Safe and Efficacious Use of Procedural Sedation and Analgesia by Non-Anesthesiologists in a Pediatric Hematology-Oncology Unit

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Background: *Children often require relief of pain and anxiety while undergoing diagnostic and therapeutic procedures. Procedural sedation and analgesia (PSA) is the safe and effective control of pain, anxiety and motion so as to allow a necessary procedure to be performed and to provide an appropriate degree of memory loss or decreased awareness.* ***Objective:*** *To prospectively describe procedural sedation and analgesia as performed in the pediatric oncology unit and to report the success of sedation and the incidence of complications.* ***Methods:*** *IV Midazolam and IV Ketamine were used for PSA in pediatric oncology patients undergoing painful procedures.* ***Results:*** *Between June 2004 and December 2004, 55 diagnostic and therapeutic procedures were performed using PSA in 16 children. There were 9 boys and 7 girls with a median age of 11 years. Twelve patients had hematolymphoid malignancies and 4 patients had solid tumors. The indication for PSA were bone marrow aspiration and/or biopsy in 7 patients, therapeutic lumbar puncture in 43 patients, bone marrow aspiration and lumbar puncture in 4 patients and skin biopsy in 1 patient. All 55 procedures were successfully completed. Adverse events occurred in 15 (27 %) episodes and included transient drop in oxygen saturation, vomiting, dizziness and disinhibition with crying spells. Average time to arousable state and full recovery was 22 minutes and 31 minutes respectively. None of the patients complained of post procedure pain nor recalled the procedure at the follow up visit.* ***Conclusion:*** *Procedural sedation and analgesia using midazolam and ketamine is a safe and efficient method of limiting anxiety and procedure related pain and can be successfully administered by non-anaesthesiologists. The complication rate is low and can be easily managed.*

Key words: *Ketamine, Midazolam, Procedural sedation and analgesia (PSA).*

CHILDREN often require relief of pain and anxiety while undergoing diagnostics and therapeutic procedures. Procedural sedation is the safe and effective control of pain, anxiety and motion so as to allow a necessary procedure to be performed and to provide an appropriate degree of memory loss or decreased awareness.

Pediatric oncology patients need several painful and anxiety provoking procedures during their treatment period. During the past two decades, most centers abroad have developed safe and effective protocols for procedural sedation and analgesia (PSA) in children. These protocols if properly administered, are safe to be provided by non-anesthesiologists, who are otherwise trained in airway management and resuscitation procedures. There is dearth of data regarding the systematic use of procedural sedation and sedation from our country. This study was aimed to describe procedural sedation and analgesia as performed in our pediatric

oncology unit and to report the success of sedation and the incidence of complications.

Subjects and Methods

Intravenous midazolam and intravenous ketamine were the drugs used for PSA. The patient and caretakers were explained about PSA and the procedure and written informed consent was obtained. All necessary age appropriate equipment for airway management, including laryngoscope, AMBU bag, endotracheal tubes, suction machine and resuscitation drugs were kept ready prior to initiating PSA. A minimum 4 hours of fasting was the prerequisite for PSA. Intravenous ondansetron or granisetron was used as premedication. Oxygen was delivered at the rate of 2 l/min via face-mask. The patients were continuously monitored using a pulse oxymeter showing heart rate and oxygen saturation; beginning before the injection of midazolam till they fully awake after the procedure. Intravenous midazolam was used in the dose of 0.05-0.1 mg/kg (maximum dose = 2 mg) diluted and given as a slow IV push over 2 minutes. This was followed by intra-venous ketamine in the dose of 0.5-1 mg/kg diluted in normal saline, titrated till the patient became unresponsive to verbal stimuli and light touch. The procedure was then initiated. At least two physicians were present during PSA; the senior physician supervised the drug administration and then performed the procedure, while the assistant continu-ously monitored the patient for complications and documented the medications adminis-tered, the response to sedation and periodic vital signs.

