Paediatric procedural sedation at a tertiary care university teaching hospital in India

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Abstract

Introduction: Although paediatric procedural sedation (PPS) using propofol is routine in the United States, its use is restricted to anaesthesiologists in many other countries like India. As a result the paediatric providers have to use other drugs for PPS.

Objective: To report a single centre experience of children receiving PPS at a tertiary care university teaching hospital.

Method: A retrospective chart review of PPS at Goa Medical College, Goa, India was provided by the paediatric senior resident, supervised by a paediatric consultant, both certified in Paediatric Advanced Life Support (PALS) and with experience in non-propofol PPS. We collected demographics, drug and dosing information, indication for PPS, procedure success rates and adverse events. Sedation related minor adverse events are complications during PPS, which are easily handled, and not expected to be associated with any sequelae. Serious adverse events include aspiration, airway obstruction, laryngospasm, emergent anaesthesia consult, cardiac arrest and death.

Results: Procedural sedation from 249 children from April-September 2015 were included in this study. Magnetic resonance imaging (MRI) 138/249 (55.4%), computed tomography (CT) scan 61 (24.5%), electroencephalogram (EEG) 26 (10.4%) and other procedures 24 (9.6%). Median age was 22 months (25th–75th: 12-36), 140 (56.2%) were female, and 227 (91.5%) were American Society of Anaesthesiologists Physical Status (ASA-PS) ≤III. Overall success was 213 (85.5%). Commonly used agents included intravenous (IV) midazolam 188 (75.5%), IV dexmedetomidine 37 (14.9%), and oral chloral hydrate 24 (9.6%). Ramsey sedation score of 3 or greater was achieved in 220 (88.4%) sedation after adding a second drug. Serious adverse events were seen in 3 (1.2%) patients. Sedation related minor adverse effects included: change in heart rate (>25% from baseline) 47 (18.9%), oxygen desaturation (<90% for 30 seconds) 32 (12.9%), and agitation/delirium 52 (20.9%). Only 21 (8.4%) required oxygen.

Conclusion: Intravenous midazolam was the commonest agent used for procedural sedation at Goa Medical College, India.

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(Key words: Procedural sedation, midazolam, propofol, adverse events)

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Introduction

Paediatric procedural sedation (PPS) is required for radiologic imaging as well as other diagnostic and therapeutic procedures. The aim of PPS is to provide sedation, analgesia, amnesia and immobility if required for the successful completion of the procedure. In the United States (US) a significant number of children receive PPS outside the operating room provided by various paediatric subspecialists such as from paediatric critical care, paediatric emergency medicine, and paediatric hospitalists[1]. Propofol, because of its pharmacological properties like quick onset and short duration of action, is the preferred sedation agent either alone or in combination with fentanyl or ketamine, allowing for rapid turnover of patients and optimal sedation[2,3]. PPS performed by paediatric subspecialists outside the operating room in the US has been shown to be highly effective, resulting in cost saving and improved parental satisfaction[4-6]. There is limited data about PPS from India[7-8]. Published surveys suggest significant variation in the sedation provider, the location of procedure (operating room vs. outside the operating room) and medications used[9,10].

Objective

To evaluate the PPS practice at a major tertiary care university teaching hospital in India.

Method

The sedation provider

Sedations were performed by a senior paediatric resident, under the supervision of an attending consultant paediatrician with experience in procedural sedation. Additionally, the consultant physician attended the paediatric BASIC course, a 2-day course, covering the essential and fundamental aspects of paediatric intensive care, a project of the World Federation of Paediatric Intensive and Critical Care Societies. *Paediatric Advanced Life Support (PALS) was mandatory for all sedation providers*. The physician team was accountable for pre-sedation assessment, physical examination, consent, administering sedation medications, monitoring patient's vital signs, airway management, and overseeing the sedation and recovery process. NPO (nil per os or nothing by mouth) guidelines recommended by the American Academy of Paediatrics (AAP) for PPS were followed[11].

