Title: Intranasal Combination Dexmedetomidine and Midazolam for Pediatric Procedural Sedation

Author(s): B Greenberg MD, J Schoonover NP, A Graf NP, K Jedlicki NP, E Overbey MD, S Auden MD

Affiliation(s): Pediatric Anaesthesia Associates, Kosair Children's Hospital, Louisville KY

Introduction: Pediatric procedural sedation continues to generate concerns over safety, efficacy, and patient and parental satisfaction (1,2). Recently, several institutions have looked at the applicability of dexmedetomidine in this setting. Several new papers have shown positive results with intravenous dexmedetomidine for pediatric procedural sedation and intranasal dexmedetomidine for preoperative sedation (3-10). Our favorable experience with IV dexmedetomidine for pediatric sedation led us to explore the intranasal route as a possible means of avoiding the distress of IV cannulation in children not requiring an IV for their procedure. In planning this approach, we postulated that the combination of intranasal midazolam and dexmedetomidine might combine the quick onset of midazolam with the longer duration and smooth emergence seen with dexmedetomidine, as well as a more profound level of sedation (11-14). After our first year of experience with this method, the combination became a valuable addition to our menu of possible sedative regimens. We report here a preliminary analysis of the safety and efficacy of this technique.

Methods: With institutional board review approval we performed a retrospective cohort study. We reviewed patients' charts from October 1, 2008 until October 1, 2009 collecting data on all patients receiving combination intranasal midazolam and dexmedetomidine as their primary sedative technique. The data was copied from the medical records and placed in a Microsoft Excel spreadsheet with no direct patient identifiers. 'Success' of the technique was defined as completion of the procedure without need for supplemental or alternative sedation. 'Failure' was separated into two categories- those patients requiring additional intranasal sedation and those requiring IV rescue before or during their study. Efficacy was further evaluated in terms of onset of sedation and timely recovery post-procedure. Hemodynamic data and need for airway intervention were evaluated for safety assessment.

Results: A total of 246 patients ranging in age from 2 months to 9.5 years were included in the study. Demographic data and baseline status of the 'successes' and 'failures' are listed in Table 1. Overall success rate of the technique was 87.4% (215/246 patients). Six patients or 2.4% required additional intranasal midazolam prior to their procedure and twenty-five patients or 10.2% required rescue IV sedation. Sedation dosing and effect including onset time (defined as time from drug administration to procedure start time or RASS score of 3) and recovery time (defined as time from drug administration to meeting discharge criteria) are listed in Table 2. Hemodynamic parameters during the study period as related to baseline are displayed in Chart 1. Only 18 out of 246 patients needed supplemental oxygen during their procedure, and only 1 patient required placement of an oral airway for obstructed ventilation. This one patient had a diagnosis of severe sleep apnea and had chronic nasal congestion and rhinorrhea prior to sedation.

Discussion: Since dexmedetomidine's introduction into clinical practice in 1990, many studies have examined its role in the perioperative and critical care settings. A simple Medline search yields more than 1100 published reports on its use over the past 20 years. Dexmedetomidine's attractiveness as a drug lies in its reliable sedative properties and outstanding safety profile-causing minimal to no respiratory depression and hemodynamic changes rarely of clinical significance (15-18). We report here the first large series of children successfully sedated with combination intranasal dexmedetomidine and midazolam for procedural sedation. A busy pediatric sedation service requires the anesthesia provider to safely and efficiently navigate many peri-procedural challenges. The psychosocial needs vary greatly depending on patient age, disease and parental dynamic. Avoiding IV cannulation in exchange for a reliable and exceedingly safe intranasal formulation has proven very valuable to our practice. Further experience with patient selection and implementation should improve on the preliminary success rate of this technique.

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Table 1	% Male	Age (months) mean	Weight (Kg) mean	ASA Status mean
Successes (n=215)	59	27	12.8	2.0
Failures (n=31)	42	36	14.8	2.0

Table 2	IN Dex Dose (mcg/Kg)	IN Midaz Dose (mg/Kg)	Onset (min)	Recovery (min)
Successes	2.8	0.3	32	95
Failures -				
IN rescue	2.7	0.4	52	125
IV rescue	2.6	0.3	69	166