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Original Article

Effects of propofol combined with sufentanil on painless gastroscopy and hemodynamics in children under general anesthesia

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Abstract: Objective: To determine the effects of propofol combined with sufentanil on painless gastroscopy and hemodynamics in children under general anesthesia. Methods: The data of 98 children who received painless gastroscopy in the Children's Hospital of Nanjing Medical University from May 2022 and November 2022 were analyzed retrospectively. Patients anesthetized with propofol (1.5-2 mg/kg) combined with sufentanil (0.03-0.05 μg/kg) were assigned to a study group (n=52), and patients anesthetized with propofol (1.5-2 mg/kg) combined with fentanyl (0.3-0.5 μg/kg) were included in a control group (n=46). The changes in hemodynamic levels (mean arterial pressure (MAP), heart rate (HR) and pulse oxygen saturation (SpO2) at T0 (before anesthesia), T1 (1 min after anesthesia induction), T2 (start of examination), T3 (2 min after the start of examination), and T4 (end of examination) in the two groups were analyzed and compared. The Ramsay sedation score was adopted to evaluate the sedation of the two groups at the anesthesia recovery and at 1 h and 2 h after the anesthesia recovery. The anesthetic effects (time to loss of consciousness, eye opening, and recovery of orientations) of the two groups were analyzed and compared. The excellent and good anesthesia outcomes, hospitalization time and dosage of propofol were compared between the two groups, and the adverse reactions in the two groups during and after the examination were analyzed. Results: At T0, the two groups were not significantly different in the levels of MAP, HR and SpO2 ($P>0.05$), but at T1, T2, T3, and T4, the study group showed a significantly higher MAP level than the control group ($P<0.05$). At T1 and T3, the study group exhibited a significantly higher HR level than the control group ($P<0.05$), and at T2 and T4, the HR level of the two groups was not greatly different ($P>0.05$). The SpO2 levels at T0, T1, T2, T3, and T4 were not greatly different between the two groups ($P>0.05$). There was no significant difference in Ramsay score between the two groups at anesthesia recovery and at 1 h and 2 h after the anesthesia recovery ($P>0.05$). Additionally, the study group experienced significantly earlier time to loss of consciousness, eye opening, and recovery of orientations than the control group ($P<0.05$). The number of patients with excellent anesthetic outcome in the study group was notably higher than that in the control group ($P<0.05$). Compared with the control group, the study group consumed less propofol, experienced shorter hospitalization time, and showed a notably lower incidence of adverse reactions ($P<0.05$). Conclusion: For children undergoing painless gastroscopy under general anesthesia, sufentanil combined with propofol can deliver better anesthetic effect than propofol combined with fentanyl, with less effect on hemodynamics and fewer gastroscopy-related adverse reactions.

Keywords: Propofol, sufentanil, painless gastroscopy under general anesthesia, anesthetic effect, hemodynamics

Introduction

Gastroscopy is a crucial means for the diagnosis and treatment of digestive tract diseases, and it is the gold standard for the diagnosis of upper gastrointestinal diseases [1]. Although it is a non-invasive examination, it still brings discomfort and fear, especially for children [2, 3]. Thus, children and their parents have some concerns about the safety profile and their tolerance to gastroscopy.

With the advancement of medical technology and the increase of patients' demand for diagnosis and treatment, painless gastroscopy came into being with a low dose of anesthesia [4]. It is also a method for the treatment of some upper gastrointestinal diseases [5].