Nil per os (NPO) guidelines recommended by the American Academy of Paediatrics (AAP) for PPS

Clear liquids*	2 hours
Breast milk	4 hours
Infant formula	6 hours
Solid food (light meal or meals rich in fat, protein or fried foods)^	6-8 hours

** includes water, juice with no pulp, carbonated beverages, tea and black coffee*

^ Meals that include fried or fatty foods or meat (which prolong gastric emptying) may require 8 hours of NPO time.

Location, equipment, and patient monitoring

Non-radiology procedures were performed in the treatment room on the paediatric in-patient floor. The senior paediatric resident was responsible for carrying the resuscitation equipment and sedation medications to the site of procedural sedation. Resuscitation equipment included an appropriate size bag and mask, laryngoscopes, endotracheal tubes, suction apparatus, and a reversal agent flumazenil. Monitoring included continuous pulse-oximetry, non-invasive blood pressure, and heart rate. No end-tidal monitoring was used.

Pre-sedation assessment

A pre-sedation evaluation was performed by the sedation provider to carefully screen patients who could be at higher risk of having airway complications. Patients with genetic syndromes, prematurity (postconceptional age <60 weeks), upper respiratory tract infection, asthma, cardiac disease, cerebral palsy, obesity (body mass index >30 kg/m^2), gastro-oesophageal reflux disease and obstructive sleep apnoea, American Society of Anaesthesiologists Physical Status (ASA-PS) classification ≥ IV were carefully screened and if deemed not to be candidates for sedation then cancelled or referred to an anaesthesiologist.

American Society of Anaesthesiologists Physical Status (ASA-PS) classification

Class	Description
I	Normal healthy patient
II	A patient with mild systemic disease
III	A patient with severe systemic disease
IV	A patient with severe systemic disease that is a constant threat to life
V	Moribund patient who is not expected to survive without surgery

Sedation medication

Chloral hydrate (50-100mg/kg/dose) was the only oral medication used. If the patient was not adequately sedated with chloral hydrate despite a supplemental dose of 25mg/kg/dose, a dose of midazolam (0.1mg/kg/dose) was used intravenously (IV) as an adjunct. Midazolam (0.1-0.6mg/kg/dose) or dexmedetomidine (1-2mcg/kg/dose) IV were used as primary agents. If the patient was not adequately sedated with either midazolam or dexmedetomidine, then ketamine IV 1mg/kg was used as an adjunct to complete the procedure. Due to institutional regulations, propofol was not allowed to be used for PPS by the sedation providers. Furthermore, the use of opioids outside the paediatric intensive care unit was not allowed. Ketamine was mainly used in combination with midazolam for procedures such as kidney and bone marrow biopsies. The depth of sedation was monitored using the Ramsey sedation scale[12].

Outcome measures

We assessed the incidence of adverse events (AE) and serious adverse events (SAE) as outcome measures. SAE were defined as any one of the following: (1) Airway obstruction, (2) laryngospasm (complete or near-complete lack of air movement with respiratory effort and/or stridor)[1,5], (3) emergent airway intervention (intubation, positive pressure ventilation, or placement of another airway

device such as an oral airway or laryngeal mask airway), (4) unplanned hospital admission, (5) aspiration, (6) cardiac arrest, (7) death. Sedation-related minor adverse events included the following: (1) Agitation, (2) brief apnoea (cessation of respiration for >15 seconds), (3) desaturation (oxygen saturation on pulse oximetry <90 for >30 s), (4) hypotension, (5) stridor.

Discharge criteria

Patients were discharged when they met standard age appropriate procedural sedation discharge criteria which include, ability to take oral liquids, a return of baseline mental status and vital signs stability is achieved[11]. Sedation duration was defined as the time of drug administration till the return to baseline mental status and vital signs were stable.

