Effects of dexmedetomidine on inflammatory response and oxidative stress in laparoscopic hysterectomy patients

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ABSTRACT

Objective: To investigate the effect of dexmedetomidine on inflammatory response and oxidative stress in patients with laparoscopic total hysterectomy. Methods: Ninety patients with laparoscopic hysterectomy under general anesthesia were selected in our hospital from January 2015 to December 2016, and randomly divided into control group and observation group, Each group of 45 cases. The observation group was given dexmedetomidine, intravenous pump injection, The control group was given the same amount of saline in the same manner, followed by anesthesia induction. The hemodynamics, inflammatory factors and oxidative stress were monitored before anesthesia (T0), 30 min after the end of pneumoperitoneum (T1), after operation (T2) and at the end of 24 h (T3). Results: Compared with T0, T1, T2 and T3, the observation group of patients with MAP and HR levels were no significant difference; T3, the control group MAP and HR levels were not significantly different; T1 and T2, MAP and HR levels in the control group were significantly increased, And significantly higher than the observation group; Compared with T0, the levels of CRP, TNF-α and IL-1β in patients were significantly increased in T1, T2 and T3, but the levels of CRP, TNF-α and IL-1β in the observation group were significantly lower than those in the control group; Compared with T0, both groups of patients with H2O2 and MDA levels were significantly increased, TAS levels were significantly reduced, the difference was statistically significant, However, the levels of H2O2 and MDA in the observation group were significantly lower than those in the control group, the level of TAS was significantly higher than the control group. Conclusion: Laparoscopic hysterectomy increases the inflammatory response and oxidative stress in patients, while the use of dexmedetomidine can maintain hemodynamic stability in a certain extent, reduce the inflammatory response and reduce oxidative stress injury; it is worth of further clinical application.

1. Introduction

Compared with the traditional surgical methods, laparoscopic surgery has the advantages of less trauma, faster recovery, less pain, and has been widely used in clinical[1]. Pneumoperitoneum is an important component of laparoscopic surgery. The study shows that pneumoperitoneum and laparoscopic surgery can lead to the changes in oxidative stress and inflammatory cytokines[2,3].

Dexmedetomidine, a selective alpha 2-adrenergic receptor agonist, produces an effective sedative and analgesic effect, which is a new type of anesthetic drug[4]. Studies have shown that dexmedetomidine can effectively inhibit inflammatory response and reduce stress damage[5,6]. However, the reports on the effect of dexmedetomidine on laparoscopic hysterectomy are not very good. This study was carried out to provide a clinical basis for the use of dexmedetomidine.
2. Materials and methods

2.1. General information

A total of 90 cases of laparoscopic hysterectomy under general anesthesia from January 2015 to December 2016 in our hospital were selected, inclusion criteria: (1) American Society of anesthesiologists (ASA) grade I and II; (2) the hospital ethics committee approval; (3) families and patients signed informed consent. Exclusion criteria: (1) liver and kidney dysfunction, endocrine disorders, diseases of nervous system; (2) bradycardia and atrioventricular block patients; (3) the recent acute inflammatory reaction or used antioxidants in the patients; (4) the history of drug allergy. The patients were randomly divided into the control group and the observation group, 45 cases in each group. The patients in the control group were 30-65 years old, and the body mass was 48-79 kg. The observation group was 31-64 years old, and the body mass was 47-78 kg. There was no significant difference between the two groups in ASA classification, age, weight and other clinical data (P>0.05).

