



CHOC Children's Hospital
Best Evidence and Recommendations

Intranasal Versed to Reduce Procedural Anxiety in Children

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PICO(T): In children undergoing minimally invasive clinical procedures, is the use of intranasal versed a safe and effective method to reduce anxiety and discomfort during the procedure?

P (Population/problem): In children undergoing minimally invasive clinical procedures

I (Intervention/issue): is the use of intranasal versed

C (Comparison): (compared to nonpharmacological interventions such as distraction)

O (Outcome): a safe and effective method to reduce anxiety and discomfort

T (Time): during the procedure?

Background:

During hospitalization, children frequently undergo a variety of minimally invasive clinical procedures, including but not limited to intravenous (IV) and nasogastric tube (NGT) placements, central line dressing changes, ultrasounds, EKGs, and radiologic imaging (MacLean, Obispo, & Young, 2007). Anxiety and fear are common barriers to the timely and successful completion of these procedures in children. For example, an extremely anxious child may kick, scream, and fight the staff attempting to perform vital parts of their care (Babl, Mandrawa, O'Sullivan, & Crellin, 2008). In such cases, multiple staff members may be needed to help restrain the patient to complete the procedure and prevent injury. This process may lead to significant delays in treatment. Restraining children in this manner also breaches the trusting and protective relationship established with the family and can cause feelings of distress in the patients, families, and staff (Babl, Mandrawa, O'Sullivan, & Crellin, 2008). Non-pharmacological interventions, such as distraction and music therapy, have proven to be effective and are well documented in the literature and should be used in concert with pharmacological interventions as needed to help reduce the child's anxiety during procedures (Birnie et al., 2014).

Practice guidelines recently published by the American Society of Anesthesiologists, defines minimal sedation as a "single, oral sedative or analgesic medication administered in doses appropriate for the unsupervised treatment of anxiety or pain" (Gross et al., 2002). Evidence-based recommendations and guidelines address moderate or deep sedation and exclude minimal sedation because "minimal sedation (anxiolysis) entails minimal risk" (2002). Benefits of minimal sedation include decreasing patient anxiety and emotional trauma, decreasing the emotional discomfort of parents and healthcare professionals, and facilitating ease and/or completion of the procedure while creating no risks to the patient's health or safety (Fantacci et al, 2018).



Midazolam (versed) is a sedating agent frequently used to provide minimal sedation in children. Although not analgesic, the advantageous properties of versed include anxiolysis, sedation, amnesia, hypnosis, anticonvulsant, and muscle relaxant. Intranasal administration of versed is emerging as a promising noninvasive method of minimal sedation in children before anxiety-producing events by rapidly delivering the medication (Fantacci et al, 2018). The dosage of intranasal midazolam (INM) is typically 0.2-0.3 mg/kg. The dose can be repeated within 5 to 15 minutes to a maximum dose of 0.5mg/kg. The maximum total dose for all ages and weights is 10 mg. INM has an average onset of 5.55 minutes, peak of 10 minutes, and duration of 23.1 minutes. INM reaches peak concentrations quickly and is more bioavailable than the orally or rectally administered drug (Lexi-Comp, 2018). INM is delivered using a Mucosal Atomization Device (MAD) and most often used for pre-procedure sedation, anxiolysis, amnesia for diagnostic or radiographic procedures, and acute treatment of seizures (Lexi-Comp, 2018).

CHOC Children's Sedation and Analgesia Guidelines currently defines minimum sedation as “a drug induced state during which patient responds normally to verbal commands. Although cognitive function and coordination may be impaired, ventilatory and cardiovascular functions remain unaffected” (CHOC Children's, 2015, p. 1) INM is sometimes used by the CHOC Children's Emergency Department to provide minimal sedation during some clinical procedures and routinely in the preoperative setting prior to taking a patient to the operating room.

The purpose of this evidence based practice project was to determine if INM can safely be administered on the inpatient units by nurses to reduce anxiety and discomfort in children undergoing minimally invasive clinical procedures. The use of INM for this purpose has the opportunity to decrease patient anxiety and emotional trauma, as well as the emotional discomfort of parents and healthcare professionals, while facilitating timely completion of the procedure. This may also result in more cost-effective use of materials and resources.

