Comparative Study of Endoscopic Esophageal Varix Ligation Anesthesia with Different Doses of Dexmedetomidine

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Abstract. Objective To investigate the ideal dosage of dexmedetomidine (DEX) with 1.0 µg/kg fentanyl for monitored anesthesia care (MAC) during endoscopic variceal ligation (EVL). Methods A total of 60 patients, of ASA physical status 2-3, aged 36–59 yr, with body weight 50–75 kg, scheduled for elective EVL, were randomly divided into 3 groups (n=20): dexmedetomidine 1.0, 1.5 and 2.0 µg/kg groups (D₁, D₂ and D₃ groups). After fentanyl 1.0 µg/kg was infused intravenously, the loading dosage of DEX 1.0, 1.5, 2.0µg/kg was separately continuous infused in 10 min. When the modified OAA / S scale > 3 points, EVL was carried out. The modified OAA/S score at the time-points of before induction (T₀), before endoscope insertion (T₁) and 5mins later(T₂), end of surgery (T₃) were recorded. The operation duration, recovery time, satisfaction of patient and doctor, incidence of nausea, body movement, bradycardia, hypotension, tachycardia, hypertension and hypoxemia was recorded. Results There were no differences in the 3 groups about the general status, operation duration and satisfaction score(P>0.05). (1) Before endoscope insertion(T₁), the improved OAA/S score in Group D₃ (4.4±0.2) were higher than D₁(3.4±0.5) and D₂ groups(3.8±0.3) (P<0.05), there were no differences between D₁ and D₂(P>0.05). At the time-point of 5mins later(T₂), the score in Group D₃ (4.5±0.3) were higher than D₁(3.5±0.6) and D₂ groups(3.7±0.4) (P<0.05),there were no differences between D₁ and D₂(P>0.05). At the end of surgery (T₃), the score were almost similar(P>0.05)(2) Compared with group D₁ (3.1±0.9) and D₂(3.8±0.8), group D₃ (6.6±1.2) had longer recovery time(min) (P<0.05).(3) The satisfaction of endoscope doctor in Group D₁(8.0±0.8) was lower than group D₂(9.4±0.6) and D₃(9.5±0.5)(P<0.05), there were no differences during the two group(P>0.05).(4)There were no incidence of tachycardia, hypertension and hypoxemia, no difference of hypotension incidence in the three groups (P>0.05). The incidences of nausea (30%) and body movement (15%) in group D₁ is significantly higher than group D₂ (5%) and D₃(0) (P<0.05), there were no differences between D₂ and D₃(P>0.05). The incidences of bradycardia (40%) in group D₃ is significantly higher than group D₁(0) and D₂(10%) (P<0.05),there were no differences between D₁ and D₂(P>0.05).Conclusion Combined with 1.0µg/kg fentanyl, 1.5 µg/kg DEX is more efficacy and safer for EVL in the status of monitored anesthesia care.

Introduction

Esophageal variceal bleeding is one of the serious complications of hepatocirrhosis. Endoscopic esophageal varix ligation is one of the main methods to treat and prevent the disease. The intravenous injection of dexmedetomidine at a loading dose of EVL can achieve the effect of monitored anesthesia care (MAC), which is safer and more effective than the Propofol deep sedation and meperidine-based anesthesia. However, at the compound routine dose of fentanyl (1.0 µg / kg), the optimal loading dose of Dexmedetomidine has not been reported at present. To this end, we conducted a study on the issue, are summarized below.
Materials and Methods

1. Objects and Groups: This study was approved by the Medical Ethics Committee of hospital (LL2014127), and esophageal varix patients who underwent elective EVL between January and August 2016 were selected as the study subjects, Inclusion criteria: esophageal varix morphology G2-G3; Liver function Child-Pugh grade B-C grade; PLT>50×10⁹/L. Sign informed consent before operation, Exclusion criteria: severe cardiopulmonary disease; renal insufficiency; sinus bradycardia; had opioids, sedative drug dependence and allergy history. The selected patients were divided into 3 groups by random digital table. The load doses used with dexmedetomidine are 1.0 μg/kg (D1 group), 1.5 μg/kg (D2 group) and 2.0 μg/kg (D3 group).