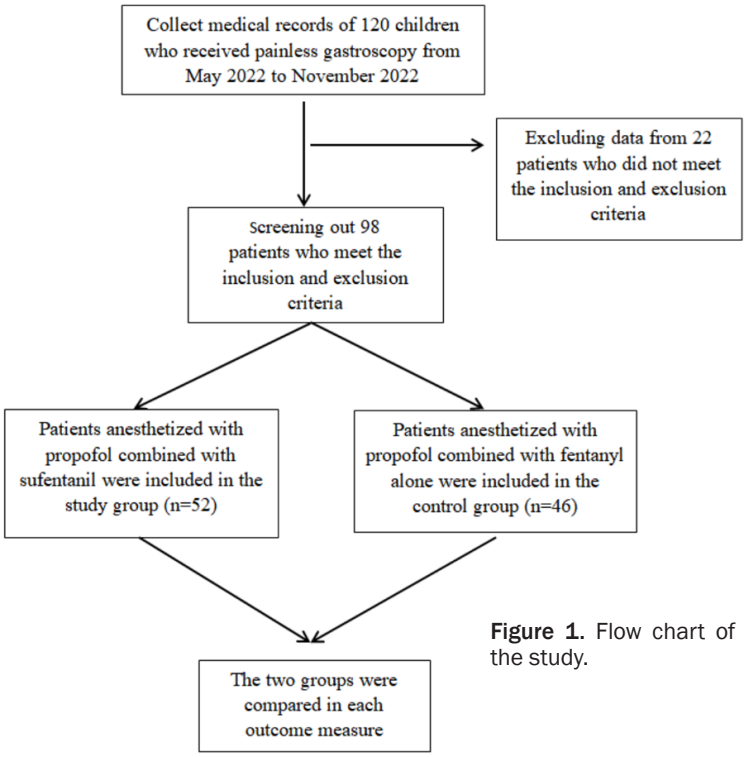

Figure 1. Flow chart of the study.

However, due to the significant difference in patients' sensitivity to pain, the procedure may still lead to different degrees of pain and discomfort to the throat and digestive tract even under anesthesia. These discomfort and pain can induce stress response and increase the risk of adverse reactions [6].

During painless gastroscopy, the painlessness is mainly achieved through narcotic drugs [4]. Under poor anesthetic effect, the patient may wake up and reject the examination, resulting in the failure of gastroscopy and the necessity of other invasive examinations, so the choice of anesthetics is of profound importance. As an effective sedative/hypnotic drug with an initial onset time of 15-40 s, short half-life and rapid recovery, propofol is the most common sedative in painless gastroscopy [7]. With a rapid onset and a quick recovery, so it can effectively inhibit the physiological reactions during the examination [8]. Propofol is frequently applied in pediatric painless gastroscopy, but because of the differences among individuals in the dosage and effect, the induction depth can be insufficient, which greatly hinders the progress of the examination [9]. In another word, single use of propofol is likely to compromise gastroscopy due to insufficient anesthesia. Sufentanil, an opioid drug, is a derivative of fentanyl, which makes up for the deficiency of propofol for its strong analgesia, quick initial onset effect, and little effect on hemodynamics [10]. However, there are few studies on the effect of propofol combined with sufentanil in children undergoing painless gastroscopy under general anesthesia.

Accordingly, this study included children who underwent painless gastroscopy under general anesthesia to determine the effects of propofol combined with sufentanil, along with the analysis of hemodynamics, aiming at providing reference for future painless gastroscopy in children.

Materials and methods

Sample collection

The data of 120 children who received painless gastroscopy in Children's Hospital of Nanjing Medical University from May 2022 to November 2022 were collected and analyzed retrospectively. The flow chart of this study is shown in **Figure 1**.

Inclusion and exclusion criteria

Inclusion criteria: Patients who received painless gastroscopy; patients between 5-10 years old; patients whose American Society of Anesthesiologists (ASA) classification was class I-II [11]; patients without a recent history of sedation or analgesia; patients with detailed clinical data.

Exclusion criteria: Patients with anemia or thrombocytopenia, patients with abnormal liver or kidney function; patients allergic to drugs adopted in this study; patients who participated in other clinical research within 3 months before the admission; patients who could not clearly express their feelings.

Sample screening

According to the inclusion and exclusion criteria, 98 patients who met the requirements were included. Among them, patients anesthetized with propofol combined with sufentanil were included in a study group (n=52), and patients anesthetized with propofol combined with fentanyl were included in a control group (n=46). This study was approved by the Medical Ethics Committee of Children's Hospital of Nanjing Medical University.

