ORIGINAL ARTICLE

Procedural moderate sedation with ketamine in pediatric critical care unit

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ABSTRACT

Objective: To evaluate the safety and efficacy of moderate sedation in the Pediatric Intensive Care Unit (PICU) settings according to moderate sedation protocol using ketamine and midazolam and to determine areas for the improvement in our clinical practice. **Settings and Design:** A retrospective study was conducted in the PICU. **Materials and Methods:** Retrospective chart review was performed for patients who had received moderate sedation between January and the end of December 2011 and who are eligible to inclusion criteria. **Results:** In this study, 246 moderate sedation sessions were included. 5.3% were in infant age, while 94.7% were children (1–14 years). Their gender distributed as 59.8% males and 40.2% females. The majority of them had hematology-oncology disease nature, i.e., 80.89% (*n* = 199). Lumbar puncture accounted for 65.3% (*n* = 160) of the producers; the rests were bone marrow aspiration 32.7%, endoscopy 8.2%, and colonoscopy 2.9%. Two doses of ketamine (1–1.5 mg/kg) to achieve moderate sedation during the procedure were given to 44.1% (*n* = 108) of the patients. One dose of midazolam was given to 77.2% (*n* = 190), while 1.22% (*n* = 3) of sessions of moderate sedation was done without any dose of midazolam. Adverse events including apnea, laryngeal spasm, hypotension, and recovery agitation were observed during moderate sedation sessions, and it has been noticed in four sessions, i.e., 1.6%, which were mild to moderate and managed conservatively. **Conclusion:** Moderate sedation in the PICU using ketamine and midazolam is generally safe with minimal side effects as moderate sedation sessions were conducted by pediatric intensivist in highly monitored and equipped environment.

Key words: Ketamine, moderate sedation, pediatric critical care

INTRODUCTION

Moderate sedation is a drug-induced depression of consciousness during which a patient responds purposefully to verbal commands. This level of sedation implies an interactive state, depending on the patient's age. With moderate sedation, no intervention is required to maintain a patent airway, adequate and spontaneous ventilation. Cardiovascular function is usually maintained.[1]

Moderate sedation can be applied for different types of pediatric procedures such as bone marrow aspiration (BMA), lumbar puncture (LP), and endoscopic procedures.[2-9]

Patients who are American Society of Anesthesiologists (ASA) Class I and II [Table 1] are considered appropriate candidates

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Table 1: American Society of Anesthesiologists physical status classification

Classification	Definition
Class I	A normally healthy patient
Class II	A patient with mild systemic disease
Class III	A patient with severe systemic disease
Class IV	A patient with severe systemic disease that is a constant threat to life
Class V	A moribund patient who is not expected to survive without the operation

for moderate sedation; children in ASA Class III and IV or children with special needs and those with anatomic airway abnormalities will usually be referred to anesthesiologist.[1]

Ketamine is one of the medications, which is used commonly for moderate sedation in pediatrics.

Previous studies evaluated moderate sedation for pediatric procedure in emergency department.[2,3,7-13] However, pediatric moderate sedation unit is uncommon. Godoy *et al*.'s study is one of the few studies, which evaluated the moderate sedation in pediatric critical care unit.[14]

Many medications used in moderate sedation include ketamine, midazolam, fentanyl, propofol, nitrous oxide, or etomidate.[13,15]

Ketamine is a desirable agent because of its good pain control with minimum side effects.

The focus will be on ketamine use in moderate sedation. Ketamine is one of the medications, which has been used increasingly and commonly since 1970 in moderate sedation. Ketamine is nonbarbiturate phencyclidine derivative dissociative agent, with sedative, hypnotic, analgesic, amnestic properties, relative preservation of airway tone, cardiovascular stability, and maintenance of spontaneous respiration.[7,8]

Mechanism of action depends on N-methyl-D-aspartate glutamate receptor antagonism; it undergoes hepatic metabolism to norketamine, which is also analgesic agent, and has approximately one-third of the activity of ketamine itself. Further, norketamine undergoes urinary excretion.[8,15] Ketamine clearance increases with decreasing age.[8,13]

In our Pediatric Intensive Care Unit (PICU), pediatric intensivist is usually responsible for daily session of moderate sedation for different types of pediatric procedures such as BMA, LP, and gastro-endoscope. In this study, the moderate sedation in PICU settings, its safety, and efficacy were reviewed.

MATERIALS AND METHODS

Objectives

To review moderate sedation in PICU settings, its safety, and efficacy using ketamine and midazolam which will provide more experience and support about future independent moderate sedation unit.

