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# Effects of Propofol anesthesia combined with remifentanil on inflammation, stress response and immune function in children undergoing tonsil and adenoid surgery

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**ABSTRACT**

The purpose of this study was to investigate the effects of propofol anesthesia combined with remifentanil on inflammation, stress response, and immune function in children undergoing tonsil and adenoid surgery. For this aim, 126 children admitted to our hospital for elective temperature-controlled radio-frequency of tonsils and adenoids from October 2020 to September 2021 were randomly divided into an observation group (n=63) and a control group (n=63). The observation group was anesthetized with propofol in combination with remifentanil, while the control group underwent propofol combined with ketamine. The mean arterial pressure (MAP), heart rate, serum C-reactive protein (CRP), interleukin-6 (IL-6), tumour necrosis factor-α (TNF-α), epinephrine, cortisol (Cor), $CD3^+$ T lymphocytes, $CD4^+$ helper T lymphocytes, $CD8^+$ suppressor T lymphocytes and $CD4^+/CD8^+$ ratio were compared between the two groups before induction of anaesthesia ($T_1$), upon intubation ($T_2$), at the beginning of surgery ($T_3$), at the end of surgery ($T_4$) and 5 min after extubation ($T_5$). -(TNF-α). The recovery time from anaesthesia and adverse reactions after extubation were observed in the two groups. Results showed that the MAP and heart rate in both groups increased significantly at $T_2$ compared to $T_1$, but the observation group had lower values than the control group after the maintenance of anaesthesia ($P<0.05$). Serum CRP, IL-6 and TNF-α levels increased with time in both groups, and the increase was considered significant ($P<0.05$). In addition, serum epinephrine and Cor levels gradually rose from $T_1$ to $T_4$ in both groups, and then decreased at $T_5$. The difference was statistically significant ($P<0.05$) between any two-time points. CRP, IL-6, TNF-α, epinephrine and Cor in the observation group were significantly lower than those in the control group from $T_3$ to $T_5$ ($P<0.05$). $CD3^+$, $CD4^+$ and CD4+/CD8+ ratio decreased whereas $CD8^+$ went up in both groups at $T_4$ and $T_5$, and which were considered statistically significant when compared with data from $T_1$ to $T_3$ ($P<0.05$). However, CD3+, CD4+, CD8+ and CD4+/CD8+ ratios did not differ statistically significantly between the two groups at each time point ($P>0.05$). In the observation group, the time to recovery of spontaneous respiration, the time to resumption of limb movements and the span from discontinuation of anaesthetic to extubation were all significantly shorter than those in the control group, and the incidence of agitation during the awakening period was lower than that in the control group ($P<0.05$). Then propofol combined with remifentanil is more effective in inflammation, stress response and immune function in anesthetizing children undergoing tonsil and adenoid surgery. The observation group presented more stable hemodynamics, lower levels of inflammation and stress reactions, rapid awakening and fewer adverse effects, so the combination therapy was worthy of clinical promotion in pediatric surgery requiring general anesthesia.

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## Introduction

Chronic tonsillitis and adenoid hypertrophy are the main causes of upper respiratory tract infections and snoring in children, and in severe cases may affect the normal development of adjacent organs, making it difficult for children to concentrate, and expose them to memory loss and even intellectual impairment (1). At present, surgical removal of the tonsils and adenoids is the main treatment method. However, the oropharynx and larynx are richly innervated, and although this type of surgery is relatively short, it can cause strong stress reactions, fluctuations in haemodynamics and even serious complications. Therefore, it is extremely important to choose the appropriate anesthetic drugs, as general anaesthesia and endotracheal intubation are often used clinically to give the child perfect analgesia and sedation, and the surgery requires rapid and complete postoperative

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awakening without agitation (2,3). In recent years, a combination of propofol and remifentanil has been applied for paediatric tonsillectomy and adenoidectomy, but its effects on haemodynamics and stress responses in children have been less well documented. By comparing the effects of propofol combined with remifentanil and propofol combined with ketamine on temperature-controlled radiofrequency ablation of pediatric tonsils and adenoids, this study aimed to investigate their influences on hemodynamics, inflammation, stress response and immune function, and to provide a reliable clinical basis for the options of anesthesia. It was reported as follows.

