Effect of different anesthesia induction on adrenal cortex and medulla activation levels as well as immune cell levels in patients after radical operation of tongue cancer
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Objective: To analyze the effect of different anesthesia induction on adrenal cortex and medulla activation levels as well as immune cell levels in patients after radical operation of tongue cancer. Methods: A total of 45 patients with tongue cancer received radical operation of tongue cancer, 24 cases of observation group received total intravenous induction and maintenance, 21 cases of control group accepted combined intravenous-inhalation induction and maintenance, and then differences in adrenal cortex and medulla activation levels as well as immune cell levels 1h after operation were compared between two groups. Results: Serum GC and ALDO as well as urine 17-OH and 17-KS levels of observation group 1h after treatment were lower than those of control group (P<0.05); serum ADM, E and NE as well as urine VMA levels were lower than those of control group (P<0.05); peripheral blood CD3-CD16+56+ and CD3-CD19+ cell levels, CD3+ and CD4+T lymphocyte levels and CD4+/CD8+ ratio were higher than those of control group (P<0.05). Conclusions: Application of sevoflurane in surgical anesthesia may be the main cause of postoperative stress and immune injury in patients with tongue cancer.

1. Introduction

Radical operation of tongue cancer causes huge trauma and is time-consuming, perioperative hypothermia in patients further increases the body’s immnosuppression, and latest studies have shown that the use of narcotic drugs during surgery is one of the important causes of the immnosuppression and strong postoperative stress state in patients[1,2]. Sevoflurane is the clinical anesthesia induction drug widely used at present, it can increase the depth of anesthesia and optimize intraoperative muscle relaxant effect, but studies have also indicated that sevoflurane can increase the severity of immnosuppression in patients with tumor[3,4]. In order to define the differences between intravenous anesthesia and intravenous-inhalation anesthesia in patients with tongue cancer, the two anesthesia induction methods were applied in patients with tongue cancer in our hospital in the study and specifically stated from two aspects: the postoperative stress reaction and immune function.

2. Materials and methods

2.1. General information

45 cases of patients with tongue cancer who received radical operation of tongue cancer in our hospital from April 2012 to April 2016 were included in the study, and the surgery, anesthesia and related testing results were retrospectively analyzed. According to different anesthesia induction, they were divided into 24 cases of observation group and 21 cases of control group. Observation group included 13 male cases and 11 female cases, they were 27-68 years old, the average age was (45.37±6.12) years, 14 cases were with T1-2 stage of TNM staging;
control group included 12 male cases and 9 female cases, they were 25-67 years old, the average age was (44.69±7.53) years, 12 cases were with T1-2 stage of TNM staging and 9 cases were with T3-4 stage. The two groups showed no statistically significant difference in the distribution of gender, age and disease severity (P>0.05).

2.2. Anesthesia induction

Observation group received total intravenous anesthesia, anesthesia induction was by propofol 2.5 mg/kg, remifentanil 2 μg/kg and cisatracurium 0.15 mg/kg, and intraoperative intravenous maintenance was by propofol (5 mg/kg•h⁻¹) and remifentanil (0.2 μg/kg•min⁻¹). Control group accepted combined intravenous-inhalation anesthesia, anesthesia induction was by 8% sevoflurane, inhaled with fresh flow rate of 5 L/min, remifentanil 2 μg/kg and cisatracurium 0.15 mg/kg, intraoperative maintenance was by propofol, remifentanil and sevoflurane (2%-3%), and the doses of propofol and remifentanil were the same as those of observation group.

2.3. Observation indexes

One hour after operation, 5 mL of peripheral venous blood was collected from two groups of patients, 3 mL was centrifuged to get plasma, and the peripheral blood and plasma were cryopreserved in -70 °C refrigerator for testing. RIA method was used to determine plasma total cortisol (GC) and aldosterone (ALDO) as well as urine 17-hydroxycorticosteroid (17-OH) and 17-ketosteroid (17-KS). RIA method was used to determine plasma adrenal medulla hormone (ADM), epinephrine (E) and norepinephrine (NE) as well as urine vanilmandelic acid (VMA). A total of 2 mL of peripheral venous blood was collected from patients, and flow cytometer was used to determine NK cells (CD3⁻CD16⁺56⁺) and B lymphocyte (CD3⁻CD19⁺) levels in it. A total of 2 mL of peripheral venous blood was collected from patients, and flow cytometer was used to determine CD3⁺, CD4⁺ and CD8⁺ T lymphocyte levels as well as CD4⁺/CD8⁺ ratio.

