Analgesic effect of dezocine in different doses on elderly patients undergoing abdominal operation under general anesthesia and its influence on stress response to postoperative tracheal extubation

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Abstract. – OBJECTIVE: To study the analgesic effect of dezocine in different doses on elderly patients undergoing abdominal operation under general anesthesia and to investigate the influence of dezocine on stress response to postoperative tracheal extubation.

PATIENTS AND METHODS: A total of 76 elderly patients undergoing abdominal operation under general anesthesia and postoperative analgesia in our hospital from January 2015 to January 2016 were selected, and patients treated with fentanyl were selected as the control group (fentanyl: 10 μg/kg, n=19). The patients were randomly divided into low-dose group (dezocine: 0.05 mg/kg, n=19), medium-dose group (dezocine: 0.1 mg/kg, n=19) and high-dose group (dezocine: 0.15 mg/kg, n=19). The patients in each group were intravenously injected with 0.1 mg/kg tropisetron. The tracheal catheter was withdrawn from patients in each group; the heart rate (HR), respiratory rate (RR), mean arterial pressure (MAP) and saturation of pulse oxygen (SpO2) of patients in each group before and at 10 min after tracheal extubation were recorded in detail; moreover, the visual analogue scale (VAS) score, Ramsay sedation score, occurrence rate of adverse reactions, Bruggrmann comfort scale (BCS) score and times of pressing analgesia pump after operation of patients in the four groups were evaluated at 4, 8, 12, 24 and 48 h after operation.

RESULTS: Compared with those before operation, there were no statistically significant differences in HR, RR, MAP and SpO2 of patients in low-dose group, medium-dose group and high-dose group at 10 min after tracheal extubation, and HR, RR, MAP and SpO2 of patients in control group were significantly increased after tracheal extubation (p<0.05). The VAS scores of patients in low-dose group within 48 h were significantly higher than those in control group, medium-dose group and high-dose group (p<0.05). The Ramsay sedation scores of patients in low-dose group and medium-dose group were significantly lower than those in control group and high-dose group (p<0.05), and the BCS score of patients in low-dose group was lower than those in medium-dose group, high-dose group, and control group (p<0.05). Besides, the occurrence rates of postoperative adverse reactions of patients in control group and low-dose group were higher than those in medium-dose group and high-dose group (p<0.05), the times of pressing analgesia pump after operation of patients in low-dose group were more than those in control group, medium-dose group and high-dose group (p<0.05), and the times were reduced successively in low-dose group, medium-dose group, and high-dose group. Finally, the results of correlation analysis showed that the dose of dezocine was positively correlated with the Ramsay sedation score, but negatively correlated with the VAS score of patients.

CONCLUSIONS: Dezocine can effectively enhance the analgesic effect on elderly patients receiving abdominal operation under general anesthesia in a dose-dependent manner. Moreover, dezocine can significantly reduce the stress response of elderly patients to postoperative tracheal extubation, and reduce the occurrence rate of adverse complications after abdominal operation under general anesthesia.

Key Words: Dezocine, Analgesia, Stress response, Operation under general anesthesia.
**Introduction**

With the continuous development of medical technology, people’s understanding of pain has been deepened constantly, and it was proposed by the World Health Organization in 2005 that “the pain is not only a symptom, but also a disease”, lifting the pain dispersing to a new height. In addition to the pain induced by the disease, the pain caused by surgery is currently one of the most common incentives for pain. A large number of studies have shown that the painless and comfortable state of patients in perioperative period can help greatly increase the success rate of surgery, and reduce the inflammatory response and stress response during operation, which is of great significance in postoperative functional recovery and organ function maintenance. China has gradually become an aging society; the requirements of elderly patients for the perioperative analgesic effect have been more intense, and the perioperative analgesic effect is closely related to the adverse reactions during and after operation. The most commonly used clinical analgesics are fentanyl-dominated opioid drugs, but these drugs lead to serious adverse reactions, such as respiratory depression and excessive sedation. Therefore, the appropriate analgesics can not only achieve the perioperative analgesic effect, but also significantly reduce the postoperative adverse prognosis of patients. Dezocine, as a kind of new drug acting on opioid receptors, can alleviate pain by specifically stimulating the μ receptor, which is characterized by high bioavailability, rapid absorption and distribution, long half-life and long-lasting and rapid-onset analgesic effect. Xu et al. showed that the occurrence rate of adverse reactions after application of dezocine is significantly lower than that after the application of traditional opioid analgesics. At present, there has been little research on the analgesic effect of dezocine in operation under general anesthesia of elderly patients, and there are few studies on the influence of dezocine on stress response to postoperative tracheal extubation. In this experiment, dezocine, as the perioperative analgesic, was studied, and its analgesic effect and influences on postoperative extubation and adverse reactions were analyzed, so as to provide a theoretical basis for the selection of analgesics in clinical anesthesia.

