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Original article

Sedative and analgesic effects of midazolam added to fentanyl or ketamine in paediatric day-case orthopaedic procedures

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Abstract

Background: Simple fractures and joint dislocations recruited for this study are among the painful procedures managed in the Emergency Room setting in children. Successful management requires adequate sedation for the relief of anxiety and analgesia for pain relief.

Aim: To compare the sedative and analgesic effects of fentanyl/midazolam (F/M) and ketamine/midazolam (K/M) combination during paediatric day-case orthopaedic procedures.

Methodology: A prospective randomized double-blind trial that involved 70 paediatric patients aged 5-12 years requiring orthopaedic procedures. The patients were randomized into two groups of 35 each. The F/M group received an intravenous (IV) bolus of fentanyl 0.5 μg/kg while the K/M group received an IV bolus of ketamine 0.5 mg/kg. The outcomes were procedural distress and anxiety from the Observational Scale of Behavioural Distress revised (OSBD-r) score, depth of sedation during and up to 120 minutes after the procedure using the Ramsay Sedation Scale (RSS), and pre-sedation and post-procedure pain scores up to 120 minutes after the procedure according to the Wong-Baker Faces Pain Scale (WBFPS) for children within the age range of 5-7 years and the Numerical Rating Scale (NRS) for children within the age range of 8-12 years.

Results: The proportion of children with severe pain was 75.3% in the F/M group compared with 68.6% in the K/M group, which occurred at baseline. Depth of sedation at baseline, every 5 minutes up to 25 minutes during the procedure and at 60 and 90 minutes post-procedure was similar. However, a significant difference was found at 30 minutes post-procedure: 12 (34.3%) K/M subjects achieved an RSS score of 1 compared to 3 (8.6%) in the F/M group, while 32 (91.4%) in the F/M group achieved an RSS of 2 compared to 21 (60.0%) among K/M subjects. During the procedure, there was a significantly lower level of OSBD-r score among K/M subjects compared with F/M subjects. No statistically significant differences were found in WBFPS and NRS scores.

Conclusion: K/M achieved better sedation and pain relief than F/M.

Keywords

Paediatric sedation, fentanyl, ketamine, fracture reduction, day case.

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Background

Procedural sedation and analgesia are important components of paediatric emergency care [1]. In the paediatric population, procedural care can be compromised even in the presence of their parents following a lack of cooperation as a result of the pain from the procedure and the inadequate analgesia given during painful medical procedures [1].

The goals of sedation in a paediatric patient for diagnostic and therapeutic purposes include: guiding the patient's safety and welfare, minimizing physical discomfort and pain, controlling anxiety, minimizing psychological trauma and maximizing the potential for amnesia, controlling behavior and movement to allow safe completion of the procedure and to return the patient to a level where discharge from medical supervision is possible [2].

Fracture reduction is one of the most painful procedures in the Emergency Department. Patients and families expect the Emergency Department to be a resource for relieving many of these pains [3]. Health care providers who care for children are found with the sometimes divergent task of providing effective analgesia and anxiolysis while ensuring timely, efficient, cost-effective, and safe care of the patient. The potential benefits of effective sedation during fracture reduction include diminished patient fear and discomfort in parents, provider and patient's satisfaction, decreased utilization of resources, improved outcome of fracture reduction and reduced reliance on general anaesthesia [2]. Several studies have documented that children receive inadequate analgesia during their visit to the Emergency Department [3]. Furthermore, there has been a wide variation in sedation practice partly because little consensus exists on the safest and most effective regimen [4].

Sedation during medical procedures involving the use of ketamine or fentanyl in association with midazolam has been shown to provide a reduction in side effect profile, enhancing short recovery time, increase the level of sedation, stable haemodynamic parameters and reduction of observational distress and anxiety of both the patients and parents. Few international studies have compared the sedative and analgesic effects of fentanyl and ketamine with a midazolam combination for paediatric orthopedic reduction [5-7]. There is a paucity of local studies using these drugs, although the pain in the paediatric population following trauma has been reported [8]. There is a dearth of knowledge regarding this study area, hence the reason for the present study [1-31].

