RESEARCH ARTICLE

Comparison of Propofol-Ketamine vs Propofol-Fentanyl for Pediatric Sedation during Upper Gastrointestinal Endoscopy

Alireza Takzare[1], Alireza Ebrahim Soltani[1], Anahid Maleki[1], Behrang Nooralishahi[1], Fariba Kaheh[1], Sagar Arab[1], Mehrdad Goudarzi[1]*

Background: Selection of the best sedative regimen during pediatric endoscopy with greater stability in hemodynamic parameters and fewer side effects is very important. The aim of this study was to compare the clinical efficacy and safety of propofol – ketamine versus propofol – fentanyl in pediatric undergoing diagnostic upper gastrointestinal endoscopy (UGIE).

Methods: In this clinical trial, 130 children aged 2 to 12 years (ASA physical status I or II) were examined. Children were divided into two groups. Propofol (1.2 mg/kg) plus ketamine (1 mg/kg) was prescribed for the first group (Group PK). The second group received propofol (1.2 mg/kg) plus fentanyl (1 µg/kg) (Group PF). Hemodynamic variables and sedation scale of patients were compared between two groups.

Results: The mean age of the children was 98.3±6.96 months and 97.15±3.56 months in group PK and group PF, respectively. Heart rate and respiratory rate values after induction in group PF were significantly lower than in group PK ($p<0.05$). Coughing, nausea and vomiting and Ramsey sedation score were significantly higher in group PK ($p<0.05$).

Conclusion: Both combinations provided effective sedation in pediatric patients undergoing UGIE, but the propofol-ketamine combination resulted in stable hemodynamics and deeper sedation although with more side effects.

Keywords: sedation; children; ketamine; propofol; fentanyl; endoscopy

Preparation for endoscopic procedure in children requires full knowledge of pycho-physiological well-being of both the child and operator [1]. The most important risk factors for successful endoscopy include sepsis, shock, dehydration, electrolyte imbalance, acute or chronic respiratory disorders, underlying cardiovascular diseases, and underlying acute hepatic or renal dysfunctions. Therefore, a full physical examination including a focused assessment of the heart, circulation, lungs, head, neck, and airway should be performed [2]. Many children complain of pre-endoscopic anxiety that makes the procedure complicated [3]. The administration of pretreatment oral midazolam (0.5 mg/kg) or intranasal midazolam (0.2 mg/kg) for peripheral intravenous cannulation and/or easy separation of the children from their parents have been found to be effective [4-6]. The prescription of sedatives in children should be done with caution and based on their weight. It is usually titrated by their therapeutic response [7-8]. It has been observed that younger children require higher dosage of these drugs [9].

Propofol is a phenol that is derived from hypnotic sedatives. It is an ultra-short-acting sedative agent with an extremely rapid onset and extremely short recovery time. This medication has anti-nausea, anti-anxiety, soporific, and anesthetic, but not analgesic, effects. Propofol can be used for children undergoing gastrointestinal procedures [10-12]. Of the possible side effects of this medication is respiratory depression and sudden apnea [13]. Ketamine is a synthetic derivative of phencyclidine with sedative and analgesic effect [14]. It is a dose-dependent analgesic and anesthetic compound. Ketamine increases heart rate, blood pressure, cardiac output and intracranial pressure. The most important side effect of this drug is laryngospasm. In different countries, a lower dose of this medication is administered with propofol, midazolam and opioid drugs. This combination can produce stable hemodynamics and reduce side effects of anesthesia [10]. Fentanyl is a highly lipid-soluble industrial effective opioid without anti-anxiety and anti-amnesia effects. This characteristic allows the drug to have a rapid onset (below 60 seconds) and short duration of action (30-45 minutes) through quick passage across the blood-brain barrier [15]. Since histamine is not released after the use of fentanyl, it is a great compound for intravenous anesthesia. Intravenous administration of this medication can easily and rapidly be used for painful procedures. Among the side effects of this medication are respiratory depression and apnea, especially when it is used with other anesthetics [16].