**Patients and Methods**

**Basic Data of Participants**

A total of 76 elderly patients undergoing abdominal operation under general anesthesia in our hospital from January 2015 to January 2016 were selected. The patients were randomly divided into the following four groups according to the difference analgesics used in operation: control group [10 μg/kg fentanyl, n=19, including 8 males and 11 females aged (62.18±6.32) years old], low-dose group [0.05 mg/kg fentanyl, n=19, including 9 males and 10 females aged (65.32±8.87) years old], medium-dose group [0.1 mg/kg fentanyl, n=19, including 10 males and 9 females aged (61.88±9.17) years old] and high-dose group [0.15 mg/kg fentanyl, n=19, including 11 males and 8 females aged (63.29±7.18) years old]. The general clinical data of patients in each group were recorded in detail; other consumptive diseases, preoperative cognitive dysfunction, cerebrovascular disease and allergy to the above analgesics were excluded from the patients enrolled. The clinical and pathological data and the complete therapeutic regimens of the above patients were saved, and the experiment was approved by the Ethics Committee of our hospital.

**Equipment and Drugs**

Fentanyl injection (Hubei Yichang Humanwell Pharmaceutical Co., Ltd., Yichang, China); dezocine injection (Jiangsu Yangtze River Hospital Co., Ltd., Jiangsu, China); tropisetron injection (Guangdong Baiyunshan Pharmaceutical Co., Ltd., Guangdong, China); anesthesia machine (Finland GE Medical Devices Group, Helsinki, Finland); analgesic pump (ACE Medical Devices Co., Ltd., Seoul, South-Korea); microcirculation function detector (Beijing Silu Medical Equipment Group, Beijing, China).

**Anesthesia Methods**

After fasting for solids for 8 h and for liquids for 4 h, patients were preoperatively evaluated by the same anesthesiologist. The visual analogue scale (VAS) score, Ramsay sedation score and Bruggermann comfort scale (BCS) score were adopted, and the patients or their families signed the informed consent of anesthesia surgery. Before the anesthesia, vital signs of patients were monitored, and the catheter was placed in the airway; after the anesthesia machine was connected, the respiratory mode was adjusted, and the relevant data were recorded. Patients were anesthetized after anesthesia induction until the operation was completed. Under patient controlled intravenous analgesia (PCIA), different doses of analgesics were given according to the grouping, and the analgesia was performed until 48 h after operation.
Dezocine in elderly patients undergoing abdominal operation

Monitoring and Observation Indexes

The heart rate (HR), respiratory rate (RR), mean arterial pressure (MAP) and saturation of pulse oxygen (SpO2) of patients in the above four groups before and at 10 min after tracheal extubation were recorded, respectively; the total times of pressing analgesia pump and all the adverse reactions within 48 h, mainly including nausea and vomiting, dizziness, hypotension and urinary retention, were recorded. VAS score, Ramsay sedation score and BCS score were given to patients at 4, 8, 12, 24 and 48 h after operation. VAS score has a total of 10 points, and 0-10 points indicate the degree of pain; the pain is evaluated by patients themselves at the corresponding time point and the pain score of patients is recorded. Ramsay sedation score has a total of 6 points: 6 points: drowsiness of patients without response to all movements outside; 5 points: drowsiness of patients with insensitive response to the loud talking outside; 4 points: drowsiness with sensitive response to the loud talking outside; 3 points: patients can effectively cooperate with the doctors in completing the task; 2 points: patients cooperate and stay calm; 1 point: patients are restless and nervous. BCS score has a total of 5 levels: 4 points: no pain when coughing; 3 points: no pain when gasping; 2 points: no pain in resting state in supine position, but pain when gasping; 1 point: no pain in calm state; 0 point: persistent pain.