2.2. Anesthesia

Two groups of patients were treated with total intravenous anesthesia, routine blood pressure, heart rate, blood oxygen saturation, right internal jugular vein puncture and apposition tube. The observation group was given dexmedetomidine (Jiangsu Nhwa pharmaceutical Limited by Share Ltd, Zhunzi H20110086), intravenous infusion, loading dose of 1 g/kg and 15 min after infusion, continuous intravenous infusion (0.5 g/kg/h) to 30 min before the end of surgery; the control group in the same way to give the same amount of physiological saline. After induction of anesthesia: Intravenous injection of midazolam 0. 05 mg/kg, propofol 2 mg/kg, fentanyl 3 μg/kg and cisatracurium 0.2 mg/kg, tracheal intubation after successful access to anesthesia machine, mechanical ventilation, tidal volume was 8-10 mL/kg, frequency of 12-15 times per minute, respiratory ratio is 1:2. Intraoperative continuous infusion of 0.1-0.2 g/(kg.min), propofol 4-6 mg/(kg.h), seven 2%-3% continuous inhalation of halothane, cisatracurium 4 mg intermittent intravenous injection, PETCO2 maintained at 30-40 mmHg/%. After the patient's consciousness is restored and the respiratory circulation is stable, the tube is pulled out and sent into the anesthesia recovery room.

2.3. Monitoring indicators

The mean arterial pressure (MAP) and heart rate (HR) were recorded between the two groups before anesthesia (T0), 30 min after the end of pneumoperitoneum (T1), Completion of surgery (T2) and end of operation 24 h (T3). Patients' venous blood was extracted at the above time points, with automatic biochemical analyzer detection of C-reactive protein (CRP), tumor necrosis factor alpha (TNF- alpha) and interleukin 1 beta (IL-1 beta) content; ELISA kit for detection of serum hydrogen peroxide (H2O2), malondialdehyde (MDA) and total antioxidant status (TAS) concentration.

2.4. Statistical methods

The data were statistically analyzed by SPSS 17.0, and the data were analyzed by t test. The mean value was added and minus standard deviation Mean ± SD, and P<0.05 was significant difference.

3. Result

3.1. Comparison of inflammatory markers of two groups

As shown in Table 1, there were no statistically significant differences in CRP, TNF-alpha and IL-1 beta levels between the two groups of T0 (P>0.05); Compared with T0, CRP, TNF-alpha and IL-1 beta levels of the two groups of patients of T1, T2 and T3 were significantly increased in the observation group, the CRP, TNF-alpha and IL-1 beta of T1, T2, T3 were respectively: (12.25 ± 0.13) mg/L, (15.71 ± 0.45) ng/mL, (14.09 ± 0.19) ng/mL, (13.65 ± 0.16) mg/L, (17.92 ± 0.58) ng/mL, (15.50 ± 0.29) ng/mL, (14.14 ± 0.08) mg/L, (19.87 ± 0.54) ng/mL, (17.26 ± 0.09) ng/mL, significantly lower than the control group, there was significant difference (P<0.05).

Table 1.

Inflammatory indexes in the two groups (n=45).

<table>
<thead>
<tr>
<th>Group</th>
<th>CRP (mg/L)</th>
<th>TNF-α (ng/mL)</th>
<th>IL-1 β (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>7.25±0.11</td>
<td>9.18±0.14</td>
<td>10.52±0.28</td>
</tr>
<tr>
<td>Control T1</td>
<td>15.74±0.10*</td>
<td>26.28±0.31*</td>
<td>18.72±0.43*</td>
</tr>
<tr>
<td>group</td>
<td>16.49±0.20*</td>
<td>27.95±0.16*</td>
<td>21.39±0.56*</td>
</tr>
<tr>
<td>T2</td>
<td>17.38±0.52*</td>
<td>29.57±0.49*</td>
<td>23.18±0.07*</td>
</tr>
<tr>
<td>T3</td>
<td>7.09±0.13</td>
<td>9.11±0.17</td>
<td>10.34±0.21</td>
</tr>
<tr>
<td>Observation T1</td>
<td>12.25±0.13*</td>
<td>15.71±0.45*</td>
<td>14.09±0.19*</td>
</tr>
<tr>
<td>group</td>
<td>13.65±0.16*</td>
<td>17.92±0.58*</td>
<td>15.50±0.29*</td>
</tr>
<tr>
<td>T2</td>
<td>14.14±0.08*</td>
<td>19.87±0.54*</td>
<td>17.26±0.09*</td>
</tr>
</tbody>
</table>

Note: *compared with T0, P<0.05; †compared with the control group, P<0.05.

