

INTRANASAL DEXMEDETOMIDINE AND MIDAZOLAM  
FOR SEDATION OF PEDIATRIC PATIENTS  
UNDERGOING AUDITORY BRAINSTEM  
RESPONSE: A RETROSPECTIVE AUDIT

DEEPAK GUPTA<sup>1</sup>, MATTHEW RYAN TUKEL<sup>2</sup>  
AND MARIA MARKAKIS ZESTOS<sup>1</sup>

**Abstract**

**Background:** The basic requirement of auditory brainstem response (ABR) testing is that the patient remains still with eyes closed to avoid the body movements confounding the ABR test results. Therefore, almost all pediatric patients require sedatives/anesthetics for conductance of ABR testing.

**Objectives:** The aim of the current study was to audit and review the efficacy and safety of intranasal dexmedetomidine plus midazolam (INDM) for pediatric patients undergoing ABR test.

**Materials and Methods:** Medical charts of all pediatric patients (age less than 18years) who had undergone ABR testing at our University Based Children's Hospital during the three-year-period (2012-2014) were reviewed. The medical charts of patients who had received INDM were analyzed.

**Results:** The data was analyzed for 203 ABR patients who had received INDM. Using the need for intravenous (IV) access as an indicator for failure of intranasal (IN) route, the failure rate was 2% among INDM patients. The patients (n=29) requiring sedative supplementations were not significantly older or bigger than the patients (n=174) who did not require sedative supplementations. Additionally, the patients (n=12) requiring oxygen supplementation were not significantly younger or smaller than the patients (n=191) who did not require oxygen supplementation.

**Conclusion:** Off-label INDM appears an effective and safe sedation regimen for pediatric patients undergoing ABR per our audit.

---

1 MD, Department of Anesthesiology Wayne State University, Detroit, Michigan, United States.

2 Undergraduate student, Department of Anesthesiology Wayne State University, Detroit, Michigan, United States.

**Corresponding Author:** Maria Markakis Zestos, MD Chief of Anesthesiology, Children's Hospital of Michigan. Associate Professor, Wayne State University 3901 Beaubien St, Suite 3B-17. Detroit Michigan 48201, United States Office: 1-313-745-5535, Fax: 1-313-745-5448. E-mail: mzestos@med.wayne.edu

## Introduction

Auditory brainstem response (ABR) is an audiology test performed to objectively assess the congenital inability to hear and/or new onset hearing loss in the pediatric population<sup>1</sup>. The basic requirement of this testing is that the patient remains still with eyes closed to avoid the body movements confounding the ABR test results. Therefore, almost all pediatric patients require sedatives/anesthetics for conductance of ABR testing. Traditionally, chloral hydrate was the medication used for ABR test under anesthesia<sup>2-4</sup>. However, over the last few years, due to discontinuation of chloral hydrate<sup>5</sup>, pediatric anesthesiologists have switched to various formulations based on their personal preferences and experiences with the currently available medications, that include but are not limited to intranasal (IN) dexmedetomidine (alpha-2 receptor agonist), IN midazolam (benzodiazepine), intravenous dexmedetomidine, intravenous midazolam, and inhalational anesthesia with sevoflurane<sup>6-9</sup>. At our institution, positive subjective experiences with IN dexmedetomidine and/or IN midazolam as premedication among other pediatric operative procedures had lead our team of pediatric anesthesiologists to begin the consistent use of IN dexmedetomidine and IN midazolam (INDM) combination for ABR test. The aim of the current study was to audit and review the efficacy and safety of INDM for pediatric patients undergoing ABR test.

## Materials and Methods

After Institutional Review Board approval for waived consent, medical charts of all pediatric patients (age less than 18years) who had undergone ABR testing at our University Based Children's Hospital during the three-year-period (2012-2014) were reviewed. The medical charts of patients who had received INDM were reviewed for the following: age, sex, weight, American Society of Anesthesiologists' (ASA) Class, prematurity, nose-throat discharge, intravenous (IV) access (if any), time when INDM dose was given (immediate pre-procedure), dexmedetomidine dose, midazolam dose, INDM time to ABR Start Time, ABR

Start Time to ABR End Time, home discharge time, documented vital signs at each monitoring time point (pulse oximetry, heart rate, respiratory rate, systolic blood pressure, diastolic blood pressure, room air/oxygen supplementation), and other documented events especially respiratory events.

## Statistical Analysis

The audit data was tabulated as means for continuous variables and as percentages for ordinal variables. Averaged (means) vital signs were charted as graphs to reflect trend over time. Statistical significance at p-value <0.05 with analysis of variance (ANOVA) was derived for continuous variables (age, weight and time) when INDM patients were grouped post-hoc depending on whether they required additional sedatives or oxygen supplementation.

