

Research Article

Intranasal Dexmedetomidine as Sedative for Non-Invasive Pediatric Diagnostic Procedures Outside Operating Room

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Abstract:

Background: Children often require sedation for long non-invasive diagnostic procedures. Dexmedetomidine is a highly selective alpha 2-adrenoceptor agonist with sedative, anxiolytic and analgesic properties. It mimics natural sleep and allows patients to easily arouse with minimal effects on respiration and airway patency.

Objective: To assess the successful completion of pediatric non-invasive diagnostic procedures with intranasal dexmedetomidine as a sedative agent.

Methods: Seventy-nine subjects of age six months to twelve years scheduled for non-invasive diagnostic procedures were included. Dexmedetomidine (4 mcg/kg) was administered intranasally 25 minutes before the scheduled time of procedure. A sedation score of two or above as per the MICHIGAN sedation scale was considered satisfactory for starting the procedure.

Results: Seventy-four (95%) out of the seventy-nine subjects were successfully sedated with Intranasal dexmedetomidine ($p < 0.0001$). The mean time and Standard deviation to achieve sedation was 18.9 ± 2.82 mins. The median time was 19 mins with a range from 15-25 minutes. Post anesthesia discharge time for Intranasal dexmedetomidine was 20 minutes with zero incidence of post procedure nausea and vomiting.

Conclusions: Intranasal dexmedetomidine can be used as an alternative to General anesthesia for non-invasive diagnostic procedures outside operating room with less adverse effects in this cohort.

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Introduction:

Approximately 220,000 children worldwide, are diagnosed with cancer every year¹ and the mainstay of its treatment is chemotherapy, radiotherapy and surgery². Regular imaging is often required to determine the disease progression and treatment response³. However, Children are mostly non-cooperative and require moderate sedation to tolerate these procedures⁴. Therefore, there is an increase in demand for sedation in pediatric population for radiological studies performed outside operating room⁵.

Various oral sedative medications are routinely used to perform such non-invasive radiological studies with

mixed results⁶. The prolonged recovery time, respiratory depression, loss of airway patency and unreliable success at achieving the desired level of sedation with these agents are undesirable and inefficient in pediatric patients⁷. However, in the last few years, intranasal dexmedetomidine has shown promising results for pediatric diagnostic procedures as a sedative agent outside operating room for its safety profile⁸.

Dexmedetomidine is a highly selective alpha 2-adrenoceptor agonist with sedative, anxiolytic and analgesic properties⁹. Administration of dexmedetomidine by the intranasal route has become a popular technique, as it is less invasive and anxiety provoking for the pediatric

population. In one recent study by Gokhan Olgun et al, intranasal dexmedetomidine was used as sole sedative agent for pediatric MRI with success rate of 94.2%¹⁰. A similar study was conducted by Natalie Behrle et al which showed success rate of 92% for pediatric procedural sedation¹¹. Additional data suggests that intranasal dexmedetomidine has a significantly lower risk of respiratory depression and hemodynamic changes¹². Other studies show that pediatric patients remained sedated successfully by intranasal dexmedetomidine for 1-2 hours¹²⁻¹⁴.

In our hospital, pediatric diagnostic scans are routinely being performed outside Operation Theater either under General Anesthesia or sedation using midazolam / Propofol. Our aim in this study was to determine the percentage of successful completion of pediatric non-invasive diagnostic procedures outside operating room with intranasal dexmedetomidine alone. Failure of dexmedetomidine was defined as requiring general anesthesia or another sedative medication to complete the procedure.

Methods:

This was a prospective observational study done at the procedural suits of a tertiary care cancer hospital over a period of one year from January 2020 to January 2021. With a Confidence Interval of 95%, Precision of 6% and Success rate of 92%, sample size was calculated to be seventy-nine¹⁴. Seventy-nine subjects listed for pediatric non-invasive radiological imaging procedures under General Anesthesia (GA) who fulfilled the criteria, were enrolled in the study after getting approval from Scientific Review Committee (SRC) and Institutional Review Board (IRB) of hospital. Continuous enrolment of patients was done until the target sample size was achieved. Informed consent was taken from the parents/legal guardians after explaining the study procedure to them. We enrolled patients from age six months to twelve years with American Society of Anesthesiologist Grade I and II. Patients refusing to participate, having Upper Respiratory Tract Infections, allergy to dexmedetomidine and anticipated difficult airway were not included in this study.