   2. Method: Routine fasting before operation, no drinking, no drugs before operation. Preparation of open venous access in the middle of the room, supplement of Ringer-Locke liquor 5 ml/kg. Into the operating room, the left lateral position, nasal catheter oxygen (oxygen flow 3 L / min), continuous monitoring of HR, noninvasive blood pressure and oxygen saturation (SPO2). Intravenous injection of fentanyl for 1.0 μg / kg, according to the group set the load dose intravenous infusion of constant velocity pump with dexmedetomidine, 10 min infusion completed, to be improved OAA / S score ≥3 can be done endoscopic [1], endoscopic operation by the same endoscopic doctors to complete. Intraoperative HR less than 50 beats / min was given to atropine, esmolol was given when more than 100 beats / min; ephedrine was given when average arterial pressure below 70% of baseline; nicardipine was given when above 130%; when SPO2 was less than 90% for jaw-lift, if necessary, assisted ventilation. After surgery, those with improved OAA/S score of 2 points were transferred to the recovery room to continue monitoring until the exit standard is met.

   3. Observed indicators:(1) Before the administration, 5 min in the operation and the improved OAA/S score at the immediate end of the operation before entering the mirror; (2) Endoscopic operating time, recovery time (Time between the end of the operation and the improved OAA/S score of 2); (3) Patient satisfaction (10 is the most satisfactory, and the 0 is the most dissatisfied.) and Endoscopic satisfaction (10 points were the most satisfactory and the 0 points were the most dissatisfied according to the esophagus and stomach secretions, peristalsis, the clarity of the field of vision, and whether the operation was affected.); (4) Intraoperative adverse reaction, including nausea, movement, bradycardia, hypotension, synchynospigmia, hypertension, hypoxia.

   4. Statistical analysis. SPSS 17.0 statistical software was used to process the data. The measurement data were expressed as mean ± standard deviation, matched t test was used for intra-group comparison, and single-factor ANOVA was used for inter-group comparison. The count data were tested by fisher's exact probability method. P < 0.05. The difference was statistically significant.

Result

1. A total of 67 patients were collected during the study, 7 of whom were excluded due to intraoperative change of procedure (using two ligators or injection of a curing agent), culminating in the study data of 60 patients (both successfully completed endoscopic treatment) Analysis of each group of 20 cases. The differences of each group in the patient's gender composition, mean age, body mass, liver function Child-Pugh grading composition, esophageal varix morphological were not statistically significant(P>0.05), baseline data is comparable, See table 1 for details.
Table 1. Basic Information of 60 Patients with esophageal varix enrolled in the study.

<table>
<thead>
<tr>
<th>Group</th>
<th>Gender (M/F)</th>
<th>Age</th>
<th>Body mass (kg, x±s)</th>
<th>Child-Pugh (B/C)</th>
<th>ASA (2/3)</th>
<th>esophageal varix morphology (2/3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1</td>
<td>19/1</td>
<td>45±9</td>
<td>59±10</td>
<td>9/11</td>
<td>13/7</td>
<td>7/13</td>
</tr>
<tr>
<td>D2</td>
<td>18/2</td>
<td>48±1</td>
<td>58±8</td>
<td>12/8</td>
<td>15/5</td>
<td>10/10</td>
</tr>
<tr>
<td>D3</td>
<td>18/2</td>
<td>50±8</td>
<td>63±12</td>
<td>10/10</td>
<td>15/5</td>
<td>8/12</td>
</tr>
</tbody>
</table>

The load doses of dexametomidine in group D1, group D2 and group D3 were 1.0, 1.5 and 2 u g/kg, respectively.

2. Modified OAA / S score results: Compared with prior administration, the scores of 5 min during operation and immediately after operation were significantly increased in the 3 groups before the operation. (P<0.05), The D3 group was (4.4±0.2) before endoscopy. higher than that of the D1 group(3.4±0.5)(P<0.05) and group D2 (3.8±0.3)(P<0.05). There was no significant difference between D1 group and D2 group.(P>0.05); At 5 min during operation ,D3 group was (4.5 ±0.3),it was also higher than that in D1 group (3.5 ±0.6),(P<0.05) and D2(3.7±0.4)(P<0.05),there was no significant difference between D1 group and D2 group.(P>0.05); Immediate after operation, There was no statistical difference between the 3 groups(P>0.05), See table 2.

Table 2. Improved OAA/S score at different observation time points in each group (x±s).

