Pediatric Anesthesia and Critical Care Journal 2017;5(2):58-65
doi:10.14587/paccj.2017.10

PACCJ

Comparison of propofol-ketamine combination versus sevoflurane sedation for gastrointestinal endoscopies in children

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Keypoints

Gastrointestinal (GI) endoscopies in children are performed world over and can range from diagnostic to therapeutic interventions. Different techniques have been employed for such procedural sedation however, there is no consensus regarding an ideal method. In this study we compare intravenous propofol ketamine sedation with sedation using sevoflurane..

Abstract

Introduction

Ideal sedation technique for endoscopic procedures which is safe and effective is yet to be determined. This study is aimed at comparing propofol and ketamine combination with sevoflurane for procedural sedation for GI endoscopy in children with respect to effectiveness, safety, recovery charecteristics and cost.

Materials and methods

We performed this observational study in 60 children aged 6 months - 18 years scheduled for GI endoscopy. Group PK (n=30) received a combination of ketamine 0.5 mg/kg and propofol 1mg/kg i.v as initial bolus followed by 0.25-0.5 mg/kg propofol incremental doses for maintenance. Group S (n=30) received 4% sevoflurane + 50% N2O in oxygen for initiation and 2% sevoflurane in oxygen for maintenance. Time required to achieve modified Ramsay sedation score of 4-5 for ease of scope insertion, need of restrain or other agents was noted.

Results

Time required to achieve MRS 4-5 was similar in both groups. Successful maintenance of sedation could be achieved in 86.7% of patients in sevoflurane group versus 56.7% in PK group (p=0.001). Overall time of recovery was also significantly shorter with sevoflurane (p<0.001). PK group had higher incidence of complications such as cough (p=0.022) and desaturation (p=0.010). Average cost of sedation in group S was Rs. 340/- compared to Rs. 110/- in PK group

Conclusion

Sevoflurane sedation is more effective, safe and offers quicker recovery as compared to propofol ketamine combination For GI endoscopies in children at a higher cost.

Keywords: endoscopy, paediatric, sedation, sevoflurane, propofol, ketamine

Introduction

Paediatric gastrointestinal (GI) endoscopy is a well-established procedure requiring moderate to deep sedation or even general anaesthesia. Though a relatively safe procedure, it has been associated with many complications including potentially fatal ones [1]. Multiple studies have been done to develop the ideal method for procedural sedation in terms of ease of administration, quality, safety of sedation and recovery profile, but the consensus seems lacking. Although both propofol-ketamine combination and sevoflurane have been used

for endoscopic procedural sedation [2,3], literature lacks any trials comparing the two of them. This observational study was planned to compare the efficacy and safety of intravenous propofol-ketamine with inhalational sevoflurane for procedural sedation in paediatric GI endoscopies.

Materials and methods

Comparative prospective observational study was performed in paediatric patients between age group 6 months – 18 years undergoing elective gastrointestinal endoscopic procedure over a period of 6 months after approval from institutional review board. Children belonging to American Society of Anaesthesiologists class I & II undergoing elective upper or lower GI endoscopic procedures were included. Exclusion criteria were ASA class III and above, known hypersensitivity to propofol or ketamine, patients with airway related problems, respiratory, cardiovascular or neurologic disorders, acute febrile illness, actively bleeding oesophageal varices, history of recent hepatitis or renal insufficiency.

All patients receiving institutional protocol based deep sedation with intravenous (IV) or inhalational agents were observed. Patients were randomized using computer generated random number table. After obtaining a thorough history, clinical examination, relevant laboratory investigations, fulfillment of inclusion criteria and confirmation of starvation status, a written informed consent was taken from the parents/guardian. Eutectic Mixture of Local Anaesthetics - with 2.5% each of Lignocaine and Prilocaine cream was applied at a suitable site for IV access one hour prior to taking the patient to the procedure room. All the patients were premedicated, under controlled environment, in the endoscopy suite with oral Midazolam 0.5 mg/kg dose, 30 minutes prior to entry to the procedure room. Meanwhile oxygen supplementation by Hudson's mask / nasal prongs was started and basic monitoring ensued which included heart rate, blood pressure, respiratory rate and pulse oximetry every 5 minutes. Degree of sedation was evaluated using Modified Ramsay Sedation Score (MRSS): 1 = anxious, agitated, restless, 2 = cooperative, oriented, tranquil, 3 = responds to commands only, 4 = brisk response to light glabellar tap or loud noise, 5 = sluggish response to light glabellar tap or loud noise, 6 = no response. A modified Ramsay sedation score target of 4-5 was suggestive of moderate to deep sedation, with spontaneous breathing maintained. In the procedure room, monitoring was instituted including electrocardiography, blood pressure, pulse oximetry and respiratory rate.

