Effect of oxycodone combined with dexmedetomidine on general anesthesia emergence agitation and stress response

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Objective: To study the effect of oxycodone combined with dexmedetomidine on general anesthesia emergence agitation and stress response in patients with abdominal operation.

Methods: A total of 118 patients who received abdominal operation under general anesthesia in our hospital between May 2014 and May 2016 were collected and randomly divided into control group (n=59) and observation group (n=59). Control group received general anesthesia + oxycodone intervention, and the observation group of patients received routine anesthesia + oxycodone combined with dexmedetomidine intervention. The incidence of emergence agitation in the PACU was compared between two groups of patients; immediately after operation (T1), 3 min after extubation (T2) and 10 min after extubation (T3), serum levels of stress-related indexes were detected.

Results: The incidence of emergence agitation in the PACU of observation group was significantly lower than that of control group. At T1, differences in serum RAS indexes, insulin resistance indexes and thyroid hormones were not statistically significant between two groups of patients; at T2 and T3, serum RAS indexes REN, Ang II and ALD, insulin resistance indexes FBG, FINS and HOMA-IR as well as thyroid hormones FT3, FT4 and TSH of both groups of patients were significantly higher than those at T1, and REN, Ang II, ALD, FBG, FINS, HOMA-IR, FT3, FT4 and TSH levels of observation group were significantly lower than those of control group.

Conclusion: Oxycodone combined with dexmedetomidine can reduce the incidence of general anesthesia emergence agitation and reduce the systemic stress reaction in patients with abdominal operation.

1. Introduction

Emergence agitation (EA) in patients with general anesthesia is a problem for all clinical anesthesiologists, severe emergence agitation may directly result in significant hemodynamic fluctuations and systemic stress reactions, and severe cases may cause cardiovascular and cerebrovascular diseases[1,2]. How to reduce or even avoid emergence agitation has been the key to improve the quality of anesthesia and ensure the surgery quality, oxycodone, as a potent analgesic drug, has been successfully applied in clinical practice at present, but the role of oxycodone analgesia alone has limitations in inhibiting EA[3]. Dexmedetomidine is the 2 adrenaline agonist that has both sedative and analgesic effect, and many studies have confirmed that it can increase the hemodynamic stability in awakening period in patients with general anesthesia[4]. In the study, oxycodone combined with dexmedetomidine was used for early intervention in anesthesia recovery period in patients with abdominal surgery, and its effect was elaborated from the incidence of EA, systemic stress reaction and other aspects.

2. Information and methods

2.1 General information

A total of 118 patients who received abdominal operation in our hospital between May 2014 and May 2016 were selected as the
research subjects, and the patients themselves and families signed the consent form. Inclusion criteria: (1) 18-80 years old; (2) undergoing elective surgery; (3) without history of surgical operation within 6 months prior to admission. Exclusion criteria: (1) intraoperative blood transfusion 500 mL; (2) without history of cerebral infarction/cerebral hemorrhage; (3) associated with systemic infectious diseases; (4) associated with hyperthyroidism/hypothyroidism, primary aldosteronism, sympathetic nerve dysfunction and other diseases that affected the endocrine system state. According to the random number table, the included patients were divided into control group (n=59) and observation group (n=59), control group included 31 male cases and 28 female cases, they were 27-69 years old, and the body weight was 49-82 kg and (59.39±9.12) kg in average; observation group included 32 male cases and 27 female cases, they were 25-72 years old, and the body weight was 48-80 kg and (59.75±9.31) kg in average. The two groups were not significantly different in terms of gender, age and body weight distribution (P>0.05), and the hospital ethics committee approved the study.