Today, sedatives have special position in outpatient

From the [1]Department of Anesthesiology and Critical Care, Tehran University of Medical Sciences, Children Medical Center, Tehran, Iran.
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*Corresponding author: Mehrdad Goudarzi, MD. Department of Anesthesiology and Critical Care, Tehran University of Medical Sciences, Children Medical Center, Tehran, Iran. E-mail: drgoudarzi@yahoo.com

procedures and advanced countries have various instructions for their administrations. However, it requires more nursing care, which prolongs recovery and hospitalization. Various medicinal interventions are used for sedation in children; however, these sedatives are associated with such complications as waking up from anesthesia, excessive sleepiness, nausea, vomiting, and hemodynamic disorders, which limit the use of this medication. In this study, the effect of two pharmaceutical compounds, namely propofol-fentanyl and propofol-ketamine, on sedation in children undergoing endoscopy of the upper gastrointestinal system was examined.

Methods

In this clinical trial, 130 children aged 2-12 years (ASA physical status I or II) were examined. ASA I included children without underlying diseases. ASA II comprised of children with underlying diseases, which were completed controlled via medication, changing lifestyle, etc. The second group was also candidate for endoscopy of the upper gastrointestinal system. After obtaining written consensus from their parents, the children were divided into two groups using the random number table based on blocks of size 4. The sample size of 130 (65 subjects in each group) was considered using STATA ver13(StataCorp LP, Texas, USA), based on the prevalence of 5% in the first and 2% in the second groups, confidence coefficient of 0.05, and research power of 80%. The exclusion criteria were patients with congenital genetic diseases, history of hypersensitivity to the drugs under study, abnormal anatomy of the jaw and face, upper respiratory tract infections, behavioral disorders, and non-Farsi-speaking families, as well as patients taking psychiatric medications, and hypnotics before entering into the operating room. In addition, those children whose parents did not consent to participate in the study were excluded. After setting up the standard monitoring equipment and cannulation, a sedative combination of propofol (1.2 mg/kg) plus ketamine (1 mg/kg) was prescribed for the first group (group PK). The patients were also ventilated with 100% oxygen during endoscopy. The second group (group PF) received propofol (1.2 mg/kg) plus fentanyl (1 µg/kg). In both groups, procedure continued until sedation score of 5 was achieved, based on the Ramsey Sedation Scale [17]. Patients with sedation score of less than 4 received additional dosages. Then, hemodynamic variables (blood pressure, heart rate per minute) and sedation (using the Ramsey Sedation Scale) of patients in both groups were measured and recorded in an information chart. Quantitative variables were compared with independent t-test. In case of abnormal distribution, comparison was done with the Mann-Whitney test. Qualitative variables were compared with Chi-square or Fisher's exact tests. SPSS 20 was used for statistical data analysis. The significance level of the tests was considered as $p<0.05$.

Results

In the current study, 65 children received propofol-ketamine induction, and 65 children received fentanyl-propofol induction. The mean age of the children was 98.3±6.96 months and 97.15±3.56 months in the first and second groups, respectively. In both groups, 50 cases (76.9%) were male and 15 cases (23.1%) were female. In terms of hemodynamic indices, the mean level of systolic blood pressure in the group PK was 93.50±3.28 mm/Hg at the baseline, and reached 93.22±2.90 mm/Hg during the procedure. On the other hand, this level was 92.94±0.93 mm/Hg in the group PF at the baseline, which reduced to 92.12±1.55 mm/Hg during the procedure. Although both groups were not different at the baseline with respect to the systolic blood pressure (p=0.664), the mean level of this factor was lower in the second group (p=0.026). The mean number of heart rate in group PK was 117.35±5.17 per minute at baseline, which reduced to 115.52±4.75 per minute during the procedure. In the group PF, the mean number of heart rate was 118.77±1.64 per minute at the baseline, which reduced to 115.12±4.05 per minute during the procedure. Although the groups were not different at the baseline with respect to the mean number of heart rate (p=0.122), this amount was lower in the group PF (p=0.042). The average number of breathing rate in group PK was 30.86±0.02 per minute at baseline, which reduced to 28.69±3.92 per minute during the procedure. In the group PF, this factor was 30.83±0.98 per minute at the baseline, which reduced to 28.86±0.93 per minute during the procedure. Two groups were similar in terms of respiratory rate at the baseline (p=0.853) and during the procedure (p=0.736). The mean level of arterial oxygen saturation in group PK was 92.42±0.70% at baseline, which reached 99.86±0.12% during the procedure. In the group PF, this factor was 92.35±0.65% at the baseline, and increased to 98.51±0.25% during the procedure. Both groups were similar in terms of arterial oxygen saturation at the baseline (p=0.605) and during the procedure (p=0.122) (Table 1).

