Clinical value of dexmedetomidine for adjuvant anesthesia and analgesia in elderly patients undergoing hip replacement

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\textbf{ABSTRACT}

\textbf{Objective:} To study the clinical value of dexmedetomidine for adjuvant anesthesia and analgesia in elderly patients undergoing hip replacement. \textbf{Methods:} The elderly patients undergoing hip replacement in our hospital between March 2015 and February 2018 were randomly divided into the control group receiving general anesthesia and the observation group receiving dexmedetomidine combined with general anesthesia. The operative conditions were observed and the serum contents of pain mediators, inflammatory factors and oxidative stress indexes were measured. \textbf{Results:} There was no significant difference in operation time, bleeding volume, intraoperative mean diastolic blood pressure and intraoperative heart rate between the two groups. During operation, serum contents of neuropeptide Y (NPY), substance P (SP), prostaglandin E2 (PGE2), C-reactive protein (CRP), tumor necrosis factor-\textsuperscript{\alpha} (TNF-\textsuperscript{\alpha}), interleukin-1\beta (IL-1\beta), interleukin-6 (IL-6), interleukin-18 (IL-18), malondialdehyde (MDA), adrenocorticotropic hormone (ACTH), cortisol (Cor) and norepinephrine (NE) of the observation group were significantly lower than those of the control group while serum content of superoxide dismutase (SOD) was significantly higher than that of the control group ($p<0.05$). \textbf{Conclusion:} The adjuvant anesthesia and analgesia with dexmedetomidine in elderly patients undergoing hip replacement will not affect the operation and can alleviate the pain, inflammation and oxidative stress during the operation.

\textbf{1. Introduction}

The elderly are at high risk of hip fracture, and hip replacement is the main method for clinical treatment of hip fracture in the elderly. Due to the poor physiological basis and the weak tolerance to surgical trauma and pain of the elderly patients, the trauma formed by surgical operation will cause relatively strong pain response, inflammatory response and oxidative stress response, which is not conducive to the recovery of local limb function and systemic body function after surgery. In the process of hip replacement in elderly patients, the establishment of effective anesthesia program is conducive to reducing the pain, inflammation and stress caused by surgical trauma\textsuperscript{[1,2]}. Dexmedetomidine is a highly selective 2-adrenergic receptor agonist increasingly used in general anesthesia in recent years, which not only exerts sedative and analgesic effect, but also has anti-inflammatory and antioxidant activities\textsuperscript{[3]}. In this study, in order to clarify the clinical value of dexmedetomidine for assistant anesthesia and analgesia during hip replacement in the elderly, we specifically analyzed the effect of dexmedetomidine on surgical conditions as well as intraoperative pain, inflammation and oxidative stress.

\textbf{2. Information and methods}

\textbf{2.1 General information}

The elderly patients who underwent hip replacement in our hospital between March 2015 and February 2018 were selected as the study subjects, and the inclusion criteria were: (1) the patients were in line with the indications of hip replacement; (2) the patients were 65 years old and with America Society of Anesthesiologist...
ASA grade I or II; (3) the hip replacement was performed by the same group of surgeons under general anesthesia; (4) the patients signed informed consent. Exclusion criteria: (1) the patients combined with central nervous system diseases or mental diseases; (2) the patients combined with autoimmune disease or chronic pain. A total of 108 patients were included and divided into two groups by random number table, with 54 patients in each group. There were 31 males and 23 females in the observation group, they were 65-74 years old and 69.33±8.12 years old on average, and body mass index was 22.19±3.38 kg/m²; there were 32 males and 22 females in the control group, they were 65-76 years old and 69.71±8.47 years old on average, and the body mass index was 22.06±3.19 kg/m². There was no significant difference in general data between the two groups (P>0.05).

2.2 Anesthesia method

Before operation, the two groups were routinely connected to ECG monitoring, and upper extremity vein access was opened; induction of anesthesia: 0.2-0.4 μg/kg sufentanil, 0.15 mg/kg cisatracurium and 0.2 mg/kg etomidate were intravenously injected successively; maintenance of anesthesia: remifentanil 30 μg/kg/h was injected continuously, and cisatracurium was intermittently administered to maintain muscular relaxation. Observation group were given dexmedetomidine on the basis of routine general anesthesia: 0.6 μg/kg of dexmedetomidine was intravenously injected via micropump 15 min before induction, followed by continuous intravenous micropump injection at 0.2 μg/kg/h.

2.3 Observation indexes

2.3.1 Observation of surgical condition

During the operation, the operation time and blood loss were observed; after joint replacement was completed, heart rate (HR), systolic arterial pressure (SAP) and diastolic blood pressure (DBP) were measured, and the mean diastolic blood pressure (MAP) was calculated.