## Materials and methods

### General data

From October 2020 to September 2021, 126 children admitted to our hospital for elective temperature-controlled radiofrequency ablation of tonsils and adenoids were randomized into an observation group (n=63) and a control group (n=63). The observation group consisted of 32 males and 31 females, ranging from 3 to 9 years old, with a mean age of (5.84±1.43) years; from 14 to 28 kg, with a mean weight of (21.68±6.30) kg; 87 to 120 cm tall, with a mean height of (102.52±13.70) cm. According to the American Society of anesthesiology (ASA) standards, 36 were classified under Grade I and 27 under Grade II, while the Mallampati scale categorized 40 under Class I and 23 under Class II. The control group constituted 34 males and 29 females, ranging from 3 to 10 years old, with an average age of (5.88±1.51) years; from 15 to 29 kg, with an average weight of (22.40±6.35) kg; from 88 to 122 cm tall, with an average heoght of (104.08±13.83) cm. According to the Mallampati scale, 40 were classified under Class I and 23 under Class II. The groups did not show significant differences in gender, age, weight, height, ASA classification and Mallampati classification (P>0.05) and were therefore comparable. The study was approved by the Medical Ethics Committee of the hospital.

Inclusion criteria: (i) Aged over 2 years old; (ii) Frequent colds, nasal congestion and runny nose sleep snoring to varying degrees, and mouth breathing; (iii) Tonsil hypertrophy not lower than Grade II, complicated with adenoid hypertrophy and other indications for tonsil and adenoid surgery; (iv) ASA Class I or II; (v) Mallampati Class I or II; (vi) Informed consent to this study and signed consent form. Exclusion criteria: (i) arrhythmia, congenital heart disease and other organ dysfunction; (ii) obesity (greater than 20% of the standard body weight); (iii) intellectual disability, neurological disability, and severe developmental disability; (iv) airway abnormalities or recent respiratory tract infection; (v) allergy to anesthetic drugs or other surgery drugs; (vi) adverse events such as severe laryngospasm and massive bleeding during the perioperative period; (vii) failure to strictly implement the study protocol due to various reasons.

### Anaesthesia method

Both groups were fasted for 6 h and abstained from drinking for 2 h before surgery. After being sent to the operating room, the children were routinely given oxygen via a face mask, and connected with a monitor, while a disposable EEG sensor was placed to detect relevant values. Then atropine (0.01mg/kg), dexamethasone (5 mg), midazolam (0.1 mg/kg), propofol (3.0 mg/kg), fentanyl (2μg/kg) and cis-atracurium (0.1 mg/kg) were administered intravenously induction of anaesthesia. The trachea was intubated with visual laryngoscopy after muscle relaxation. Afterward, the observation group was continuously pumped with propofol (6-8 mg/kg.h) and remifentanil (20-40 μg/kg.h), whilst the control group was maintained in anaesthesia by continuous pumping of propofol (6-8 mg/kg.h) and intravenous drip of 0.1% ketamine solution. The intraoperative dose of propofol was adjusted according to the Bispectral Index (BIS). It was kept unchanged at a BIS of 45-55, reduced for BIS less than 45, and adjusted to 0.5 mg/kg for BIS greater than 55. The drug administration was stopped 5 min before the end of the procedure. The tracheal tube was removed after the children's consciousness, cough reflex and tidal volume had recovered, and the oropharyngeal secretions and blood were aspirated. The children were observed to be free of nausea, vomiting, choking, agitation and other adverse reactions before being returned to the ward.

**Observation indicators**

**Haemodynamics**

Hemodynamic parameters include mean arterial pressure (MAP) and heart rate before induction of anaesthesia ($T_1$), upon intubation ($T_2$), at the beginning of surgery ($T_3$), at the end of surgery ($T_4$) and 5 minutes after extubation ($T_5$) were compared between the two groups.

**Inflammation, stress response and immune function**

Fasting venous blood was collected from both groups at $T_1$-$T_5$ and centrifuged after clotting to collect the serum. Serum levels of C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor (TNF-α), and epinephrine were measured by an enzyme-linked immunosorbent assay, Cortisol (Cor) by a radioimmunoassay, $CD3^+$ T lymphocytes, $CD4^+$ helper T lymphocytes, and $CD8^+$ suppressor T lymphocytes by BD Facscalibur flow cytometry to calculate the CD4+/CD8+ ratio.

