Comparative study between inj. Ketamine hcl-Midazolam hcl & inj. Fentanyl citrate-Midazolam hcl in Paediatric Patient for Procedural Sedation (RT/CT/MRI)

Deepa Jadav*, Nita D Gosai**, Dipika Patel**, Priyadarshini ***, Rajdip Kubavat*** Bipin M Patel****

Abstract

Introduction: Interaction with medical providers is stressful experience for children. Because of this stress and the anxiety, minor procedures often require mild to moderate sedation. Sedation of the paediatric patient is a process carefully planned by the anaesthesia provider while maintaining the heart rate, respiration & oxygen saturation levels at the patient's baseline values. **Methodology:** We studied 80 patients of either sex aged 2-10 years of ASA grade-1 and 2, undergoing Radiation therapy, CT Scan and MRI. They were randomly allocated in two groups 40 each to compare the efficacy, safety, and tolerability of inj. Ketamine - Midazolam combination to inj. Fentanyl - Midazolam combination for sedation of children during Radiation Therapy (RT)/Computerised Tomography Scan (CT Scan)/Magnetic Resonance Imagine(MRI). Both the groups were given IV inj. Midazolam 0.05 mg/kg before giving IV inj. Ketamine 1 mg/kg in group 1 while IV inj. Fentanyl 2 µg/kg in group 2. Result: In both groups after giving sedation, there were no significant changes in heart rate. Degree of sedation was better in group I than in group II. Recovery from sedation was more prolonged in group 1 than in group 2. **Conclusion:** It was found that inj. Ketamine-Midazolam combination offers good sedation without compromising respiration but more prolonged recovery and higher incidence of post procedural vomiting, while inj. Fentanyl-Midazolam combination has lower sedation score and higher incidence of respiratory depression.

Key Words : Fentanyl, Ketamine, Midazolam, Paediatric procedural sedation

Introduction

MRI & CT Scan; non-invasive radiographic tests, are used to aid the diagnosis of diseases abnormalities. It requires a cooperative & immobile patient. Sedation of the paediatric patient is a process carefully planned by the anaesthesia provider [1] while maintaining the heart rate, respiration & oxygen saturation levels at the patient's baseline values.

Goals of sedation in the paediatric patient for diagnostic and therapeutic procedures are defined as: guard the patient's safety and welfare, minimize physical discomfort and pain, control anxiety, minimize psychological trauma and maximize the potential for amnesia, control behaviour and/or movement to allow the safe completion of the procedure, less side effects, shorter recovery time and return the patient to a state in which safe discharge from medical supervision, as determined by recognized criteria, is possible.[2]

* Assistant Professor, Department of Anaesthesia, GCS Medical College Hospital & Research Centre
** Associate Professor
*** Resident
****Professor & Head, Department of Anaesthesia, Gujarat Cancer Research Institute, New Civil Hospital, Ahmedabad, Gujarat, India

This study was therefore designed to compare the inj. Ketamine Midazolam & inj. Fentanyl Midazolam for sedative procedures in paediatric patients.

Methodology

80 paediatric patients ranging from 2-10 years of age and from both sex undergoing RT, CT Scan, MRI. Patients were assessed pre operatively through history and clinical examination. Investigations were carried out and analysed. Only patients belonging to ASA 1 and 2 were selected for the study. We exclude the patients having following features; (1) Children ≤ 1 year of age (2) Significant medical co-morbidities (3) Patients having known allergy to study drugs (4) Airway abnormalities (5) Congenital anomalies. After obtaining institutional ethical board approval, written informed consent was obtained from 80 paediatric patient's parents and were placed in two different groups (40 in each group)

