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Original Research Article

Comparative study of intravenous and oral midazolam in pediatric CT scans for non CNS pathology

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Abstract

Introduction: There has been a dramatic increase in the use of computed tomography (CT) scan to diagnose conditions and to monitor treatment in the pediatric setting. Infants and children require sedation during procedure to maintain a motionless state to ensure high quality imaging.
The target sedation depth required depends on imaging procedure and individual patient characteristics. CT scans with modern multislice scanners do rapid image acquisition and procedure may require minimal sedation. But some children need to be asleep to tolerate the study scan. Procedures may be rescheduled and repeated if the movement is excessive which leads to additional radiation burden which leads to increasing the cost of the procedure and patient stress. Careful planning of sedation is important in such scenarios.[1]
Many drug regimens have been recommended to achieve satisfactory sedation for such painless procedure. Most of these medications can be administered through various routes and selecting the drug varies on the procedure, level of pain, optimum depth of sedation required and the patient's condition.[2] Midazolam has been widely used as a sedative in children for a long time.[3]
This study compares the effect of intravenous and oral Midazolam in paediatric age group with respect to degree of sedation levels achieved, and the need for a rescue dose for non CNS Computed Tomography scans.
Materials and Methods: In this prospective study, oral Midazolam verses IV Midazolam was studied for sedation in paediatric patients of 2 to 6 years of age for non CNS CT scan. 0.5mg/kg of oral Midazolam and 0.01mg/kg of IV Midazolam was used. 1mg/kg Propofol used as the rescue drug and 0.5mg/kg subsequently till the desired sedation score was achieved.
70 patients were divided into 2 groups of 35in each group. 1: Group A received oral 0.5 mg/kg body weight Midazolam 20 minutes prior to the scan (a maximum dose of 10 mg); 2: Group B received IV 0.01mg/kg body weight Midazolam 5 minutes prior to scan.
Statistical Analysis: Calculation of sample size using the Open Epi software considering α error 5% and β error 20% was 66 (Kelsey). The statistical analysis done by SPSS-20, unpaired 't' test and Chi-Square test.
Results: In oral midazolam group:
At the end of 20 minutes 54% achieved the desired sedation score. At the beginning of scan i.e. at 25 minutes from the drug administration, 60% achieved desired sedation score.
40% required the rescue drug. There was no incidence of haemodynamic or respiratory disturbances after giving the rescue drug.
In IV Midazolam group: At the end of 5 minutes (sedation end point) 8.5% achieved required sedation level. At the beginning of scan i.e 5 minutes later 11.4% of the study population achieved sedation level. 88.6% required the rescue drug with multiple subsequent doses.
There was no incidence of haemodynamic or respiratory disturbances after giving the rescue drug.
Conclusion: 1: As compared to IV route, Midazolam by oral route in the dose of 0.5mg/kg was effective in achieving desired sedation level with slower onset time but lesser incidence of rescue drug requirement; 2: The recovery with oral Midazolam was comparatively of longer duration than with IV Midazolam; 3: The incidence of haemodynamic and respiratory disturbances such as desaturation was not observed in either the groups.

Introduction

Paediatric sedation requires anxiety relief, pain control and control of excessive movement[4] for specific imaging procedure.

Sedation in the paediatric patient for procedures has to be safe, has to control anxiety, should minimize physical discomfort and psychological trauma and minimize movements.[5]

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There are pharmacological and other non-pharmacological methods like sleep deprivation, hypnosis, play therapy etc.[6,7]

Sedation agents are used when these methods fail or are not indicated. The search for ideal pharmacological agent continues.

Aims and Objectives

1. To study the effect of intravenous and oral Midazolam paediatric age group undergoing non CNS CT scan for sedation levels and need for rescue drug.
2. To study any complications that may arise from administration of Midazolam by intravenous and oral routes.