Preoxygenation with 100% O_2 for 1 minute, by appropriate sized endoscopic face mask attached to an appropriate breathing circuit (Jackson Rees circuit for children ≤ 20 kg and Bain circuit for children >20 kg) was done. Inj. glycopyrrolate 0.004 mg/kg was administered intravenously. Patients in Propofol-Ketamine (Group PK) group received 0.5 mg/kg IV ketamine and 1mg/kg IV propofol as loading dose followed by incremental doses of 0.25-0.5mg/kg IV propofol alone for maintenance as per the requirement. Loading dose was considered as adequate if adequate jaw relaxation for scope insertion and MRSS 4-5 occurred. Induction time was considered as time from beginning of IV agent to achievement of MRSS 4-5.

Patients in inhalational group received Sevoflurane (Group S) at 4% dial concentration in O_2:N_2O mixture (50:50) to begin with. Adequacy of sedation was taken as adequate jaw relaxation for the scope insertion and attainment of MRSS 4-5. Induction time was considered as time from beginning of inhalational agent to achievement of MRSS 4-5. Sedation was maintained using O_2 with sevoflurane at 2% dial concentration with endoscopy mask.

Both Groups received at least 10 ml/kg/hr of an IV lactated Ringer's solution with 5% dextrose perioprocedure.

All endoscopies were performed in the left lateral position. The oxygenation was maintained using an endoscopic face mask. Duration of procedure was taken as time from insertion to removal of endoscope. The dura-

tion of deep sedation was the time from beginning of induction to achievement of MRSS ≥ 3.

Outcome measures were effectiveness, safety and recovery profile. Effectiveness was assessed in terms of induction time as defined above, success of induction and maintenance i.e induction doses sufficient to allow easy passage of endoscope and maintenance doses sufficient to carry out the procedure respectively. Need of changeover from one group to the other i.e use of other agents or need of restraint was considered as failure. Variation in doses/dial settings as described in methodology; in their respective groups was also included in failure. Safety was assessed in terms of occurrence of complications. Oxygen desaturation was defined as SpO_2 <95% for > 30 seconds, bradycardia as 30% decrease in heart rate from baseline, hypo/hypertension as 20% variation from baseline. Emergence was assessed as emergence time i.e time from end of procedure till achievement of MRSS ≤ 3. Other variables recorded were time to respond to light painful stimulus, time to spontaneous eye opening, time to achievement of purposeful limb movements, time to child becoming oriented (older children). Post procedure emergence agitation was rated on a 4-point scale: 1 = Awake, calm and cooperative; 2 = Crying, requires consoling; 3 = Irritable/restless, screaming, inconsolable; 4 = Combative, disoriented, thrashing. Children with an agitation score of 3 or 4 were classified as agitated. Post procedure nausea vomiting was rated on a 4 point scale as 0 = No nausea, 1 = Nausea but no vomiting, 2 = Vomiting once in 30 minutes or more, 3 = Persistent nausea (>30 minutes) or 2 or more vomits in 30 minutes. Recovery time was defined from end of procedure till Steward Recovery score of 6 was reached (Table 1).

The consumption of sevoflurane per patient was determined as follows: Flow rates were set at twice the minute ventilation of the patient, dial concentration kept at 4% for induction along with 50% N_2O and at 2% for maintenance with 100% O_2. Any change in flow rates during procedure was also recorded. The amount consumed was calculated using Dions equation [4]:

Sevoflurane consumed (ml) = PFTM/2412 d

Where P: Vapor concentration; F: flow in l/min; T: time in minutes; M: Mol mass of sevoflurane in gms = 200.055gms; d: density of sevoflurane in gm/ml = 1.52g/ml

Sample size calculation

Following assumptions were made for calculation of sample size: 1) Difference in recovery times between two groups of 5 minutes; 2) Standard deviation of 6 minutes; 3) Alpha error of 0.05; 4) Beta error of 0.2 i.e. power of study 80%. Power and sample size software Version 3.0.43 calculated the sample size of 24 per group [5]. We studied 30 cases per group.

