Effect of dexmedetomidine assisted anesthesia on the inflammatory cytokines and T lymphocyte subsets in elderly patients with Alzheimer disease underwent total hip replacement

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Objective: To explore the effect of dexmedetomidine assisted anesthesia on the inflammatory cytokines and T lymphocyte subsets in elderly patients with Alzheimer disease (AD) underwent total hip replacement (THR).

Methods: A total of 60 patients with AD who were admitted in our hospital from October, 2014 to October, 2016 for THR were included in the study and randomized into the observation group and the control group with 30 cases in each group. Strict preoperative preparation was performed. The patients in the two groups were given intravenous injection of midazolam (0.04 mg/kg), propofol (0.5–1.5 mg/kg), cisatracurium (0.15 mg/kg), and fentanyl (4 μg/kg) for anesthesia induction, continuously venous pumping of propofol [1.5–2.5 mg/(kg·h)] and remifentanil [0.04–0.4 μg/(kg·min)] in maintaining the anesthesia depth, and cisatracurium for intermittent muscle relaxation. The patients in the observation group were given venous pumping of dexmedetomidine (1 μg/kg) 15 min before anesthesia induction, and dexmedetomidine [0.2–0.7 μg/(kg·h)] for maintenance until the end of operation. The peripheral venous blood before operation, the time immediately after operation, 12 and 24 h after operation in the two groups was collected. ELISA was used to detect CRP, IL-6, and TNF-α. FCM was used to detect T lymphocyte subsets (CD3+, CD4+, and CD8+). CD4+/CD8+ was calculated. Ramsay sedation grading was performed before operation, the time immediately after operation, 12 and 24 h after operation.

Results: Ramsay sedation score the time immediately after operation and 12 h after operation in the observation group was significantly greater than that in the control group (P<0.05). The serum CRP, IL-6, and TNF-α levels the time immediately after operation, 12 and 24 h after operation in the observation group were significantly lower than those in the control group (P<0.05). The serum CD3+, CD4+, CD8+, and CD4+/CD8+ the time immediately after operation, 12 and 24 h after operation in the observation group were significantly higher than those in the control group (P<0.05).

Conclusions: Dexmedetomidine applied in patients with AD underwent THR has an unique analgesia and sedation effect, and can effectively inhibit the release of inflammatory cytokines in order to improve the immunological function.

I. Introduction

Total hip replacement (THR) is the most effective method in the treatment of hip joint disease in the terminal stage, but the postoperative pain will affect the rehabilitation.[1] The surgical trauma can cause the release of inflammatory cytokines, especially for the elderly patients with Alzheimer disease (AD), the anesthesia is relatively difficult, due to their function degeneration, weakened body resistance, communication difficulty, and being accompanied by systemic disease.[2] Dexmedetomidine has effects of analgesia, sedation, sympathetic activity inhibiting, anti-anxiety, hypnosis, improvement of cardiovasculary stability during the perioperative period, and anti-inflammation, and has a
preferable effect in alleviating the perioperative stress reaction and inflammatory reaction[3]. The study is aimed to explore the effect of dexmedetomidine assisted anesthesia on the inflammatory cytokines and T lymphocyte subsets in elderly patients with AD underwent THR.

2. Materials and methods

2.1. General materials

A total of 60 patients with AD who were admitted in our hospital from October, 2014 to October, 2016 for THR were included in the study. Inclusion criteria: (1) those who had intelligence disturbance; (2) those who could not preferably communicate with others and cooperate with the anesthesia, with ASA II–III grade; (3) those whose relatives had signed the informed consents. The study was approved by the Ethical Committee of our hospital. Those who were merged with heart, liver, and renal dysfunction, hemorrhagic disease, and coagulation dysfunction were excluded from the study. The patients were randomized into the observation group and the control group with 30 cases in each group. In the observation group, 18 were male, and 12 were female; aged from 68 to 75 years old, with an average age of (72.3±2.5) years old; 21 on the left, and 9 on the right. In the control group, 17 were male, and 13 were female; aged from 67 to 76 years old, with an average age of (71.2±2.6) years old; 20 on the left, and 10 on the right. The comparison of gender, age, and limb between the two groups was not statistically significant ($P$>0.05).

2.2. Methods

Strict preoperative preparation was performed. The venous channel was opened. BP, HR, RR, and SPO2 were strictly monitored. The patients in the two groups were given intravenous injection of midazolam (0.04 mg/kg), propofol (0.5–1.5 mg/kg), cisatracurium (0.15 mg/kg), and fentanyl (4 μg/kg) for anesthesia induction, continuously venous pumping of propofol [1.5–2.5 mg/(kg • h)] and remifentanil [0.04–0.4 μg/(kg • min)] in maintaining the anesthesia depth, and cisatracurium for intermittent muscle relaxation. The patients in the observation group were given venous pumping of dexmedetomidine (1 μg/kg) 15 min before anesthesia induction, and dexmedetomidine [0.2–0.7 μg/(kg • h)] for maintenance until the end of operation.