Materials and Methods

A prospective, comparative and observational study carried out in a tertiary care hospital in 70 paediatric patients aged between 2 -6 years undergoing various non CNS Computed Tomography scans which were less than 20 minutes were included in the study. Institutional ethics committee approval and written informed consent was taken from patient's parents

Inclusion Criteria

1. Age 2 years to 6 years
2. ASA grade I and grade II patients
3. Duration of scan: up to 20 minutes
4. Patients whose parents gave valid written consent

Exclusion Criteria

1. Patient's parents' refusal
2. Patients undergoing CT scan for CNS lesions
3. Patients with hemodynamic and respiratory instability, congenital anomaly, physical disability
4. Patients receiving anticonvulsants or sedatives
5. Patients who vomit out the drug after oral administration
6. Patients who required prolonged period of sedation (more than 20 minutes).

Preanesthetic evaluation was done. NBM period for a minimum of 6 hours as per ASA standard guidelines[8] prior to the procedure was confirmed. The weight of the children was recorded.

They were divided into

Group A (35 cases): oral Midazolam 0.5 mg/kg was given20 minutes prior to the procedure (a maximum dose of 10 mg)

Group B (35 cases): IV Midazolam 0.01mg/kg was given 5 minutes before the procedure.

An IV cannula of appropriate size was secured in all the patients before administering the study drug.

To mask the bitter taste of the drug, the calculated dose was mixed with apple juice to a total quantity of 4ml as oral formulation in group A

IV dose of the study drug was prepared by taking 0.5 ml of Midazolam and diluting it to 0.01 mg/ml with normal saline and in group B.

The baseline heart rate, SBP, DBP, SpO_2, respiratory rate and baseline sedation score were recorded just prior to administration of the drug.

The sedation scores were assessed using Modified Ramsay Sedation Score:[9]

Group A patients were given the calculated dose of oral Midazolam (0.5mg/kg). These patients were made to wait in a quiet room with their parents and signs of onset of sedation and hemodynamic parameters were observed for 20 minutes after drug administration, expecting the action of drug to commence within the said time period. [42]Glazed look, delayed eye movement, lack of muscle coordination, slurred speech and sleep were the signs for onset of sedation. The heart rate, SBP, DBP, SpO_2, respiratory rate and sedation scores were recorded after 20 minutes time interval, which was taken as sedation end point in group A.

Group B patients were given IV Midazolam at 0.01mg/kg. The heart rate, SBP, DBP, SpO_2, respiratory rate and sedation scores were recorded after 5 minutes of administration of IV Midazolam expecting the patients to be sedated adequately for the procedure. This time interval was taken as the sedation end point of group B.

Patients were then moved to the procedure room and pulse oximeter, BP cuff was attached.

All patients were supplemented with oxygen on venti mask at flow rate 4 litre/minute until discharge.

If there was movement or failure to achieve the desired sedation score, Propofol 1mg/kg was given intravenously as the rescue drug, 5 minutes from the sedation end points in either of the groups. Subsequent dose of Propofol at 0.5mg/kg of body weight was supplemented if there was a failure to achieve a sedation score< 3.

Patient's monitored for sedation score, heart rate, Systolic and diastolic BP, SpO_2, respiratory rate at the end of procedure and every 10 minutes in the recovery room till discharged. Patients were considered fit for discharge when they reached a Modified Ramsay Sedation score of 2 or less.

If HR < 50/ min: Inj. Glycopyrrolate 0.004mg/kg

Apnoea or SpO2 < 90%: Oxygen flow increased, ventilation assisted; airway secured if necessary

BP <20% of baseline: Ringer lactate or Inj. Ephedrine 0.012 mg/kg

Results

The male (19): female (16) ratio in group A was comparable with Group B: male (17) female (18) p=0.632

The mean age in group A and group B were 3.80 years and 3.88 years respectively (p = 0.780).

The mean weight of group A and group B were 12.47 kg and 12 kg (p= 0.46).

The mean duration of the scan in Group A and Group B were 7.86 minutes and7.43 minutes (p=0.458).