<table>
<thead>
<tr>
<th>Group</th>
<th>Pre-dose</th>
<th>Before endoscopy</th>
<th>Intraoperative 5 min</th>
<th>Immediate after operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1</td>
<td>1.0</td>
<td>3.4±0.5</td>
<td>3.5±0.6</td>
<td>3.1±0.2</td>
</tr>
<tr>
<td>D2</td>
<td>1.0</td>
<td>3.8±0.3</td>
<td>3.7±0.4</td>
<td>3.2±0.5</td>
</tr>
<tr>
<td>D3</td>
<td>1.0</td>
<td>4.4±0.2</td>
<td>4.5±0.3</td>
<td>4.0±0.3</td>
</tr>
</tbody>
</table>

note: The load doses of dexametomidine in group D1, group D2 and group D3 were 1.0,1.5 and 2 u g/kg, respectively; comparison before administration, aP<0.05; Comparison with D1 group, bP<0.05; Comparison with group D2; P<0.05.

3. Endoscopic operation time, patient recovery time, patient and endoscopes satisfaction: The duration of endoscopic operation was longer than that of the D2 and D3 groups, but the difference was not statistically significant. (P>0.05), The recovery time of patients in D3 was significantly longer than that in group D1 and D2, and the difference was statistically significant.(P<0.05),The satisfaction of endoscope doctors in group 1 was lower than that in group D2, and the difference was statistically significant.(P<0.05), There was no significant difference in patient satisfaction among the three groups.(P>0.05), See table 3.

Table 3. Endoscopic operating time, recovery time, endoscopic physician and patient satisfaction.

<table>
<thead>
<tr>
<th>Group</th>
<th>Operation(min )</th>
<th>Recovery time</th>
<th>Endoscopist satisfaction</th>
<th>Patient satisfaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1</td>
<td>25.3±5.7</td>
<td>3.1±0.9</td>
<td>8.0±0.8</td>
<td>9.2±0.5</td>
</tr>
<tr>
<td>D2</td>
<td>23.8±2.9</td>
<td>3.8±0.8</td>
<td>9.4±0.6</td>
<td>9.5±0.3</td>
</tr>
<tr>
<td>D3</td>
<td>22.9±3.6</td>
<td>6.6±1.2</td>
<td>9.5±0.5</td>
<td>9.3±0.4</td>
</tr>
</tbody>
</table>

note: The load doses of dexametomidine in group D1, group D2 and group D3 were 1.0,1.5 and 2 u g/kg, respectively; Comparison with D1 group, aP<0.05;Comparison with group D2,bP<0.05
4. Occurrence of adverse reactions: The incidence of nausea, body movement in group D1 was significantly higher than that in group D2, and in group D3, the difference was statistically significant \((P<0.05)\). But there was no significant difference between D2 group and D3 group \((P>0.05)\). The incidence of bradycardia in group D3 was significantly higher than that in group D1, group D2. The difference was statistically significant \((P<0.05)\). But there is no significant difference between D1 group and D2 group \((P>0.05)\). The incidence of hypoxia was similar among the three groups. There was no statistically significant difference between groups \((P>0.05)\), Sychnosphygemia, hypertension and hypoxemia did not occur in the three groups, Table 4.

<table>
<thead>
<tr>
<th>Group</th>
<th>Nausea</th>
<th>Movement</th>
<th>Bradycardia</th>
<th>Hypotension</th>
<th>Sychnosphygemia</th>
<th>Hypoxia</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1</td>
<td>6(30)</td>
<td>3(15)</td>
<td>0(0)</td>
<td>2(10)</td>
<td>0(0)</td>
<td>0(0)</td>
</tr>
<tr>
<td>D2</td>
<td>1(5*)</td>
<td>1(5*)</td>
<td>2(10)</td>
<td>3(15)</td>
<td>0(0)</td>
<td>0(0)</td>
</tr>
<tr>
<td>D3</td>
<td>0(0*)</td>
<td>0(0*)</td>
<td>8(40*)</td>
<td>3(15)</td>
<td>0(0)</td>
<td>0(0)</td>
</tr>
</tbody>
</table>

note: The load doses of dexmedetomidine in group D1, group D2 and group D3 were 1.0, 1.5 and 2 u g/kg, respectively; Comparison with D1 group, \(^*P<0.05\); Comparison with group D2, \(^*P<0.05\)

**Discussion**

The MAC is used to administer certain anesthetics to patients undergoing diagnostic or therapeutic procedures to relieve anxiety, fear and discomfort, relieve pain and other noxious stimuli, improve safety and comfort, and increase the rate of successful operation [1]. The load doses of dexmedetomidine in group D1, group D2 and group D3 were 1.0, 1.5 and 2 u g/kg, respectively. Neral anesthesia, with the goal of moderate sedation, analgesia, elimination of anxiety, rapid recovery, autonomous maintenance of airway and circulatory function, continuous reduction of local anesthetic injection pain and reduced body movement [2].