Statistics and data collection

This is a retrospective study of all PPS performed at Goa Medical College, Goa, India from April-September 2015. *The study was approved by the institutional ethics committee*. Descriptive statistics were calculated using counts and frequencies, medians and ranges, or means and confidence intervals (CI) for patient demographics and sedation procedure characteristics, risk factors and AEs. Rates of events were calculated, and 95% CIs for these rates were provided. Chi-square tests and Wilcoxon-rank sum tests were used to compare characteristics of patients experiencing a sedation event to those that did not. Statistical significance was assessed using a significance level of 0.05 unless otherwise noted, and two-sided statistical tests are reported.

Results

Patient demographics are shown in Table 1.

A total of 249 patients who underwent PPS were included in this study. The most common indication for PPS was neurological in 201 (81%) followed by oncology/ gastrointestinal in 13 (5%) of the cases respectively. PPS was performed on 150 (60%) outpatients who were given appointments on selected days whereas 99 (40 %) of the patients were inpatients who needed PPS for certain diagnostic procedures. Types of procedure for which PPS was provided are shown in Figure 1. Sedation medications (primary and secondary drugs) used are shown in Table 2.

Table 1: ***Patient demographics (n=249)***

Characteristic	Result
Age (months), median (25^{th}–75^{th})	22 (12 – 36)
Weight (kg), median (25^{th}–75^{th})	10 (08 – 12)
Sex-Female, No. (%)	140 (56.2)
ASA-PS Score, No. (%)	
I	21 (08.5)
II	206 (83.1)
III	21 (08.5)
Admission Status, No. (%)	
Inpatient	99 (39.8)
Outpatient	150 (60.2)
Nil per os (NPO) status	
NPO for clears ≥ 2 hrs. No. (%)	248 (99.6)
NPO status for solids ≥ 6 hrs. No. (%) (n = 247)	105 (42.5)
Procedure Type, No. (%)	
Computed Tomography (CT) scan	61 (24.5)
Magnetic resonance imaging (MRI)	105 (42.5)
Others	50 (20.1)

ASA-PS: American Society of Anaesthesiologists Physical Status

Table 2: ***Sedation medication used for PPS***

Sedation medication used	No. (%)
Primary medication	
Midazolam	188 (75.5)
Dexmedetomidine	37 (14.9)
Chloral Hydrate	24 (09.6)
Adjunctive medication	113 (45.4)
Midazolam→ Dexmedetomidine	56 (22.5)
Midazolam→ Ketamine	38 (15.3)
Chloral hydrate→ Midazolam	15 (06.0)
Dexmedetomidine→ Midazolam	03 (01.2)
Dexmedetomidine →Ketamine	01 (0.4)
Drug infusion	0