2.2 Anesthesia

Both groups of patients received general anesthesia and endotracheal intubation, and the specific anesthesia induction was as follows: sufentanil (Yichang Humanwell Pharmaceutical Co., LTD., approved by H20054171) 0.3 μg/kg, propofol (Guangdong Jiabo Pharmaceutical Co., LTD., approved by H20051842) 1.5-2.0 mg/kg and cis atracurium (Shanghai Pharma, Dongying (Jiangsu) Pharmaceutical Co., Ltd., approved by H20060927) 0.15 mg/kg, pure oxygen intake for 3 min, then oral trachea cannula, connecting the respirator and setting respiratory parameters according to the situation of individual patients. Anesthesia maintenance: target controlled infusion of propofol and remifentanil (Yichang Humanwell Pharmaceutical Co., LTD., approved by H20030197), propofol BIS value 40-50, remifentanil effector site concentration 3-5 ng/mL, composite sevoflurane inhalation (Shanghai Hengrui Pharmaceutical Co., LTD., approved by H20070172) and maintaining inspired concentration within 0.5 minimum alveolar concentration (MAC). Sevoflurane inhalation was stopped when abdominal closure started, and target controlled infusion of intravenous anesthetics was stopped when skin suturing was finished.

2.3 Adjuvant drugs

The control group received pump injection of oxycodone (Beijing Hwellsopharmaceutical Co., LTD., approved by H20090228) 0.08 mg/kg 30 min before the end of surgery. Observation group received intravenous drip of dexmedetomidine (Sichuan Guorui Pharmaceutical Co., LTD., approved by H20110097) 1 μg/kg within 10 min before anesthesia induction, which was maintained at the speed of 0.3 μg/(kg·h) until 30 min before the end of surgery. Oxycodone usage and dosage were the same as those of the control group. After operation, patients were sent into postanesthesia care unit (PACU).

2.4 Observation indexes

Incidence of emergence agitation of two groups of patients in the PACU was recorded. Immediately after operation (T1), 3 min after extubation (T2) and 10 min after extubation (T3), 1.5 mL peripheral venous blood was extracted from two groups of patients, anti-coagulated and centrifuged to get supernatant, and stress-related parameter levels were determined, specifically as follows: (1) the renin-angiotensin aldosterone system (RAS) indicators: RIA method was used to detect serum renin (REN), angiotensin (Ang II) and aldosterone (ALD) contents; (2) insulin resistance indexes: the glucose meter (Guilin Urit Medical Electronics Co., LTD., the article number U80) was used to determine fasting blood glucose (FBG), fasting insulin (FINS) and insulin resistance index (HOMA-IR) levels; (3) thyroid hormones: RIA method was used to detect serum free triiodothyronine (FT3), free thyroxine (FT4) and thyroid stimulating hormone (TSH) contents.

2.5 Statistical methods

Data calculation in the study was by software SPSS 20.0, and the personnel received professional statistical training. Incidence of emergence agitation and other count data were in terms of percentage and comparison between groups was by chi-square test; RAS indexes, insulin resistance indexes, thyroid hormones and other measurement data were in terms of mean ± standard deviation, and the comparison between groups was by grouping t test. P<0.05 was the standard of statistical significance in differences between groups.

3. Results

3.1 Incidence of emergence agitation

Comparison of EA incidence in the PACU between two groups of patients was as follows: the incidence of emergence agitation in the PACU of control group was 22.03% (13/59) and the incidence of emergence agitation in the PACU of observation group was 5.08% (3/59). The incidence of emergence agitation in the PACU of observation group was significantly lower than that of control group, and differences were statistically significant (P<0.05).

| Table 1. | Comparison of RAS index levels at different points in time between two groups. |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Groups          | n               | T1              | T2              | T3              | T1              | T2              | T3              |
| Control group   | 59              | 1.72±0.28       | 3.04±0.45*      | 4.18±0.52*      | 1.17±0.15       | 1.68±0.24       | 2.94±0.35*      | 114.38±16.59   | 204.44±26.82*  | 294.36±35.71*  |
| Observation group| 59              | 1.71±0.25       | 2.24±0.34*      | 2.61±0.39*      | 1.90±0.14       | 1.34±0.18*      | 1.86±0.24*      | 116.52±19.73   | 154.82±19.53*  | 189.36±23.41*  |
| T value         |                 | 0.281           | 6.492           | 8.293           | 0.193           | 5.932           | 7.182           | 0.583           | 12.181         | 18.394         |
| P value         |                 | >0.05           | <0.05           | <0.05           | >0.05           | <0.05           | <0.05           | >0.05           | <0.05          | <0.05          |

