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Original Article

Effects of epidural analgesia with different concentrations of bupivacaine plus fentanyl on pain in patients undergoing thoracic surgery

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Abstract: Objective: To investigate and compared the efficacy and safety of epidural analgesia with different concentrations of bupivacaine plus fentanyl on pain in patients undergoing thoracic surgery. Methods: 120 cases undergoing elective thoracic surgery were randomly divided into A, B, C and D four groups each with 30 cases, and they were treated with 0.25% (A group), 0.375% (B group), 0.50% (C group) and 0.75% (D group) bupivacaine plus fentanyl 0.4 mg. The pain conditions postoperative 4 h, 8 h, 12 h, 24 h and 48 h were evaluated by visual analogue scale (VAS). The PCA pressing numbers and incidence of adverse reactions were compared between the four groups. Results: By postoperative 4 h, the VAS in D group were obviously lower than those in the other three groups (*P* all <0.05), and the other three groups showed no significances (P>0.05). However, the four groups showed no significant differences in VAS by postoperative 8 h, 12 h, 24 h and 48 h (*P* all >0.05). The incidences of respiratory depression in C and D groups were markedly higher than those in A and B groups (*P* all <0.05). Conclusions: 0.25%~0.375% bupivacaine plus fentanyl 0.4 mg using in epidural analgesia in patients undergoing thoracic surgery can lead to safe and effective analgesic effect.

Keywords: Epidural analgesia, patient-controlled analgesia, bupivacaine, respiratory depression

Introduction

The trauma of thoracotomy is large, and with severe postoperative pain, causing severe stress response. It not only affects the wound healing, but also causes the instability of circulatory and respiratory systems, resulting in a series of severe complications [1]. Patient-controlled analgesia (PCA) is the patients based on the situation of pain to decide the time and dose of medication by themselves, ensuring the effectiveness of analgesic and avoiding adverse drug reaction induced by high concentration. Bupivacaine is a long-acting amide local anesthetics with many advantages, including strong analgesic effects, low minimum impact concentration low impact time and rapid onset [2]. Currently, the recommended concentration of epidural block is 0.25%~0.75%. However, due to the influence of the size of trauma and the degree of muscle relaxation, the reports about the bupivacaine plus fentanyl used in epidural analgesia after thoracic surgery are relatively less, and the applied concentration of bupivacaine is not inconsistent. In order to take consideration to the efficacy and safety, in this paper, we have systematically discussed the best concentration of bupivacaine in epidural analgesia after thoracic surgery. The reports are as follows.

Materials and methods

General information

From January 2012 to June 2014, 120 cases undergoing elective thoracic surgery were selected in our hospital. All patients without serious liver and kidney dysfunction, have no allergy of drugs and without blood coagulation dysfunction, as well as no epidural analgesia contraindications. This study has been audited and approved by the Hospital Ethics Committee, and all patients were given the right of informed consent and voluntarily signed the informed consent. The study was divided into open, par-

allel and control trial. 120 cases based on random number table were randomly divided into A, B, C and D four groups each with 30 cases.

The methods of anesthesia and analgesia

The patients in the four groups were all treated with epidural block combined with general anesthesia. 30 min before patients came into operation room, the patients were injected with 0.1 g phenobarbital sodium and 0.5 mg atropine. After came into the operation room, the vein passage was established for the monitoring of electrocardiogram (ECG), blood pressure (BP), heart rate (HR), blood oxygen saturation (SpO_2) and partial pressure of carbon dioxide in end expiratory gas ($P_{ET}CO_2$). Before induction of anesthesia, the epidural space was punctured near the T6 and injected 5 ml 1% lidocaine. If the blocking effect was satisfactory, then measure the block plane. The drugs to induce anesthesia were 1 mg/kg propofol, 0.1 mg/kg vecuronium bromide, 0.4 μg/kg fentanyl and 0.04 mg/kg midazolam. The drugs to maintain anesthesia were 3 mg/kg propofol, and by intermittent injection of fentanyl and vecuronium bromide. During operation, the epidural space was intermittently injected with 10 ml lidocaine. Before about 15 min, the epidural space stopped giving the drugs.

After operation, it's connected to the patient-controlled analgesia device. The analgesia drug was bupivacaine plus fentanyl. The concentrations of bupivacaine of A, B, C, D groups were 0.25%, 0.375%, 0.50% and 0.75%, respectively, and all were added with 0.4 mg fentanyl for making 100 ml 0.9% sodium chloride solution. The loading dose of 6 ml, continuous dose 2 ml/h, single patient-controlled analgesia dose of 0.5 ml, at the same time, the lockout time was set at 15 min and the analgesia time was set at 48 h.

The observe content

Pain: Based on the visual analogue scale (VAS) to evaluate the situation of patients' pain, the pain was divided into 0~10 score by this evaluation, where 0 is no pain, and 10 was the pain that can't stand. Comparing the pain conditions of four groups after 4, 8, 12 and 48 h of operation.

Pressure times of PCA: The pressure times of PCA of four groups within 48 h were recorded.

Adverse reactions: The postoperative gastrointestinal reaction (nausea, vomiting), dizziness, pruritus, urinary retention and the respiratory depression of four groups were counted.

Statistical methods

Statistical packages SPSS 17.0 is used for the data processing, continuous variables are expressed as x±s, multiple groups were compared by Kruskal-Wallis test, two groups was compared by t test, and the data was count by using χ^2 test. $P<0.05$ was considered statistically significant.