3.2. Comparison of oxidative stress between two groups

Table 2 shows, two groups MDA, TAS and H2O2 levels of T0 showed no significant difference (P>0.05); compared with T0, the H2O2 and MDA levels in two groups of patients of T1, T2 and T3 were significantly increased, TAS level were significantly decreased, the difference was statistically significant (P<0.05); the observation
group H$_2$O$_2$ and MDA levels of T1, T2 and T3 were (43.8 ± 0.66) mmol/L, (5.86 ± 0.05) mmol/L, (58.77 ± 0.40) mmol/L, (7.66 ± 0.13) mmol/L, (61.67 ± 0.57) mmol/L, (8.29 ± 0.06) mmol/L, (126.4 ± 1.45) ng/L, significantly higher than those in the control group, there was significant difference (P<0.05).

Clinical often by adding marijuana drunk method to reduce the amount of stress in patients, but the high amount of anesthesia will increase the adverse reactions of patients, to make it in a deep state of anesthesia for a long time, and seriously increased the patient’s discomfort after recovery[9]. Dexmedetomidine is a selective alpha 2-adrenergic receptor agonist, can be applied to patients with locus coeruleus on adrenergic receptor regulation of noradrenaline release, so as to achieve the effect[10] sedation and hypnosis; acting on postsynaptic membrane receptor, inhibition of sympathetic nerve activity, prevent blood pressure and heart rate increased[11]. The study found that dexmedetomidine for laparoscopic hysterectomy patients, MAP and HR level of patients did not appear significantly increased, compared with no significant difference before anesthesia (P>0.05), that of dexmedetomidine in patients with stable hemodynamics play a certain role. Dexmedetomidine is a selective 2-adrenergic receptor agonist that acts on the adrenal nerve on the patient's locus coeruleus and regulates the release of norepinephrine, thus achieving sedative and hypnotic effects[10]; Acting on the postsynaptic membrane receptor, inhibits sympathetic activity, prevents blood pressure and heart rate rise[11]. This study found that dexmedetomidine for laparoscopic total hysterectomy patients, patients with MAP and HR levels did not appear significantly increased, compared with no significant difference before anesthesia (P>0.05), indicating that the United States tomdine plays a role in stabilizing hemodynamics in patients.

Under normal circumstances, the body can effectively scavenge reactive oxygen in its antioxidant system under the action of the (ROS), to prevent the injury of the body. But some stimuli outside the body will lead to excessive increase in body ROS, more than their own antioxidant system to remove the limit, too much ROS will attack the body of protein, nucleic acid and other macromolecules, resulting in oxidative stress response[7]. During surgery and anesthesia, patients suffer from trauma, bleeding, hypoxia and other stimuli, resulting in a large number of free radicals, so that the body is in a high oxidation state, causing organ damage by oxidative damage[12]. H$_2$O$_2$ is a strong oxidative activity of oxygen, can consume the body's antioxidant substances, promote the body's free radicals[13]; MDA is an important product of lipid peroxidation, its content in the body reflects the body fat quality of the degree of peroxide[14]; TAS represents the sum of various antioxidants in the body, reflecting the relationship between the antioxidants and the relationship between the antioxidant, the higher the level, the greater the antioxidant capacity of the body[15]. Studies have found that dexmedetomidine can significantly reduce the level of free radicals, reduce oxidative stress injury[16,17]. In this study, the levels of H$_2$O$_2$ and MDA were significantly increased in both groups at T1, T2 and T3 compared with those before anesthesia, and the levels of increased blood pressure, heart rate and other a series of reactions[8].

