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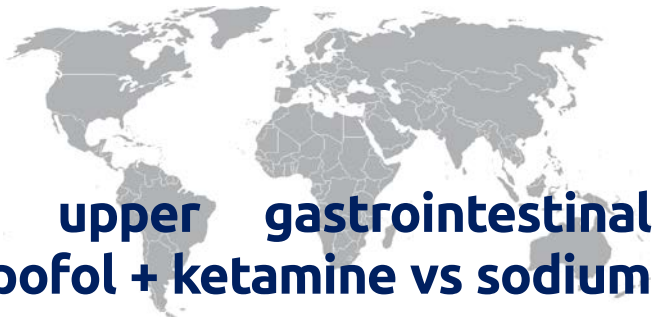

Paediatric sedation during upper gastrointestinal endoscopy: Comparison of propofol + ketamine vs sodium thiopental + fentanyl

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ABSTRACT

Background: Different drug regimens can be used for management of anxiety before endoscopy. This study aimed to compare the sedation effects of propofol+ketamine (PK) and sodium thiopental+fentanyl (TF) in children during upper gastrointestinal (UGI) endoscopy.

Methods: A triple-blind clinical trial was conducted on 88 children aged 2-12 years who were candidate for UGI endoscopy at Children's Medical Centre, Tehran, Iran, during 2012-2013. It was administered propofol (2.1 mg/kg) + ketamine (1 mg/kg) and 100% oxygen in PK group, and thiopental (5 mg/kg) + fentanyl (1 mg/kg) in TF group. The haemodynamic status and degree of sedation by Ramsay's criteria were measured.

Results: The mean age in PK and TF groups was 92.2±38.2 and 98.6±49.5 months, respectively. The systolic blood pressure and heart rate significantly increased and decreased in PK and TF groups during the procedure, respectively. The frequency of Ramsay's Sedation Scales of 5 and 6 were respectively 72.7% and 27.3% for PF, and 54.5% and 45.5% for TF group (p=0.076).

Conclusion: Although both groups were similar in the degree of sedation, PK can be a more appropriate choice for sedation in children with special diseases undergoing endoscopy due to small changes in haemodynamic parameters and, consequently, their higher stability.

Keywords: propofol, ketamine, thiopental, fentanyl, esophagogastroduodenoscopy

INTRODUCTION

Preparation for the endoscopy procedure in children requires full knowledge of physiology and suitable mental state of both the child and the person performing the procedure (1). According to the American Paediatric Academy, preparations for a successful endoscopy entails obtaining a suitable medical history, measuring anaesthesia score from the physical condition, collecting medication history, allergies assessment, age and weight measurements, and assessment of the children's vital signs (2,3). In terms of indications for sedation, according to the instructions of the American Society of Anaesthesiologists, performing general anaesthesia for endoscopy in children should be in fasting condition for four hours before breastfeeding and for six hours before eating solids (2). Almost all the procedures used in gastrointestinal endoscopy should be performed after a medium or deep anaesthesia under careful supervision of an anaesthesiologist (4-6). Many children complain about anxiety before endoscopy, making the procedure complicated (7). There are various methods for solving this problem, such as oral or intranasal midazolam administration in order to facilitate the separation of the child from the mother (8-10). Compared with adults, small and thin air route causes more air flow resistance in children and increases oedema or mucus. In children, tongue fills a higher portion of the air duct compared to adults. This happens mainly in children younger than 3-5 months. These children are also more prone to hyperactive airways after the occurrence upper respiratory tract infections, which make the upper endoscopy in these patients impossible (11). In addition, episodes of hypoxemia occur more often in these children due to their higher oxygen consumption. In this respect, routine administration of oxygen during the endoscopic procedures is an inexpensive way to improve breathing condition and the sedation required for endoscopy in children (12-14).