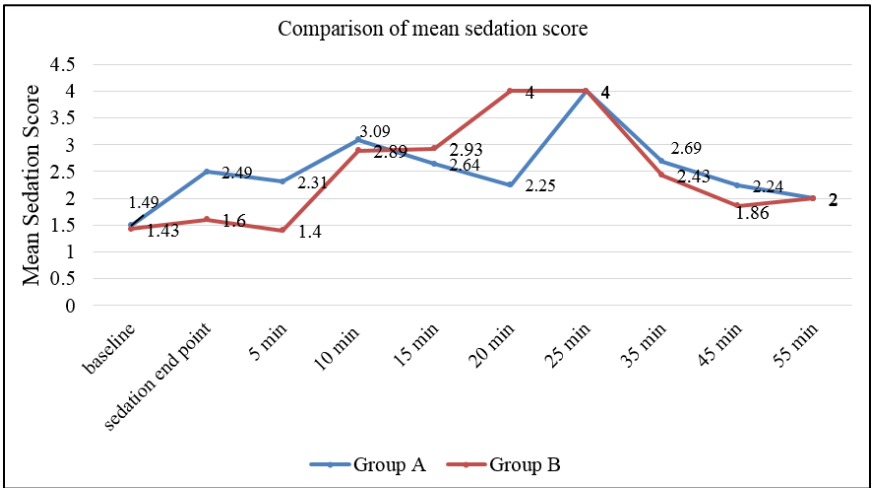
Sedation

The baseline sedation scores of both groups were statistically comparable. At the sedation end point and at 5 minutes of procedure, mean sedation scores was statistically highly significant in group A.

Table 1: Comparison of mean sedation score between the groups

Event	Time (min.)	Group A (ORAL)			Group B (IV)			Inter Group P Value
		N	Mean SS ±SD	Intra Group P Value	N	Mean SS ±SD	Intra Group P Value	
Baseline		35	1.49 ± 0.507	0.000	35	1.43 ± 0.502	0.225	0.620
Sedation end point	0*	35	2.49 ± 0.853		35	1.6 ±0.651		0.000
During Procedure	5	35	2.31 ± 0.963	0.421	35	1.4 ± 0.695	0.218	0.000
	10	35	3.09 ± 0.781	0.003	35	2.89 ±0.963	0.000	0.343
	15	14	2.64 ± 0.633	0.503	15	2.93 ±1.238	0.000	0.425
	20	4	2.25 ± 1.258	0.712	2	4 ±1.414	0.023	0.213
	25	1	4	0.000	1	4	0.000	
During Recovery	35	35	2.69 ± 0.631	0.269	35	2.43 ±0.558	0.000	0.072
	45	21	2.24 ± 0.436	0.127	15	1.87 ±0.352	0.067	0.008
	55	5	2	0.002	2	2	0.000	

Graph 1: Comparison of mean sedation score



The sedation end point was taken as 20 minutes for group A and 5 minutes for group B, designated as 0 minute. The mean SS at various time intervals was compared with the respective mean SS at sedation end point in each of the groups.

The mean sedation scores was statistically comparable at 10 minutes (p = 0.343), 15 minutes (p=0.425) and 20 minutes (p = 0.213)

At sedation end point, group A had 19 patients (54.28%) and group B had 3 patients (8.57%) in the desired sedation score.

During recovery, the mean sedation score between both the groups was statistically comparable at 35 minutes, but was significant at 45 minutes of study period in group A.

Group A had 21 patients (60%) in the desired sedation score at 5 minutes of procedure and group B had 4 patients (11.43%). Group A had 26 patients (74.28%) and group B had 25 patients (71.4%) in the desired sedation score at 10 minutes. 2 patients in group A and 1 patient in group B had sedation score of 5 at 20 minutes of the study period. Group A had 14 patients (40%) and group B had 21 patients (60%) with sedation score of <3and were fit for discharge at 35 minutes.

Group A had 5 patients (14.3%) and group B had 2 patients (5.7%) at 45 minutes with a sedation score of 3 or 4were observed till a sedation score of 2 or less was achieved.

Requirement of Rescue Drug

All patients who fail to achieve the desired sedation score at start of the procedure were given the rescue drug (Propofol 1mg/kg).

Additional dose of the rescue drug at 0.5mg/kg was administered whenever required.

In group A, 14 patients (40%) required the rescue drug at the start of procedure of which one patient needed one more dose of the rescue drug.