Methods

The prospective study was conducted among 70 patients between the ages of 5-12 years scheduled for day-case at the Emergency Department of University College Hospital (UCH), Ibadan, Nigeria, from February 2022 to August 2022. The ethical approval for this study was obtained from the University of Ibadan (UI)/UCH Ethics Committee (UI/EC/20/0561). Consent to participate in the study was obtained from the parent/guardian of the children.

The study was a randomized controlled, double-blind trial of two groups of paediatric patients with limb fractures scheduled for closed reduction of fracture in the Emergency Department under sedation in the UCH, Ibadan. The type of orthopedic procedure are manipulation under anaesthesia, close reduction, and application of Plaster of Paris. The patients were grouped into two groups, i.e., fentanyl/midazolam (F/M) group and ketamine/midazolam (K/M) group. One group received intravenous (IV) F/M (0.5 µg/kg / 0.1 mg/kg, respectively) and the other group received IV K/M (0.5 mg/kg / 0.1 mg/kg, respectively). The sample size was calculated using the modified Kirkwood formula for two independent groups of 10:

$$N = \frac{2\,\delta^2(Z_{(1-\alpha/2)} + Z_{(1-\beta)})^2}{\Delta^2}$$

The inclusion criteria were paediatric patients with American Society of Anaesthesiologist (ASA) status 1 or 2 and paediatric patients aged 5-12 years who were scheduled for day-case emergency fracture reduction procedure, while the exclusion criteria were patients with cardiovascular disorders, respiratory diseases, previous opioid use or non-prescribed narcotic drug use within 6 hours of the procedure, adverse reaction to the study drugs (ketamine, fentanyl, or midazolam) and those with cognitive impairment. Independent outcomes were the level of distress and anxiety in the two groups during the procedure, measured using the Perioperative score of the Observational Scale of Behavioural Distress revised (OSBD-r) score, while the dependent outcomes were the depth of perioperative sedation (Ramsay Sedation Scale [RSS] scores) attained during and after the procedure and pain scores (Numerical Rating Scale [NRS] scores and Wong-Baker Faces Pain Scale [WBFPS] scores) before sedation and every 30 minutes up to 120 minutes post-procedure.

Ramsay Sedation Scale

RSS is a simple scale that allows a numeric score of a patient's sedation level from 1 (RSS 1) to 6 (RSS 6) based on the responsiveness of the patient. This sedation scale helped to rate the patient's level of sedation into 6 categories, ranging from severe agitation (RSS 1) to deep coma (RSS 6).

Numerical Rating Scale

In the NRS, the respondent provides his or her feedback in terms of numerical values. The pain rating scale was used for patients between the age of 8-12 years. The NRS did not include any line but was administered as a script asking the child to rate his or her pain from 0 to 10. Patients were asked to circle the number between 0 and 10 that fits best to their pain intensity. Zero represented "no pain at all", whereas 10 represented "the worst pain ever possible".

Wong-Baker Faces Pain Rating Scale

The WBFPS is a pain rating scale that was used in this study for pain assessment in children within the age range of 5-7 years. The scale consists of a series of faces ranging from a happy face at 0, or "no hurt", to a crying face at 10, which represents "hurts like the worst pain imaginable". Based on the faces and written descriptions, the patient chooses the face that best describes their level of pain.

The similarity, between NRS and WBFPS, is that they both utilize numbers to rate pain intensity, while the key difference between the two pain scales is that NRS relies solely on numbers to communicate pain and does not include facial expression while WBFPS does.