2.4. Statistical methods

Obtained data was input in SPSS21.0 for analysis and processing, measurement data was in terms of average ± standard deviation, comparison between two groups was performed by t test, and P<0.05 was the standard of statistical significant differences.

3. Results

3.1. Adrenal cortex activation–related indexes

Plasma GC and ALDO as well as urine 17-OH and 17-KS levels of observation group 1h after treatment were lower than those of control group (P<0.05), shown in Table 1.

3.2. Adrenal medulla activation–related indexes

Plasma ADM, E and NE as well as urine VMA levels of observation group 1h after treatment were lower than those of control group (P<0.05), shown in Table 2.

3.3. NK cell and B lymphocyte

Peripheral blood CD3⁺CD16⁻56⁻ and CD3⁺CD19⁻ cell levels per 100 cells of observation group 1h after treatment were higher than those of control group (P<0.05), shown in Table 3.

3.4. T lymphocyte subsets

Postoperative venous blood CD3⁺ and CD4⁺/CD8⁺ T lymphocyte levels and CD4⁺/CD8⁺ ratio of observation group were higher than those

| Table 1 | Comparison of postoperative adrenal cortex activation index values. |
|---|---|---|---|---|
| Groups | Case No. | GC (nmol/L) | ALDO (ng/L) | 17-OH (μmol/24 h) | 17-KS (μmol/24 h) |
| Observation group | 24 | 683.29±71.04 | 156.28±18.39 | 35.42±4.13 | 69.36±7.21 |
| Control group | 21 | 1132.64±184.59 | 247.55±28.38 | 51.37±5.92 | 92.45±10.23 |
| t | 13.293 | 11.054 | 8.262 | 9.183 |
| P | <0.05 | <0.05 | <0.05 | <0.05 |

| Table 2 | Comparison of postoperative adrenal medulla activation index values. |
|---|---|---|---|---|
| Groups | Case No. | ADM (μmol/24 h) | E (mmol/L) | NE (mmol/L) | VMA (pg/mL) |
| Observation group | 24 | 109.26±17.62 | 1.83±0.21 | 1.21±0.17 | 13.58±1.62 |
| Control group | 21 | 187.53±22.49 | 2.59±0.34 | 1.98±0.25 | 20.43±2.51 |
| t | 12.183 | 5.732 | 5.384 | 8.293 |
| P | <0.05 | <0.05 | <0.05 | <0.05 |
of control group ($P<0.05$), and differences in CD8$^+$T lymphocyte levels per 100 cells were not statistically significant between two groups ($P>0.05$), shown in Table 4.

4. Discussion

Radical operation of tongue cancer requires distant skin flap transplantation and repair, causes great trauma and is time-consuming, and perioperative hypothermia can appear in patients and activate the sympathetic-adrenal medulla system, or directly act on the immune system and cause different degree of postoperative immunosuppression. In addition to the intraoperative blood loss and surgical trauma, the choice of anesthetic drugs can also further affect the immune function in patients[5]. In order to define the effect of different anesthesia induction on postoperative stress state and immune function in patients with tongue cancer and predict postoperative recovery of patients, both total intravenous anesthesia and combined intravenous-inhalation anesthesia were used in patients with radical operation of tongue cancer, and the effect of different anesthesia induction on stress levels and immune state in patients was mainly analyzed.

