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A study of injection Midazolam, ketamine and combination of both as premeditation in pediatric surgeries: A tertiary care teaching hospital study.

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Keywords:
Premeditation, Pediatrics surgeries, Ketamine, Midazolam.

Abstract:
Background: The pediatric surgeons deal with the congenital anomalies, trauma, tumors, major surgical infections, antenatal diagnosis and counseling related to various sub specialties such as Pediatric neurosurgery, thoracic, urology, plastic, gastrointestinal, traumatology, oncology, and neonatal surgery including many others belonging to man's land from newborn stage to 14 or sometimes even 18 years of age. In 1960s, there was an enormous challenge to operate upon children.
Aims and Objectives: To Assess and compare the Midazolam, ketamine and combination of both as premeditation in pediatric surgeries in our tertiary care hospital.
Materials And Methods: A total of 52 children were enrolled. Only children less than 12 years and more than 2 years of age were included. Complete demographic and clinical details of all the subjects was recorded. Inclusion criteria for the present study included children undergoing orthopedic, pediatric, ophthalmic or plastic surgery lasting for 40 minutes to 150 minutes. Thorough pre-treatment examination of all the patients was carried out. Random division of all the patients was done into two study groups as follows:Group 1: 25 pediatric patients subjected to Intranasal Midazolam (0.2 mg/kg), and Group 2: 25 pediatric patients subjected to Intranasal Midazolam (0.15 mg/kg) with Ketamine [1 mg/kg].
Results and Observations: Among group 1, there were 14 boys and 12 girls while among group 2, there were 16 boys and 10 girls. Significant results were obtained while comparing the level of sedation at 20 minutes. While comparing the emotional reaction at 20 minutes in between the two study groups, significant results were obtained. Mean onset time of sedation among patients of group 1 and group 2 was 10.95 minutes and 10.08 minutes respectively. Mean postoperative recovery time was 22.12 minutes and 29.23 minutes respectively. Postoperative analgesic requirement was seen in 64 percent of the patients of group 1 while it was seen in 16 percent of the patients of group 2.
Conclusion: Children can be sedated quickly and predictably with intranasal premedication. The midazolam plus ketamine group considerably provides superior analgesia, sedation, and comfort.

Introduction: The pediatric surgeons deal with the congenital anomalies, trauma, tumors, major surgical infections, antenatal diagnosis and counseling related to various sub specialties such as Pediatric neurosurgery, thoracic, urology, plastic, gastrointestinal, traumatology, oncology, and neonatal surgery including many others belonging to man's land from newborn stage to 14 or sometimes even 18 years of age.[1- 3]In 1960s, there was an enormous challenge to operate upon children. To administer intravenous fluid a venous cut down was mandatory for insertion of a plastic cannula. It was difficult to get the right sizes of endotracheal tubes to anesthetize the child. It was even more challenging to find anesthetists who were confident and knowledgeable about pediatric anesthesia.[4, 5] Not only is it possible to avoid general anesthesia and its related risks, such as unpredicted difficult airway management, cardiovascular collapse and malignant hyperthermia,

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but it is especially important in low resource settings, where keeping spontaneous breathing and avoiding general anesthesia might reduce patient's morbidity and mortality rate. Ketamine is an anesthetic agent widely used for pediatric sedations in many settings where its safety and efficacy has been extensively reviewed.[6,7] Hence; the present study was conducted for comparatively evaluating between Midazolam Ketamine and combination of both as premedication.

Materials And Methods: The present study was conducted in the department of Anaesthesiology of R D Gardi Medical College Ujjain, Madhya Pradesh, India, for comparatively evaluating between Midazolam, Ketamine and combination of both as premedication in pediatric surgeries. A total of 52 children were enrolled. Only children less than 12 years and more than 2 years of age were included. Complete demographic and clinical details of all the subjects was recorded. Inclusion criteria for the present study included children undergoing orthopedic, pediatric, ophthalmic or plastic surgery lasting for 40 minutes to 150 minutes. Thorough pre-treatment examination of all the patients was carried out. Random division of all the patients was done into two study groups as follows: Group 1: 25 pediatric patients subjected to Intranasal Midazolam (0.2 mg/kg), and Group 2: 25 pediatric patients subjected to Intranasal Midazolam (0.15 mg/kg) with Ketamine [1 mg/kg]. Two ml syringes were used for giving premedication. For around thirty minutes, the patients were observed preoperatively, intraoperatively and postoperatively. Haemodynamic variables were recorded. Induction ofgeneral anaesthesia was done with sevoflurane (six percent) and air and oxygen (ratio of sixty to forty). Tracheal intubation was done. Paracetamol was used for providing postoperative analgesia. Sedation scale adapted from Wilton and Colleagues was used for estimation of sedation score. Findings were recorded in Microsoft excel sheet followed by statistical analysis using SPSS software.

Results and Observations:
Among group 1, there were 14 boys and 12 girls while among group 2, there were 16 boys and 10 girls. Mean age of the subjects of group 1 and group 2 was 6.35 years and 7.12 years respectively. Mean weight of the subjects of group 1 and group 2 was 17.2 Kg and 17.9 Kg respectively. At 20 minutes, level of sedation was drowsy in 64 percent of the patients of group 1 while it was present in 56 percent of the patients of group 2. Significant results were obtained while comparing the level of sedation at 20 minutes. While comparing the emotional reaction at 20 minutes in between the two study groups, significant results were obtained. Mean onset time of sedation among patients of group 1 and group 2 was 10.95 minutes and 10.08 minutes respectively. Mean postoperative recovery time was 22.12 minutes and 29.23 minutes respectively. Postoperative analgesic requirement was seen in 64 percent of the patients of group 1 while it was seen in 16 percent of the patients of group 2.