Group 1: Receives IV inj. Midazolam 0.05 mg/kg + inj. Ketamine 1 mg/kg while Group 2: Receives IV inj. Midazolam 0.05 mg/kg + inj. Fentanyl 2 µg/kg. Patients were kept NBM for 5 hours. On arrival of patient in the procedure room, patient's baseline heart rate, respiratory rate and oxygen saturation was

recorded. The resuscitation cart was brought to bedside. Oral airway, bag valve mask and suction made immediately available. After securing venous access inj. Glycopyrrolate 0.004mg/kg and inj. Midazolam 0.05 mg/kg was given IV slowly over 1-2 minutes in both groups. After 3 minutes, this was followed by IV Ketamine 1 mg/kg (1-2 mg/kg) in group 1, while IV Fentanyl 2µg/kg (1-3 µg/kg) in group 2 slowly over 1-2 minutes. Vital signs, SpO2, sedation score and recovery time were recorded every 5 min during procedure and for 15 min after until ensuring that they were fully awake, coherent and able to tolerate oral food. Patients who could not remain immobile after giving recommended doses, another 1mg/kg incremental dose of ketamine and 1µg/kg incremental dose of fentanyl was given in patients of group 1 and group 2 respectively. If patients still remain mobile inj. ketamine 0.5mg/kg was given as rescue drug for group 2 patients. Sedation score was assessed using Ramsay sedation scale described by Michael A.E. Ramsay which was as below: [3]

1. Anxious and agitated or restless or both
2. Co-operative, oriented and calm
3. Responsive to commands only
4. Exhibiting brisk response to light glabellar tap or loud auditory stimulus
5. Exhibiting a sluggish response to light glabellar tap or loud auditory stimulus
6. Unresponsive

Transient desaturation was defined as SpO_2 <90%. Supplemental oxygen was given to any patient with an oxygen saturation <90% that did not respond to any airway repositioning or suction. Recovery time was defined as the time that elapsed from when the last dose of medication was given to when the patient returned to his or her baseline sensorium. The patient's recovery from sedation was judged by muscle activity, respiration, circulation. [4] Patients able to move all four limbs, able to breathe deeply and/or cry and cough and able to follow oral commands consider recovered from sedation. Written and verbal after-care instructions are given to the patient's caregiver prior to discharge. Data calculation and p value calculation is done by unpaired t-test using SPSS software.

Results

The present study includes 80 paediatric patients belonging to ASA group 1 and 2 undergoing RT, CT Scan, MRI requiring sedation. They were randomly

Table 1: Demographic Data: age, sex and weight distribution of study participants

Group Mean± S.D.	Age(years) Mean ± S.D.	Weight(kg) M:F	Sex procedure (min)	Duration of
Group 1(n=40)	3.8±1.8	11.7±2.574	25:15	8.575±11.349
Group 2(n=40)	3.925±1.716	12.088±2.736	26:14	8.75±6.262

Table 1 shows there was no significant difference in the parameters mentioned above in both the groups.

Table 2: Comparison of Heart Rate in both groups

Time Interval Mean± S.D.	Group 1 (n=40)bpm Mean± S.D.	Group 2 (n=40)bpm
Baseline	110.7±10.13	109.1±10.71
5min	111±8.55	109.6±9.831
15min	111.5±6.699	108.9±9.932
30min	107.8±6.648	107.3±8.098
45min	107.45±7.249	106.4±7.121

P < 0.05: significant, P >0.05: Not Significant

Table 3: Comparison of Sedation Score in both groups

Variables	Group 1 (n=40) Mean± S.D.	Group 2 (n=40) Mean± S.D.
Sedation score	5.025±0.946	3.575±1.083

P < 0.05: significant, P >0.05: Not Significant

Table 4: Comparison of Recovery Time in both groups

Variables	Group 1 (n=40) Mean± S.D.	Group 2 (n=40) Mean± S.D.
Recovery time	28.525±3.558	18.95±4.212

P < 0.05: significant, P >0.05: Not Significant

Table 5: Comparison of side effects in both groups

Side effect	Group 1 No. of pt. (%)	Group 2 No. of pt. (%)	Total No. of pt. (%)
None	36 (90%)	35 (87.5%)	71 (88.75%)
Respiratorydepression	1 (2.5%)	4 (10%)	5 (6.25%)
Nausea/vomiting	3 (7.5%)	1 (2.5%)	4 (5%)
Total	40 (100%)	40 (100%)	80 (100%)

assigned into two groups of 40 each. All the patients were given the drug according to methodology of our study.