2.3.2 Determination of serum indexes

1 d before the operation and after joint replacement was completed in the operation, 3 mL of cubital venous blood was collected respectively, let stand and centrifuged to isolate serum. Enzyme-linked immunosorbent assay was used to detect neuropeptide Y (NPY), substance P (SP), prostaglandin E2 (PGE2), C-reactive protein (CRP), tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), interleukin-6 (IL-6), interleukin-18 (IL-18), malondialdehyde (MDA), superoxide dismutase (SOD), adrenocorticotrophic hormone (ACTH), cortisol (Cor) and norepinephrine (NE) levels.

2.4 Statistical methods

SPSS21.0 software was used to input data, the analysis of measurement data before or during surgery between the two groups was performed with group t test, the comparison of measurement data before and during surgery within group was performed with paired t test, and P<0.05 meant that the differences were statistically significant.

3. Results

3.1 Comparison of surgical conditions between the two groups of patients

The differences in operation time, bleeding volume, intraoperative MAP and intraoperative HR were not statistically significant between the two groups of patients (P>0.05).

3.2 Comparison of pain mediators between the two groups

Before operation, serum NPY, SP and PGE2 contents were not significantly different between the two groups of patients (P>0.05); during operation, serum NPY, SP and PGE2 contents of both groups were significantly higher than those before operation (P<0.05), and serum NPY, SP and PGE2 contents of the observation group were significantly lower than those of the control group (P<0.05).
Table 4.
Comparison of serum oxidative stress index contents between the two groups of patients.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>MDA(μmol/L)</th>
<th>SOD(U/mL)</th>
<th>ACTH(pg/mL)</th>
<th>Cor(ng/mL)</th>
<th>NE(pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>54</td>
<td>Before operation</td>
<td>8.38±1.13</td>
<td>93.92±10.38</td>
<td>54.94±7.83</td>
<td>224.58±31.82</td>
<td>203.12±24.83</td>
</tr>
<tr>
<td></td>
<td></td>
<td>During operation</td>
<td>11.31±1.38*</td>
<td>74.59±9.82*</td>
<td>70.28±9.39*</td>
<td>256.41±22.93*</td>
<td>255.28±31.72*</td>
</tr>
<tr>
<td>Control group</td>
<td>54</td>
<td>Before operation</td>
<td>8.52±1.09</td>
<td>95.12±10.38</td>
<td>55.41±7.23</td>
<td>225.13±29.38</td>
<td>202.89±22.93</td>
</tr>
<tr>
<td></td>
<td></td>
<td>During operation</td>
<td>15.48±1.88</td>
<td>66.65±8.12</td>
<td>89.48±11.38</td>
<td>289.48±33.26</td>
<td>294.21±32.94</td>
</tr>
</tbody>
</table>

Note: comparison between before and during operation within group, \(*P<0.05; \#P<0.05\). comparison between the two groups during operation, \(^*P<0.05\).

3.3 Comparison of inflammatory cytokines between the two groups

Before operation, serum CRP, TNF-α, IL-1β, IL-6 and IL-18 contents were not significantly different between the two groups of patients \((P>0.05)\); during operation, serum CRP, TNF-α, IL-1β, IL-6 and IL-18 contents of both groups were significantly higher than those before operation \((P<0.05)\), and serum CRP, TNF-α, IL-1β, IL-6 and IL-18 contents of the observation group were significantly lower than those of the control group \((P<0.05)\).

3.4 Comparison of oxidative stress indexes between the two groups

Before operation, serum MDA, SOD, ACTH, Cor and NE contents were not significantly different between the two groups of patients \((P>0.05)\); during operation, serum MDA, ACTH, Cor and NE contents of both groups were significantly higher than those before operation \((P<0.05)\), and serum MDA, ACTH, Cor and NE contents of the observation group were significantly lower than those of the control group while SOD content was significantly higher \((P<0.05)\).

4. Discussion

Hip fracture is a common type of fracture in the elderly population. Its incidence is increasing year by year with the aggravation of aging of population and the increase of the number of people with osteoporosis. If not treated in time, it will not only cause disability, but also increase the risk of death. Hip replacement is an effective method for treatment of hip fracture in the elderly. However, due to the physical degeneration and the obviously reduced ability to tolerate surgical trauma and pain in the elderly, it also puts forward higher requirements for surgical anesthesia. Dexmedetomidine is a highly selective α2 adrenergic agonist receptor, which exerts sedative and analgesic effect through the excitement of α2 adrenergic receptor in nucleus ceruleus. Compared with the similar drug clonidine, this drug has a higher selectivity to α2 adrenergic receptor and will not affect circulation and respiration\(4,5\). In order to define the value of dexmedetomidine for hip replacement in elderly patients, the surgical conditions after the application of dexmedetomidine were analyzed at first in the study, the surgery time, bleeding volume, intraoperative MAP and intraoperative HR of the observation group with dexmedetomidine combined with conventional general anesthesia were not significantly different from those of the control group with conventional general anesthesia. The results indicate that the addition of dexmedetomidine on the basis of conventional general anesthesia will neither affect the operation of hip replacement nor cause changes in the intraoperative vital signs in elderly patients.