## Results

A total of 260 ABR patient charts were screened for INDM use over a three-year period (2012-2014). The data was analyzed for 203 ABR patients who had received INDM: only 14% patients required repeat supplemental INDM doses but 6% patients required oxygen supplementation. Assuming the need for IV access after IN medication administration as an indicator for failure of IN route, failure rate was 2% among INDM patients. The patients (n=29) requiring sedative supplementations (mean age 2yrs with mean weight 13kg) were not significantly older or bigger than the patients (n=174) who did not require sedative supplementations (mean age 2yrs with mean weight 11kg). Similarly, the patients (n=12) requiring oxygen supplementation (mean age 1yr with mean weight 9kg) were not significantly younger or smaller than the patients (n=191) who did not require oxygen supplementation (mean age 2yrs with mean weight 12kg). Detailed data points for further analysis were only available in 95 INDM patients: 54% were males, 96% were ASA Class II-III, and other data is tabulated in Table 1. As shown in Figure 1, averaged oxygen saturations decreased somewhere in the middle of the procedure that required averaged oxygen supplementations around the same time to

Fig. 1  
Changes In Averaged Values of Vital Signs Over Time Among 95 INDM Patients.

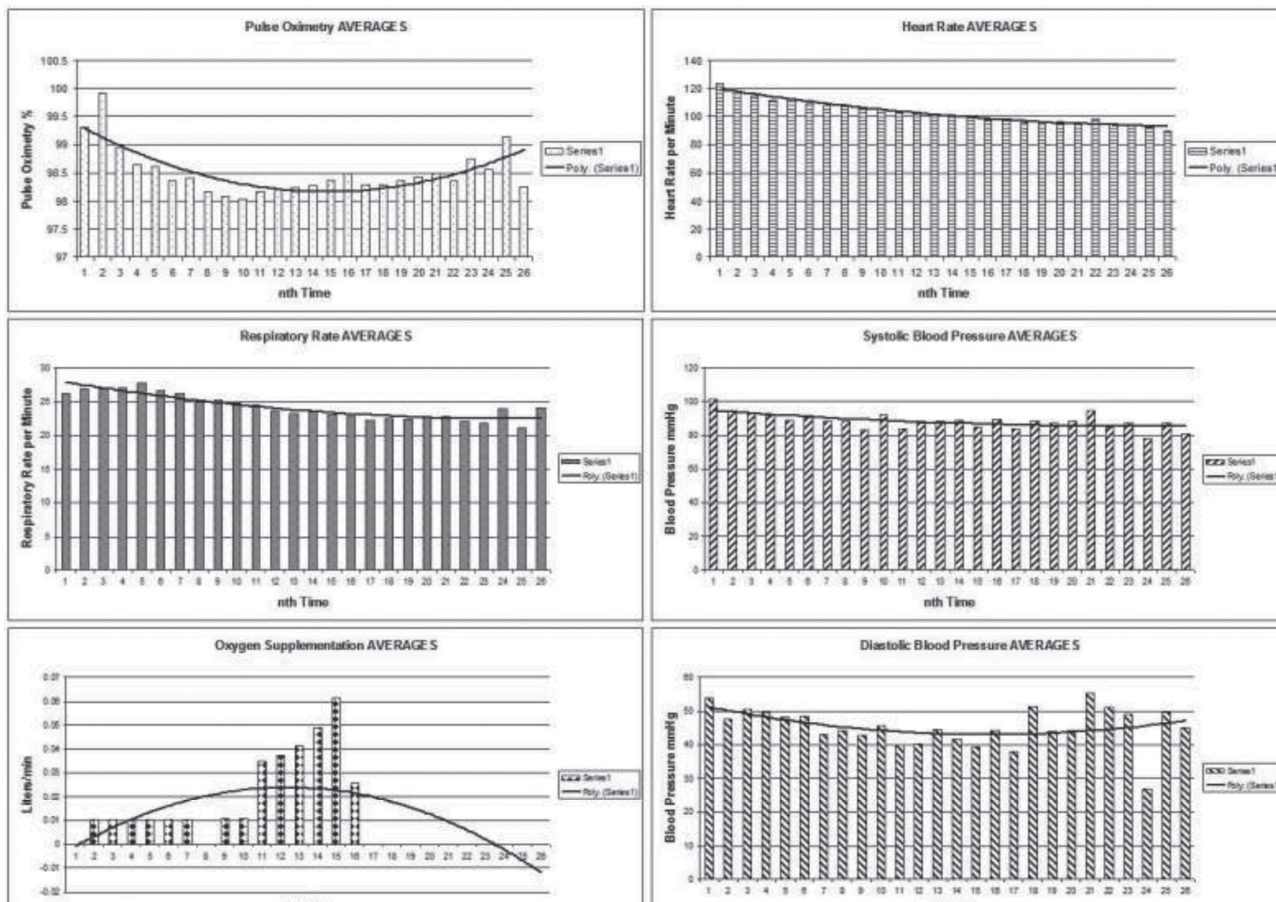


Table 1  
Patients' Characteristics  
(n=95) who underwent Auditory  
Brainstem Response (ABR) with  
Intranasal Dexmedetomidine  
and Intranasal Midazolam  
(INDM).