**Recovery from anaesthesia**

Time to return of spontaneous circulation, time to resumption of limb movements and period between the withdrawal of anesthesia and extubation were recorded in both groups. Also, the occurrence of adverse reactions after extubation was observed.

**Statistical processing**

SPSS 19.0 software was used for data analysis. The measurement data were expressed as x±s, and the count data as a number of cases or rate, both undergoing repeated measures ANOVA, q-test, paired t-test and $\chi^2$ test. Differences were considered statistically significant at $P < 0.05$.

**Results and discussion**

**Comparison of haemodynamic parameters**

The MAP of the observation group significantly rose from $T_1$ to $T_2$ before it remained low until the end of the operation, and then went up at $T_5$ to an unprecedented level, suggesting statistically significant differences ($P<0.05$). The control group had a significantly higher MAP value from $T_1$ to $T_2$ until the end of the operation and also experienced an increase in MAP level at $T_5$, suggesting statistically significant differences ($P < 0.05$). Further, the findings indicated no significant difference in MAP at $T_1$ and $T_2$ between the two groups ($P > 0.05$), while lower MAP levels in the observation group between $T_3$ and $T_5$ were considered as statistically significant ($P<0.05$). The observation group was observed at significantly faster heart rates at $T_2$ than at $T_1$, indicating a statistically significant difference ($P<0.05$). The control group also had significantly faster heart rates at $T_2$ than $T_1$, but remarkably lower from $T_3$ to $T_4$, indicating statistically significant differences ($P<0.05$), and then faster at $T_5$, without a statistically significant difference from $T_1$ ($P>0.05$). To put together, the heart rates did not show a significant difference from $T_1$ to $T_2$ ($P>0.05$), but the observation group had lower rates than the control group from $T_3$ to $T_5$, indicating statistically significant differences ($P<0.05$) (Table 1).

**Table 1.** Comparison of haemodynamic parameters between the two groups (x±s)

| Haemodynamic indicators | Observation (n = 63) | Control (n = 63) | t | P |
|---|---|---|---|---|
| MAP(mmHg) | | | | |
| $T_1$ | 74.58±6.74 | 73.97±6.68 | 0.468 | 0.640 |
| $T_2$ | 77.44±7.35a | 79.42±7.50a | 1.372 | 0.172 |
| $T_3$ | 74.77±6.91 | 78.33±7.24a | 2.587 | 0.010 |
| $T_4$ | 72.42±6.57b | 75.25±6.78bc | 2.180 | 0.031 |
| $T_5$ | 81.51±7.83abcd | 85.46±8.15abcd | 2.542 | 0.012 |
| Heart rate (bmp) | | | | |
| $T_1$ | 100.62±10.38 | 104.95±12.24 | 1.963 | 0.051 |
| $T_2$ | 120.80±13.73a | 122.52±13.90a | 0.641 | 0.522 |
| $T_3$ | 99.60±10.67b | 113.71±12.49ab | 6.249 | 0.001 |
| $T_4$ | 96.73±9.94b | 100.64±9.88abc | 2.030 | 0.044 |
| $T_5$ | 100.51±10.14b | 108.23±12.45bcd | 3.498 | 0.001 |

a: $P<0.05$, compared with the same group at $T_1$; b: $P<0.05$, compared with the same group at $T_2$; c: $P<0.05$, compared with the same group at $T_3$; d: $P<0.05$, compared with the same group at $T_4$.

**Comparison of inflammatory indicators**

Both groups showed time-dependent higher serum levels of CRP, IL-6 and TNF-α, indicating statistically significant differences ($P<0.05$), but suggesting no statistically significant differences between $T_1$ and $T_2$ ($P>0.05$). In addition, the levels in the observation group were significantly lower than those in the control group from $T_3$ to $T_5$ ($P<0.05$), as shown in Table 2.

**Comparison of the stress response**

In both groups, serum levels of Epinephrine and Cor increased gradually from $T_1$ to $T_4$, and decreased

at $T_5$, with statistical significance (P<0.05). However, the observation group presented significantly lower levels than the control group from $T_3$ to $T_5$, with statistical significance (P<0.05), as shown in Table 3.