Statistical analysis

Parametric data was presented as mean ± standard deviation and analyzed using unpaired t test. Repeated measurements data was analyzed using paired t test and binary data was analyzed using Chi-squaretest. Nonparametric data was analyzed using Mann Whitney U test.

Conciousness		Airway		Motor	
Awake	2	Cough on command or cry	2	Moves limbs purposefully	2
Response to verbal/tactile stimuli	1	Maintains good airway	1	Non purposeful movement	1
Not responding	0	Requires airway assistance	0	Not moving	0

Table 1. Steward Recovery Score

Results

Both the groups were comparable in terms of age, weight, gender, ASA physical status and duration of procedure (Table 2).

Parameters	Group S	Group PK	P Value
No. of Cases	30	30	
Age (yrs)· Mean ± SD	5.43±3.00	6.64±4.42	0.220
Weight (kg)· Mean ± SD	15.00±5.40	16.30±7.84	0.458
Sex (Male/Female)▪ (Number of patients)	17/13	21/9	0.284
ASA I/II▪ (Number of patients)	28/02	27/03	0.640
Duration of Procedure£ (Minutes) Median (IQR)	07.50 (7.00)	8.00 (10.25)	0.998
Duration of deep sedation£ (Minutes) Median (IQR)	12.00 (9.75)	15.00 (13.25)	0.216

Table 2. Group S – group sevoflurane; Group PK – group propofol-ketamine
·By Unpaired 't' Test
▪By Chi – Square Test
£By Mann-Whitney U test as data was not normally distributed
P > 0.05, Not Significant

The types of procedures included 27 upper and 3 lower GI endoscopies in group S; 26 upper and 4 lower GI procedures in Group PK (Table 3). Both groups were statistically similar in terms of types of procedures. Intra operative heart rate, mean blood pressure, respiratory rate and haemoglobin oxygen saturation at regular intervals were comparable in both groups. MRSS of 4-5 was maintained during the procedure in both the groups. Time of induction required to achieve MRSS of 4-5 was statistically similar in both the groups (Table 4). Success of induction appears to be better with sevoflurane, however, the difference is statistically not significant. Failure of maintenance was observed in 13 cases in PK group out of which 5 required addition of sevoflurane and 8 required restraint. Whereas in sevoflurane group, four patients required use of propofol during maintenan-

ce and none required restraint. In both the groups, endoscopists were able to negotiate the endoscope with ease after induction with respective agents, however, success during the maintenance phase turned out to be significantly better with sevoflurane. In all 11 events in group S and 31 in P-K group were noted.

Indication	Group S (n=30)	Group PK (n=30)
Foreign body	11	12
History of haematemesis	12	8
Stricture oesophagus	1	3
Recurrent vomiting	2	1
Ulcers	0	1
Pain abdomen	1	3
Bleeding per rectum	2	2
Recurrent diarrhea	1	0

Table 3. Types of procedures

As evident in the Table 5, the incidence of complications was more in the PK group with hypoxia and cough being significantly higher than in group S. Six patients desaturated in PK group, of these, three occurred at the time of scope insertion, one midway during endoscopy and two at the time of scope removal.

Parameter	Group S (N= 30)	Group PK (N= 30)	P Value
Time of Induction (minutes)	01.93 ± 0.63	01.70 ± 0.45	0.913
Success of induction (Number of patients)	23 76.7%	17 63.3%	0.100
Restraint at induction (Number of patients)	03 10.0%	09 23.3%	0.052
Success of maintenance (Number of patients)	26 86.7%	17 56.7%	0.001*
Restraint at maintenance (Number of patients)	- -	08 26.7%	0.038*

Table 4. Effectiveness of agents in the two groups.
Group S – group sevoflurane; Group PK – group propofol-ketamine
By Chi - Square Test; *P < 0.05 Significant

Of those occurring at the time of scope insertion, two were due to partial laryngospam requiring temporary procedural interruption and one was due to cough. Endoscopy was resumed in the above after addition of other agents. The other episodes were in patients where PK combination failed during maintenance phase and other agents or restraint was being used. Two patients,

who aspirated in this group, were managed by oxygen supplementation intra and post procedure and did not require any further intervention. None of these patients required any intensive care.