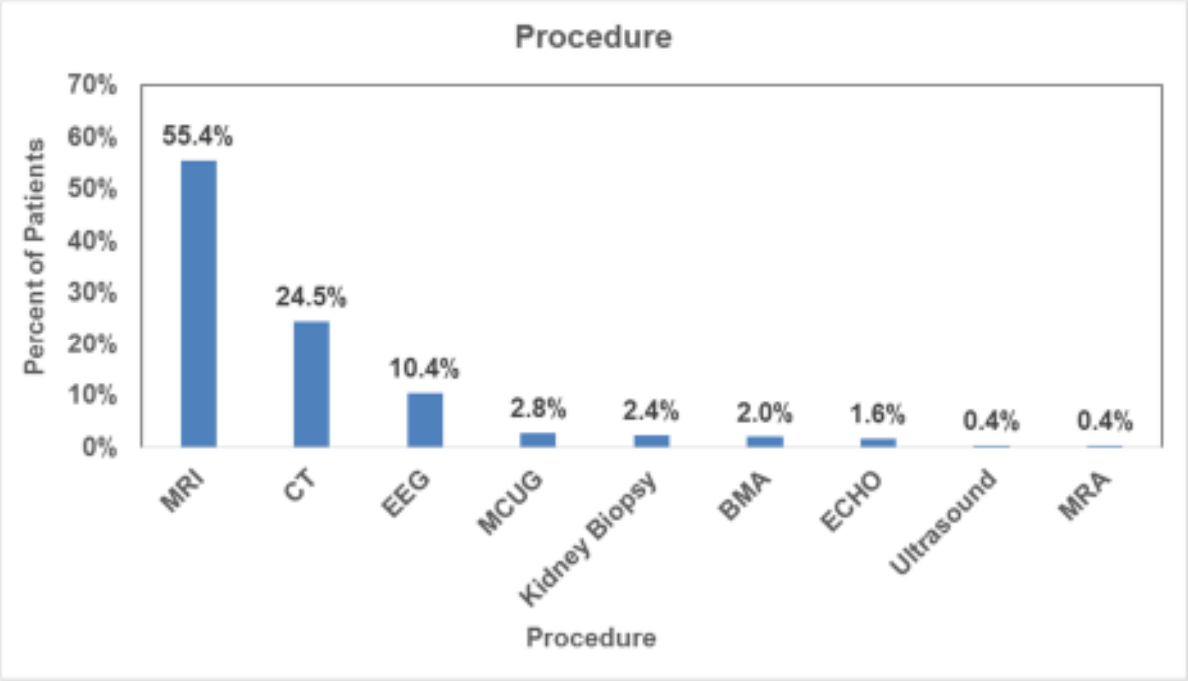

Figure 1: ***Types of procedure for which PPS was provided***

CT = computed tomography, EEG= electroencephalogram, ECHO = echocardiography, MCUG = micturating cystourethrogram, MRI = Magnetic resonance imaging, BMA = bone marrow aspiration, MRA = magnetic resonance angiography

Midazolam and dexmedetomidine (DEX) given IV were the most commonly used primary agents. Chloral hydrate was used by the oral route and not rectally. Secondary drug (adjunct) was used in case of inadequate Ramsey sedation score despite using a supplemental dose of the primary drug. A secondary drug was required in 113 (45.4 %) of the patients after administration of the primary drug. Adverse events/interventions and procedure success rates are shown in Table 3.

Table 3: ***Adverse events/interventions and procedure success rates (n=249)***

	No. (%)
Study completed	213 (85.5)
Serious adverse events (SAE)	**03 (01.2)**
Upper airway obstruction	02 (0.8)
Transfer to PICU	03 (01.2)
Emergency anaesthesia Consult	02 (0.8)
Minor adverse events	**94 (37.8)**
Desaturation	32 (12.9)
Coughing	18 (07.2)
Change in heart rate > 30%	47 (18.9)
Hypotension	11 (04.4)
Agitation/ Delirium	52 (20.9)
Required Intervention	**24 (9.6%)**
Oxygen	21 (08.4)
Suctioning	03 (01.2)
Fluid Bolus	02 (0.8)
Atropine	03 (01.2)
Parent Satisfaction	**213 (85.5)**
Radiology Satisfaction	**213 (85.5)**

No patient had cardiac arrest, death, or aspiration. Airway obstruction was seen in two patients. The clinical profile of patients who developed severe upper airway obstruction was as follows: patients were infants aged six months and nine months respectively of ASA-PS Class II with the former infant being premature. Both received midazolam and ketamine combination for sedation. Both patients were rescued using jaw thrust, oxygen via bag-mask and required monitoring in the paediatric intensive care unit (PICU) prior to discharge. A 36 month old female with cerebral palsy and a history of cardiac disease (ASA PS Class II) who received midazolam with adjunctive ketamine for an MRI of the brain and spine had to be admitted to PICU because patient experienced desaturation, hypotension, agitation and excessive secretions. Patient required suctioning, fluid bolus and atropine.