Surgical incision pain is an important factor affecting postoperative recovery, and it can also cause changes in the internal environment of the body, which is not conducive to the stability of vital signs. Surgical trauma to local tissues can induce changes in the synthesis and secretion of various pain mediators, which can cause pain in the body through the respective biological activities of the pain mediators. NPY and SP are two kinds of peptide pain mediators, which can reduce the pain threshold of the nervous system and facilitate the generation and amplification of pain\(6,7\); PGE2 is a liposoluble pain mediator, which is massively produced during the metabolism of arachidonic acid and can induce aseptic inflammation in peripheral tissues to promote the generation of pain\(8\). In this study, the changes of serum pain mediators before surgery and during surgery were analyzed, and the levels of serum NPY, SP and PGE2 in both groups during surgery were significantly higher than...
those before surgery, suggesting that surgical trauma can increase the secretion of various pain mediators and cause pain through the biological activities of the pain mediators. Dexmedetomidine has powerful analgesic and sedative activity. The analysis of the pain mediators after the application of dexmedetomidine in this study showed that the serum NPY, SP and PGE2 levels in the observation group during surgery were significantly lower than those in the control group. The results show that the addition of dexmedetomidine on the basis of conventional general anesthesia can reduce the secretion and release of various pain mediators during surgery, and thus exert analgesic effect.

Under the combined action of surgical trauma and body pain, the internal environment of the body will change significantly, among which the over-activation of inflammatory response is one of the important features of the internal environment change. During the activation of inflammatory response, a variety of inflammatory factors are released in the cascade form, which, after entering the blood circulation, can increase the risk of damage to multiple tissues of the body and also increase the pain degree of the body. CRP is an acute phase protein massively synthesized by hepatocytes under the stimulation of pro-inflammatory factors, which is positively correlated with the activation degree of inflammatory response; TNF-α is a pro-inflammatory cytokine that is massively secreted by the activated mononuclear macrophages, which can further recruit a variety of inflammatory cells and mediate the cascade amplification of inflammation; IL-1β, IL-6 and IL-18 are cytokines in the interleukin family involved in the regulation of inflammatory response, which can promote the activation of inflammatory cells and increase the secretion of inflammatory factors. In this study, the changes of serum inflammatory factors before surgery and during surgery were analyzed, and the serum CRP, TNF-α, IL-1β, IL-6 and IL-18 contents in both groups during surgery were significantly higher than those before surgery, suggesting that the trauma caused by operation can activate the inflammatory response. Dexmedetomidine has anti-inflammatory and anti-oxidative stress effect and can reduce the production of oxygen free radicals and promote the scavenging of oxygen free radicals, and further analysis of the oxidative stress indicators after the use of dexmedetomidine in this study showed that serum MDA, ACTH, Cor and NE contents in both groups were significantly higher than those before surgery while SOD contents were significantly lower than those before surgery, suggesting that the trauma caused by operation can activate the oxidative stress. Dexmedetomidine has anti-inflammatory and anti-oxidative stress effect and can reduce the production of oxygen free radicals and promote the scavenging of oxygen free radicals, and further analysis of the oxidative stress indicators after the use of dexmedetomidine in this study showed that serum MDA, ACTH, Cor and NE contents in both groups were significantly higher than those before surgery while SOD contents were significantly lower than those before surgery, suggesting that the trauma caused by operation can activate the oxidative stress. Dexmedetomidine has anti-inflammatory and anti-oxidative stress effect and can reduce the production of oxygen free radicals and promote the scavenging of oxygen free radicals, and further analysis of the oxidative stress indicators after the use of dexmedetomidine in this study showed that serum MDA, ACTH, Cor and NE contents in both groups were significantly higher than those before surgery while SOD contents were significantly lower than those before surgery, suggesting that the trauma caused by operation can activate the oxidative stress.

To sum up, it can be concluded that routine general anesthesia combined with dexmedetomidine for hip replacement in the elderly will not affect the surgical conditions or intraoperative vital signs. Compared with conventional anesthesia, the combined anesthesia program can reduce the degree of pain, inflammation and oxidative stress during operation.

References

[3] Li L, Li J, Mi WD. Research progress on the anti-inflammatory effect of