Study procedure

A study proforma was used to collect information on the socio-demographic data such as age, weight, height, body mass index (BMI), gender, ethnicity, fracture type, parent's phone numbers, ASA classification, allergies, medications administered to the patient with doses, time of drug administration, procedure time, reduction time, pain scores. Interventions, haemodynamic changes, and adverse effects during the procedure and post-procedure were all recorded in the proforma, and time to onset of sedation, sedation duration, and recovery times were also assessed and compared.

The investigator visited the patient before the procedure for a detailed history taking. A general and systemic examination of all systems was done, including measuring of patient's weight.

The investigator explained the study to each patient's parent before the commencement of the procedure. The patients in the age range 8-12 years were educated on the use of a NRS while the various faces on the WBFPS and how to match the varied faces to a corresponding level of pain was explained to the children within age 5-7 years. Patients were placed on *nil per oris* (2 hours for clear fluids, 4 hours for liquids, and 6 hours for solid food).

All patients received IV glycopyrolate and IV ondansetron as premedication at induction. The attending Anaethetist administered the study medication. Before the drug administration, each patient's weight communicated to the Pharmacist by the investigator earlier during the study was used by the Pharmacist to prepare the study drug for each patient based on the generated random numbers. The prepared drugs were then handed over to the attending Anaesthetist to administer.

Results

Seventy patients were recruited, and no patients dropped out of the study population. There were 41 (58.6%) males and 29 (41.4%) females in the study population. The mean age of the study population was 8.9 ± 2.8 years. **Tab. 1** shows that there was no significant difference in the two groups in terms

of gender distribution (p = 0.332), mean age (p = 0.100), weight (p = 0.369), height (p = 0.934), and BMI (p = 0.575).

Baseline characteristics of study participants are presented in **Tab. 2**.

Tab. 3 shows a comparison of the depth of sedation at baseline and 5-minute intervals during the procedure using RSS between children who received F/M and those who received K/M. At baseline, the proportion of children who had RSS 1 and those with RSS 2 was similar between the groups who received F/M and those who received K/M.

At 5 minutes into the procedure, those who had RSS 3 were 28 (80.0%) among those who received F/M, compared with 26 (74.3%) among those who received K/M. Those who had RSS 4 were comparable in the two study groups (5 [14.3%] in both the F/M group and K/M, respectively). None of the participants in the groups attained RSS 5 or RSS 6. The difference in depth of sedation at 5 minutes into the procedure was not statistically significant (p = 0.864).

At 10 minutes into the procedure, the proportion of children who were asleep and responsive to command only (RSS 3) was slightly higher amongst those who received F/M compared to those who received K/M: 28 (80.0%) for F/M and 23 (65.7%) for K/M, with no significant difference (p = 0.76).

At 15 minutes into the procedure, the proportion of children who had RSS 3 was slightly lower in the F/M group (23 [65.7%]) compared to the K/M group (28 [80.0%]), with no significant difference (p = 0.71). At this point, also, those who had RSS

Table 1. Comparison of demographic and clinical characteristics of patients in the fentanyl/midazolam (F/M) and ketamine/midazolam (K/M) groups.

		F/M group (n = 35)	K/M group (n = 35)	Total (n = 70)	Test statistics	p-value
Gender	**Male**	18 (51.4)	23 (65.7)	41 (58.6)	1.472	0.332
	Female	17 (48.6)	12 (34.3)	29 (41.4)		
Age group (years)	**5-7**	9 (25.7)	17 (48.6)	26 (37.1)	3.916	0.082
	8-12	26 (74.3)	18 (51.4)	44 (62.9)		
Mean ± SD (years)		9.4 ± 2.5	8.3 ± 3.0	8.9 ± 2.8	1.669	0.100
Weight (kg)		27.1 ± 6.1	28.8 ± 9.3	28.4 ± 7.5	0.905	0.369
Height (m)		1.3 ± 0.1	1.3 ± 0.2	1.3 ± 0.2	0.083	0.934
BMI (kg/m^2)		15.9 ± 1.5	16.2 ± 2.4	16.4 ± 2.3	0.564	0.575

Results shown as number (%) or mean ± SD.
BMI: body mass index; F/M: fentanyl/midazolam; K/M: ketamine/midazolam; SD: standard deviation.