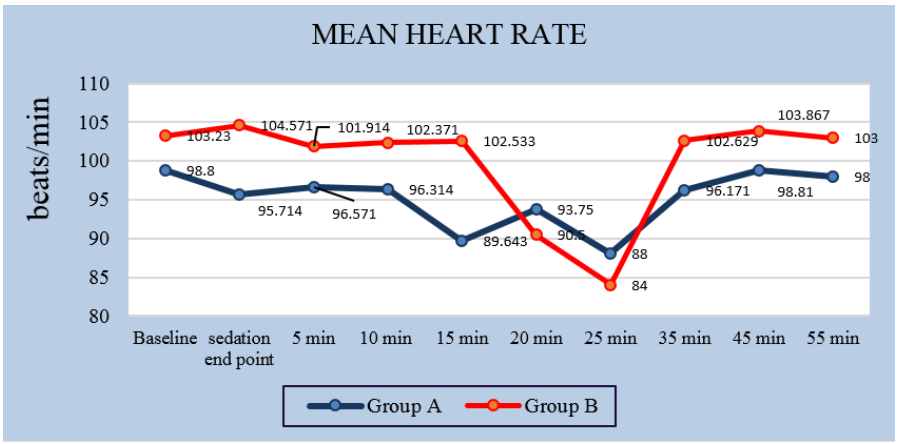
4 patients (11.4%) in group B completed the scan with the dose of the study drug. The rescue drug was required in

31 patients (88.6%), of which 9 patients (25.7%) needed an additional dose, 4 patients (11%) needed two additional doses and 1 patient (3%) needed a third additional dose of the rescue drug.

Heart Rate

Both the groups were statistically comparable at baseline, during procedure and recovery (p>0.05). However at sedation end point, at 10 minutes and at 35 minutes in the study period, there was a statistical difference between the groups (p= 0.003, 0.001 and 0.02 respectively).

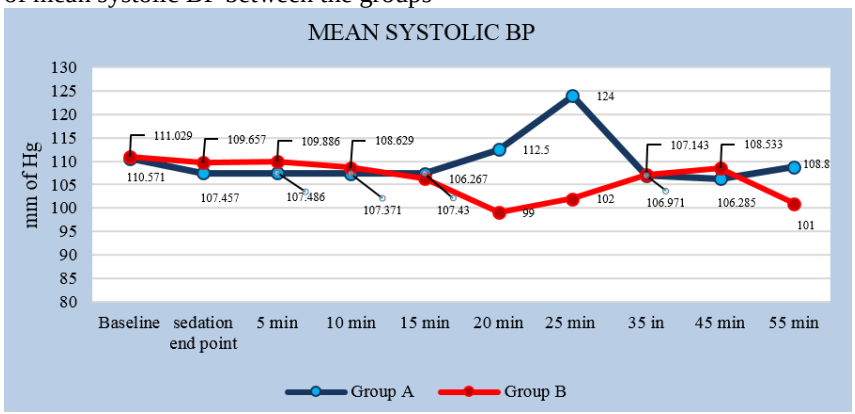
Graph 1



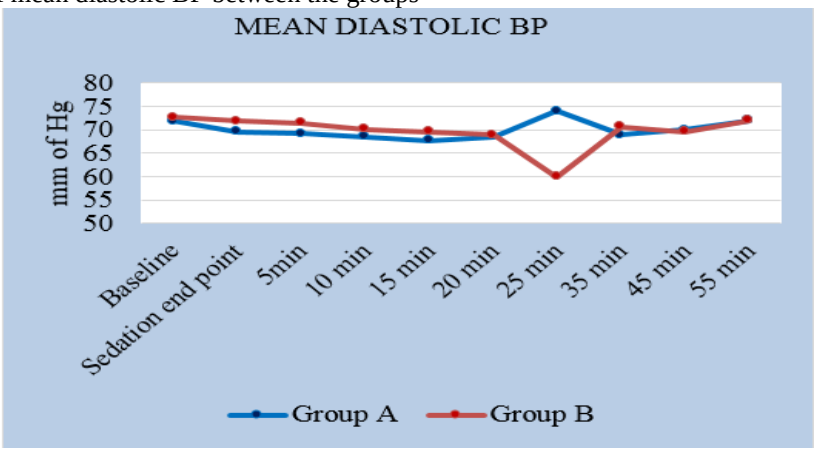
Blood pressure (SBP, DBP)

The groups were comparable at all times during the study (p>0.05).