**Table 2.** Comparison of inflammatory indicators between the two groups (x±s)

| Inflammatory indicators | Observation (n = 63) | Control (n = 63) | t | P |
|---|---|---|---|---|
| CRP(mg/L) | | | | |
| $T_1$ | 56.76±6.81 | 57.02±6.85 | 0.197 | 0.844 |
| $T_2$ | 67.20±7.75a | 67.63±7.78a | 0.286 | 0.775 |
| $T_3$ | 93.57±10.48ab | 114.27±12.52ab | 9.223 | 0.001 |
| $T_4$ | 116.38±12.86abc | 129.56±13.20abc | 5.204 | 0.001 |
| $T_5$ | 134.15±14.07abcd | 145.70±15.11abcd | 4.071 | 0.001 |
| IL-6 (ng/L) | | | | |
| $T_1$ | 26.03±3.24 | 25.88±3.16 | 0.242 | 0.809 |
| $T_2$ | 32.14±3.78a | 31.25±3.67a | 1.228 | 0.222 |
| $T_3$ | 40.26±4.17ab | 54.31±5.73ab | 14.406 | 0.001 |
| $T_4$ | 52.37±5.65abc | 62.44±6.38abc | 8.589 | 0.001 |
| $T_5$ | 66.51±6.78abcd | 73.63±7.45abcd | 5.140 | 0.001 |
| TNF-α (ng/L) | | | | |
| $T_1$ | 45.81±5.35 | 46.02±5.40 | 0.202 | 0.840 |
| $T_2$ | 49.75±5.83a | 50.10±5.91a | 0.307 | 0.759 |
| $T_3$ | 56.28±6.44ab | 62.93±6.82ab | 5.154 | 0.001 |
| $T_4$ | 61.33±6.92abc | 67.75±7.14abc | 4.695 | 0.001 |
| $T_5$ | 69.57±7.36abcd | 75.28±7.67abcd | 3.906 | 0.001 |

a: P<0.05, compared within the group at $T_1$; b: P<0.05, compared within the group at $T_2$; c: P<0.05, compared within the group at $T_3$; d: P<0.05, compared within the group at $T_4$.

**Table 3.** Comparison of stress response between the two groups (x±s)

| Stress response indicators | Observation (n = 63) | Control (n = 63) | t | P |
|---|---|---|---|---|
| Epinephrine (ng/mL) | | | | |
| $T_1$ | 38.95±4.56 | 40.14±4.72 | 1.318 | 0.190 |
| $T_2$ | 49.77±6.38a | 51.06±6.47a | 1.033 | 0.303 |
| $T_3$ | 61.62±7.81ab | 77.45±8.68ab | 9.859 | 0.001 |
| $T_4$ | 78.14±8.45abc | 85.22±9.63abc | 4.008 | 0.001 |
| $T_5$ | 53.36±5.60abcd | 68.40±7.56abcd | 11.606 | 0.001 |
| Cor(pg/mL) | | | | |
| $T_1$ | 149.51±15.68 | 151.36±15.85 | 0.605 | 0.546 |
| $T_2$ | 167.37±17.23a | 168.91±17.52a | 0.457 | 0.648 |
| $T_3$ | 182.70±19.44ab | 236.84±24.28ab | 12.667 | 0.001 |
| $T_4$ | 203.45±20.75abc | 272.54±28.40abc | 14.296 | 0.001 |
| $T_5$ | 191.68±19.56abcd | 219.42±22.77abcd | 6.726 | 0.001 |

a: P<0.05, compared within the group at $T_1$; b: P<0.05, compared within the group at $T_2$; c: P<0.05, compared within the group at $T_3$; d: P<0.05, compared within the group at $T_4$.

## Comparison of immune function indicators

$CD3^+$, $CD4^+$ , $CD4^+/CD8^+$ levels decreased while $CD8^+$ increased in both groups at $T_4$ and $T_5$, indicating statistically significant differences (p<0.05) from the data at $T_1$-$T_3$. The levels did not vary significantly between the two groups from $T_1$ to $T_5$ (Table 4).