Anesthesia regimens

All children in the two groups were required to fast for over 8 hours before the examination. A multifunctional monitor was adopted to monitor the mean arterial pressure (MAP), heart rate (HR) and pulse oxygen saturation (SpO2) before and throughout the examination. The control group was intravenously anesthetized with propofol (1.5-2 mg/kg) (Xi'an Libang Pharmaceutical Co., Ltd., specification: 50 ml: 0.5 g, State Food and Drug Administration (SFDA) approval number: H19990281) and fentanyl (0.3-0.5 μg/kg). In addition to anesthesia with propofol, the study group was anesthetized with sufentanil (Yichang Humanwell Pharmaceutical Co., Ltd., specification: 1 ml: 75 μg, SFDA approval number: H20054171) instead of fentanyl. Sufentanil was given at a dose of 0.03-0.05 μg/kg intravenously for more than 1 min, and propofol was given at a dose of 1.5-2 mg/kg.

During gastroscopy, in the case of body movement, tachycardia, swallowing or MAP level rising more than 20%, the propofol dosage was increased by about 0.5-1 mg kg-1 according to the child's condition. In the case of HR less than 60 times/min, 0.1 mg kg-1 atropine was given. In cases where SpO2 level droped below 90% or there was apnea lasting longer than 30 s, the child's head would be tilted back and the lower jaw would be propped up. If there was no improvement, an upper mask would be put on to provide pressure and assist with ventilation. In the case of hypotension, 5-8 mg ephedrine (Sinopharm Group Xinjiang Pharmaceutical Co., Ltd., SFDA approval number: H65020272) was given according to the specific situation.

Outcome measures

Primary outcome measures: The general data and measurements during examinations were collected from electronic medical record system and LIS inspection system. The changes in hemodynamic levels (MAP, HR and SpO2) at T0 (before anesthesia), T1 (1 min after anesthesia induction), T2 (start of examination), T3 (2 min after the start of examination) and T4 (end of examination) in the two groups were analyzed and compared. The excellent and good anesthesia outcomes in the two groups were evaluated according to the following criteria [12]. Excellent: there was no limb movement in the process of gastroscopy; good: there were light limb movements that did not affect the examination; poor: there were limb movements that affected the progress of the examination. The Ramsay sedation score was used to evaluate the sedation of the two groups at anesthesia recovery and at 1 h and 2 h after the anesthesia recovery [13].

Secondary outcome measures: The anesthetic effects (time to loss of consciousness, eye opening and recovery of orientations) of the two groups were analyzed and compared. The time to loss of consciousness refers to the time it takes for a patient to be at a state of unconsciousness after the use of anesthetic drugs. Time to eye opening is from the time the patient stops receiving anesthetics to the time the patient opens his eyes. Time to recovery of orientations refers to the time from the cessation of anesthetic administration to the recovery of normal cognitive, thinking and reaction ability. In addition, the dosage of propofol and hospitalization time were compared between the two groups, and the adverse reactions in the two groups during and after the examination were evaluated.

Statistical analyses

This study adopted SPSS 22 statistical software for statistical analyses and GraphPad Prism 8 for visualization of data. The counting data were described by rate and analyzed using the chi-square test. The measurement data were described by mean ± SD, and their intragroup comparison of these data was conducted using paired t test, and intergroup compari-

Table 1. Comparison of baseline data

Factors	Study group (n=52)	Control group (n=46)	X^2 value	*P* value
Age			0.111	0.739
≥8	30	25		
<8	22	21		
Sex			1.050	0.306
Male	28	20		
Female	24	26		
BMI			1.855	0.173
≥20 kg/m^2	32	22		
<20 kg/m^2	20	24		
ASA classification			1.639	0.201
I	40	30		
II	12	16		
Place of residence			1.467	0.226
Rural areas	35	36		
Urban areas	17	10		
Reason for painless gastroscopy			0.1109	0.739
Gastrointestinal discomfort	30	25		
Epigastric pain	22	21		
Comorbid disease			0.635	0.426
Obstructive sleep apnea syndrome	21	15		
Asthma	31	31		
Final diagnosis			1.639	0.200
Reflux esophagitis	40	30		
Acute and chronic colitis	12	16		

BMI: body mass index; ASA: American Society of Anesthesiologists.

son was conducted using independent sample t test. Repeated analysis of variance was used for comparison among three groups of data or more, and the Bonferroni method was used for post hoc test. P<0.05 suggests a significant difference.