The prevalence of coughing and straining, bronchospasm or laryngospasm in recovery in the group PK and the group PF was 9% and 2%, respectively. This between-groups difference was significant (p=0.042). The frequency of Ramsey sedation score V and VI was 44.6% and 55.4% in the group PK, and 64.6% and 35.4% in the group PF, respectively. This between-groups difference was significant (p=0.022). In addition, the prevalence of nausea and vomiting was 53.8% in the group PK and 32.3% in the group PF. This between-groups difference was also significant (p=0.013). The degree of full satisfaction of nurses of recovery was 23.1% in the group PK and 12.3% in the group PF. This between-groups difference was not significant (p=0.459). The average time for recovery was 17.2±0.98 per minute in the group PK and 15.5±0.96 per minute in the group PF. This between-groups difference was not significant (p=0.096) (Table 2).

Table 1- Basic features of patients with hemodynamic parameters before and after the procedure

Variables	Group PK (n=65)	Group PF (n=65)	p-value
Age (month)	98.3±6.96	97.15±3.56	0.368
Sex (female)	50 (76.9%)	50 (76.9)	1
Weight (kg)	22.35±1.02	22.11±1.86	0.352

Table 1- Basic features of patients with hemodynamic parameters before and after the procedure (Continued)

Variables	Group PK (n=65)	Group PF (n=65)	p-value
Hemodynamic parameters in baseline			
Systolic blood pressure	93.5±3.28	92.94±0.93	0.664
Heart rate	117.35±5.17	118.77±1.64	0.122
Respiratory rate	30.86±0.92	30.83±0.98	0.853
Oxygen saturation	92.42±0.7	92.35±0.65	0.605
Hemodynamic parameters during procedure			
Systolic blood pressure	93.22±2.9	92.12±1.55	0.026
Heart rate	115.52±4.75	115.12±4.05	0.042
Respiratory rate	28.69±3.92	28.86±0.93	0.736
Oxygen saturation	99.86±0.12	98.51±0.25	0.122

Table 2- Sedation-induced complications after the procedure

Variables	Group PK (n=65)	Group PF (n=65)	p-value
Bronchospasm or laryngospasm	9%	2%	0.042
Ramsay score			0.022
5	44.6%	55.4%	
6	64.6%	35.4%	
Nausea and vomiting	53.8%	32.3%	0.013
Nurses' degree of satisfaction			0.459
Very poor	1.5%	1.5%	
Poor	6.2%	12.3%	
Don't Know	29.2%	29.2%	
Good	40%	44.6%	
Very good	23.1%	12.3%	
Mean score of satisfaction	17.2±0.98	15.5±0.96	0.096

Discussion

This study was conducted to compare two pharmaceutical compounds (namely propofol-ketamine and propofol-fentanyl) on sedation in children undergoing endoscopy of the upper gastrointestinal system. Findings showed that the groups were not significantly different in terms of demographic variables. Regarding the greater drop of systolic blood pressure and heart rate in the group PF, it seems that the propofol-ketamine compound produces greater cardiovascular stability than propofol-fentanyl compound.