Table 2. Comparing the baseline vital signs among the groups.

Baseline vital signs'	Statistics	F/M group (n = 35)	K/M group (n = 35)	Total (n = 70)	t-test	p-value
HR	**Mean ± SD**	94.9 ± 18.2	91.5 ± 15.7	92.2 ± 17.1	1.323	0.190
	Range	72-134	48-128	48-134		
SBP	**Mean ± SD**	108 ± 14.3	103 ± 10.6	105 ± 12.0	1.748	0.085
	Range	85-130	85-130	85-130		
DBP	**Mean ± SD**	58.9 ± 6.5	61.0 ± 6.6	60.0 ± 6.6	1.319	0.192
	Range	50-70	50-85	50-85		
MAP	**Mean ± SD**	75 ± 8.4	75 ± 7.2	75 ± 7.8	0.203	0.840
	Range	62-90	65-100	62-100		
SPO_2	**Mean ± SD**	98.8 ± 0.5	98.9 ± 0.5	98.8 ± 0.5	1.133	0.261
	Range	98-100	97-100	97-100		
RR	**Mean ± SD**	23.0 ± 4.1	22.6 ± 3.1	22.8 ± 3.6	0.461	0.646
	Range	20-30	15-28	15-30		
Temperature	**Mean ± SD**	36.3 ± 1.1	36.4 ± 0.3	36.3 ± 0.8	0.507	0.613
	Range	30.3-37	36-38	30.3-37.4		

DBP: diastolic blood pressure; F/M: fentanyl/midazolam; HR: heart rate; K/M: ketamine/midazolam; MAP: mean arterial pressure; RR: respiratory rate; SBP: systolic blood pressure; SD: standard deviation; SPO_2: oxygen saturation.

4 were comparable in both groups: 12 (34.3%) for F/M and 7 (20.0%) for K/M groups (p = 0.179).

At 20 minutes into the procedure, the number of patients who had RSS 3 were 11 (31.4%) and 10 (28.6%) for F/M and K/M groups, respectively. Those who had RSS 4 were similar in both groups: 24 (68.6%) in the F/M group and 25 (71.4%) in the K/M group (p = 0.794).

At 25 minutes into the procedure, 27 (77.1%) achieved RSS 4 in the F/M group and 30 (85.7%) achieved RSS 4 in the K/M group (p = 0.356).

So, there was no significant difference in depth of sedation between children who received F/M and those who received K/M at different time intervals during the procedure.

Time to achieve RSS 3 among the groups is presented in **Tab. 4**.

Tab. 5 shows a comparison of the depth of sedation after the procedure between children

Table 3. Comparison of depth of sedation (according to the Ramsay Sedation Scale [RSS]) at baseline and 5-minute intervals during the procedure between children who received fentanyl/midazolam (F/M) and ketamine/midazolam (K/M).

Time interval	Depth of sedation	Baseline	Time interval				
			5 mins	10 mins	15 mins	20 mins	25 mins
F/M group (n = 35)	RSS 1	32 (91.4)	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	RSS 2	3 (8.6)	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	RSS 3	0 (0.0)	28 (80.0)	28 (80.0)	23 (65.7)	11 (31.4)	8 (22.0)
	RSS 4	0 (0.0)	5 (14.3)	7 (20.0)	12 (34.3)	24 (68.6)	27 (77.1)
	RSS 5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	RSS 6	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
K/M group (n = 35)	RSS 1	32 (91.4)	2 (5.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	RSS 2	3 (8.6)	2 (5.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	RSS 3	0 (0.0)	26 (74.3)	23 (65.7)	28 (80.0)	10 (28.6)	5 (14.3)
	RSS 4	0 (0.0)	5 (14.3)	2 (5.7)	7 (20.0)	25 (71.4)	30 (85.7)
	RSS 5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	RSS 6	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Results shown as number (%).
F/M: fentanyl/midazolam; K/M: ketamine/midazolam; RSS: Ramsay Sedation Scale.