Sedation-related minor adverse events (AE) were seen in 94 (37.8%) patients undergoing PPS. A change in heart rate >30% from the baseline was seen with DEX but did not require any intervention. Hypotension was a minor adverse event noted in 4.4% of the cases. Only two patients required a fluid bolus of normal saline. No respiratory depression was noted following midazolam administration used as a sole agent or along with a secondary IV agent. Agitation/delirium was seen in 52 (20.9)% of the cases more following chloral hydrate administration along with a concurrent use of a secondary agent like midazolam. Flumazenil was not used in any patients

as the agitation/delirium was of short duration and self-resolved

Procedure success (completion of the procedure using PPS) was seen in 213 (85.5%) patients. Of the 36 patients who did not complete the study, 34 had an inadequate Ramsey sedation score and 2 patients developed severe upper airway obstruction and could not successfully complete the procedure. Overall parental satisfaction with PPS was 85.5%.

Risk factor analysis for adverse events are provided in table 4. Comparisons among patients that experienced an AE to those that did not showed that younger age (p=0.025), higher ASA-PS classification (p=0.015), the presence of cerebral palsy (p=0.040), the use of dexmedetomidine (p=0.013) and need for a secondary agent were associated with an adverse event.

Table 4*: Risk factors associated with sedation related complication or serious adverse event*

Characteristic	No event *(n=155)*	Event *(n=94)*	*p* value
Sex, No. (%)			
Male	70 (64.2)	39 (35.8)	0.571
Female	85 (60.7)	55 (39.3)	
Age in months, median (25^{th} – 75^{th})	18 (11 – 36)	24 (14 – 48)	0.025*
Weight in kg, median (25^{th} – 75^{th})	10 (08 – 12)	11 (09 – 14)	0.052
Inpatient, No. (%)			
Yes	59 (59.6)	40 (42.6)	0.483
No	96 (64.0)	54 (36.0)	
ASA Class, No. (%)			
1	13 (61.9)	08 (38.1)	
2	135 (65.5)	71 (34.4)	0.015*
3	07 (33.3)	14 (66.7)	
Comorbidities No. (%)			
Premature			
Yes	32 (64.0)	18 (36.0)	0.775
No	123 (61.8)	76 (38.2)	
Gastro-oesophageal reflux			
Yes	09 (42.9)	12 (57.1)	0.055
No	146 (64.0)	82 (36.0)	
Cerebral palsy			
Yes	18 (47.4)	20 (52.6)	0.040*
No	137 (64.9)	74 (35.1)	
Cardiac disease			
Yes	06 (54.6)	05 (45.5)	0.752
No	149 (62.6)	89 (37.4)	
Procedure type, No. (%)			
Computed tomography	42 (68.9)	19 (31.2)	
Magnetic resonance imaging	82 (59.4)	56 (59.6)	0.449
Other	31 (62.0)	19 (38.0)	
Primary drug used, No. (%)			
Chloral Hydrate	16 (66.7)	08 (33.3)	
Dexmedetomidine	15 (40.5)	22 (59.5)	0.013*
Midazolam	124 (66.0)	64 (34.0)	
Adjunctive medication, No. (%)			
No	97 (72.4)	37 (27.6)	< 0.001*
Yes	58 (50.4)	57 (49.6)	

Discussion

The goals of PPS as outlined by the AAP include patient safety, minimization of pain and discomfort, anxiolysis, amnesia, immobility and return of patient to a baseline level which is safe for discharge[11]. Furthermore, Cote *et al* have stressed on the use of the fewest number of drugs and the lowest dose possible to match the type of procedure[11,13]. This study focuses on the sedation provided by general paediatricians at a tertiary care university teaching hospital in India. Several barriers to PPS in resource limited countries like India result in wide practice variation, violation of AAP paediatric sedation guidelines resulting in a lower success rate of PPS[9,10]. The restriction of drugs (by institutional or anaesthesia policy) which provide analgesia such as opioids, or deep sedation such as propofol, can result in inability to provide adequate pain control or immobilization required for non-radiology procedures. The restriction of drugs also necessitates

the use of more than one agent which can result in an increased incidence of AE[13]. Additionally the shortage of anaesthesiologists, operating room availability, a dedicated sedation service comprised of paediatric subspecialists, places the burden of providing PPS on the general pediatricians, as in this study.