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Propofol is a phenol derived from hypnotic sedatives. Its effect start fast (less than a minute). It is short-acting and has a quick return. It has anti-nausea, anti-anxiety, sedative and aesthetic effects but does not have analgesic effect. Propofol can be used in children in gastrointestinal procedures (15-17), intensive care (18) and emergencies (19-26). Respiratory depression and sudden apnoea are the major possible side effects of propofol. In general, it has a rapid action combined with a quick return. Ketamine is a synthetic derivative of phencyclidine with palliative and analgesic effects. It is one of analgesic and anaesthetic compounds, but is dose-dependent. Ketamine causes increased heart rate, blood pressure, cardiac output, intracranial pressure and intraocular pressure, while its main problem is laryngospasm. In different countries, low doses of Ketamine are used along with propofol, midazolam and opioid drugs. This combination creates a stable haemodynamic condition and can reduce the side effects associated with anaesthesia (27-31). Sodium thiopental is a barbiturate drug and creates anaesthesia by affecting the reticular activating system. It is generally used in short-term anaesthesia. Respiratory system depression and bronchospasm are among its side effects. It also increases heart rate and reduces blood pressure but is short-acting with rapid onset of action (32-34). In general, different drug regimens can be used in the presence of an anaesthesiologist; however, these drugs have side effects such as delay in waking up from anaesthesia, excessive sleepiness, as well as nausea, vomiting, and haemodynamic disorders, which limit the use of these drugs. In this study, the effectiveness of two methods and sedation of two drug combinations of propofol ketamine and Sodium thiopental were examined on sedation in children's upper gastrointestinal endoscopic procedures.

MATERIALS AND METHODS

This clinical trial study was conducted on 88 children aged two to twelve years candidate for upper gastrointestinal endoscopy at Children's Medical Centre during 2012-2013. The trial was initiated after the approval of the institutional ethic committee review board at Tehran University of Medical Sciences. After obtaining consent from parents, children were divided into two groups with blocks of four based on table of random numbers. It was a triple-blind study. The number of samples in each group was determined as 44 by taking into account an incidence of 0.5 in the first group and 0.2 in the second group, confidence level of 0.5, and study power of 80% using STATA. Exclusion criteria included congenital genetic diseases, hypersensitivity to study drugs, abnormal anatomy of the jaw and face, upper respiratory tract infections, behavioural disorders, use of psychiatric drugs, family language other than Persian, and lack of parents' consent. Those who had used hypnotics before arriving the operating room were also excluded. In the first group, after installing the standard monitoring equipment and performing venepuncture, sedation was conducted using a combination of propofol 2.1 mg/kg and ketamine 1 mg/kg and administration of one hundred percent oxygen in the endoscopy room. In the second group, thiopental 5 mg/kg and fentanyl 1 mg/kg were administered. The haemodynamic variables and degree of sedation of patients were measured in both groups using the Ramsay's criteria and recorded in a data collection chart. If patients needed higher degree of sedation, additional doses of propofol in the first group and thiopental in the second group were administered. Independent t-test was used to compare the quantitative variables. Mann-Whitney test was used in the case of abnormal distribution. Chi-square test or Fisher's exact was used for comparisons between the qualitative variables. SPSS 20 was used for statistical analysis. The significance level was considered less than 0.05.

RESULTS

In this study, 44 children were induced with propofol+ketamine, and 44 children were induced with thiopental. The mean age of subjects was 92.2 ± 38.2 and 98.6 ± 49.5, respectively, while the difference was not significant (p=0.529). In terms of haemodynamic parameters, the mean baseline systolic blood pressure in the group induced with propofol+ketamine was 92.21±10.17 mm Hg, which increased to 94.85±18.58 mm Hg during the procedure. In the group induced with thiopental + fentanyl, the mean baseline systolic blood pressure was 93.16±16.58 mm Hg, which was reduced to 87.56±10.29 during the procedure. The mean heart rate in the propofol+ketamine group was 115.12±23.36 per minute, which was increased to 130.02±13.33 per minute during the procedure, while in the sodium thiopental + fentanyl group, the mean baseline heart rate was 117.29±26.10 per minute, which was reduced to 111.24±25.29 per minute during the procedure. The mean respiration rate in the propofol+ketamine group was 31.23±5.36 per minute, which reached 31.02±3.70 during the procedure, while in the sodium thiopental + fentanyl group, it was 32.32±3.98 per minute, which was reduced to 28.82±8.35 during the procedure. The mean baseline arterial oxygen saturation in the propofol+ketamine group was 91.31±8.81 percent, which reached 95.86±4.91 percent during the procedure, while in