Table 4. Time to achieve Ramsay Sedation Scale (RSS) score 3 (RSS 3) among the groups.

	Statistics	F/M group (n = 35)	K/M group (n = 35)	Total (n = 70)	t-test	p-value
Time (minutes)	Mean ± SD	8.5 ± 4.2	8.5 ± 3.9	8.5 ± 3.9	0.00	1.000
	Range	3.0-19	3.0-17	3.0-19		

F/M: fentanyl/midazolam; K/M: ketamine/midazolam; SD: standard deviation.

Table 5. Comparison of depth of sedation (according to the Ramsay Sedation Scale [RSS]) after procedure between children who received fentanyl/midazolam (F/M) and ketamine/midazolam (K/M).

Time interval	Depth of sedation	Time interval			
		Immediately after the procedure	30 mins	60 mins	90 mins
F/M group (n = 35)	RSS 1	0 (0.0)	3 (8.6)	33 (94.3)	35 (100.0)
	RSS 2	7 (20.0)	32 (91.4)	2 (5.7)	0 (0.0)
	RSS 3	27 (77.1)	0 (0.0)	0 (0.0)	0 (0.0)
	RSS 4	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)
	RSS 5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	RSS 6	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
K/M group (n = 35)	RSS 1	0 (0.0)	12 (34.3)	32 (91.4)	34 (97.1)
	RSS 2	9 (25.7)	21 (60.0)	3 (8.6)	1 (2.9)
	RSS 3	24 (68.6)	2 (5.7)	0 (0.0)	0 (0.0)
	RSS 4	2 (5.7)	0 (0.0)	0 (0.0)	0 (0.0)
	RSS 5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	RSS 6	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Results shown as number (%).
F/M: fentanyl/midazolam; K/M: ketamine/midazolam; RSS: Ramsay Sedation Scale.

who received F/M and those who received K/M. Immediately after the procedure, those with RSS 2 were 7 (20.0%) in the F/M group compared to 9 (25.7%) in the K/M group. Those who had RSS 3 were higher (27 [77.1%]) among those who received F/M, compared with those who received K/M (24 [68.6%]). On the other hand, those who had RSS 4 were 2 (5.7%) among those who received K/M, compared with 1 (2.9%) among those who received F/M. At this time (immediately after sedation), none of the children in the two study groups, who received either K/M or F/M, returned to RSS 1. Hence, there was no significant difference in the depth of sedation between participants in the two study groups immediately after the procedure ($p = 0.657$).

At 30 minutes post-procedure, the number of children who had RSS 1 was lower among those who received F/M (3 [8.6%]) compared with the K/M group (12 [34.3%]). The number of children who had RSS 2 was higher (32 [91.4%]) among those who received F/M compared with children who received K/M (21 [60.0%]). The number of children who had RSS 3 was 2 (5.7%) in the K/M group and none in the F/M subjects. The depth of sedation 30 minutes after the procedure was better in the K/M subjects as more patients in this group were observed to attain RSS 1 compared to patients in the F/M group, with a statistically significant difference ($p < 0.001$).

At 60 minutes after the procedure, the majority of the children had RSS 1 (33 [94.3%] in the F/M group and 32 [91.4%] in the K/M group), while the remaining few had RSS 2 (2 [5.7%] in the F/M group and 3 [8.6%] in the K/M group). The depth of sedation 60 minutes after the procedure was similar, as a similar proportion of patients in the two groups were found to attain RSS 1 ($p = 1.000$)

At 90 minutes after the procedure, all the children 35 (100.0%) who received F/M were in RSS 1, and 34 (97.1%) who received K/M were in RSS 1. The depth of sedation at 90 minutes after the procedure was similar ($p = 1.000$).