2.3. Observation indicators

The peripheral venous blood before operation, the time immediately after operation, 12 and 24 h after operation in the two groups was collected. ELISA was used to detect CRP, IL-6, and TNF-α. FCM was used to detect T lymphocyte subsets (CD3+, CD4+ and CD8+). CD4+/CD8+ was calculated. Ramsay sedation grading was performed before operation, the time immediately after operation, 12 and 24 h after operation: 1 score: irritable and restless; 2 scores: cooperation and quietness; 3 scores: somnolence and obeying the order; 4 scores: sleep state and being awakening; 5 scores: slow response when calling; 6 scores: not awaking when calling.

2.4. Statistical analysis

SPSS 19.0 software was used for the statistical analysis. The measurement data were expressed as mean±SD, and t test was used. Chi-square test was used for the enumeration data. $P$<0.05 was regarded as statistically significant.

3. Results

3.1. Comparison of the levels of the inflammatory cytokines before and after operation between the two groups

The serum CRP, IL-6, and TNF-α levels the time immediately after operation, 12 and 24 h after operation in the two groups were significantly elevated when compared with before operation ($P$<0.05). The serum CRP, IL-6, and TNF-α levels the time immediately after operation, 12 and 24 h after operation in the observation group were significantly lower than those in the control group ($P$<0.05) (Table 1).

3.2. Comparison of the levels of T lymphocyte subsets before and after operation between the two groups

The serum CD3+, CD4+, CD8+, and CD4+/CD8+ the time immediately after operation, and 12 h after operation in the two groups were significantly reduced when compared with before operation ($P$<0.05), the above indicators were recovered 24 h after operation, but were still significantly lower than those before operation ($P$<0.05). The serum CD3+, CD4+, and CD8+ the time immediately after operation, 12 and 24 h after operation in the observation group were significantly higher than those in the control group ($P$<0.05) (Table 2).

3.3. Comparison of Ramsay sedation score before and after operation between the two groups

Ramsay sedation score the time immediately after operation and 12
of strong sedation, rapid effect taking, and short half-life period, Locus coeruleus is also a key part in responsible of sleep and can produce analgesia, sedation, and anti-anxiety effects when α2 adrenergic receptor, and terminate the conduction of pain signal. Some researches [8] demonstrate that operation can mediate the inflammatory reaction, increase the expression of inflammatory cytokines, and aggravate the postoperative complications and severity degree. Operation can activate the immune system to cause strongly peripheral inflammatory reaction, while the inflammatory cytokines can directly or indirectly cause the central nervous system inflammatory reaction, resulting in neurotoxicity, synaptic transmission dysfunction, and neurodegeneration [9]. In the central nervous system inflammatory reaction, CRP, IL-1, IL-6, and TNF-α are regarded as the typical pro-inflammatory cytokines, and are usually served as indicators to evaluate the central nervous system inflammatory reaction [10]. Some researches [11,12] demonstrate that stimulating on the central α2 adrenergic receptor can produce an anti-inflammatory effect, while stimulating on the peripheral α2 adrenergic receptor can produce an pro-inflammatory effect.

Table 1
Comparison of the levels of the inflammatory cytokines before and after operation between the two groups (n=30, mean±SD).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Time</th>
<th>CRP</th>
<th>IL-6</th>
<th>TNF-α</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Before operation</td>
<td>3.72±1.43</td>
<td>12.87±3.21</td>
<td>14.36±4.55</td>
</tr>
<tr>
<td></td>
<td>The time immediately after operation</td>
<td>7.57±2.37±</td>
<td>23.62±4.72±</td>
<td>28.31±6.18±</td>
</tr>
<tr>
<td></td>
<td>12 h after operation</td>
<td>9.52±2.56±</td>
<td>27.46±5.28±</td>
<td>37.54±5.26±</td>
</tr>
<tr>
<td></td>
<td>24 h after operation</td>
<td>12.34±3.34±</td>
<td>30.56±5.72±</td>
<td>40.26±6.38±</td>
</tr>
<tr>
<td>Control</td>
<td>Before operation</td>
<td>3.65±1.61</td>
<td>12.69±4.24</td>
<td>14.29±5.16</td>
</tr>
<tr>
<td></td>
<td>The time immediately after operation</td>
<td>15.42±3.23±</td>
<td>32.71±5.44±</td>
<td>38.42±6.61±</td>
</tr>
<tr>
<td></td>
<td>12 h after operation</td>
<td>19.43±4.28±</td>
<td>40.53±7.45±</td>
<td>52.47±8.29±</td>
</tr>
<tr>
<td></td>
<td>24 h after operation</td>
<td>22.71±5.46±</td>
<td>48.53±6.19±</td>
<td>65.31±7.65±</td>
</tr>
</tbody>
</table>

*P<0.05, when compared with before operation; †P<0.05, when compared with the control group.