Our study shows that the general paediatricians provide PPS for children in the age range of 12-36 months, usually ASA-PS I or II for a variety of procedures, majority of which involves radiologic imaging. Similar findings were reported by Monroe *et al* when they analysed procedural sedations provided by paediatricians in the US from a large sedation database (PSRC) that paediatricians sedate younger patients, mostly ASA-PS I or II, non-painful, non-emergency procedures such as radiologic imaging when compared to PPS provided by paediatric subspecialists[14]. The overall procedure success rate was about 85% which can be attributed to the medications used for PPS in this study. The primary agent used in 76% of patients in this study was IV midazolam. Intravenous DEX was the second most commonly used agent. IV midazolam was also used if patients were inadequately sedated by chloral hydrate, another commonly used agent besides the above two agents. The liquid formulation of chloral hydrate is no longer available in the US and the use of this agent is on the decline[11]. Ketamine was used as a secondary agent in 15% of the patients if inadequately sedated by midazolam. Interestingly no opioids, barbiturates or any sedative infusions were utilized in this study. The use of a single bolus rather than an infusion of the sedative could also explain the lower success rate compared to studies that utilize propofol or ketamine which report much higher procedure success rates[15,16]. It is possible that due to the fear attributed to ketamine's side effect profile especially laryngospasm, the paediatricians were reluctant to use that as a first line agent for non-radiology procedures[17,18]. The overall parental or radiology satisfaction was also low. This can be probably attributed to the higher failure rate due to inadequate sedation or AE. Parents have to take off work or travel long distances to bring the child to the hospital.

The overall incidence of sedation related minor AE was much higher (37%) compared to studies in which PPS was provided by paediatric subspecialists. Serious AE rate was however low (1.2%) compared to other studies and could be attributed to the type of medications used in our study (i.e. no propofol)[15]. None of the patients had aspiration, required cardiopulmonary resuscitation or died.

When we examined risk factors for AE, we found that younger age, higher ASA-PS, use of multiple drugs was associated with increased incidence of AE. These findings are similar to what has been published previously[5,11,15]. Additionally patients with a diagnosis of cerebral palsy were at a higher risk of AE and this is consistent with findings from other studies especially with use of midazolam which has been to shown to give rise to agitation and delayed recovery[19]. This higher incidence of AE in patients with cerebral palsy could be attributed to multiple factors such as muscle tone, pharyngeal collapse, increased secretions and drug interactions with various medications used daily such as baclofen[20]. We excluded all patients with a recent active upper respiratory infection as sedation candidates as there are some publications which have elucidated to the higher risk of adverse events and sedation failure in these patients[21] The risk for AE in our patients with prematurity, gastro-oesophageal reflux disease and cardiac disease was not statistically significant, although studies have shown that these patients are at higher risk for AE with sedation[15,22,23, 24].

This study has several limitations. The results of this observational study are from a single centre with a small sample size. Because there is no control group, we are unable to draw a direct cause and effect from our study. Additionally, the drug regimen used was not uniform in all patients, therefore, the AE reported may have varied on that account. We did not follow-up on patients once they were discharged from the hospital. Adverse reactions could have occurred at home and we would not have been aware of them. Finally, we did not take into account AE in relation to the level of sedation. There is a possibility that rate of AEs increase as the depth of sedation increases. There is no pre-screening of high risk patients prior to their appointment and patient are frequently cancelled on the day of their arrival. Distraction techniques to accomplish procedures were not utilized in our study due to resource limitation. End-tidal monitoring was also was not available for PPS provided in this study.

Conclusions

Midazolam IV was the commonest agent used for procedural sedation at Goa Medical College, India.

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