A PSA form was designed and used to record pertinent clinical and demographic characteristics of patients, information related to the procedure, vital signs and the occurrence of complications. Success of sedation was defined as successful completion of the procedure in a minimally responsive subject. Complications were defined as apnea, hypoxia (sustained pulse oxymetry <93%), seizures, arrhythmia, laryngospasm, stridor, hypotension, rash, vomiting, disinhibition or aspiration. Patients were discharged 2 hours after the procedure after ensuring that they were fully awake, coherent and able to tolerate oral feeds. Information regarding late complications after discharge was recorded at the subsequent follow-up visit.

Results

Between June 2004 and December 2004, 55 diagnostic and therapeutic procedures were performed using PSA in 16 children.(9 boys and 7 girls). The median age was 10 years (range 4-18 years). The primary diagnosis was acute lymphoblastic leukemia in 5 patients, acute myeloid leukemia in 4 patients, Non Hodgkins lymphoma in 3 patients, and 4 patients had solid tumors. The indications for PSA were bone marrow aspiration and/or biopsy in 8 episodes, lumbar punctures in 43 episodes, bone marrow aspiration and lumbar puncture in 3 episodes and skin biopsy in one patient.

Intravenous midazolam and intravenous ketamine was used for all the patients. Procedural sedation and analgesia was successfully completed in all 55 episodes. The average time to arousable state and full recovery was 22 minutes (range 12-30 minutes) and 31 minutes (range 20-40) respectively. Adverse events occurred in 15 (27%) episodes. Transient hypoxia was recorded in 5 (9%) episodes, vomiting in 3 (5.4%) episodes, dizziness in 3 (5.4%) and disinhibition with crying spells in 4 (7.2%) episodes.

All episodes of hypoxia were encountered within 3-5 minutes after administering the sedation and were treated by increasing the

flow rate of nasal oxygen. None needed bag and mask ventilation nor intubation. There were only 2 episodes of vomiting after discharge. None of the patients complained of post procedure pain nor recalled the procedure at the follow up visit.

Discussion

The management of acute pain and anxiety in children undergoing therapeutic and diagnostic procedures outside the operating room has developed substantially in the past 15 years. The widespread availability of noninvasive monitoring, short acting opioids and sedatives, and specific opioid and benzodiazepine antagonists has enabled clinicians to administer sedation safely for procedures in diverse settings.

The progression from mild sedation or analgesia to general anaesthesia is a continuum. As the dose increases and the level of the drug in the central nervous system rises, consciousness decreases and the risk of cardiorespiratory depression increases. As the dose increases further, the patient continues to advance along the sedation continuum until protective airway reflexes are lost and general anaesthesia is induced.

The definitions of the states of sedation as applicable to children have been well described in literature (1-4). Most pediatric procedures can be successfully performed with the patient in the state of primary sedation. Several safe and effective protocols have been successfully used by anesthesiologists for PSA in children(1-3). More recently, PSA is being administered by non-anesthesiologists with equally good results.

The combination of midazolam and ketamine is one such protocol(5,11). Midazolam is an ultra short acting benzodiazepine, which provides potent sedation, loss of memory and anxiolysis but no analgesia. Given intravenously, its onset of action is within 2-3 minutes and lasts for 45-60 minutes. The effects of midazolam can be rapidly reversed with the antagonist flumazenil. Due to these properties it has emerged as a safe and popular drug for procedural sedation in both children and adults(5-7).

Ketamine has been used as an anesthetic since 1970s and for PSA in American emergency departments since the early 1990s. It rapidly induces a trance-like cataleptic condition characterized by profound analgesia, sedation, amnesia and immobilization. Ketamine preserves upper airway muscular tone, protects airway reflexes and spontaneous respiration is maintained. With intravenous administration, action starts within a minute, lasting 15 to 30 minutes. This unique state of cortical dissociation permits painful procedures to be performed more consistently and effectively. Due to its preservation of protective airway reflexes, ketamine has an extremely low incidence of respiratory adverse events (5,7-10,12-15). In the last 30 years there have been no reported cases of aspiration following ketamine when used without contraindications. The efficacy and safety of ketamine is comparable when used by the intramuscular and the intravenous routes, though the recommended doses differ by the two routes(9).