During the procedure, there was a significantly lower level of OSBD-r score among K/M subjects compared with F/M subjects.

Using NRS and WBFPS, the children who had severe pre-sedation pain were 26 (74.3%) in the

Table 6. Comparison of mean pre-sedation and post-procedure pain scores (according to the Numerical Rating Scale [NRS] for children within the age range of 8-12 years and the Wong-Baker Faces Pain Scale [WBFPS] for children within the age range of 5-7 years) between children who received fentanyl/midazolam (F/M) and ketamine/midazolam (K/M).

Variable		F/M group (n = 35)	K/M group (n = 35)	Total (n = 70)	Test statistics	p-value
Pre-sedation pain scores	No pain (0)	2 (5.7)	3 (8.6)	5 (7.1)	2.413	0.500
	Mild pain (1-3)	1 (1.9)	4 (11.4)	5 (7.1)		
	Moderate pain (4-6)	6 (17.1)	4 (11.4)	10 (14.3)		
	Severe pain (7-10)	26 (74.3)	24 (68.6)	50 (71.4)		
Mean pre-sedation pain scores		7.45 ± 2.18	7.13 ± 2.81	7.30 ± 2.48	T-test, 0.121	0.665
30 minutes post-procedure	No pain (0)	13 (37.1)	13 (37.1)	26 (37.1)	2.293	0.557
	Mild pain (1-3)	9 (25.7)	6 (17.1)	15 (21.4)		
	Moderate pain (4-6)	13 (37.1)	14 (40.0)	27 (38.6)		
	Severe pain (7-10)	0 (0.0)	2 (5.7)	2 (2.9)		
Mean 30 minutes post-procedure pain score		3.6 ± 0.7	4.1 ± 1.6	3.9 ± 1.3	T-test, 1.141	0.260
60 minutes post-procedure	No pain (0)	11 (31.4)	18 (51.4)	29 (41.4)	3.680	0.157
	Mild pain (1-3)	22 (62.9)	14 (40.0)	36 (51.4)		
	Moderate pain (4-6)	2 (5.7)	3 (8.6)	5 (7.1)		
	Severe pain (7-10)	0 (0.0)	0 (0.0)	0 (0.0)		
Mean 60 minutes post-procedure pain score		2.2 ± 0.8	2.1 ± 0.9	2.1 ± 0.9	T-test, 0.359	0.721
90 minutes post-procedure	No pain (0)	22 (62.9)	24 (68.6)	46 (65.7)	5.558	0.067
	Mild pain (1-3)	13 (37.1)	7 (20.0)	20 (28.6)		
	Moderate pain (4-6)	0 (0.0)	4 (11.4)	4 (5.7)		
	Severe pain (7-10)	0 (0.0)	0 (0.0)	0 (0.0)		
Mean 90 minutes post-procedure pain score		1.2 ± 0.7	2.1 ± 0.4	1.6 ± 0.5	T-test, 1.953	0.070
120 minutes post-procedure	No pain (0)	31 (88.6)	31 (88.6)	62 (88.6)	0.000	1.000
	Mild pain (1-3)	4 (11.4)	4 (11.4)	8 (11.4)		
	Moderate pain (4-6)	0 (0.0)	0 (0.0)	0 (0.0)		
	Severe pain (7-10)	0 (0.0)	0 (0.0)	0 (0.0)		
Mean 120 minutes post-procedure pain score		1.0 ± 0.1	1.2 ± 0.5	1.0 ± 0.3	T-test, 0.380	0.713

F/M: fentanyl/midazolam; K/M: ketamine/midazolam.