One day prior to scan patients were advised to remain nil per oral for six hours before the scan time. All patients were taken to the respective holding area before

the start of the scan and baseline vitals including non-invasive blood pressure (NIBP), oxygen saturation and heart rate were recorded. Undiluted Dexmedetomidine 4ug/kg was drawn up in 1 ml syringe by the lead investigator (counter checked by second investigator) and administered in the form of drops in both nostrils 25 minutes before the start of the procedure.

A predesigned data collection Performa was used to note the vitals, sedation score and side effects if any. Vitals and sedation score were noted every five minutes. Level of sedation was measured using UNIVERSITY OF MICHIGAN SEDATION SCALE (Table 1). Satisfactory sedation score was considered to be two as per the Michigan Sedation Scale. Throughout the procedure, patients were accompanied by parents/legal guardians throughout the procedure.

Table 1: *University of Michigan Sedation Scale*

0	Awake and alert
1	Minimally sedated, tired / sleepy, appropriate response to verbal conversation
2	Moderately sedated, somnolent, sleeping, easily aroused with tactile stimulation or a verbal command.
3	Deeply sedated, aroused only with maximal physical stimulation.
4	Unarousable

After completion of the scan, patients were transferred to Post Anesthesia Care Unit (PACU) where nurses did the routine post-operative monitoring. Patients remained in recovery area till they met PACU discharge criteria. Adverse events were defined as the following; a 20 % change in baseline heart rate or blood pressure, an apnea lasting more than 20 seconds and oxygen desaturation to 90 %. In addition to these, discharge time from PACU and post procedure nausea and vomiting were also recorded.

Statistical analyses were performed by using SPSS software version 22. To check significance of success Binominal distribution was used. Success was defined as completion of the procedure without the requirement of any additional sedative medication or conversion to GA. For continuous variables mean and median were calculated. Whereas for categorical variables frequency and percentages were calculated. Moreover, the side effects, PACU discharge time, PONV incidence and

procedural cost were compared with procedure under general anaesthesia.

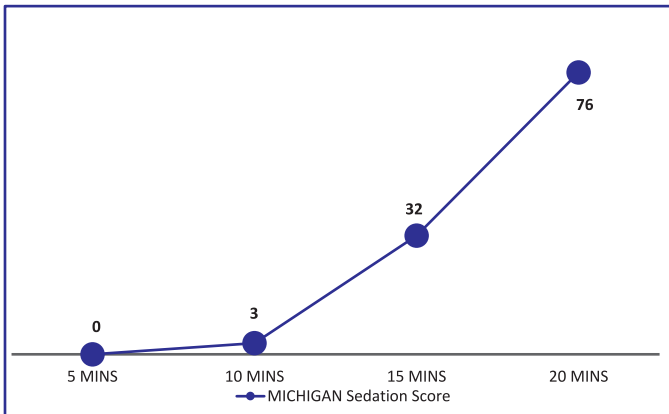


Fig. 1: Time taken to Achieve Satisfactory Sedation Score (2)

Results:

Seventy-five subjects (95% population) had a successful outcome with a statistically remarkable p value <0.001 using Binominal distribution. Two patients moved during the scan and required additional sedative medications. Whereas the other two patients did not achieve the desired sedation score and were given GA.

The mean age and weight of the patients were three years and 12.4 kg, respectively. Forty-nine patients (62%) enrolled in the study were males and thirty patients (38%) were females. The time taken to achieve satisfactory sedation score was 18.9 ± 2.8 minutes. The maximum time to achieve the desired sedation was 25 minutes and the minimum time was as low as nine minutes with the median of 19 minutes and a range from 9-25 minutes (Figure 1). Fifty-three patients (67.1%) underwent MRI scans, twenty-one (26.6%) had Renogram and five (6.3%) patients had Positron Emission Tomography.

There was no considerable difference in the oxygen saturation of all the patients from the time of drug administration to the start of scan. Heart rate decreased by 4.5%. The most significant drop was seen in the systolic and diastolic blood pressures, 6.1% and 6.3% respectively. After the scan, all patients were shifted to PACU where the sedation score on arrival was 0 in 32 subjects (42.7%) whereas 42 children (56%) were sedated at a score of 1 and only one patient was deeply sedated with a score of two. The mean PACU discharge time was 20 ± 1.36 minutes. The minimum time of PACU stay was five minutes whereas the maximum time

was 55 minutes. Oxygen supplementation was not required in any patient during the scan and in recovery.