### 3.3 Comparison of hemodynamic parameters of two groups

Table 3 shows the two group MAP and HR levels of T0 showed no significant difference (P>0.05); compared with T0, there were no significant differences between the MAP and HR levels of the observation group of T1, T2 and T3; At T3, there was no significant difference in the levels of MAP and HR in the control group. The levels of MAP and HR in the control group increased significantly (P<0.05) when T1 and T2, significantly higher than those in the observation group (P<0.05) at the same time.

### 4. Discussion

The operation will produce a strong stimulus to the body, resulting in stress response, strong stress response can stimulate the sympathetic adrenal medulla system, the catecholamines, accelerate the blood supply; also stimulation of the hypothalamic adrenal system makes the release of adrenaline increases, resulting in

### Table 2.

Indexes of oxidative stress in the two groups (n=45).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>H$_2$O$_2$(nmol/L)</th>
<th>MDA (nmol/L)</th>
<th>TAS (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>T0</td>
<td>35.23±0.81</td>
<td>5.1±0.11</td>
<td>201.47±2.71</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>47.23±0.35</td>
<td>6.18±0.06</td>
<td>121.1±4.81</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>65.8±1.05</td>
<td>9.35±0.08</td>
<td>81.8±4.95</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>69.1±0.20</td>
<td>10.18±0.06</td>
<td>63.3±4.15</td>
</tr>
<tr>
<td>Observation</td>
<td>T0</td>
<td>35.23±0.95</td>
<td>5.01±0.10</td>
<td>201.5±2.57</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>43.8±0.66</td>
<td>5.86±0.05</td>
<td>164.2±7.35</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>58.77±0.40</td>
<td>7.66±0.13</td>
<td>135.3±3.76</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>61.67±0.57</td>
<td>8.29±0.06</td>
<td>126.4±1.45</td>
</tr>
</tbody>
</table>

Note: *compared with T0, P<0.05; †compared with the control group, P<0.05.

### Table 3.

Hemodynamic indexes of two groups (n=45).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>MAP (mmHg)</th>
<th>HR (bit/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>T0</td>
<td>86.07±1.27</td>
<td>67.83±0.76</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>99.77±0.55</td>
<td>84.53±1.23</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>117.07±1.47</td>
<td>89.47±0.59</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>85.40±0.95</td>
<td>68.15±1.02</td>
</tr>
<tr>
<td>Observation</td>
<td>T0</td>
<td>85.43±0.91</td>
<td>68.50±0.79</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>87.17±1.46</td>
<td>69.97±0.61</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>87.93±1.34</td>
<td>70.30±0.20</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>85.67±0.57</td>
<td>68.47±0.85</td>
</tr>
</tbody>
</table>

Note: *compared with T0, P<0.05; †compared with the control group, P<0.05.
H₂O₂ and MDA were significantly lower in the observation group than in the control group, TAS level significantly higher than the control group (P<0.05). Indicating that laparoscopic hysterectomy to promote the production of oxidative stress, and dexametomorphan application to a certain extent, reduce the level of oxidative stress and reduce damage.

Laparoscopic hysterectomy in patients with stress, when the body's immune cells will secrete a large number of inflammatory cytokines, which led to a series of inflammatory response of the body, in these inflammatory factors, TNF-α, IL-1β is to promote Inflammatory factors, also known as proinflammatory cytokines, are key substances in initiating antiinflammatory responses, and CRP is an important indicator of inflammatory response, and the magnitude of the response reflects the level of inflammation[18]. The levels of CRP, TNF-α and IL-1β were significantly higher in patients with T1, T2 and T3 than those before exercise (P<0.05), but the level of observation group was significantly lower than that of the control group (P<0.05). Indicating that laparoscopic surgery to promote the release of inflammatory factors in patients with dexmedetomidine to a certain extent, reduce the level of inflammatory factors, reduce the inflammatory response.

In summary, dexmedetomidine for laparoscopic hysterectomy can significantly reduce the patient's inflammatory response, to maintain hemodynamic stability, reduce oxidative stress injury, it is worth further clinical application.

Reference