Both anesthesia and surgical trauma can make patients in postoperative stress state, which causes that the hypothalamus-pituitary-adrenal cortex axis and the sympathetic-adrenal medulla system are activated, and a large number of relevant hormones are released into the bloodstream and detected[6]. In the study, detection of adrenal cortex and medulla system factor levels of two groups 1h after treatment showed that plasma cortex indexes GC and ALDO as well as urine 17-OH and 17-KS levels of observation group were lower, and medulla indexes ADM, E, and NE as well as urine VMA levels were lower than those of control group. GC, ALDO, 17-OH and 17-KS are the typical adrenal cortex-related indicators, it has been confirmed that GC and ALDO are at high levels in stress state, 17-OH and 17-KS are the active ingredients after GC is degraded in the liver and then discharged to the urine, and the levels are consistent with the change of GC content[7,8]. ADM, E, NE and VMA are the adrenal medulla-related parameters, and many studies have shown that plasma ADM, E and NE are at high levels after surgical trauma and anesthesia, and VMA is the catecholamine metabolite and is positively correlated with the body’s stress state[9]. The study results show that the application of sevoflurane for anesthesia induction in radical operation of tongue cancer may increase systemic stress state and is not conducive to postoperative trauma recovery and tumor cell viability inhibition, and the specific mechanism needs to be clarified by further research.

NK cells mediate innate immunity, B lymphocytes mediate the humoral immunity, and the two play a nonnegligible role in the anti-tumor aspect. NK cells can kill tumor cells, the domestic study has shown that the decrease in the number of NK cells is one of the key causes of death in patients with malignant tumor, and the latest research shows that after the number of NK cells decreases, free tiny tumor emboli will occur in radical operation of cancer, and cause intraoperative lymph node metastasis[10,11]. B lymphoid cells can be differentiated into plasmacytes, further secrete a variety of immune globulins, and participate in humoral immunity of tumor patients. Patients with decrease in B lymphocytes cannot secrete enough antibodies, which further weakens the patients’ overall immune function, and leads to the weakened inhibiting and killing effect of the body on the residual tumor cells, and the increased long-term recurrence rate[12]. CD3$^+$CD16$^+$56$^+$ is a marker factor of NK cells, CD3$^+$CD19$^+$ is a marker factor of B lymphocytes, and the study results showed that peripheral blood CD3$^+$CD16$^+$56$^+$ and CD3$^+$CD19$^+$ cell levels of observation group were higher 1h after operation, indicating that after total intravenous anesthesia induction, NK cell and B lymphocyte function in patients were suppressed to a lesser degree, the innate immunity and humoral immunity function in patients with sevoflurane induction were greatly damaged, and the results might be related to the massive production of cytotoxic cells in sevoflurane induction[13].

T lymphocytes mediate the process of cellular immunity and play an extremely important role in the body’s anti-tumor immunity. The suppression of cellular immune function is discovered in patients with lung cancer, liver cancer, colon cancer and the vast majority of malignant tumors, the negative effect of surgical trauma on immune function of cancer patients has already been confirmed, but the effect of anesthetics on cellular immune function in surgery is still less covered[14]. In the study, CD3$^+$ and CD4$^+$T lymphocyte levels and CD4$^+/CD8^+$ ratio of observation group were higher 1h after operation, indicating that the damage of total intravenous induction to cellular immune function was smaller than that of sevoflurane induction. Sevoflurane can suppress the ligand binding function of lymphocyte-related factor LFA-1, make LFA-1 unable to be transformed to active form, and eventually lead to the suppression of T cell proliferation, and it may be the internal mechanism of the suppressed cellular immune function after control group of the study received sevoflurane induction[15].

To sum up, application of sevoflurane in surgical anesthesia may increase postoperative stress and immunosuppression in patients with radical operation of tongue cancer, and total intravenous

<table>
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<th>Groups</th>
<th>Case No.</th>
<th>CD3$^+$</th>
<th>CD4$^+$</th>
<th>CD8$^+$</th>
<th>CD4$^+/CD8^+$</th>
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<td>24</td>
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Table 4
Comparison of postoperative distribution of peripheral blood T lymphocyte subsets.
anesthesia induction is a more ideal way of anesthesia induction for patients with tongue cancer.

References