Statistical Analysis

The data in this study were presented as mean ± standard deviation, and processed using Statistical Product and Service Solutions (SPSS) 19.0 software (SPSS Inc., Chicago, IL, USA). The t-test was used for the intergroup comparison, and analysis of variance was used for the comparison among groups. The homogeneity test of variance was performed; if the variance was homogeneous, Bonferroni method was used for the pairwise comparison; if the variance was heterogeneous, Welch method was used for analysis. Logistic regression analysis was used for the correlation analysis of data in each group; p<0.05 suggested that the difference was statistically significant.

Results

General Data

The general data and clinicopathologic data of patients enrolled were analyzed. The results showed that there were no statistically significant differences in age, gender, body weight, basal heart rate and operation time of patients among the four groups (p>0.05) (Table I).

Analgesic Effect

VAS scores were given to patients in each group at 4, 8, 12, 24 and 48 h after operation. The results showed that there was no significant difference in the VAS score at 4 h among groups, the VAS scores of patients in low-dose group at 8, 12, 24 and 48 h were significantly higher than those in control group, medium-dose group and high-dose group (p<0.05), and there were no statistically significant differences among control group, medium-dose group and high-dose group (p>0.05) (Figure 1).

Sedative Effect

Ramsay sedation scores were given to patients in each group at 4, 8, 12, 24 and 48 h after operation. The results showed that the Ramsay scores of patients in low-dose group and medium-dose group at 4, 8, 12, 24 and 48 h were significantly lower than those in control group and high-dose group, and the differences were statistically significant (p<0.05). There were no statistically significant differences between control group and high-dose group (p>0.05) (Figure 2).

Table I. General data analysis of patients in each group (x±s).

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (years old)</th>
<th>Gender (male/female)</th>
<th>Body weight (kg)</th>
<th>Basal heart rate (time/min)</th>
<th>Operation time (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>62.18±6.32</td>
<td>8/11</td>
<td>53.2±6.9</td>
<td>66±5.4</td>
<td>1.9±0.3</td>
</tr>
<tr>
<td>Low-dose group</td>
<td>65.32±8.87</td>
<td>9/10</td>
<td>58.7±7.1</td>
<td>68±3.2</td>
<td>2.1±0.5</td>
</tr>
<tr>
<td>Medium-dose group</td>
<td>61.88±9.17</td>
<td>10/9</td>
<td>52.5±8.9</td>
<td>70±3.1</td>
<td>1.8±0.2</td>
</tr>
<tr>
<td>High-dose group</td>
<td>63.29±7.18</td>
<td>11/8</td>
<td>57.1±5.3</td>
<td>67±6.9</td>
<td>1.8±0.3</td>
</tr>
<tr>
<td>p</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>t</td>
<td>0.356</td>
<td>0.532</td>
<td>0.296</td>
<td>0.685</td>
<td>0.568</td>
</tr>
</tbody>
</table>
BCS Score

BCS scores were given to patients in each group at 4, 8, 12, 24 and 48 h after operation. The results revealed that the BCS scores of patients in low-dose group at 4, 8, 12, 24 and 48 h were lower than those in control group, medium-dose group and high-dose group, and the differences were statistically significant ($p<0.05$), and there were no statistically significant differences among control group, medium-dose group and high-dose group ($p>0.05$) (Figure 3).

Times of Pressing Analgesia Pump After Operation

The total times of pressing analgesia pump after operation of patients in each group were recorded in detail. The results revealed that the total times of pressing analgesia pump after operation of patients in low-dose group were more than those in medium-dose group, high-dose group and control group, and the differences were statistically significant ($p<0.05$), and the times were reduced successively in low-dose group, medium-dose group and high-dose group (Figure 4).

Changes in Circulation Indexes

Circulation indexes, mainly including HR, RR, MAP and SpO$_2$, of patients in each group before operation and after tracheal extubation were recorded to measure the stress response of patients to tracheal extubation. The results showed that compared with those before operation, there were no statistically significant differences in HR, RR, MAP and SPO$_2$ of patients in low-dose group, medium-dose group and high-dose group at 10 min after tracheal extubation, and HR, RR, MAP and SPO$_2$ of patients in control group were significantly increased after tracheal extubation ($p<0.05$) (Figure 5).

Occurrence Rates of Adverse Reactions

The occurrence rates of adverse reactions within 48 h after operation of patients enrolled were statistically analyzed. The results revealed that the occurrence rates of postoperative adverse reactions of patients in control group and low-dose group were higher than those in medium-dose group and high-dose group ($p<0.05$) (Table II).