Table 1: Demographic data

Variable	Group 1	Group 2
Mean age (years)	6.35	7.12
Mean weight (Kg)	17.2	17.9
Boys (n)	14	16
Girls (n)	12	10

Table : 2 Level of sedation at 20 minutes

Score	Group 1		Group 2	
	Number	Percentage	Number	Percentage
Agitated	1	4	0	0
Alert	3	12	1	4
Calm	5	20	10	40
Drowsy	17	64	15	56
Asleep	0	0		
p- value	0.0012 (Significant)			

Table: 3 Emotional reaction at 20 minutes

Score	Group 1		Group 2	
	Number	Percentage	Number	Percentage
Crying	2	8	0	0
Apprehension	18	68	5	20
Calm	6	24	21	80

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p- value	0.0001 (Significant)

Table 4: Comparison

Variables	Group 1	Group 2	p- value
Onset time of sedation (minutes)	10.95	10.08	0.129
Postoperative recovery time (minutes)	22.12	29.23	0.017 (Significant)
Postoperative analgesic requirement	64 percent of patients	16 percent of patients	0.006 (Significant)

Discussion:

Any clinical defect in children that necessitates invasive operations, excision, and wound closure is classified as a pediatric surgical disorder. Surgically treatable diseases account for roughly 28–30% of the worldwide illness burden. Around 67% of children and adolescents who require medical assistance around the world do not have timely access to surgical care. In addition, death from postoperative complications was on the rise among children and adolescents. Congenital malformations, injuries, cancer-related illnesses, gastrointestinal conditions, particularly appendicitis, and intussusceptions were the most common reasons for pediatric surgical admissions. Surgical disorders that necessitate surgical and conservative therapy contribute significantly to the worldwide burden of mortality and morbidity rates, and this burden is exacerbated in economically impoverished countries. Even though children make up nearly half of a developing country's population, there is a slight focus on childhood surgical disorders, with attention instead being given to communicable disease and obstetrics care.[6- 9]Currently, there is a wide variation on the choice of sedating drugs for children in different disciplines and in different parts of the world. Midazolam and ketamine are among those most commonly used sedatives, either alone or in combination. Midazolam is a short-acting benzodiazepine for sedation without analgesia. It also provides anxiolysis and amnesia. Ketamine is a phencyclidine derivative that induces rapid and profound sedation, analgesia, and amnesia. In contrast to benzodiazepines and narcotics, protective airway reflexes are maintained during sedation with ketamine, with minimal cardiovascular and respiratory side effects.[10, 11]Hence; the present study was conducted for comparatively evaluating between Midazolam, Ketamine and combination of both as premedication in pediatric surgeries. Among group 1, there were 13 boys and 12 girls while among group 2, there were 15 boys and 10 girls. Mean age of the subjects of group 1 and group 2 was 6.35 years and 7.12 years respectively. Significant results were obtained while comparing the level of sedation at 20 minutes. While comparing the emotional reaction at 20 minutes in between the two study groups significant results were obtained. Mean onset time of sedation among patients of group 1 and group 2 was 10.95 minutes and 10.08 minutes respectively.In a previous study conducted by Cheuk DKet al, authors evaluated efficacy and adverse effects of intravenous midazolam and ketaminein pediatric ward setting.Altogether, 369 minor operations were performed in 112 patients. All achieved adequate sedation, with 96% within 30 s and 75% required just the starting dose. Younger children required a higher dosage. The median recovery time was 87 min, with no association with age, sex, or dosage of sedation, but was longer in patients having hallucination (p=0.001). Adverse effects included tachycardia (27.9%), increased secretion (17.6%), agitation (13.6%), nausea and vomiting (9.2%), hallucination (8.7%), desaturation (8.4%), and cataleptic reaction (0.8%). Half of the children who received 0.3 mg/kg midazolam developed desaturation.Intravenous midazolam-ketamine can provide rapid, effective, and safe sedation for children undergoing minor operations in ward setting.[12] Mean postoperative recovery time was 22.12 minutes and 29.23 minutes respectively. Postoperative analgesic requirement was seen in 64 percent of the patients of group 1 while it was seen in 16 percent of the patients of group 2.In another similar study conducted by Narendra PL et al, authorscompared the efficacy and side-effects of Ketamine and Midazolam administered nasally for the pediatric premedication.50 children were evaluated for nasal ketamine (using 50 mg/ml vials) at the dose of 5 mg/kg and the other 50 received nasal midazolam 0.2 mg/kg. Midazolam showed a statistically significant early onset of sedation. Significant tachycardia and ‘secretions were observed in the ketamine group intra operatively. Postoperatively emergence (8% vs. 0%) and secretions (28% vs. 4%) were significant in the ketamine group. Nausea and vomiting occurred in l6% versus 10% for midazolam and ketamine group.Both midazolam and ketamine nasally are an effective pediatric premedication.[13]Safety of intranasal (IN) ketamine and midazolam as premedication in children was compared in another pervious study by Khoshrang H et al.Recovery time was significantly longer in group K (ketamine) compared to group M (midazolam) 27.86±4.42 vs 38.19± 6.67 minutes respectively (P=0.01). No significant difference was observed in terms of sedation score between two groups of K & M; 3.29±0.78 vs 3 ±0.71

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www.jchr.org
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respectively (P=0.17), and not regarding separation score; 2.51±0.61 & 2.31±0.52 respectively (P=0.01). Vital signs were kept within the physiological limits in both groups with no marked fluctuations.To produce sedation in young children, both midazolam and ketamine were effective and safe by IN route.[14]

Conclusion:
From the above results, the authors conclude that children can be sedated quickly and predictably with intranasal premedication. The midazolam plus ketamine group considerably provides superior analgesia, sedation, and comfort

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