Complication	Group S (N= 30) No.	%	Group PK (N= 30) No.	%	P value
Bradycardia	-	-	-	-	
Oxygen desaturation (≤95% for >30secs)	-ᵛ	-	06	20.0	0.010*
Hyperventilation	02	06.7	03	10.0	1.00
Hypoventilation	03	10.0	01	03.3	0.612
Laryngospasm	-	-	02	06.7	0.492
Procedural interruption	-	-	02	06.7	0.492
Coughing	*01	03.3	07	23.3	*0.022
Salivation	-	-	03	10.0	0.237
Apnoea	02	06.7	01	03.3	1.00
Assisted ventilation	03	10.0	03	10.0	1.00
Aspiration	-	-	02	06.7	0.492
Breath holding	-	-	01	03.3	1.00
Patients developing ≥1 Complication	07	23.3	09	30.0	0.559

Table 5. Profile of complications. Group S – group sevoflurane; Group PK – group propofol-ketamine; ᵛBy Chi – Square Test using Yates correction; By Chi – Square Test
*P < 0.05 Significant

Time to emergence i.e end of procedure to achievement of MRSS </=3, spontaneous eye opening, purposeful limb movements, orientation and recovery (Steward recovery score = 6) was significantly shorter in the sevoflurane group as compared to the PK group (Table 6).

Parameters (minutes)	Group S (N= 30) Mean ± SD	Group PK (N= 30) Mean ± SD	P Value
Time of emergence	03.00 ± 1.91	04.82 ± 3.43	*0.014
Time to spontaneous eye opening	05.00 ± 3.18	09.53 ± 4.95	*0.001
Time to purposeful limb movements	05.53 ± 3.33	10.77 ± 4.99	*0.001
Time to orientation	6.00 ± 3.10	11.03 ± 4.77	*0.001
Time to recovery	6.00 ± 3.10	11.57 ± 5.40	*0.001

Table 6. Comparison of emergence in two groups. Group S – group sevoflurane; Group PK – group propofol-ketamine; By Student 't' test; *P < 0.05 Significant

The endoscopist rated the sedation as good in both the groups. The emergence agitation score was 2 for six children in group PK and five in group S. Rest had a score of 1 (P=0.741 by Mann Whitney U test). There was no significant difference in the scores. None of the patients vomited in the PK group and 2 patients vomited in the sevoflurane group (P =0. 154 by Mann Whitney U test). Excellent / Good / Fair / Poor experience was noted by endoscopist in 0/25/5/0 patients in sevoflurane group and 2/22/6/0 patients in PK group (p=0.457). Excellent / Good / Fair / Poor satisfaction was noted by parents in 0/28/2/0 patients in sevoflurane group and 0/27/3/0 patients in PK group (p=1.00).

The average amount of sevoflurane consumed per patient based on Dions equation was 9.48±6.51ml. Considering the cost of one bottle as Rs 8500, per patient cost of sevoflurane anaesthesia was Rs 340.

Average amount of propofol used was 4.69±2.74 ml and that of ketamine was 0.163±0.078 ml per patient. Cost of ketamine was neglected considering multiuse vial and requirement being too low. One vial of propofol costs Rs 110 for 10ml, so the cost per patient was estimated as Rs 55-60. Since propofol is dispensed in a single use vial, cost per patient comes to Rs 110.

Discussion

GI endoscopies are being performed world over both for diagnostic and therapeutic purposes. It is preferably done under moderate sedation in adults. Children require anywhere from moderate to deep sedation to general anaesthesia. Even though GI endoscopies are being performed for a couple of decades now, an ideal method of sedation has still not been documented.

Most studies on GI endoscopic sedation have been done using only propofol, or in combination with opiods or benzodiazipines, ketamine [1,2,6]. Only propofol sedation seems to be the preferred method, however, this has been associated with haemodynamic instabilites such as bradycardia and hypotension [1,6]. The combination of propofol and ketamine has been successfully tried to balance out this effect [2,7]. At the same time, this combination offers deeper sedation and better tolerance to endoscopy [2].