Correlation Analysis

The correlations of dezocine dose with Ramsay sedation score and VAS score of patients were analyzed via Logistic regression analysis. The results showed that the dose of dezocine was posi-
Dezocine in elderly patients undergoing abdominal operation

Table II. Occurrence rate of adverse reactions of patients in each group (x±s).

<table>
<thead>
<tr>
<th>Group</th>
<th>Incidence rate of adverse reactions (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>36.8*</td>
</tr>
<tr>
<td>Low-dose group</td>
<td>31.5*</td>
</tr>
<tr>
<td>Medium-dose group</td>
<td>10.5</td>
</tr>
<tr>
<td>High-dose group</td>
<td>15.7</td>
</tr>
<tr>
<td>t</td>
<td>0.865</td>
</tr>
</tbody>
</table>

The occurrence rates of postoperative adverse reactions of patients in control group and low-dose group are significantly increased compared with those in medium-dose group and high-dose group (p < 0.05).

Discussion

Due to the external stimuli acting on the peripheral receptors of the body and entering the spinal cord via nerve, the pain reflex is formed, which will be transmitted to the more advanced...
central nervous system, producing the sense of pain. Studies have shown that the pain is a kind of feeling and reaction controlled and integrated by the central system, whose main manifestations are in the physical, behavioral and psychological aspects. The pain can lead to complications in the cardiovascular system, significantly increase the hospital stays, and cause poor prognosis in patients. The above complications occur in elderly patients easily. With the deepening of research on pain, its occurrence mechanisms have been constantly cleared, so a large number of analgesic drugs are developed and used clinically, effectively reducing the pain of patients due to various causes and significantly increasing the success rate of multiple surgeries. Choosing the appropriate analgesics to reduce the postoperative pain, increase the success rate of surgery, postoperative recovery of patients and increase the postoperative review rate of patients is of great significance.

In this work, the analgesic effect of dezocine in different doses on elderly patients undergoing abdominal operation under general anesthesia and its influence on stress response to postoperative tracheal extubation were studied with fentanyl as the control drug. It was found that the medium- and high-dose dezocine could produce the similar analgesic effect to fentanyl, and the occurrence rate of postoperative adverse reactions of patients in the dezocine group was significantly decreased. Dezocine is the inhibitor of opioid μ receptors, and the opioid κ receptors distributed in the cerebral cortex can have an effective inhibitory effect on pain and have a good treatment effect on chronic dull pain and acute sharp pain triggered by surgery and other various causes. Solanki et al. found that dezocine has an excellent analgesic effect after the abdominal operation under general anesthesia, which may be related to its strong inhibitory effect on the μ receptor, and its dual effect of activation and antagonism of μ receptors; moreover, dezocine can effectively reduce the occurrence rate of adverse reactions. In this experiment, VAS score was used to evaluate the analgesic effect on patients in each group, Ramsay score was used to evaluate the sedative effect on patients, and the times of pressing analgesia pump after operation were recorded to analyze the analgesic effect of dezocine from various perspectives. All the above indexes showed that dezocine has a strong analgesic effect in a certain dose-dependent manner. The effect of analgesics on the stress response to postoperative extubation was detected via monitoring the circulation indexes of patients in each group before operation and at 10 min after postoperative extubation. The results revealed that the protective effect of dezocine on postoperative stress was significantly superior to that of fentanyl, and even if the dose of dezocine is lower, the stress response to postoperative extubation can also be effectively reduced. Zhou et al. observed that the strength of postoperative stress is closely related to the postoperative recovery of patients, and the stress response of patients should be reduced as far as possible in the clinical surgery. Besides, the correlation analysis showed that the dose of dezocine was positively correlated with the Ramsay score but negatively correlated with the VAS score of patients, indicating that the analgesic effect of dezocine is dose-dependent and the higher dose of dezocine within the safety range can improve the postoperative pain effectively.

Conclusions

Dezocine can effectively reduce the postoperative pain of elderly patients, and its analgesic effect is dose-dependent. Moreover, dezocine can
also significantly reduce the stress response to postoperative tracheal extubation and the occurrence rate of postoperative adverse reactions. It is recommended that the higher dose of dezocine be used for analgesia in abdominal operation under general anesthesia.

Conflict of interest
The authors declare no conflicts of interest.

References