**Table 4.** Comparison of immune function indicators between the two groups (x±s)

| Immune function indicators | Observation (n = 63) | Control (n = 63) | t | P |
|---|---|---|---|---|
| $CD3^+$(%) | | | | |
| $T_1$ | 51.91±5.82 | 52.12±5.86 | 0.186 | 0.853 |
| $T_2$ | 50.84±5.75 | 51.67±5.78 | 0.741 | 0.460 |
| $T_3$ | 51.35±5.80 | 51.78±5.83 | 0.381 | 0.704 |
| $T_4$ | 43.06±4.41abc | 42.94±4.35abc | 0.142 | 0.887 |
| $T_5$ | 42.58±4.37abc | 42.36±4.31abc | 0.261 | 0.794 |
| $CD4^+$ (%) | | | | |
| $T_1$ | 31.77±3.34 | 32.12±3.41 | 0.533 | 0.595 |
| $T_2$ | 31.53±3.30 | 31.85±3.36 | 0.494 | 0.622 |
| $T_3$ | 30.91±3.27 | 30.88±3.24 | 0.048 | 0.961 |
| $T_4$ | 22.15±2.33abc | 21.91±2.28abc | 0.535 | 0.596 |
| $T_5$ | 21.82±2.26abc | 21.74±2.23abc | 0.184 | 0.856 |
| $CD8^+$(%) | | | | |
| $T_1$ | 20.85±2.12 | 21.04±2.15 | 0.457 | 0.648 |
| $T_2$ | 21.09±2.18 | 21.31±2.23 | 0.512 | 0.609 |
| $T_3$ | 21.02±2.16 | 21.27±2.28 | 0.578 | 0.566 |
| $T_4$ | 29.78±3.04abc | 30.10±3.09abc | 0.537 | 0.592 |
| $T_5$ | 30.24±3.07abc | 30.14±3.13abc | 0.167 | 0.867 |
| $CD4^+/CD8^+$ | | | | |
| $T_1$ | 1.52±0.45 | 1.53±0.46 | 0.112 | 0.911 |
| $T_2$ | 1.48±0.42 | 1.49±0.43 | 0.119 | 0.905 |
| $T_3$ | 1.47±0.40 | 1.46±0.39 | 0.128 | 0.898 |
| $T_4$ | 0.73±0.19abc | 0.71±0.20abc | 0.503 | 0.617 |
| $T_5$ | 0.71±0.18abc | 0.70±0.17abc | 0.279 | 0.780 |

a: P<0.05, compared within the group at $T_1$; b: P<0.05, compared within the group at $T_2$; c: P<0.05, compared within the group at $T_3$.

## Comparison of recovery from anaesthesia

In the observation group, the time to recover spontaneous breathing, the time to resume limb movements and the time from stopping the anaesthetic to extubation were all significantly shorter than those in the control group (P<0.05) (Table 5).

**Table 5.** Comparison of recovery from anaesthesia between the two groups (x±s, min)

| Indicators | Observation (n = 63) | Control (n = 63) | t | P |
|---|---|---|---|---|
| Time to return spontaneous breathing | 4.13±1.88 | 6.94±2.52 | 6.535 | 0.001 |
| Time to resume limb movements | 5.04±1.27 | 8.35±1.43 | 12.692 | 0.001 |
| From stopping anaesthetic to extubation | 6.26±1.49 | 10.73±2.58 | 10.972 | 0.001 |

## Comparison of adverse events

The observation group was much less likely to agitate than the control group, with statistical significance (P<0.05), but there was no statistically

significant difference in the incidence of upper airway obstruction or breath-holding spells, nausea and vomiting between the two groups (P>0.05) (Table 6).

**Table 6.** Comparison of the incidence of adverse events between the two groups [n(%)

| Adverse events | Observation (n = 63) | Control (n = 63) | $\chi^2$ | P |
|---|---|---|---|---|
| Emergence agitation | 6 (9.52) | 23 (36.51) | 12.738 | 0.001 |
| Upper airway obstruction/breath-holding | 4 (6.35) | 11 (17.46) | 3.286 | 0.068 |
| Nausea & vomiting | 8 (12.70) | 10 (15.87) | 0.069 | 0.083 |

The small size of the paediatric oropharyngeal cavity and the fragile mucosa, as well as the tendency for uvula, swelling of the operative cavity and increased respiratory resistance in the pharyngeal cavity after temperature-controlled radiofrequency ablation of tonsils and adenoids, place the paediatric population at high risk of serious adverse events. Currently, general anaesthesia is often used for these short procedures, requiring intraoperative anaesthesia and a rapid awakening at the end of the procedure, without delayed respiratory depression and metabolic residual anaesthetic drugs. However, the paediatric organs are not yet fully developed and may affect the metabolism of intravenous anaesthetic drugs, leaving drug residue in the body. Therefore, it is crucial to choose appropriate anaesthetic drugs.