Inclusion criteria

- Both male and female patients
- Age 1 month to 14 years
- ASA I: Healthy patient or ASA II
- Nothing by mouth (NPO) for the last 6 h.

Exclusion criteria

- Intubated patients
- Patients who had moderate sedation by other sedative drugs (e.g., propofol, dexmedetomidine).

Outcomes

Primary outcome

- To evaluate the safety and efficacy of moderate sedation in PICU settings using ketamine and midazolam.

Secondary outcome

- To identify categories of diseases for whom underwent for moderate sedation
- To review ketamine doses given for procedural sedation
- To identify moderate sedation-related adverse events.

Definitions

- Optimal moderate sedation: Drug-induced depression of consciousness during which a patient responds purposefully to verbal commands (e.g., "open your eyes") either alone or accompanied by light tactile stimulation, such as a light tap on the shoulder or face, not a sternal rub. With moderate sedation, no intervention is required to maintain a patent airway, adequate and spontaneous ventilation. Cardiovascular function is usually maintained[8]
- Optimal ketamine dose (as described in sedation protocol): 1–1.5 mg/kg[2,5]
- Adverse events to moderate sedation: Unwanted and usually harmful events, moderate sedation-related, such as hypotension, bradycardia, stridor, or hypoxemia.[2,5]

Study design

This is a retrospective, by charts review, which was conducted in the PICU. The study started after Research Office's approval. The patients who had received moderate sedation during 2011, as we had approved and are eligible to inclusion criteria, were included in the study.

Data collection

Patients had come from pediatric wards to the PICU for procedural sedation only. After the procedure, they stayed in PICU until appropriate discharge criteria [Table 2].

Moderate sedation was managed by pediatric intensivist, pediatric intensive care nurse, according to moderate sedation protocol in our institution. This protocol includes preassessment [Table 1], vital signs monitoring, discharge criteria, and medications. These moderate sedation medications consist of ketamine (1–1.5 mg/kg), midazolam (0.1–0.05 mg/kg), and atropine. For each moderate sedation session, a sedation record sheet was filled and completed before the procedure, together with the informed consent. During the procedure, the following data were monitored and recorded every 5 min: Vital signs (heart rate, respiratory rate, O_2 saturation, blood pressure), oxygen requirement, administered drugs, and associated adverse events.

All patients received supplemental oxygen with nasal cannula during sedation.

Analysis of the data included demographic details (age, gender) weight, procedure(s) performed, doses of each medication per kilogram body weight, and adverse effects.

RESULTS

A total of 253 moderate sedation sessions were performed over the study period (2011). Seven patients were excluded from the study because of incomplete moderate sedation sheet data.

All of the 246 patients who had moderate sedation and received ketamine were included in the study. Some patients required extra doses, especially ketamine (71.4% for ketamine), during the procedure.

There were 59.8% ($n = 147$) males and 40.2% ($n = 99$) females, infant 5.3% ($n = 13$), and children (1–14 years) 94.7% ($n = 233$). Majority of procedures were LP 65.3% ($n = 160$).

Regarding diseases nature, the most common was hematology-oncology disease 80.89% ($n = 199$), followed by gastrointestinal disease 10.16% ($n = 25$) and neurological disease 8.94% ($n = 22$). Details are shown in Tables 3-5.

Most of the patients received two doses of ketamine or more (ketamine dose 1–1.5 mg/kg) (71.4%) [Table 6]. We could not obtain enough data to evaluate the ketamine doses number relation to the procedure type or duration of moderate sedation session.

In midazolam side, most of the patients received only one dose of midazolam 77.2% ($n = 190$) as shown in Table 7. Three patients were sedated with only ketamine, and they did not receive midazolam. Only 22.8% of patients received more than one dose of midazolam to achieve good sedation [Table 7].

Patients have multiple visits (repeated procedures). The patients have been sedated either by giving them a single dose or multiple doses of ketamine. Each dose was assumed as an episode; hence, the total number of episodes is 515 for ketamine.