Dexmedetomidine is a highly selective \(\alpha\)2 adrenergic receptor agonist. It acts on the central, peripheral and sympathetic nervous system excitation, plays a role in tranquilizing, relieving pain, and inhibiting the release and anti-injury effects [3]. Dexmedetomidine has strong sedative effect and weak analgesia. It cannot inhibit pharynx and larynx reflex caused by gastroscope and tracheoscopy alone. It often needs to be used in conjunction with 1 \(\mu\) g / kg fentanyl. Using it as the only sedative in mac, endotracheal intubation, intraoperative arousal, and imaging examination of children is superior to deep sedation [4,5]. But for the dose differences of different anesthesia DEX large (0.8-2u g/kg \([4,5]\)), so it is necessary to study the optimal dose for Mac under EVL. The study showed that the composite 1\(\mu\)g/kg fentanyl, 1\(\mu\)g/kg dexmedetomidine can maintain EVL sedation (modified OAA /s score >3) and higher patient satisfaction, No hypertension and Sychnosphygemia occurred, but the incidence of nausea and unconscious movement is high, requiring the suspension of surgery to comfort patients. Although the aim of MAC is not to forget and completely avoid movement, it is not necessary to increase the dose of medication for short-term awakening of patients [6]. However, frequent movements prolong the operation time, reduce the satisfaction of endoscopists and increase the risk of inducing intraoperative esophageal veins bleeding, vomiting, and aspiration risk. Dexmedetomidine at a dose of 2.0 \(\mu\)g / kg resulted in
greater intraoperative sedation but significantly longer patient recovery times, adversely affecting
the turnaround of outpatient surgery, and the incidence of nausea and movement, as well as patient
and endoscopist satisfaction Degree scoring results and 1.5 \( \mu g / kg \) dose group showed no
significant difference, but the incidence of bradycardia increased significantly, suggesting that large
doses of Dexmedetomidine increased the actual effect was not obvious, and significantly increased
adverse reactions, which is consistent with the literature.

Dexmedetomidine inhibition of peripheral sympathetic nerve, reduction of catecholamine release,
reduction of heart rate and reduction of hypoxia. When the drug dose and surgical stress level match,
such as D2 group, the patient hemodynamics is more stable, independent maintenance of circulation.
At a loading dose of 2.0 \( \mu g / kg \), the over-inhibition increased the incidence of bradycardia in the
D3 group by 40%, although it was rapidly relieved at the start of surgery or after drug support [7],
but significantly increased the risk of anesthesia. The rate of bradycardia may be higher when given
too fast or when drug levels are high. In this study, the incidence of hypoxia in group 3 did not
increase with the increase of dose. The mechanism is for patients with general anesthesia or brachial
plexus blockade who have blocked sympathetic reflexes. Dexmedetomidine directly activates \( \alpha \)
2aron on the surface of endothelial cells of the great arteries and venules, causing vasoconstriction
in the extremities [8]. To some extent, hypoxia was avoided. Although fentanyl was used
cooperatively, no hypoxemia was found in all three groups. Accord with the literature report [5,7].
Dexmedetomidine inhibits nucleus coeruleus to produce a senescence-like quiescence similar to
normal sleep. Slight reduction in resting minute ventilation does not affect chemo sensitivity to
bulbus medullae even at 10-15 times the recommended dose. End-tidal carbon dioxide
Concentration and arterial blood gas results [9]. This result is also related to the patient's position in
the supine position, adequate nasal catheter oxygenation, slow pump infusion, and endoscopic
support.

In summary, at composite of 1.0 \( \mu g/kg \) fentanyl, 1.5\( \mu g/\)kg load dose of dexmedetomidine,
intravenous constant speed pump for 10 min, Esophageal varix endoscopic ligation can achieve a
satisfactory effect of monitored anesthesia care, With this loading dose of Dexmedetomidine,
patients have moderate depth of anesthesia and wakefulness, stable hemodynamics, less
symptomatic treatment, swallowing and suppression of body movement with instructions. Patient
satisfaction is higher and anesthesia management is more safe and convenient.

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References


versus propofol target-controlled infusion for sedation during fibreoptic nasotracheal intubation [J].

respiratory effects of dexmedetomidine and propofol in children undergoing magnetic resonance