Graph 2: Comparison of mean systolic BP between the groups



Graph 3: Comparison of mean diastolic BP between the groups



Mean Oxygen Saturation

The groups were statistically comparable at baseline and at the sedation end points. They were also comparable at 5 minutes and at all times during recovery period ($p>0.05$). However, there was statistical significance at 10 and 15 minutes during the procedure ($p=0.024$ and 0.046 respectively)

There was no clinically significant changes in the SpO_2.

Both the groups were statistically comparable with respect to respiratory rate ($p>0.05$ at all times).

Mean Duration of Scan

The mean duration of the scan was 7.86 minutes in Group A and 7.43 minutes in Group B. By applying Chi-square Test, the difference in mean duration between the two groups was not significant. ($p=0.458$).

Discussion

In this study, oral and IV Midazolam for sedation in CT scan in 70 children aged 2 years to 6 years was studied and compared.

1. Group A: 0.5 mg/kg oral Midazolam 20 minutes prior to the procedure
2. Group B: 0.01mg/kg IV Midazolam 5 minutes prior to the procedure.

In group A, 20 minutes interval from the administration of oral Midazolam was taken as sedation end point and in group B, 5 minutes interval after administration of IV Midazolam was taken as sedation end point. The sedation end point was considered as '0' minute interval. The administration of rescue drug was considered only after 5 minutes interval after sedation end point (i.e., '0' minute interval) in respective groups. In both the groups, the sedation scores after these end points were noted at 5 minutes interval during the procedure and at 10 minutes interval during recovery period.

The efficacy of the study drug by either route was assessed by:

1. Sedation score achieved at sedation end point i.e, at 20 minutes in group A and 5 minutes in group B,
2. The need for rescue drug in both the groups if the desired sedation score was not achieved after, 5 minutes interval from sedation end point,
3. The adverse effect of the study drug on the haemodynamic and respiratory parameters.

Sedation has been the method of choice to make children cooperative and immobile to obtain good quality images of CT scan. There is increased restlessness, and anxiety in children in the environment of CT suite.[10] These reactions interfere with the acquisition of good quality images in children and lead to changes in physiologic parameters such as heart rate, blood pressure and respiration. Selection of an appropriate sedative agent will reduce the artifacts in the images, decrease the requirement for a rescue drug and increase the safety of the procedure.[11] Benzodiazepines have been widely used to achieve sedation, anxiolysis and amnesia in children. Midazolam has been most commonly used because of its shorter duration of action and lesser side effects.

Comparison of Demographic Data

The mean age in group A and group B was 3.80 and 3.88 years respectively. The mean weight of group A and group B was 12.47kg and 12kg. The ratio of male to female in group A and Group B was 19:16 and 17:18 respectively. The mean duration of the scan was 7.86 and 7.43 minutes in Group A and Group B. The mean duration of scan and demographic data were comparable.

The demographic data of the patients in the present study is in concurrence with the studies done by Moro-Sutherland et al,[12] Singh R et al,[13] Deshmukh PV et al,[14] Anshu Gupta et al,[15] Maryam H Norousalitehrani et al,[16] Barzegari H et al.[17]

Sedation Score

In group A, oral Midazolam was given 20 minutes prior to the procedure. The mean sedation score at sedation end point was significantly higher compared to its baseline score. The mean sedation scores at all times during the procedure and recovery was comparable, except at 10 minutes interval. This is because, at 5 minutes interval of procedure, 14 patients (40%) had not achieved the desired sedation score, and received the rescue drug, resulting in a higher mean sedation score at 10 minutes.

In group B, the mean sedation score at sedation end point was comparable with the baseline score, suggesting that the desired sedation score was not achieved after IV Midazolam at the sedation end point. Significant increase in the mean sedation score was noted only after the rescue drug was given, from 10 minute onwards during the procedure which continued till the end of the study. In this group 31 patients (88.6%) had not achieved the desired sedation score, and hence received the rescue drug in multiple doses at various time intervals, resulting in a higher mean sedation score at subsequent intervals.