In recent years, propofol has been widely used as an alkylphenolic intravenous anaesthetic, characterized by quick drug potency, short duration of action, rapid awakening and controlled anaesthetic depth. However, it works poorly as an analgesic and produces somatic reactions when used alone, while causing circulatory and respiratory depression at a larger dose, so it is often used in combination with other analgesics or local anaesthetics (4). Ketamine is a traditional intravenous anaesthetic, often used in combination with propofol for paediatric surgery in the early days, and is still widely used in primary care hospitals. Despite quick drug potency, low respiratory impact and good surface analgesia, the drug in repeated administration will develop drug resistance among patients and lead to more adverse events (5). The development of anaesthesia medicine enables the new generation, opioid agonist, remifentanil, to be clinically combined with propofol. Remifentanil is suitable for minor operations as it has a rapid onset of action with a blood-brain equilibrium half-life of 1 minute and is rapidly degraded by nonspecific plasma and tissue esterases, in addition to the short duration of action, complete elimination, rapid awakening, minor damage to liver and kidney function, high safety, strong anesthetic effect (6).

Although the combination of drugs used to induce anaesthesia in this study was reasonable, a few children experienced intubation stress responses that resulted in a moderate increase in MAP and heart rate. Dose-dependent bradycardia and hypotension have been documented with remifentanil, while ketamine has been shown to cause an increase in blood pressure (7). In this study, the combination of remifentanil at 20-40 μg/kg.h with propofol in the maintenance of anaesthesia did not generate severe bradycardia and hypotension. While the changes in MAP and heart rate were not completely consistent at all time points, the two indicators were significantly lower in the observation group than in the control group after the maintenance of anaesthesia, in line with the references (7). Furthermore, the observation group continued with a smoother MAP and heart rate until the end of the surgery, which was consistent with the study by UNSAL et al. (2). It was assumed that the adverse events of remifentanil were dose-dependent possibly due to its synergy with propofol in the combined therapy and could be alleviated by reducing respective dosages. In addition, the drug concentration in the plasma is stabilized better via intravenous pumping so as to effectively control the injurious stimuli, thus keeping steady hemodynamics.

Numerous studies have long established that anesthesia and surgical stimuli trigger multiple inflammatory and stress responses in the body, and suppress the immune system, yet the degree of responses produced by different anesthetic drugs and methods varies considerably (8). This study was consistent with the research by Yuan Fen (9) who reported that remifentanil combined with propofol reduced inflammatory factor production in elderly orthopaedic surgery, as it found that propofol in combination with remifentanil was effective in reducing inflammation. Injurious stimulus signals to the nociceptors can stimulate two systems, hypothalamic-pituitary-adrenocortical and sympathetic-adrenal medullary, leading to the synthesis of the adrenal cortex and adrenal medulla, and thus increased secretion of Cor and epinephrine.

Hence, serum epinephrine and Cor can reflect the stress response (10). This study further showed that remifentanil with propofol had an inhibitory effect on the stress response, which coincided with the results reported by Ye Linyang et al. (11) that the combined anaesthesia could effectively inhibit the stress response in patients with acute abdomen complicated by infectious shock. This was because remifentanil may affect the release of inflammatory factors by interfering with the synthesis of prostaglandins. At the same time, it activates opioid receptors in central and peripheral nerves, resulting in a reduced release of noxious neurotransmitters by C-fibers, and the suppression of the sensitization of noxious receptors caused by inflammatory mediators. Ultimately, it works as analgesic and reduces inflammatory and stress responses. However, this study was also consistent with the findings of Zhang Yang et al (12) in that the anesthetic drugs and methods used herein had little effect on the immune function of the children. Separately, the observation group took obviously less time to recover after anesthesia than the control group, which was in line with the results reported in the earlier literature (13). This was associated with the following factors: (i) The pharmacokinetic profile of remifentanil is unique as its metabolism is independent of the liver and kidneys, hence few individual differences. This enables children to have a similar elimination rate to adults. (ii) Norketamine, a metabolite of ketamine, has 1/5 to 1/3 of the anesthetic potency of ketamine and a longer elimination half-life, often leading to drowsiness after awakening. In this study, the incidence of agitation during the awakening period was significantly lower in the observation group than in the control group, in keeping with the results reported in the references that ketamine triggers psychiatric symptoms such as hallucinations, nightmares, delirium and restlessness during the recovery period from anesthesia (14-16).