Table 2
Comparison of the levels of T lymphocyte subsets before and after operation between the two groups (n=30, mean±SD).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Time</th>
<th>CD25+</th>
<th>CD4+</th>
<th>CD8+</th>
<th>CD4+/CD8+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Before operation</td>
<td>985.11±128.46</td>
<td>632.65±85.76</td>
<td>395.68±89.42</td>
<td>1.59±0.19</td>
</tr>
<tr>
<td></td>
<td>The time immediately after operation</td>
<td>796.64±121.32±</td>
<td>461.13±78.57±</td>
<td>332.37±72.54±</td>
<td>1.47±0.16±</td>
</tr>
<tr>
<td></td>
<td>12 h after operation</td>
<td>786.42±124.51±</td>
<td>425.64±82.34±</td>
<td>309.57±58.38±</td>
<td>1.41±0.16±</td>
</tr>
<tr>
<td></td>
<td>24 h after operation</td>
<td>928.83±131.56±</td>
<td>596.64±95.25±</td>
<td>371.25±76.45±</td>
<td>1.49±0.18±</td>
</tr>
<tr>
<td>Control</td>
<td>Before operation</td>
<td>986.42±131.23</td>
<td>635.28±83.71</td>
<td>396.78±91.22</td>
<td>1.59±0.20</td>
</tr>
<tr>
<td></td>
<td>The time immediately after operation</td>
<td>663.54±113.56±</td>
<td>319.41±68.74±</td>
<td>225.37±69.35±</td>
<td>1.37±0.15±</td>
</tr>
<tr>
<td></td>
<td>12 h after operation</td>
<td>517.16±123.25±</td>
<td>242.57±65.42±</td>
<td>203.24±54.72±</td>
<td>1.22±0.18±</td>
</tr>
<tr>
<td></td>
<td>24 h after operation</td>
<td>772.34±16.47±</td>
<td>474.15±54.49±</td>
<td>324.54±68.49±</td>
<td>1.42±0.16±</td>
</tr>
</tbody>
</table>

*P<0.05, when compared with before operation; †P<0.05, when compared with the control group.

Table 3
Comparison of Ramsay sedation score before and after operation between the two groups (n=30, mean±SD)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Before operation</th>
<th>The time immediately after operation</th>
<th>12 h after operation</th>
<th>24 h after operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>1.96±0.21</td>
<td>4.11±1.16†</td>
<td>2.35±0.36†</td>
<td>2.07±0.18</td>
</tr>
<tr>
<td>Control</td>
<td>2.01±0.17</td>
<td>2.63±0.47†</td>
<td>1.98±0.22</td>
<td>2.05±0.16</td>
</tr>
</tbody>
</table>

*P<0.05, when compared with before operation; †P<0.05, when compared with the control group.
Dexmedetomidine, as α<sub>2</sub> adrenergic receptor agonist, can stimulate the central nervous system to inhibit the sympathetic activity, and strengthen the parasympathetic activity to control the inflammatory reaction. The results in the study showed that the serum CRP, IL-6, and TNF-α levels the time immediately after operation, 12 and 24 h after operation in the observation group were significantly lower than those in the control group (P<0.05), indicating that dexmedetomidine applied in patients with AD for THR can significantly reduce the expressions of inflammatory cytokines.

Some researches[13] demonstrate that the immunological status is an important factor to affect the perioperative prognosis, while anxiety, anesthesia, hypothermia, surgical trauma, bleeding, pain, and stress reaction can affect the immunological status. T lymphocyte subsets are the sensitive indicators to reflect the immunological status[14,15]. It is reported that after being given dexmedetomidine in different dosages for elderly patients underwent spinal operation during the perioperative period, the results show that dexmedetomidine can effectively reduce the expressions of T lymphocyte subsets and NK cell, in a dose dependent manner, and improve the immunological function[16].

In conclusion, dexmedetomidine applied in patients with AD underwent THR has an unique analgesia and sedation effect, and can effectively inhibit the release of inflammatory cytokines in order to improve the immunological function.

References