Results

Baseline data of patients

The two groups were not significantly different in age, sex, body mass index, ASA classification, and place of residence (P>0.05, **Table 1**).

Comparison of hemodynamic indexes between the two groups

At T0, the two groups were not greatly different in terms of the levels of MAP, HR and SpO2 (P>0.05), but at T1, T2, T3, and T4, the study group showed a notably higher MAP level than the control group (P<0.05). At T1 and T3, the study group exhibited a notably higher HR level than the control group (P<0.05), and at T2 and T4, the HR level was not greatly different between the two groups (P>0.05). The SpO2 levels at T0, T1, T2, T3, and T4 were not greatly different between the two groups (P>0.05, **Figure 2**).

Comparison of sedation depth between the two groups

Ramsay sedation score was used to evaluate the sedation depth in the two groups. According to the results, there was no significant difference in Ramsay score between the two groups at anesthesia recovery and at 1 h and 2 h after the anesthesia recovery (P>0.05, **Figure 3**).

Comparison of anesthesia effect between the two groups

The study group experienced significantly earlier time to loss of consciousness, eye opening, and recovery of orientations than the control group (P<0.05, **Figure 4**).

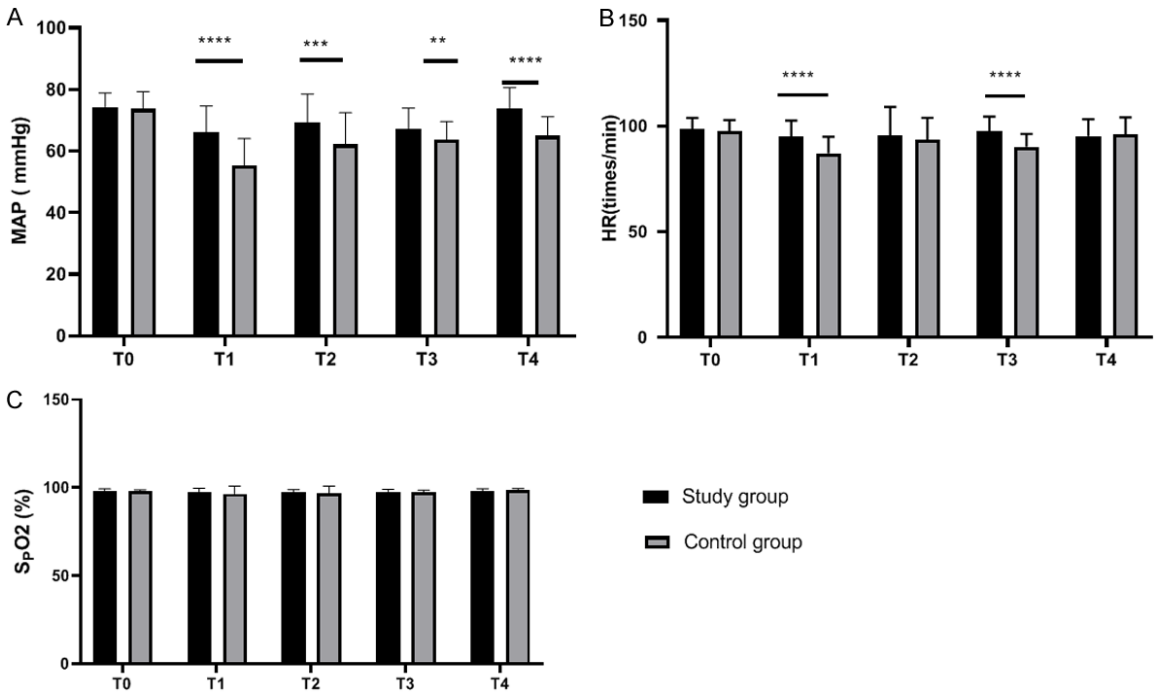

Figure 2. Comparison of hemodynamic indexes between the two groups. A: Comparison of MAP. B: Comparison of HR. C: Comparison of SpO2. Notes: MAP: Mean arterial pressure; HR: Heart rate; SpO2: Pulse oxygen saturation. **P<0.01 *vs.* the control group; ***P<0.001 *vs.* the control group; ****P<0.0001 *vs.* the control group.