Characteristic	Mean ±SD
Age (years)	1.89 ±1.88
Weight (kg)	11.22 ±4.89
Initial Dexmedetomidine Dose (mcg/kg)	3.17 ±0.31
Repeat Dexmedetomidine Dose (mcg/kg) (n=9)	1.18 ±0.34
Initial Midazolam Dose (mg/kg)	0.32 ±0.05
Repeat Midazolam Dose (mg/kg) (n=3)	0.11 ±0.02
INDM to ABR Start Time (Time To Sedation in mm:ss)	30:46 ±12:50
ABR Start To ABR End (ABR Total Duration in mm:ss)	52:13 ±23:53
End to Discharge (Recovery Period in mm:ss)	57:32 ±33:40
PERCENT CHANGE IN THE VITAL SIGNS FROM PRE-INDM VALUES	
To Lowest Heart Rate During ABR (%)	-16% ±9%
To Lowest Respiratory Rate During ABR (%)	-33% ±18%
To Highest Respiratory Rate During ABR (%)	15% ±28%
To Lowest Systolic Blood Pressure During ABR (%)	-11% ±13%
To Lowest Diastolic Blood Pressure During ABR (%)	-26% ±22%
To Lowest Pulse Oximetry During ABR (%)	-2% ±3%
Time To Lowest Pulse Oximetry Post INDM (mm:ss)	32:47 ±25:36

bounce back up to their averaged baselines at the end of the procedures; averaged heart rates and averaged respiratory rates decreased over time and were lower post-procedure than their averaged pre-procedural values; and averaged blood pressures (systolic and diastolic) remained almost stable throughout the procedures.

## Discussion

The key findings of our audit; (a) fourteen percent of INDM patients required additive supplementation with IV and/or IN sedatives and (b) decreased oxygen saturation requiring oxygen supplementation was a common occurrence among INDM patients.

Recently, there had been studies investigating IN dexmedetomidine as well as IN midazolam which were independently compared with oral chloral hydrate for ABR<sup>10-12</sup>. Our study did not have a comparative group but the data elicited in our study was different because we had audited our practice of combination medication use as INDM. In our retrospective audit, our team had used median IN dose of 3.14 mcg/kg dexmedetomidine and IN dose of 0.31 mg/kg midazolam that was similar in dosing to 3mcg/kg dexmedetomidine reported by Reynolds et al<sup>10</sup> and lower in dosing than 0.5mg/kg midazolam reported by Stephen et al<sup>12</sup> when compared with 50mg/kg oral chloral hydrate<sup>10,12</sup>.

In the study of Reynolds et al<sup>10</sup>, single dose of IN dexmedetomidine was successful in sedating 89% patients with overall median time to sedation being 25 minutes, and the median procedural duration of ABR was 99 minutes (inclusive of time to sedation); and 2% patients required oxygen supplementation while 2% patients required only head repositioning maneuvers.

In another study by Stephen et al<sup>12</sup>, single dose of IN midazolam was successful in sedating only 37% patients with overall median time to sedation being 50 minutes, and the mean procedural duration of ABR was 27 minutes (exclusive of time to sedation) with average recovery time being 102 minutes; and 2% patients required head repositioning maneuvers.

Comparatively, per our audit results procedure

completion rate for ABR was 100%. Single-dose INDM successfully sedated 91% patients with overall median time to sedation being 29 minutes, and the median procedural duration of ABR was 45 minutes (exclusive of time to sedation) with median recovery time being 57 minutes; and 2% patients required oxygen supplementation. Among the 9% patients who required repeat IN doses, median time to sedation (39 minutes), median procedural duration of ABR (52 minutes) and median recovery time (63 minutes) were longer than the measures of central tendency among the single-dose INDM patients with level of significance achieved only for averaged longer time to sedation among the re-dosed patients ( $p=0.002$ ). Additionally, the likelihood of requiring oxygen supplementation was insignificantly higher among the re-dosed patients (1/9) than among the single-dose INDM patients (1/86).