F/M group compared with 24 (68.6%) in the K/M group; the difference was not statistically significant (p = 0.5) (**Tab. 6**). Six patients in the F/M group had moderate pain (17.1%) whereas 4 (11.4%) patients in the K/M group had moderate pain. Also, the mean pre-sedation pain score was similar among children in the F/M and K/M groups (7.45 ± 2.18 versus 7.13 ± 2.81, p = 0.665). The post-sedation pain scores in the two groups were comparable at 30 minutes post-procedure (p = 0.557), 60 minutes post-procedure (p = 0.157), 90 minutes post-procedure (p = 0.067), and at 120 minutes post-procedure (p = 1.000). The mean post-procedure pain scores at 30 minutes were similar in both groups: 3.6 ± 0.7 in the F/M group and 4.1 ± 1.6 in the K/M group (p = 0.260).

Discussion

The study aimed to compare the effects of F/M versus K/M in pediatric day-case orthopedic procedures regarding sedation depth, pain scores, recovery time, distress levels, anxiety. No significant difference was observed in hemodynamic parameters between the two groups, and both groups had similar pre- and post-sedation pain scores.

The majority of patients were male, consistent with the higher prevalence of fracture injuries in males [12-16]. Fracture/dislocation injuries were more common in children aged 8-12 years, in line with previous research findings [12, 17]. Children in the school-age group are particularly susceptible to injuries, with a significant portion resulting from road traffic accidents, at 50.0%. Falls and mechanical injuries follow closely, at 25.0%. The higher activity levels and tendency to explore, compounded by peer pressure and group play dynamics, contribute to their increased vulnerability to injuries compared to younger children [12].

Sedation depth during and after the procedure was comparable between the two groups, except for a lower sedation depth at 30 minutes post-procedure in the K/M group. Post-procedure pain scores and recovery time were similar in both groups, but the F/M group experienced significantly higher levels of OSBD-r score during the procedure.

These results are similar to those of other researchers [14, 18]. Kennedy et al. [14] found sedation depth to be similar in both F/M and K/M groups (87% vs 89%, respectively). Damle et al. [19] compared the effect of oral doses of ketamine and midazolam and also found sedation levels to be similar in the two groups (90% of patients in each group).

In the current study, there was no significant difference in the time taken to achieve RSS 3 between the F/M and K/M groups. Sedation depth during the procedure and immediately afterward was similar in both groups, but at 30 minutes post-procedure, more children in the K/M group reached a sedation level of RSS 1 compared to those in the F/M group, indicating better sedation depth with K/M at that time point, which is in line with previous studies [16, 24].

The duration of the procedure was similar in both groups. Previous studies have also found comparable sedation levels between K/M and F/M groups, with variations depending on factors like dosage and assessment timing [14, 19, 25, 26]. Comparisons with other studies [26-28] highlight differences in sedation depth and onset times, likely influenced by factors such as medication dosage, route of administration, and patient age.

Pain assessment using the NRS and WBFPS showed comparable pre- and post-procedure pain scores between the F/M and K/M groups, consistent with findings from other studies [12, 20]. Despite variations in pain assessment tools and medication dosages, relief of pain and anxiety was similar across different sedation protocols, as demonstrated by Godambe et al.'s study [29].

The current study shares similarities with previous research, such as Kennedy et al. [14], which found no difference in parental ratings of pain handling between groups receiving F/M and K/M. Barcelos et al. [30] also observed comparable outcomes between K/M and morphine/midazolam groups in terms of procedure time, satisfaction, and analgesia. Jamal et al. [17] noted no significant pain score difference between F/M and ketamine-only groups, similar to the current study's findings. Conversely, Akelma et al. [16] reported lower pain scores with ketamine/fentanyl due to their synergistic analgesic effect, contrasting with the present study's comparable pain scores between K/M and F/M groups. Cevik et al. [13] and Abdolrazaghnejad and Banaie [25] found lower pain scores in K/M groups, likely due to assessment during sedation, which could affect ketamine-administered patients' ability to judge pain accurately. Overall, while other studies have shown lower pain scores with K/M, the current study's similar pain scores may be attributed to the sedoanalgesic effect of fentanyl and the hypnotic/analgesic effect of ketamine.