Most patients 87.37% ($n = 450$) received the ketamine within the recommended dosage (1–1.5 mg/kg) according to the

Table 2: Recommended discharge criteria

Cardiovascular function and airway patency are satisfactory and stable
The patient is easily reusable, and protective reflexes are intact
The patient can talk (if age appropriate)
The patient can sit up unaided (if age appropriate)
For very young or handicapped child incapable of the usually expected response, the presedation level of responsiveness or a level as close as possible to the normal level for that child should be achieved
The state of hydration is adequate

Table 3: Age, *n* (%)

	n (%)
Infant (1-12 months)	13 (5.3)
Child (1-14 years)	233 (94.7)
Gender	
Male	147 (59.8)
Female	99 (40.2)

Table 4: Type of procedure, *n* (%)

	n (%)
Bone marrow aspiration	80 (32.7)
Lumbar puncture	160 (65.3)
Endoscopy	20 (8.2)
Colonoscopy	7 (2.9)

Table 5: Disease type, *n* (%)

	n (%)
Hematology-oncology	199 (80.89)
Gastroenterology	25 (10.16)
Neurology	22 (8.94)

Table 6: Number of ketamine doses received (*n*=246)

One dose (%)	Two doses (%)	Three doses (%)	Four doses (%)	Five doses (%)
70 (28.6)	108 (44.1)	49 (20)	11 (4.5)	7 (2.9)

Table 7: Number of midazolam doses received (*n*=246)

No midazolam (%)	One dose (%)	Two doses (%)	Three doses (%)	Four doses (%)
3 (1.22)	190 (77.2)	45 (18.3)	7 (2.8)	1 (0.4)

protocol, while 12.62% (n = 65) of them received less than recommended dose of ketamine [Table 8].

The patients have been given a supplemental midazolam single dose or multiple doses. Each dose was assumed as an episode; hence, the total number of episodes is 306 for midazolam.

The majority 96.08% (n = 294) of the patients received regular doses of midazolam; only 3.92% (n = 12) of them received either suboptimal or exceeded doses [Table 9].

Adverse events including apnea, laryngeal spasm, hypotension, and recovery agitation were observed during moderate sedation. It has been noticed in four sessions, i.e., 1.6%, which includes hypoxia, laryngeal spasm, and hypotension, while we did not notice recovery agitation in our patients [Table 10], all of it were mild to moderate and managed conservatively.

DISCUSSION

Ketamine dose was studied by a lot of research.[7,10] The studies compare administration of initial dose 1 mg/kg intravenous (IV), with 1.5 mg/kg IV. Dose of 1 mg/kg IV is suitable for short procedure which is <5 min because 90% of them will have <0.75 mg/L at 10 min of administration, while the dose of 1.5 mg/kg IV seems to be suitable more for longer procedure because 50% of those who received 1.5 mg/kg IV have <0.75 mg/L at 10 min and no cardiopulmonary effects were noted with either doses.[7,10]

In another randomized, double-blind clinical trials, midazolam combined with ketamine did not reduce recovery agitation and other side effects related to ketamine sedation, and its use appears unnecessary.[16]

Table 8: Ketamine doses (n=515)

Regular dose (1-1.5 mg/kg), n (%)	Less than regular, n (%)
450 (87.37)	65 (12.62)

Table 9: Midazolam doses (n=306)

Regular dose (0.1-0.05 mg/kg), n (%)	Less or more than regular dose, n (%)
294 (96.08)	12 (3.92)

Table 10: Distribution of adverse events

	n (%)
Apnea	None
Hypoxia	2 (0.8)
Laryngeal spasm	1 (0.4)
Hypotension	1 (0.4)
Recovery agitation	None

Most (108) 44.1% of our patients received two doses of ketamine; the number of ketamine doses differs from one patient to another and also relates to type of procedure. Some of the patients have multiple exposure to moderate sedation, which may play a role in the number of ketamine doses, which could not be investigated in our patients.

Some of our patients received less than the recommended dose of ketamine. Again, this may increase the dose frequency of ketamine, but different types of procedures and different number of exposure may affect the results.

In relation to moderate sedation's safety, the side effects encountered were minimal. All of them occurred with patients who received optimal doses of ketamine and midazolam. All patients responded quickly to the appropriate management; hypoxemia episodes and laryngeal spasm were managed by supplying oxygen, positioning, and secretion suction. Advanced airway was not required.

This study evaluates protocol-based moderate sedation procedure in PICU and by pediatric intensivist. In conclusion, results of our analysis showed that most of our patients required more than one dose of ketamine (71.4%) plus a dose of midazolam to achieve moderate sedation, with minimum side effects. This suggests that moderate sedation sessions in PICU are safe for different types of procedures such as LP, BMA, endoscopy, and colonoscopy.

The timing and the type of procedures in relation to dosages of ketamine were not examined because of the different types of procedures and different times of exposure to moderate sedation sessions, and this can be considered as a limitation of this review.

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Conflicts of interest

There are no conflicts of interest.

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