In conclusion, propofol combined with remifentanil is worthy of clinical promotion in pediatric surgery requiring general anesthesia for its advantages in anesthetizing children undergoing tonsil and adenoid surgery, including more stable hemodynamics, lower levels of inflammation and stress responses, rapid awakening and fewer adverse events.

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None.

**Conflict interest**

The authors declare no conflict of interest.

**References**

1. Pan Hg, Yang H, Chen Gw, et al. Olfactory function in children with adenoid hypertrophy who underwent adenotonsillectomy during pre-and post-operative period.Zhonghua Er Bi Yan Hou Jing Wai Ke Za Zhi, 2017,52(6) ; 453-457.
2. Unsal O, Bozkurt G, Esen Akpinar M, et al. Albuminuria in Pediatric Patients With Adenotonsillar Hypertrophy. J Craniofac Surg 2017;28(7):e640-643.
3. Smiianov Y V, Smiianov V A, Sniehirova I A, et al. Algorithm of adenoiditis treatment in adults, depending on the pharyngeal tonsil hypertrophy stage. Wiad Lek 2018;71(3 pt 1):564-568.
4. Ullman D A, Saleem S A, Shahna Waz A, et al. Relation of viscous lidocaine combined with propofol deep sedation during elective upper gastrointestinal endoscopy to discharge. Proc(Bayl Univ Cent) 2019; 32(4):505-509.
5. O'brien M E, Fuh L, Raja AS, et al. Reduced-dose intramuscular ketamine for severe agitation in an academic emergency department. Clin Toxicol(Phila) 2020;58(4):294-298.
6. Ouyang R, Ren H, Liu W, et al.Remifentanil inhibits the traumatic stress response in emergent trauma surgery. J Clin Lab Anal 2019;33(8):e22971-22975.
7. Jelting Y, Weibel S, Afshari A, et al. Patient-controlled analgesia with remifentanil versus alternative parenteral methods for pain management in labour: a Cochrane systematic review. Obstetric Anesthesia Digest 2018; 38(2): 65-66.
8. Bal W Y, Yang YC, Teng XF, et al. Effects of transcutaneous electrical acupoint Stimulation on the stress response during extubation after general anesthesia in elderly patients undergoing elective supratentorial craniotomy: a prospective randomized controlled trial. J Neurosurg Anesthesiol,2018,3094） : 337-346.
9. Yuan F. Effects of remifentanil combined with propofol on inflammatory factors and postoperative cognitive function in elderly patients undergoing orthopaedic surgery. Chin J Gerontol 2017; 37(3): 673-675.
10. Zakharov A V. Features of relaxation of a stress tensor in the microscopic volume of nematic phase under the action of a strong electric field. Physics Solid State 2018;60(602):412-421.
11. Ye LY, Nie YY, Wang QX, et al. Effects of remifentanil combined with propofol on hemodynamics and inflammatory stress response in patients with septic shock . Chin Prim Med 2019, 26(11): 1325-1330.

12. Zhang Y, Feng Y, Shang Y. Effects of different anesthesia methods on hemodynamics, inflammatory stress response and immune function in patients with acute abdominal septic shock. Medical Herald 2017; 36 (5): 520-523.
13. Du X Y, Zheng Q J, Wang C H, et al. Clinical anesthetic effect of remifentanil in adenoidectomy in children. Chin Continu Med Edu 2019, 11 (4): 82-84.
14. Rahbar-Karbasdehi E, Rahbar-Karbasdehi F. Clinical challenges of stress cardiomyopathy during coronavirus 2019 epidemic. Cell Mol Biomed Rep 2021; 1(2): 88-90. doi: 10.55705/cmbr.2021.145790.1018
15. Aryafar S, Sirousmehr A, Najafi S. The Impact of Compost on Seed Yield and Essential Oil of Black Cumin under Drought Stress Conditions. Agrotech Ind Crops 2021; 1(3): 139-148. doi: 10.22126/atic.2021.7184.1026
16. Lopez-Gil X, Jimenez-Sanchez L, Canpa L, et al. Role of serotonin and noradrenaline in the rapid antidepressant action of ketamine. ACS Chem Neurosci 2019; 10(7):3318-3326.