Although, taking a certain measure is not required in normal patients and it is not clinically significant, it can be concluded that due to reduction of hemodynamic parameters of this pharmaceutical group, the propofol-fentanyl compound in patients with hemodynamic disorders (hypovolemia and gastrointestinal bleeding) undergoing endoscopy is not a suitable choice, and propofol-ketamine produces a greater cardiovascular stability. In terms of the respiration rate, it seems that the prescription of propofol-fentanyl causes a greater drop than propofol-ketamine during the procedure, as compared to the baseline. However, this between-groups difference is not statistically significant, which can be attributed to the studied sample size.

In a study conducted by Tosun et al., patients were randomly divided into propofol-ketamine induction and propofol-fentanyl induction groups. Findings suggested that the heart rate and respiration rate were significantly lower in the second group. Although both groups had appropriate sedation during the endoscopy, hemodynamic stability and depth of sedation were greater among ketamine recipients [17]. This finding is consistent with the findings of the current study. In a study, Kb N et al. compared changes in blood pressure and arterial oxygen saturation induced by sedation with propofol-ketamine and propofol-fentanyl. Results indicated that fentanyl-recipients had greater blood pressure drop in 5 minutes and also greater diastolic blood pressure drop in 10 minutes after the injection. In addition, arterial oxygen saturation drop was greater in fentanyl-recipient group. On the other hand, ketamine-recipients had shorter recovery time and less pain [18]. These findings are consistent with the findings of the present study.

Khutia et al. compared the anesthetic effects of ketamine-propofol and fentanyl-propofol methods on children undergoing short emergency surgery and observed that hypotension was significantly lower in ketamine group than fentanyl group. In addition, the mean level of arterial blood pressure was significantly lower in the fentanyl group than ketamine group during the surgery [19]. Results were completely consistent with our findings asserting the

superiority of ketamine in hemodynamic parameters. Moreover, Singh R et al. compared children who randomly underwent anesthesia with ketamine-propofol and fentanyl-propofol during the laryngeal mask airway placement. Results showed that the heart rates, as well as systolic and diastolic blood pressures were significantly higher in ketamine group [20]. In other words, findings indicated higher hypertension in fentanyl group, which suggested the greater effectiveness of ketamine administration than other pharmaceutical regimens.

After both interventions, we observed a transient drop in oxygen-saturated hemoglobin which was quickly resolved after the administration of oxygen, and exceeded 98%. This change was not statistically significant. The incidence rate of coughing and straining was higher in propofol-ketamine group, which may be due to the effect of fentanyl on airway reflexes. In addition, the depth of anesthesia (based on the Ramsey sedation scale) was greater in ketamine induction group than fentanyl induction group. On the other hand, the prevalence of nausea and vomiting during the procedure was higher in ketamine group than fentanyl group, which may be due to the direct effect of ketamine and its pharmaceutical complications. According to the overall score of recovery nurse satisfaction of patient's sedation, the propofol-ketamine compound was more effective; however, the groups were not significantly different in this regard.

Chandar et al. compared the effect of two pharmaceutical regimens (namely propofol-ketamine versus propofol-fentanyl) on anesthesia in children undergoing esophagogastroduodenoscopy. They found that pain caused by propofol injection was greater in fentanyl group than ketamine group [21]. In other words, the depth of anesthesia was greater in ketamine group. This finding was consistent with the finding of our study. In addition, Ghatak et al. compared the effect of anesthesia induction with ketamine, fentanyl, and propofol on hemodynamic conditions, and concluded that average blood pressure and heart rate were in better conditions in the ketamine group than fentanyl and normal saline groups. The incidence of prolonged apnea was higher in fentanyl group than ketamine and normal saline groups [22].

Conclusion

According to this study, it can be said that both propofol-ketamine and propofol-fentanyl compounds are good sedatives in children undergoing endoscopy. However, due to the greater stability of hemodynamic indices in propofol-ketamine group, it is a more suitable medication than propofol-fentanyl compound in patients with hemodynamic disorders (dehydration, hypovolemic and gastrointestinal bleeding).

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