On the other hand, sevoflurane, a relatively newer inhalational agent, though considered ideal for induction of general anaesthesia in children, has not been thoroughly investigated for sedation in GI endoscopies. Though there are retrospective studies [1,3] which mention the use of sevoflurane for GI endoscopic sedation, there are few lacunae requiring further investigation on the use of sevoflurane for the same. Lack of consensus regarding an ideal method of procedural sedation and paucity of data on use of sevoflurane in paediatric GI endoscopy prompted us to conduct this study comparing the combination of propofol-ketamine with sevoflurane for endoscopic sedation. Use of endoscopic face masks of appropriate sizes helped us maintain uninterrupted inhalational anaesthesia. To avoid discrepancy, the same mask was used in intravenous group as well.

Both methods of sedation were similarly effective in terms of induction time and ease of endoscope insertion. The success of induction of sedation was greater in sevoflurane group than P-K group, however, this difference was not statistically significant. Maintenance of sedation was significantly better in sevoflurane group. Also, use of restraint was significantly lower in sevoflurane group during the maintenance phase. Hence, sevoflurane was able to maintain an overall better plane of sedation. These results seem to be consistent with those obtained in other studies. Montes et al also score ease of procedure and adequacy of sedation better with sevoflurane compared with plain propofol, though method of assessment and statistical figures have not been documented [3].

In terms of complications, the incidence of coughing and desaturation during the procedure was significantly higher in PK group. Tosun et al also recorded a higher incidence of cough in PK group when compared with propofol-fentanyl combination [2].This being inspite of pre procedure use of 10% lignocaine spray into pharynx of all their patients. The cut off for hypoxia in our study was ≤95% for >30 seconds compared to <90% in study by tosun et al [2]. Moreover they did not see any significant desaturation requiring intervention. The average age in their study was 10 years as compared to 6 years in ours [2]. As explained in the results, the occurrence of these complications was a consequence of failure of induction or maintenance of sedation in the PK group. On the other hand, sevoflurane group was by and large free from the above complications. Three patients in each group required assisted ventilation due to apnea or hypoventilation. Studies using sevoflurane did not define the adverse events and hence could not be used for comparison. None of the patients in any of the groups

had haemodynamic complications nor did anyone require conversion to general anaesthesia.

Emergence was quicker with sevoflurane compared to PK group (03.00±1.91 minutes vs 04.82±3.43 minutes (p=.014). The overall time to recovery in sevoflurane group was almost half of that in PK group (6.00±3.10 minutes vs 11.57±5.40 minutes; p=0.001). Montes et al recorded time to awaken as 5.7±3.18 mins with sevoflurane against 36.12±25.48 minutes with propofol alone [3].They used sevoflurane with N_2O and O_2 at 5% concentration for induction and at 3% concentration with O_2 for maintenance using laryngeal insufflation. The dosage of propofol used was not available for comparison. Nonetheless, we did not encounter such huge difference in recovery time between our groups. The duration of endoscopies was longer in their study compared to ours (28.19±23.07 vs 10.07±9.73 minutes for propofol group and 20.58±12.54 vs 8.47±6.68 minutes for sevoflurane group) [3]. Since the duration of procedure is short in our study, the time difference in recovery can have a significant impact in improving the efficiency and per day turn over in GI endoscopy suites.

Comparing the cost of these agents, P-K group is far superior to sevoflurane group. The concern of waste gas scavenging also exists in the latter. However, sevoflurane surpasses the intravenous agents in terms of quality and safety of endoscopic sedation as well as the recovery profile. The endoscopy facemasks used in our study were convenient to the endoscopists. They helped circumvent intubation or laryngeal insufflation for administering sevoflurane sedation. Our study has few limitations. It is a unicentric study. We used semi closed circuits with high flow rates without scavenging. However, considering the short duration of procedure, it is questionable whether use of inhalational anaesthesia would significantly contribute to environmental pollution. Moreover, initial high flow rate is necessary before switching over to low flow anaesthesia.

Conclusion

Sevoflurane is an effective agent for procedural sedation in GI endoscopies, associated with fewer complications and faster recovery when compared with propofol and ketamine combination, albeit at a higher cost.

Acknowledgements

This study was registered with CTRI, India. CTRI number: CTRI/2015/12/006450, registered on 21/12/2015.

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