In the current study, there was a slightly lower level of distress and anxiety observed in children who received K/M compared to those who received F/M during IV insertion and before sedation, although the

difference was not statistically significant. However, during the procedure, the K/M group exhibited significantly lower levels of distress and anxiety compared to the F/M group. This finding is consistent with previous research, including the Kennedy et al's [14] study, where children receiving K/M had significantly lower distress scores compared to those receiving F/M. Similar results were found in studies by Lee-Jayaram et al. [18], indicating a consistent trend of lower distress and anxiety with K/M administration.

Recovery agitation was comparable between the K/M and F/M groups in the current study. While some previous studies have reported a higher incidence of emergence agitation with K/M, the current study did not find a statistically significant difference. The incidence of emergence agitation was lower than that reported in some previous studies by Barcelos et al. [30] and Wathen et al. [31], suggesting that factors such as pre-sedation psychological preparation of children, as well as the specific orthopedic procedures performed may have influenced the lower agitation outcomes observed. The tranquil recovery environment provided may also have contributed to the reduced agitation seen in our study population. This discrepancy may also be attributed to variations in dosing regimens and patient populations across different studies. Despite the concurrent administration of midazolam intended to mitigate emergency agitation, the current study found that the incidence of agitation was not completely prevented. However, the incidence of emergence agitation was lower than that reported in some previous studies by Barcelos et al. [30] and Wathen et al. [31], suggesting that factors such as pre-sedation psychological preparation of children may influence agitation outcomes.

In the current study, the tranquil recovery environment might have contributed to the lower overall incidence of emergence agitation observed. While dizziness was more prevalent among children who received F/M, the difference was not statistically significant. This finding aligns with previous research, including Kennedy et al.'s study [14], which found a comparable incidence of dizziness between K/M and F/M groups. However, Kennedy et al.'s study [14] reported a slight increase in dizziness after 24 hours and 7 days post-procedure, which was not observed in the current study because our study was for 24 hours. This difference could be attributed to variations in follow-up protocols and patient monitoring between studies.

Finally, the success rate of procedures was similar in both study groups, with all fracture reductions and joint dislocation manipulations carried out successfully on the first attempt. This aligns with findings from previous studies of Jamal et al. [17] and Abdolraxhenjad and Banaie's [25], indicating comparable success rates between K/M and F/M groups during reduction procedures. The limitation of this study was that the bi-spectral index monitoring could have been used to provide a more objective measure of assessing the sedation level of the patients, but it was not used in this study because it was not available in our Centre.

Conclusion

The current study demonstrated that K/M and F/M provided adequate depth of sedation and pain control with stable haemodynamics. Recovery time and incidence of side effects were also comparable in the two groups; however, the level of distress and anxiety was significantly lower amongst patients who received K/M.

Abbreviations

ASA: American Society of Anesthesiologists
BMI: body mass index
DBP: diastolic blood pressure
F/M: fentanyl/midazolam combination
HR: heart rate
IV: intravenous
K/M: ketamine/midazolam combination
MAP: mean arterial pressure
NRS: Numerical Rating Scale
OSBD-r: Observational Scale of Behavioral Distress revised
RR: respiratory rate
RSS: Ramsay Sedation Scale
SBP: systolic blood pressure
SD: standard deviation
SPO_2: oxygen saturation
UCH: University College Hospital
UI: University of Ibadan
WBFPS: Wong-Baker Faces Pain Scale

Ethics approval

The study was approved by the institutional Ethical Committee of the University College Hospital and the College of Medicine, University of Ibadan.

Informed consent

All participants in this study gave voluntary written informed consent.

Declaration of interest

The Authors declare that there is no conflict of interest. This study did not receive any funding.

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