Table 1: *Initial characteristics of patients with haemodynamic parameters before and after the intervention*

parameter	propofol+ketamine (n=44)	sodium thiopental + fentanyl (n=44)	p-value
Age (month)	92.2±38.2	98.6±49.5	0.611
Sex (female)	32 (72.7)	34 (77.3)	0.323
Weight (kg)	25.2±20.9	22.1±16.2	0.529
haemodynamic parameters in baseline			
systolic blood pressure	92.21±10.17	93.16±16.58	0.747
Heart rate	115.12±23.36	117.29±26.1	0.682
Respiratory rate	31.23±5.36	32.32±3.98	0.282
oxygen saturation	91.31±8.81	92.12±8.34	0.659
haemodynamic parameters during procedure			
systolic blood pressure	94.85±18.58	87.56±10.29	0.025
Heart rate	130.02±13.33	111.24±25.29	0.003
Respiratory rate	31.02±3.7	28.82±8.35	0.042
oxygen saturation	95.86±4.91	93.07±5.84	0.017

Table 2: *Complications of sedation after the procedure*

parameter	propofol+ketamine (n=44)	sodium thiopental + fentanyl (n=44)	p-value
Bronchospasm or laryngospasm	3 (6.8)	2 (4.5)	0.64
Ramsay score			0.076
5	32 (72.7)	24 (54.5)	
6	12 (27.3)	20 (45.5)	
Nausea and vomiting	12 (27.3)	14 (31.8)	0.644
Nurses' degree of satisfaction			0.268
Very poor	1 (2.3)	1 (2.3)	
Poor	3 (6.8)	4 (9.1)	
Don't Know	12 (27.3)	12 (27.3)	
Good	18 (40.9)	21 (47.7)	
Very good	10 (22.7)	6 (13.6)	
Mean score of satisfaction	3.57±0.97	3.61±0.92	0.5

the sodium thiopental + fentanyl group, the mean baseline arterial oxygen saturation was 92.12±8.34 percent, which was reduced to 93.07±5.84 percent during the procedure. In evaluation of haemodynamic changes during procedures compared with the baseline values, changes in all indicators between the two groups was significant, so that mild increases in blood pressure, heart rate, respiratory rate and oxygen saturation were observed in the propofol+ketamine group, while all four indicators decreased significantly in the sodium thiopental + fentanyl group (**Table 1**).

The incidence of bronchospasm or laryngospasm during recovery in the propofol+ketamine group and the sodium thiopental + fentanyl group was 6.8% and 4.5%, respectively, while the difference between the two groups was not significant (p=0.64). The frequency of Ramsay's Sedation Scales of 5 and 6 in the propofol+ketamine group was 72.7% and 27.3%, respectively, while it was 54.5% and 45.5% in the sodium thiopental + fentanyl group, respectively. The difference between the two groups was not significant (p=0.076). The prevalence of nausea and vomiting during the procedure in the propofol+ketamine group was 27.3%, while it was 31.8% in the sodium thiopental + fentanyl group, and difference was not significant (p=0.664). The nurses' degree of satisfaction with the course of recovery was 22.7% in the propofol+ketamine group and 13.6% in the sodium thiopental + fentanyl group, while the difference between the two groups was not significant (p=0.664) (**Table 2**).