Trying to perform a painful procedure in a struggling child can be a very traumatic experience for the patient, the parents and the entire medical team including the doctors and the nurses. Although there are a few reports on the use of ketamine by non anesthesiologists from the developing countries, there is dearth of published data from our country regarding the systematic use of pediatric PSA (16,17). In an attempt to limit the pain and anxiety of the patients and their parents and encouraged by the abundant data from the West regarding the safety and the ease of using PSA protocols in experienced hands, we initiated this study in

our pediatric oncology unit.

The results are extremely satisfactory. The commonest adverse effect noted was transient hypoxia, which could be reverted by increasing the oxygen concentration via face mask. None of the patients needed bag-mask ventilation or intubation, and none needed reversal with flumazenil. Among the other adverse effects noted, vomiting was easily controlled with antiemetics, either on– dansetron or domperidome. Dizziness and disinhibition were transient with complete recovery with one hour. Late complications (after 2 hours post procedure) were noted in only 2 patients who had vomiting after discharge.

All patients had complete amnesia regarding the procedure and none complained of post procedure pain. At the time of subsequent procedures, none of the patients nor their parents displayed nor conveyed any anxiety related to the procedure or the sedation. Patients who had experienced the same or similar procedure earlier without sedation, said they would definitely choose to be sedated if they had to undergo it again.

There are some issues that need to be addressed regarding PSA in children:

1. *Pre-PSA fasting requirement:* Guidelines of the American Society of Anesthesiologists require that children should not consume clear liquid for 2-3 hours or solids for 4-8 hours before PSA for elective procedures(4). Literature however does not strongly support this view point. Agarwal, *et al.*(18) have studied 1014 patients undergoing PSA in the emergency department, only 44% of who met fasting requirements. There was no significant difference in the incidence of adverse events especially vomiting in the fasting and non-fasting patients. In another prospective study, Treston(19) concluded that prolonged pre-procedure fasting (>3 hours) led to increased incidence of vomiting. In our study, 4 hours fasting was the prerequisite and the incidence of vomiting was an acceptable 5.4%

2. *Supplemental oxygen:* The need for supplemental oxygen for PSA has not been formally studied. Given the lack of evidence, supplemental oxygen is not mandatory for all patients and is at the physician's discretion. We used supplemental oxygen in all patients and had transient hypoxia in 9% episodes.

3. *Monitoring:* Continuous pulse oximetry is mandatory during PSA in children(4). Patients are at highest risk for complications during 5-10 minutes after the intravenous administration of medication and during the period immediately after the end of the procedure when procedural stimuli are discontinued. Vital signs should be measured at base line, after the administration of the drugs, after completing the procedure, during early recovery and at the completion of recovery.

4. *Discharge criteria:* Before discharge, children should be alert and oriented or should have returned to an age appropriate base line and their vital signs should be stable(4). Newman, *et al.* (20) studied 1341 sedation events over a 2-year period for optimal timing of discharge following PSA and concluded that 30 minutes after final sedation medication administration is a safe time for discharge if no adverse events have occurred till then. In our study all patients in whom the procedure was performed in the day care unit were discharges two hours after the procedure. Several other agents, *e.g.*, propofol(21-23), etidromate, fentanyl(5) *etc*. have been successfully used for PSA in children by non-

Key Messages

- Procedural sedation is necessary for pediatric patients undergoing painful procedures to decrease the trauma and anxiety associated with such procedures.
- The combination of midazolam and ketamine when properly used is a safe and efficient method of procedural sedation in children.

anesthesiologists in various settings.

Contributors: AB designed the study, AB and IA performed the procedures under sedation. AB was responsible for recording and collection of data, its analysis and interpretation. AB prepared the initial draft of the manuscript. RG and SA assisted in revising the draft and provided important intellectual content. AB will stand guarantor for the paper.

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