mean VAS pain scores at rest and with activity.¹¹ One randomized controlled trial demonstrated a non-inferior analgesic effect of CWC compared with thoracic epidural in liver surgeries.¹² In our study, patients with open abdominal partial hepatectomy reported mild to moderate postoperative pain. The analgesic effect of CWC

was comparable with traditional PCEA and PCIA at most time points. Patients in the CWC group had a tendency for early recovery of bowel movement and fewer incidence of PONV. But these findings failed to show statistical significance. In the surgical center where this study was carried out, most patients are encouraged to sit up and ambulate 24 to 48 hours after surgery. The level of pain on movement is accompanied by an increase in mobilization and cannot be effectively managed with a CWC alone. Having only a continuous infusion mode without patient-controlled mode is another disadvantage of CWC. There are nociceptive nerve endings in viscera, and they contribute to visceral pain.¹³ A possible contribution from the visceral element of postoperative pain is another possible explanation for inferior analgesic effects with CWCs. A multimodal pain management strategy incorporating CWC infiltration and another analgesic that covers breakthrough pain and visceral pain could be a reasonable approach.

Epidural analgesia is considered the gold standard to manage postoperative pain after major abdominal surgeries due to the possible superior analgesic effect.¹⁴⁻¹⁵ However, unwanted complications and the possibility of a labor-intensive and non-functioning epidural catheter make epidural analgesia not an ideal analgesic method for hepatectomy. Large hepatectomy can lead to postoperative coagulopathy,¹⁶ which was confirmed in our study. Recently, epidural analgesia has been suggested to be an independent risk factor for AKI after hepatectomy.¹⁷ For the reasons mentioned above, epidural analgesia is no longer favored by Enhanced Recovery after Surgery guidelines.¹⁸

This study was a non-randomized study with a limited sample size. Future randomized study designing with a larger sample size is needed to further evaluate analgesic efficacy of CWC infiltration combined with different intravenous analgesics in open abdominal partial hepatectomy.

In conclusion, we speculate that multimodal analgesic management combining CWC infiltration with another intravenous analgesic could be a suitable regiment for patients undergoing open abdominal partial hepatectomy.

Conflict of Interest Statement

The authors have no conflict of interest to disclose.

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