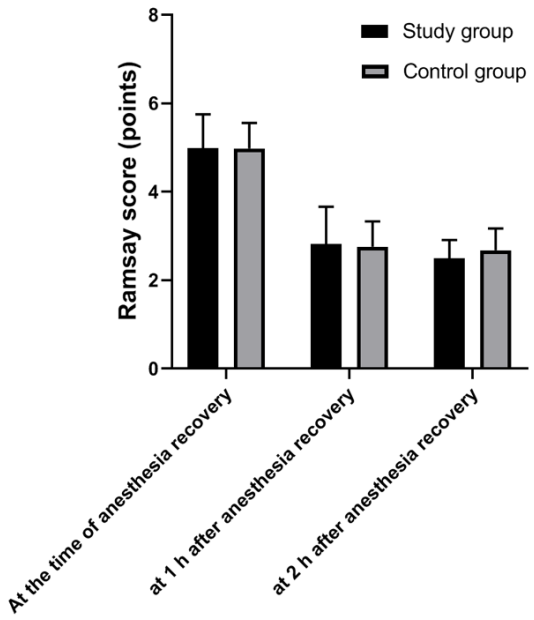

Figure 3. Comparison of Ramsay scores between the two groups.

Comparison of anesthetic outcomes between the two groups

The number of patients with excellent anesthetic outcome in the study group was notably higher than that in the control group (P<0.05, **Table 2**).

Comparison of the propofol dosage and hospitalization time between the two groups

The study group consumed notably less propofol than the control group (P<0.0001) and experienced a notably shorter hospitalization time than the control group (P=0.0315, **Figure 5**).

Comparison of adverse reactions between the two groups

The study group exhibited a notably lower incidence of adverse reactions than the control group (P=0.0476, **Table 3**).

Discussion

Painless gastroscopy is favored by patients due to its advantages of short examination time and increased comfort level. It has become one of the common clinical examinations and treatments, and is gradually becoming the first choice of gastroscopy [14]. Compared with conventional gastroscopy, painless gastroscopy can greatly reduce instrument-caused stimuli to patients, especially for patients with fear