Results

Comparison of each baseline data

After determine the treatment plan, there was 1 case in group B and group C exited the research due to the patients were transferred to another hospital. Thus, there were 118 cases can be used for the final evaluation. There were 30, 29, 29 and 30 cases in A, B, C and D group, respectively. The baseline data of four groups were tested by using Kruskal-Wallis test or χ^2 test. The results show no significant differences ($P>0.05$), thus it was comparable, as is shown in **Table 1**.

The comparison of VAS scores of four groups at different points

After surgery 4 hour, D group VAS score significantly lower than the other three groups. The difference was statistically significant ($P<0.05$). After surgery 8, 12, 24 and 48 hour and the difference between the three groups was not statistically significant ($P>0.05$); the difference was not statistically significant ($P>0.05$) (**Table 2**).

The pressure times of PCA of four groups within 48 h

The pressure times of PCA of four groups within 48 h were 8.25±2.33, 5.46±1.32, 3.24±0.72 and 2.11±0.48, respectively, showing significant difference ($P<0.05$).

The comparison of incidence of adverse reactions within 48 h of four groups

The gastrointestinal reaction, dizziness, pruritus and urinary retention of four groups within

Table 1. Comparison of general information of four groups

Groups	Cases	Age (years)	Gender (male/female)	Body weight (kg)	ASA (I/II)	Operation time (min)
A	30	62.31±8.47	17/13	60.65±6.13	10/20	105.42±20.47
B	29	63.04±7.82	15/14	59.75±6.62	11/18	110.16±18.85
C	29	62.63±8.16	17/12	60.48±6.45	12/18	108.23±19.71
D	30	62.55±7.68	16/14	60.11±6.38	11/19	112.29±21.36

Group A: treated with 0.25% bupivacaine + fentanyl 0.4 mg, group B: 0.375% bupivacaine + fentanyl 0.4 mg, group C: 0.50% bupivacaine + fentanyl 0.4 mg, and group D: 0.75% bupivacaine + fentanyl 0.4 mg.

Table 2. The comparison of VAS scores of four groups (x±s)

Groups	Cases	After operation 4 h	After operation 8 h	After operation 12 h	After operation 24 h	After operation 48 h
A	30	1.68±0.70	1.16±0.57	0.74±0.45	0.42±0.31	0.22±0.24
B	29	1.62±0.61	1.12±0.56	0.68±0.48	0.44±0.29	0.24±0.27
C	29	1.52±0.68	1.15±0.61	0.71±0.46	0.41±0.33	0.22±0.25
D	30	1.22±0.62	1.08±0.53	0.70±0.43	0.40±0.30	0.21±0.24

Table 3. The comparison of incidence of adverse reactions within 48 h of four groups [case (%)]

Group	Cases	Gastrointestinal reaction	Dizziness	Pruritus	Urinary retention	Respiratory depression
A	30	3 (10.00)	0	0	3 (10.00)	1 (3.33)
B	29	4 (13.79)	0	1 (3.45)	4 (13.79)	2 (6.90)
C	29	4 (13.79)	1 (3.45)	1 (3.45)	4 (13.79)	6 (20.69)
D	30	5 (16.67)	1 (3.33)	1 (3.33)	3 (10.00)	7 (23.33)

48 h has no significant difference (P>0.05), but the incidence of respiratory depression of group A and group B were evidently higher than that of group C and group B, the difference was statistically significant (P<0.05), as is shown in **Table 3**.

Discussion

Based on the reference [3] and combined with therapeutic dose of bupivacaine used in the PCA of thoracic surgery, this study the drug used for patient-controlled analgesia (PCA) was set as bupivacaine combined with fentanyl, and set the concentrations at 0.25%, 0.375%, 0.50% and 0.75%, these four concentrations were in the safety range of epidural block. What' more, according to the methods of pain assessment in the references [4, 5], the situation of pain at difference points was evaluated by using VAS score.

The results indicated that the VAS scores of four groups after operation 4 h have statistical significance. After the comparison of two groups, it was found that the VAS score of D group was evidently lower than other three groups, while other three groups has no statistical significance, this may related to the loading dose. Although the loading dose of each group was 6 ml, the content of bupivacaine has significant difference.

The pressure times of PCA of four groups were significant difference, with the increasing concentration of bupivacaine, the pressure times reduced. It indicates that the reason to determine the effect of analgesic is not it's concentration but maybe it's absolute dose, indicating by using low concentrations of bupivacaine with large volume can also obtain satisfactory pain analgesic effect, these results were in accord with the studies of Freire etc. [6] and Eva etc. [7].

Respiratory depression is a complication of thoracic surgery which must be taken into consideration. The results indicated that the incidences of respiratory depression at 0.50% and 0.75% were significantly higher than that at 0.25% and 0.375%, suggesting an increased incidence of adverse reaction, and less safety. A study from domestic Jiang Daming [8] has showed that the patients taken with 0.50% bupivacaine during epidural anesthesia in thoracic surgery can significantly affect the intrapulmonary shunt and oxygenation compared with the concentration of 0.25%. It indicated that the concentration of bupivacaine less than

0.50% in thoracic epidural anesthesia may be relatively safe and effective.

In a word, the concentration of bupivacaine at 0.25%~0.375% in PCA of epidural anesthesia after thoracic surgery can make safe and effective analgesia effect.

Disclosure of conflict of interest

None.

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