Group 1: Receives IV Inj. Midazolam 0.05 mg/kg + Inj. Ketamine 1 mg/kg

Group 2: Receives IV Inj. Midazolam 0.05 mg/kg + Inj. Fentanyl 2 mcg/kg

Discussion

There is often heavy demand for paediatric sedation services throughout the usual work day as well as off hours, and these cases must be performed in a wide variety of locations involving many different services, including radiology, dentistry, paediatric inpatient service, emergency department, and nuclear medicine.[5] The major goals of paediatric procedural sedation may vary with the specific procedure, but generally encompass anxiety relief, pain control, and control of excessive movement.[6]

Sachdeva et al. [7] studied Ketamine-Midazolam & Fentanyl-Midazolam for sedation & analgesia in children for out Patient Basis procedures. The dose of Ketamine was 1mg/kg (R = 0.5-5mg/kg). The complications were airway malalignment (3 cases), transient apnea (1 case). There were no sequelae. Emesis was reported in 1 patient. 1 child was agitated on recovery. Fentanyl 2µg/kg and midazolam 0.1 mg/kg. 2 children had hypoxia, which responded to oxygen therapy & found that Ketamine can be administered safely, is effective, preserves protective airway reflexes & has a wide margin of safety. One should be careful about the position of airway. FM can be safely administered for procedures with appropriate monitoring. It is very effective, has a good safety profile & also very cost effective.

We used IV inj. Midazolam 0.05mg/kg combined with inj. Ketamine 1mg/kg and inj. Midazolam 0.05mg/kg combined with inj. Fentanyl 2 mcg/kg in our study. As MRI has longer duration patients were given supplemental dose of ketamine 1mg/kg. In our study, 3 patients of group 2 need rescue drug- inj. ketamine 1mg/kg IV and 1 patient in group 2 was given incremental dose of IV inj. fentanyl 1µg/kg, Despite this patient was not remain immobile & rescue drug IV inj. Ketamine 1 mg/kg was given. In our study 10% patient of group 2 needed rescue drug.

Roback et al [8] compared the frequency and severity of adverse events associated with parenteral drugs commonly used for procedural sedation and analgesia (PSA) in a pediatric emergency department. They used four major drug combinations: ketamine alone, ketamine/midazolam, midazolam/fentanyl, and midazolam alone & conclude that drug types used in pediatric PSA are associated with different adverse event profiles. Patients receiving ketamine with or without midazolam experienced fewer respiratory adverse events but more vomiting than the commonly used combination of midazolam and fentanyl. Adverse events may occur in any patient receiving parenteral PSA. We observed our patients for 45 minutes after procedure and found that the decrease oxygen saturation was in 10% patients of group 2 and approximately 2.5% patients of group 1within 5 minutes of sedation. Muniz et al. [9] compared two conscious sedation drug regimens, ketamine versus opioid/midazolam for conscious sedation in children in the emergency department. They used Ketamine in 67 (56.7%) procedures, with average dose 1.2±0.4 mg/kg (range 0.8 - 3.1 mg/kg). Midazolam was given in 21 (31.3%) procedures. There were 4 (5.9%) patients with respiratory rate less than 12 per minute, and 5 (7.4%) patients required supplemental oxygen. Average sedation score was 2.8±1.0, which was lower (more sedated) than that of the opioids/midazolam group (P<.05). Mean recovery time was 24.0±14.4 minutes. There was no difference between the ketamine group and opioid/midazolam group in recovery time. Fentanyl or morphine plus midazolam were used in 51 (36.9%) procedures. Fentanyl was used in 12 (23.5%) procedures, with an average dose of 1.3±0.5 µg/kg (range 0.4 - 3.2 µg/kg). Morphine was used in 39 (76.4%) procedures, with an average dose of 0.13±0.06 mg/kg (range 0.02 - 0.3 mg/kg). Midazolam was used with an average dose of 0.08±0.04 mg/kg (range 0.02 - 0.23 mg/kg). There were 4 (7.8%) patients with RR < 12 per minute, and 2 (3.9%) patients required supplemental oxygen administration. Average sedation score was 3.5±0.9. Mean recovery time was 22.0±12.3 minutes. They concluded that ketamine was used more often in younger children than opioid/midazolam and resulted in a deeper sedation score but no difference in total recovery time.