Note: compared with same group at T1, *P<0.05.
Table 2.
Comparison of insulin resistance index levels at different points in time between two groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>FBG</th>
<th>FT3</th>
<th>FINS</th>
<th>HOMA-IR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>T1</td>
<td>T2</td>
<td>T3</td>
<td></td>
</tr>
<tr>
<td>Control group</td>
<td>59</td>
<td>6.83±0.71</td>
<td>7.21±0.78</td>
<td>6.93±0.62</td>
<td>6.89±0.77</td>
</tr>
<tr>
<td>Observation group</td>
<td>59</td>
<td>5.31±0.68</td>
<td>5.92±0.59</td>
<td>6.13±0.68</td>
<td>5.16±0.58</td>
</tr>
</tbody>
</table>

T value: 0.201, P value: 0.05

Note: compared with same group at T1, P<0.05.

Table 3.
Comparison of thyroid hormone contents at different points in time between two groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>FT3</th>
<th>FT4</th>
<th>TSH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>T1</td>
<td>T2</td>
<td>T3</td>
</tr>
<tr>
<td>Control group</td>
<td>59</td>
<td>12.27±1.89</td>
<td>15.31±1.94</td>
<td>2.19±0.34</td>
</tr>
<tr>
<td>Observation group</td>
<td>59</td>
<td>2.52±0.34</td>
<td>2.12±1.85</td>
<td>2.17±0.31</td>
</tr>
</tbody>
</table>

T value: 0.102, P value: 0.05

Note: compared with same group at T1, P<0.05.

3.2 RAS indexes

Comparison of serum RAS indexes REN (μg/L), AngⅠ (pg/mL) and ALD (pg/mL) contents at different points in time between two groups of patients was as follows: at T1, differences in serum REN, AngⅠ and ALD contents were not statistically significant between two groups of patients (P>0.05); at T2 and T3, serum REN, AngⅠ and ALD contents of both groups of patients were significantly higher than those at T1, and serum REN, AngⅠ and ALD contents of observation group were lower than those of control group, and differences were statistically significant (P<0.05), shown in Table 1.

3.3 Insulin resistance indexes

Comparison of serum insulin resistance indexes FBG (mmol/L), FINS (μU/mL) and HOMA-IR levels at different points in time between two groups of patients was as follows: at T1, differences in serum FBG, FINS and HOMA-IR levels were not statistically significant between two groups of patients (P>0.05); at T2 and T3, serum FBG, FINS and HOMA-IR levels of both groups of patients were significantly higher than those at T1, and serum FBG, FINS and HOMA-IR levels of observation group were lower than those of control group, and differences were statistically significant (P<0.05), shown in Table 2.

3.4 Thyroid hormones

Comparison of serum thyroid hormones FT3 (pmol/L), FT4 (pmol/L) and TSH (μU/mL) contents at different points in time between two groups of patients was as follows: at T1, differences in serum FT3, FT4 and TSH contents were not statistically significant between two groups of patients (P>0.05); at T2 and T3, serum FT3, FT4 and TSH contents of both groups of patients were significantly higher than those at T1, and serum FT3, FT4 and TSH levels of observation group were lower than those of control group, and differences were statistically significant (P<0.05), shown in Table 3.