During the scan, three patients (3.79%) had arrhythmias, four patients (5.06%) developed hypotension and six (7.59%) went in to bradycardia. All of the patients with hypotension had a mean arterial pressure >65 mmhg and hence no corrective measures were taken. Similarly, patients having bradycardia had a heart rate of >60 beats per minute and did not need any intervention. Arrhythmias were of sinus origin without hemodynamic instability. All of these side effects were self-limiting and no intervention was required. There was no episode of desaturation or apnea documented.

Discussion:

In our study, we have demonstrated that intranasal dexmedetomidine provides adequate sedation in pediatric population for diagnostic radiological procedures. Contrary to the majority of routine sedatives, dexmedetomidine has a least impact on respiratory drive and on airway patency.

Although Dexmedetomidine is registered only for intravenous use but it can be given by various routes⁹. The bioavailability after oral use is only 16% due to extensive first pass metabolism¹⁵. But it is well absorbed through the intranasal route with bioavailability of 82%¹⁶⁻¹⁷. There are many documented advantages of intranasal administration of dexmedetomidine, e.g., it avoids first pass hepatic metabolism and is rapidly transported to the brain through the olfactory mucosa. Furthermore, in comparison to intravenous administration, intranasal route demonstrates delayed serum concentration with reduced levels of plasma peak and a lower risk of side effects.

In one study Li et al. compared 3 mics/kg intranasal dexmedetomidine, administered by atomizer or drops in 279 children under 3 years of age. Both were equally effective with favorable results of 82.5% and 84.5% respectively¹⁸. In addition, the average time for onset of sedation was 15 minutes. Whereas, the mean time taken for sedation to begin was 25 mins and 92% of the patients were successfully sedated¹¹. Surprisingly in our study the percentage of success was high (95%) as compared to other studies and the average time taken for onset of sedation in patients was 18.9 minutes, which

could be attributed to the different genetic characteristics in this part of the world.

While there are concerns that prolong exposure to most commonly used sedatives and anesthetic agents in the developing brain can have detrimental effects on the development of brain in children along with learning disability¹⁹⁻²⁰. In some animal models, even short-term use of ketamine has been observed to have detrimental effects on brain²¹. Conversely, dexmedetomidine may be linked to neuroprotective properties in animal and laboratory studies²². However, further studies are required to prove this evidence.

There were various challenges which had to be overcome while administering dexmedetomidine via nasal route. Such as the movement of the child while putting drops in the nose, size of the drops, frequency with which the drops were put and the anxiety of the child. To minimize the issues as much as possible, single operator was assigned for the task of administering drops and parents were explained about the whole procedure beforehand. In addition to that, for relieving the anxiety of children a demonstration of drops insertion was done before proceeding. For this study, intravenous access was secured before the beginning of sedation. But in another study by Natalie et al. it was considered safe to proceed without obtaining the access¹¹. Hence, further decreasing the emotional stress of children and parents. Even after all the above, it was not possible to completely eliminate anxiety.

Table 2: Comparison of General Anesthesia and Intranasal Dexmedetomidine

Parameters	General Anesthesia	Intranasal Dexmedetomidine
PACU Discharge Time	37 mins	20 mins
Post Procedure Nausea Vomiting	11.4%	0%
Cost	11,000 PKR	6,000 PKR

Another important aspect of cost benefit was calculated for this study. Until now in Shaukat Khanum Memorial Cancer Hospital and Research Center

(SKMCH & RC) pediatric patients coming for MRI patients were given GA. The Cost of GA for one MRI is 11,000 Pak Rupees (PKR) whereas the expense for sedation is 6,000 PKR (Table 2). Hence by using dexmedetomidine 265,000 PKR were saved in this study for 53 patients. Thereby estimating this projection, SKMCH & RC can save approximately 4 million Pak rupees annually for 774 patients (number of pediatric patients given GA for MRI in 2020)²⁴.

Our study had several limitations such as: 1) This study is done in a single center and by one operator. 2) It is a prospective observational study and not a randomized control trial. 3) The sample size is small. 4) Investigator Bias was not ruled out of the study. Further research using intranasal dexmedetomidine would benefit from large multicenter trial, which could include investigation of the effect of procedure type on success.

In conclusion Intranasal Dexmedetomidine can be used as an alternative to GA for pediatric noninvasive diagnostic procedures, having lesser side effects, more cost effective and easy to administer.

Ethical Approval: Given

Conflict of Interest: The authors declare no conflict of interest.

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