It is not clear whether there was potential additive/synergistic effect in play with INDM because despite adding IN midazolam for procedural sedation to perform the ABR, the time to sedation with INDM in our audit was longer as compared to IN dexmedetomidine used by Reynolds et al<sup>10</sup> although our single INDM dose success rate at sedating patients was marginally better than with IN dexmedetomidine used by Reynolds et al<sup>10</sup>. Recovery time, observed with IN midazolam by Stephen et al<sup>12</sup> was almost double compared to our audit results, perhaps secondary to the higher dose of IN midazolam used by Stephen et al<sup>12</sup>.

Our study has limitations. It was a retrospective audit with no comparative medication groups. However, we were able to ascertain that single dose combined medication use in the form of INDM was clinically successful in more than 85% of our ABR patients. However, based on heterogeneity of clinical practice regarding sedating ABR patients, it may seem prudent to investigate in the future whether IV dexmedetomidine and midazolam (IVDM) can be a safer alternative to INDM from the beginning especially among the older and bigger pediatric patients.

## **Conclusion**

In summary, off-label INDM appears an effective and safe sedation regimen for pediatric patients undergoing ABR per our audit; however future clinical investigations into the use of INDM for ABR are needed to validate our audit results.

## **Acknowledgements**

The authors are sincerely thankful to Divya Mukhija BDS, Clinical Research Associate, Department of Anesthesiology, Children's Hospital of Michigan, Detroit, Michigan, United States, for administrative support and research coordination during our retrospective audit.

## References

1. Children's Hospital Of Pittsburgh Of Upmc: Auditory brainstem response (ABR) test. <http://www.chp.edu/CHP/Auditory+Brainstem+Response> Accessed on June 28, 2016.
2. AVLONITOU E, BALATSOURAS DG, MARGARITIS E, GIANNAKOPOULOS P, DOUNIADAKIS D, TSAKANIKOS M: Use of chloral hydrate as a sedative for auditory brainstem response testing in a pediatric population. *Int J Pediatr Otorhinolaryngol*; 75:760-763, 2011.
3. FÁVERO ML, PONCE FA, PIO MR, TABITH JUNIOR A, CARVALHO E SILVA FL: Chloral hydrate to study auditory brainstem response. *Braz J Otorhinolaryngol*; 76:433-436, 2010.
4. REICH DS, WIATRAC BJ: Methods of sedation for auditory brainstem response testing. *Int J Pediatr Otorhinolaryngol*; 38:131-141, 1996.
5. Drugs.Com: Chloral hydrate oral solution and capsules. <https://www.drugs.com/drug-shortages/chloral-hydrate-oral-solution-and-capsules-902> Accessed on June 28, 2016.
6. TALON MD, WOODSON LC, SHERWOOD ER, AARSLAND A, MCRAE L, BENHAM T: Intranasal dexmedetomidine premedication is comparable with midazolam in burn children undergoing reconstructive surgery. *J Burn Care Res*; 30:599-605, 2009.
7. YUEN VM, HUI TW, IRWIN MG, YUEN MK: A comparison of intranasal dexmedetomidine and oral midazolam for premedication in pediatric anesthesia: a double-blinded randomized controlled trial. *Anesth Analg*; 106:1715-1721, 2008.
8. AKIN A, BAYRAM A, ESMAOGLU A, TOSUN Z, AKSU R, ALTUNTAS R, BOYACI A: Dexmedetomidine vs midazolam for premedication of pediatric patients undergoing anesthesia. *Paediatr Anaesth*; 22:871-876, 2012.
9. NORRIS LW, TREPANIER S, ATLAS M, KIM D: The auditory brainstem response: latencies obtained in children while under general anesthesia. *J Am Acad Audiol*; 23:57-63, 2012.
10. REYNOLDS J, ROGERS A, MEDELLIN E, GUZMAN JA, WATCHA MF: A prospective, randomized, double-blind trial of intranasal dexmedetomidine and oral chloral hydrate for sedated auditory brainstem response (ABR) testing. *Paediatr Anaesth*; 26:286-293, 2016.
11. REYNOLDS J, ROGERS A, CAPEHART S, MANYANG P, WATCHA MF: Retrospective Comparison of Intranasal Dexmedetomidine and Oral Chloral Hydrate for Sedated Auditory Brainstem Response Exams. *Hosp Pediatr*; 6:166-171, 2016.
12. STEPHEN MC, MATHEW J, VARGHESE AM, KURIEN M, MATHEW GA: A Randomized Controlled Trial Comparing Intranasal Midazolam and Chloral Hydrate for Procedural Sedation in Children. *Otolaryngol Head Neck Surg*; 153:1042-1050, 2015.