DISCUSSION

This study aimed to compare the outcomes of sedation with propofol+ketamine admixture and thiopental sodium in children undergoing upper gastrointestinal tract endoscopy. In terms of demographic variables (age, sex and weight), there was no statistically significant difference between the two groups. Given the drop in systolic blood pressure and heart rate in the thiopental sodium group and its significance, even though the normal patients did not require specific action and the difference was not clinically significant, and considering the reduction in haemodynamic parameters in this drug class, it seems that thiopental sodium is not a suitable choice in patients undergoing endoscopy with haemodynamic compromise (hypovolemia, gastrointestinal bleeding), and propofol+ketamine admixture is associated with higher cardiovascular stability. Moreover, in terms of oxygen saturation of haemoglobin and respiratory rate, it seems that thiopental sodium is associated with higher incidence of respiratory depression and transient desaturation

and is not an appropriate choice compared to ketamine+propofol in children's endoscopy procedures, where maintaining spontaneous breathing is especially important. In previous studies, other sedation regimes have been compared. In a study conducted by the Tosun et al., patients were randomly assigned to two groups induced by propofol+ketamine or propofol+fentanyl. Heart rate and respiration rate values were considerably lower in the group receiving fentanyl than the one receiving ketamine. Therefore, even though both groups had appropriate sedation during endoscopy, haemodynamic stability and deeper sedation were observed in the group receiving ketamine (35), which is in agreement with our findings about haemodynamic stability following administration of ketamine. Abu-Shahwan et al. evaluated the effectiveness of propofol+remifentanil admixture administration in deep anaesthesia in children under 7 years undergoing upper gastrointestinal endoscopy. In their study, the propofol+remifentanil admixture led to reduced heart rate, blood pressure and respiratory rate. However, no respiratory depression or oxygen desaturation was observed. Our study suggested that although remifentanil is associated with reduced vital parameters, these changes can be compensated through combining remifentanil with ketamine (36).

In this study, the incidence of coughing was higher in the propofol+ketamine group, but there was no statistically significant difference between the groups which may be attributed to the sample size. Considering the direct association between complications (hypotension, heart rate, respiratory depression and rate, and oxygen saturation of haemoglobin) and sedation score of 6 in the thiopental sodium group, the administered dose seem to be high, and complications are likely to be reduced at a lower dose or at more gradual administration. Nausea and vomiting in the thiopental sodium group was higher compared to the propofol+ketamine group; however, the difference was not statistically significant. It seems that despite the sample size factor, these drugs do not increase the incidence of nausea and vomiting. In terms of mean nurses' score of satisfaction with calmness, the propofol+ketamine group performed better, which was statistically significant. It can be concluded that propofol+ketamine administration results in more satisfaction in terms of calmness in recovery nurses. In a study by Barbi et al., very limited complications was observed in sedation with propofol for upper endoscopy in children, clinically confirming the effectiveness of the drug (37). Burgeat et al. used propofol in combination with sodium thiopental and reported more analgesic consumption at 6 hours after the procedure and higher incidence of nausea and vomiting in the thiopental group (38). In a study by Larrson in the U.S., the group receiving propofol fentanyl experienced higher incidence of bradycardia during surgery, whereas the incidence nausea and vomiting was lower in this group. The period of spontaneous respiration and extubation was lower in the group receiving propofol fentanyl. The apprehension score was also higher in this group compared to the thiopental halothane group, which again indicates the superiority of administration of propofol over thiopental (39). In the study by Motamed in Iran, the effects of oral ketamine and oral fentanyl administration were compared. The required midazolam dose for sedation was lower in the ketamine group. The patients in the ketamine group experienced lower distress levels in IV line insertion and separation from parents for the procedure. Deeper sedation, higher comfort level, and higher endoscopists' satisfaction level were reported in this group. Recovery period was significantly shorter in the ketamine group, which all indicated higher efficiency of ketamine administration compared to other drug regimens (40).

CONCLUSION

Findings showed that the effects of both drugs used in this study were similar in terms of degree of sedation; however, propofol+ketamine can be a more appropriate choice for sedation in children with special diseases undergoing endoscopy due to small changes in haemodynamic parameters and, consequently, their higher stability.

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