In our study, IV Inj. midazolam + ketamine provide higher sedation score (5.025±0.946) compared to IV Inj. midazolam + fentanyl (3.575±1.083). Recovery time was approximately 1.5 times longer in IV inj. midazolam + ketamine group than in IV inj. midazolam + fentanyl group. Remadevi [10] used Midazolam and Ketamine by oral route as premedicants in pediatric anesthesia. Ketamine (6 mg/kg) p.o. and Midazolam (0.5 mg/kg)] p.o. given. Heart rate, arterial pressure, respiratory rate, sedation score, anxiolysis score were notes before drug administration, 15 min and 30 min after drug administration. Parental separation score at 30 min and mask acceptance score were also noted. They observed that sedation score, anxiolysis score and mask acceptance score were significantly higher in Group-K than in Group-M (p<.05). Hemodynamic parameters, parental separation and drug acceptance were similar in both groups. In our study there were no significant changes in heart rate in both groups. No evidence of any convulsion or laryngospasm was seen in any of the patients in any group in our study.

Conclusion

It was concluded that midazolam-ketamine combination offers good sedation without compromising respiration but more prolonged recovery and higher incidence of post procedural vomiting, while midazolam-fentanyl combination has lower sedation score and higher incidence of respiratory depression.

References

1. WCW Chu, WWM Lam, Sedation of paediatric patients undergoing magnetic resonance imaging examination: A clinical Audit J HK Coll Radiol 2002;5:176-182
2. Anaesthesia or sedation for MRI in children Leonie Schulte-Uentrop and Matthias S. Goepfert Current Opinion in Anaesthesiology 2010,23:513 517
3. Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedation with alphaxalone-alphadolone. Br. Med.J.1974; 2:656-659.
4. J. Antonio Aldrete, M.D. Diane Kroulik, M.D. Denver, Colorado A: Postanesthetic Recovery Score Anesthesia and analgesia. Current Researches Vol. 49, No. 6, Nov.-Dec., 1970.
5. Joseph P. Cravero & George T. Blike, Review Articles, review of paediatric sedation , Anesth Analg 2004, 99: 1355-64
6. S. Malviya, T. Voepel-Lewis, O.P. Eldevik, D.T. Rockwell, Br J Anaesth 84(6): 743-8 (2000)
7. Sachdeva, S. Gupta, S.P. Yadav , D. Gupta, A. Soni, and C. Palta Safety of Ketamine-Midazolam [KM] & Fentanyl-Midazolam [FM] Sedation for Pediatric Procedures on Out Patient Basis Presented at SIOP XXXIV meeting Medical & Pediatric Oncology 2002; 39:406
8. Roback MG, Wathen JE, Bajaj L, Bothner JP. Adverse events associated with procedural sedation and analgesia in a pediatric emergency department: a comparison of common parenteral drugs. Acad Emerg Med. 2005 Jun; 12(6):508-13.
9. A.E. Muniz, C. Woleben, R.L. Foster, S. Bartle Ketamine versus opioids and midazolam for conscious sedation in children in the emergency department Annals of Emergency Medicine Volume 44, Issue 4, Supplement , Pages S57-S58, October 2004
10. Remadevi R, Ezhilarasu P, Chandrasekar L J, Vasudevan A: Comparison of Midazolam and Ketamine as Oral premedicants in pediatric patients Journal of Anesthesiology;2009, Vol. 21 Issue 2, p5