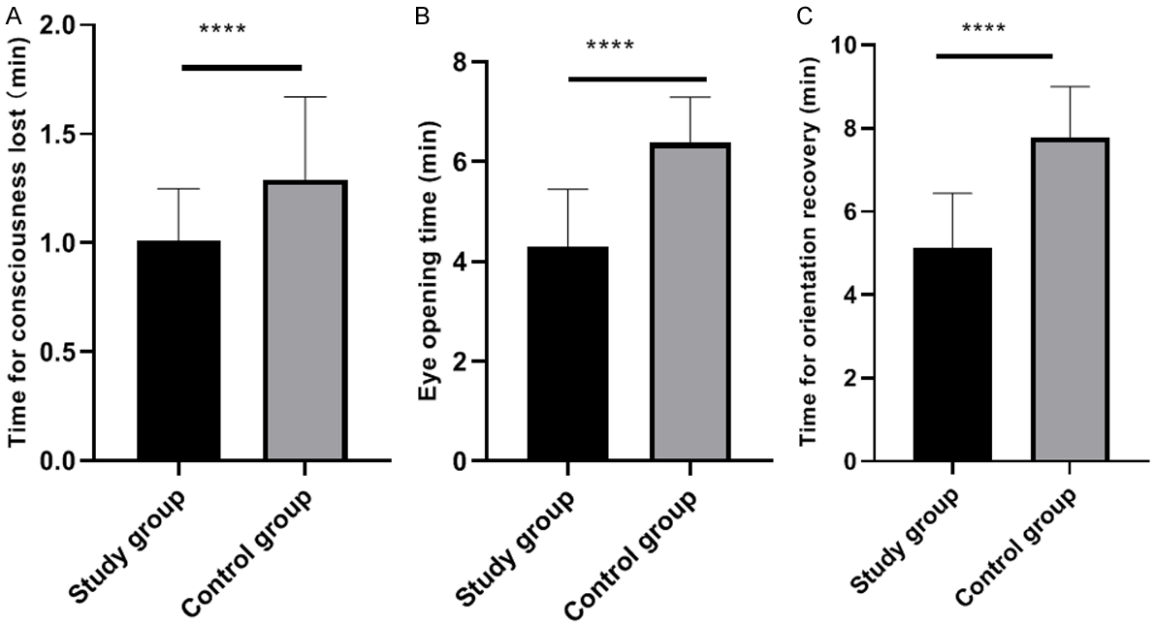

Figure 4. Comparison of anesthesia effect between the two groups. A: Comparison of the time to loss of consciousness. B: Comparison of eye opening time. C: Comparison of time to recovery of orientations. Note: ****P<0.0001 *vs.* the control group.

Table 2. Comparison of anesthetic outcomes between the two groups [n (%)]

Group	Excellent	Good	Poor
Study group (n=52)	45 (86.54)[a]	7 (13.46)	0 (0.00)
Control group (n=46)	31 (67.39)	13 (28.26)	2 (4.35)
X^2	5.140, 1	3.291, 1	2.308, 1
P value	0.0234	0.0697	0.1287

Note: [a]P<0.05 *vs.* the control group.

anxiety for the examination, and it can substantially alleviate the pain that can be brought by conventional gastroscopy and enhance patient compliance with the treatment [15]. During painless gastroscopy, the use of short-acting anesthetics is particularly important, as a good anesthesia can alleviate the pain, as well as reduce tension, anxiety and fear [16].

As a kind of phenolic derivative, propofol exerts its sedative and hypnotic effect by activating the central inhibitory amino acid, receptor γ-aminobutyric acid [17, 18]. Even though it is common anesthetic drug in clinical practice, its anti-injury effect is unsatisfactory, because it can easily bring adverse reactions such as body movements and cough when being used alone [19, 20]. Propofol and opioids have a synergistic effect, resulting in increased blood concentration and improved sedative and analgesic effect, so propofol combined with opioid analgesics is often adopted in painless gastroscopy [21]. Qu et al. [22] confirmed the effect of sufentanil combined with propofol on stabilizing intraoperative hemodynamic parameters, and reducing perioperative stress response and pain in patients undergoing radical surgery. With strong sedative and analgesic effects, sufentanil can inhibit afferent nerve impulses and reduce adrenal medulla hormone secretion and stress response, so it can be adopted for anesthesia induction, maintenance, postoperative analgesia, labor analgesia, as well as in painless endoscopic examination [23, 24]. This study collected children who underwent painless gastroscopy under general anesthesia with propofol combined with fentanyl or with propofol and sufentanil to explore the effect of the combination in children undergoing painless gastroscopy.

In this study, the MAP and HR levels decreased in all children 1 min after anesthesia induction, and did not recover until the end of the exami-