It was observed that sedation scores at baseline were comparable. At the sedation end point and at 5 minutes of procedure mean sedation scores was highly significant because the desired sedation score was not achieved in group B at sedation end point. After administration of the rescue drug, the desired score achieved in group B and hence the sedation score was comparable at all times in both groups.

In group A, the number of patients at sedation end point were 54.28%, which increased to 60% at 5 minutes during procedure and 74% after receiving the rescue drug. The number of patients in group Bat sedation end point were 8.57% which increased to 11.43% at 5 minutes during procedure and 71% after receiving the rescue drug.

Our results were concurrent with studies done by Deshmukh PV et al,[14] Ahmad Khodadad et al,[18] Barzegari H et al,[19] Majidinejad S et al.[20]

It was observed that at the recovery intervals, the percentage of patients with sedation score < 3 was higher in group B than group A. The recovery from sedation in IV group (group B) was more than oral Midazolam (group A).

The procedure was not abandoned in any patient because of lack of sedation.

Need for Rescue Drug

Only 40% patients in group A required the rescue drug at the start of procedure whereas 88.6% of patients in group B required the rescue drug.

Group B required additional doses of the rescue drug in 40% patients and group A had 25.7% who wanted single additional dose, 11% patients received two additional doses and 1 patient (2.9%) needed a third additional dose of the rescue drug. In group A, only 1 patient (2.9%) needed an additional dose of rescue drug.

Thus rescue drug requirement in the group A was in less than group B which required multiple doses of the rescue drug. This correlates with studies done by Anshu Gupta et al,[15] Ahmad Khodadad et al,[18] Barzegari H et al[19] Comparison of haemodynamic parameters:

Mean Heart Rate

Mean HR at baseline and at all times during procedure and recovery was statistically comparable with the respective mean HR at sedation end point, except at 25 minutes when it was statistically highly significant. This was because of the reduced number of patients (single patient) at 25 minutes and the single reading at that interval was not representative of the generalized tendency of the group.

Mean Systolic and Diastolic Blood Pressure

In the oral Midazolam group, the baseline mean SBP and DBP and at all times during procedure and recovery was statistically comparable at sedation end point, except at 25 minutes during procedure statistically highly significant difference noted. There was a reduced number of patients during this time interval because majority of patients had completed the scan before this time interval.

In group B also, the baseline SBP, DBP as well as mean SBP, DBP during procedure and recovery was comparable to the mean at sedation end point. At 20 and 25 minutes during procedure statistically highly significant difference seen due to reduced number of patients during these time intervals.

Mean Oxygen Saturation

Groups were comparable at baseline, at the end point of sedation, and at majority of time intervals during the procedure and recovery. However, there was statistical significance between the groups at 10 and 15 minutes during the procedure. But these changes had no clinical significance

Mean Respiratory Rate

In group A, the mean RR at sedation end point was comparable to mean RR at baseline, 5 minutes, 20 minutes, 45 minutes and 55 minutes.

In group B, the mean RR at baseline and at all time intervals during procedure and recovery was statistically comparable to the mean RR at sedation end point. Although difference was significant statistically at 15 minutes (p=0.027) and highly significant at 25 minutes. Similar results were seen in studies conducted by Ahmad Khodadad et al,[18] Majidinejad S et al,[20] Sequeira Trevor et al,[21] Katayoun Salem et al.[22]

Conclusion

The efficacy of oral and IV Midazolam with the selected doses for sedation in paediatric age group for non CNS CT scan was compared.

1. Adequate sedation scores was achieved at the initiation of the CT scan with oral Midazolam compared to IV Midazolam.
2. The requirement of rescue drug in the oral group was less compared to IV group.
3. Haemodynamic or respiratory disturbances were not observed.

Summarizing, Oral Midazolam in its therapeutic dose on weight basis was better at sedation in paediatric age group for CT scan without any adverse haemodynamic or respiratory effects as compared to IV Midazolam.

Conflict of Interest: None.

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