4. Discussion

Oxycodone is one of the most popular analgesic drugs in anesthesiology, and it is mostly used via intravenous injection before the end of surgery to reduce the incision pain in patients after recovery. The analgesic effect of oxycodone has been confirmed in many studies, but in abdominal surgery and other surgeries with larger trauma, the EA incidence after oxycodone analgesia alone is still high[5]. Dexmedetomidine has central anti-sympathetic and anti-anxiety effect, it can increase the depth of sedation, but it is relatively insufficient in analgesia effect, so some scholars recommend joint application of oxycodone and dexmedetomidine in surgeries with larger trauma so that the two can draw on each other's strength to exert potent sedative and analgesic action[6,7]. In the study, patients with abdominal surgery were selected as the research subjects, the incidence of EA under different drug compatibility was compared at first, and it was found that the incidence of emergence agitation in the PACU of observation group was significantly lower than that of control group, thus indicating that oxycodone combined with dexmedetomidine can effectively reduce the EA in patients with abdominal surgery, and increasing the depth of sedation in patients helps to increase the patients' smoothness in awakening period.

The systemic stress response caused by insufficient intraoperative sedation depth, pain in awakening period and so on is the root cause of EA in surgical patients, dexmedetomidine excites 2 adrenergic receptor, exerts sedative and anti-sympathetic nerve effect, deepens the depth of anesthesia and increases the pain threshold, and this is also the root cause for it to further stabilize the internal environment and reduce the EA in patients after compatibility with oxycodone[8]. In the study, the homeostasis in patients was furthered studied from RA system indexes, insulin resistance and thyroid hormones, and the reason for oxycodone combined with dexmedetomidine to lower postoperative incidence of EA in patients with abdominal surgery was explored from the aspect of serology.
REN, Ang II and ALD are the major indexes of RAS, RAS is activated when operation and other huge stimuli occur; the above indexes in serum are massively secreted, and their secretion volume is consistent with the body’s stress level[9,10]. It was found in the study that serum REN, Ang II and ALD contents of both groups of patients at T2 and T3 were higher than those at T1 suggesting that postoperative anesthetic effect extinction, extubation and other stimuli can all stimulate the RAS and lead to the increased synthesis of corresponding factors, but serum REN, Ang II and ALD contents of observation group at T2 and T3 were significantly lower than those of control group, confirming that oxycodone combined with dexmedetomidine will reduce the RAS activation at different time points after extubation in patients with abdominal surgery, and this is directly related to the anti-sympathetic activity of dexmedetomidine. The increased glycogen decomposition and the decreased insulin sensitivity under stress state lead to hyperglycemia and hyperinsulinemia, and sustained hyperglycemia can inhibit surgical incision healing and increase the risk of incision infection[11-13]. Affected by the stimuli such as incision pain and extubation, serum FBG, FINS and HOMA-IR levels of both groups after extubation were higher than those at T1, but the serum levels of above indexes of observation group after extubation were lower than those of control group, thus indicating that oxycodone combined with dexmedetomidine will reduce the degree of insulin resistance after extubation in patients with abdominal surgery, and indirectly reflecting that the stress damage after extubation is lighter.

More and more studies have confirmed that the hypothalamus-pituitary-thyroid axis plays an important role in adjusting acute stress response, its perception to the strength of pressure is sensitive, acute stress can result in the elevation of T3, T4 and TSH levels, and when stimulus continues or the stimulus intensity increases, the hypothalamus-pituitary-thyroid axis can be converted into inhibited state, and TSH levels drop[14,15]. In this study, serum T3, T4 and TSH levels of both groups of patients after extubation were higher than those during operation, it indicates that the patients undergo a certain intensity of stimulation during extubation, and the serum T3, T4 and TSH levels of observation group after extubation were lower than those of control group, and it indicates that the hypothalamus-pituitary-thyroid axis stimulation is relieved after oxycodone combined with dexmedetomidine intervention, and indirectly confirms that the combination of the two drugs plays a positive role in reducing stress reaction.

To sum up, it can be concluded that oxycodone combined with dexmedetomidine can reduce the incidence of postoperative EA in patients with abdominal surgery, and the specific mechanisms are directly correlated with its reducing the peri-extubation systemic stress response. In the same surgical intervention in the future, this drug compatibility solution can be referred to further stabilize the hemodynamics and internal environment, and ensure the implementation of operation effect.

References