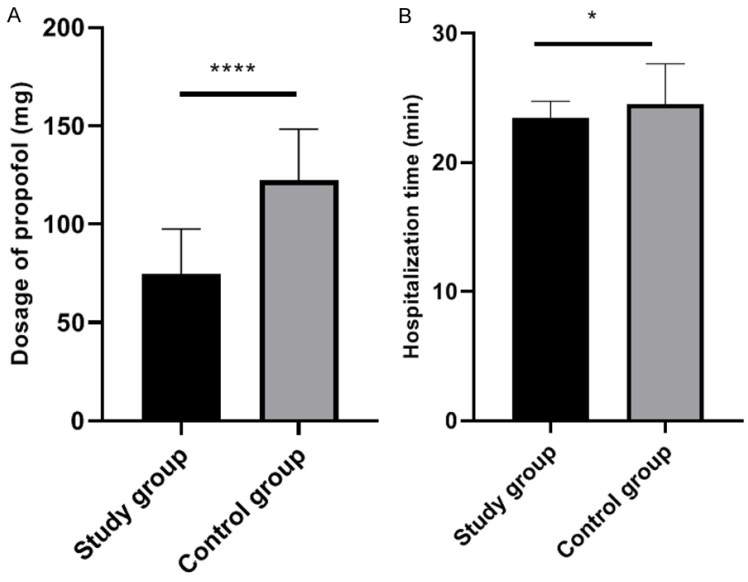

Figure 5. Comparison of propofol dosage and hospitalization time between the two groups. A: Comparison of the dosage of propofol. B: Comparison of the hospitalization time. Note: *P<0.05 *vs.* the control group; ****P<0.0001 *vs.* the control group.

nation, but the decrease of MAP and HR in children treated with propofol combined with sufentanil was milder and within the normal range. The possible reason is that sufentanil can excite the vagus nerve and inhibit the sympathetic nerve. Therefore, the combination of propofol and sufentanil can inhibit the stress response during operation and maintain the stability of hemodynamics. In addition, the SpO2 level in both groups did not fluctuate greatly, indicating that both anesthesia ways had little effect on SpO2. In this study, the study group experienced earlier time to loss of consciousness, eye opening, and recovery of orientations than the control group. Besides, the number of patients with excellent anesthetic outcomes in the study group was notably higher than that in the control group. The results imply better anesthetic effect of propofol combined sufentanil than that of propofol combined with fentanyl. Our results are similar to those acquired by Chung et al. [25], who revealed that 0.3 μg/kg sufentanil, along with propofol microemulsion injection, could reduce the pain, without increasing arterial pressure and HR after endotracheal intubation.

This study also compared and analyzed the consumed dosage of propofol and hospitalization time between the two groups. We found a lower consumed dosage of propofol and shorter hospitalization time in the group given sufentanil combined with propofol than those in the control group. These results suggest that sufentanil combined with propofol can reduce the use of propofol, which is consistent with the results of Contreras-Dominguez et al. [26], who revealed that intrathecal injection of 2.5 mg or 5 mg sufentanil could reduce the use of propofol in patients with spinal anesthesia. Moreover, this study compared the occurrence of adverse reactions between the two groups and revealed a notably lower incidence of adverse reactions in the study group than that in the control group. The reason may be the rapid onset and quick metabolism of sufentanil, allowing for smoother examination procedures in children. The results indicate that sufentanil combined with sufentanil is safe and reliable because it can helps to avoid the risk associated with adverse reactions.

This study has verified the effects of propofol combined with sufentanil in children undergoing painless gastroscopy and on their hemodynamics, but the study still has some limitations. The sample sizes included in this study is small and all from the same region, which may introduce potential bias to the results. In addition, this study did not analyze the optimal compatible dose of the drugs, so the optimal dose of the combination requires further study. We hope these deficiencies can be addressed in future studies.

To sum up, for children undergoing painless gastroscopy under general anesthesia, sufentanil combined with propofol can deliver better anesthetic effect compared with propofol combined with fentanyl, with less effect on hemodynamics, and fewer examination-related adverse reactions.

Disclosure of conflict of interest

None.

Table 3. Adverse reactions in the two groups [(n)%]

Group	Apnea	Respiratory depression	Nausea and vomiting	Dizziness	Adverse reactions
Study group (n=52)	4 (7.69)	1 (1.92)	4 (7.69)	0 (0.00)	9 (17.31)[a]
Control group (n=46)	7 (15.22)	3 (6.52)	5 (10.87))	1 (2.17)	16 (34.78)
X^2	1.387	1.318	0.295	1.142	3.922
P value	0.239	0.251	0.587	0.285	0.048

Note: [a]P<0.05 *vs.* the control group.

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