Search Strategies and Databases Reviewed:

- Databases searched for this review included CINAHL, Medline in EBSCO and PubMed. Key search words: intranasal midazolam, anxiolysis, procedures, radiology, pediatric. This search yielded 18 articles.
- Websites reviewed included the American Society of Anesthesiologists, choc.org, and the American Dental Association.

Synthesis of Evidence:

- Articles reviewed focused on the use of INM in children undergoing procedures varying widely, including IV starts, laceration repairs, radiological imaging, and closed reduction of nasal fractures.
- INM has no respiratory depression when used alone (Abrams et al, 1993; Chokshi et al., 2013; Lane et al., 2008; Mellion et al., 2017; Roback et al., 2016).
- The only reported adverse event for INM is vomiting, but with very low frequency (Filho et al, 2013; Klein et al., 2011). NPO time prior to INM administration has the potential to decreased rate of emesis (Lane et al., 2008).



- INM is contraindicated in patients with hypersensitivities to midazolam or other benzodiazepines. When used with other CNS depressants, such as opioids, there is high risk for respiratory depression (Mellion et al., 2017).
- There is some nasal discomfort with INM affecting successful administration, but intranasal lidocaine has been shown to decrease discomfort and increase acceptance of INM (Smith et al., 2017).
- When plasma concentration of INM is specifically measured it was shown to be 90% above the maximum levels from 5 to 17 minutes (Filho, 2013), determining the best time for procedures to be completed

Practice Recommendations:

- INM can be safely used in concert with non-pharmacological techniques to provide minimal sedation during minimally invasive clinical procedures. Abrams et al. (1993) suggests INM be used in minimally invasive clinical procedures lasting 10 minutes or less when success is hampered by movement, fear, or general irritability. These procedures include but are not limited to:
 - IV starts, NGT placement, X-ray, CT, ultrasound, EKG
- Collaborate with the multidisciplinary team (nursing, pharmacy, providers, the pain team, and families) to develop an organizational policy on the use of INM in the inpatient units. Policy should include:
 - An appropriate sedation scale to be completed q15 minutes for at least one hour, or until patient returns to baseline.
 - Continuous monitoring for one hour with blood pressures q15 minutes after administration.
 - Exclusion criteria including but not limited to: benzodiazepines 24 hours prior to procedure, excessive epistaxis, nasal trauma, nasal deformity, copious rhinorrhea, or underlying neurologic condition making observational assessment difficult (Mellion et al., 2017).
 - Recommendations on use and safety of INM based on best available evidence.
 - Reference to policy on proper use of Mucosal Atomization Device (MAD).
- Collaborate with multidisciplinary team to create an order set on PowerChart that will be ordered along with safe INM dosage. Order set will include:
 - Heart tasks reminding administering nurse to take vital signs and complete sedation scores at determined times.
 - Medication order for Flumazenil, the appropriate antidote (CHOC Children's, 2015).
 - Order to remove MAD from pyxis.
- Develop and disseminate educational materials to nurses and other key stakeholders on proper use of MAD, proper dosage and administration of INM, appropriate monitoring and necessary assessments per INM administration policy.
- Measure the outcomes of INM use could through:
 - Pre- post- tests of nursing opinion of success in INM usage in decreasing anxiety with procedures and number of attempts to complete procedure.
 - Monitoring for changes in specific HCAHP scores concerning patient and family satisfaction with pain control while hospitalized.



Acknowledgements:

- The Evidence-Based Scholars Program was supported by a grant from the Walden and Jean Young Shaw Foundation
- Jennifer Hayakawa, DNP, PCNS-BC, CNRN, CCRN, Nurse Scientist, CHOC Children's.
- Vicky R. Bowden, DNSc, RN, Azusa Pacific University, CHOC Children's Hospital EBP Scholars Mentor.

Bibliography:

- Abrams, R., Morrison, J. E., Villasenor, A., Hencmann, D., Da Fonseca, M., & Mueller, W. (1993). Safety and effectiveness of intranasal administration of sedative medications (ketamine, midazolam, or sufentanil) for urgent brief pediatric dental procedures. *Anesthesia Progress*, 40(3), 63-66.
- Babl, F. E., Mandrawa, C., O'Sullivan, R., & Crellin, D. (2008). Procedural pain and distress in young children as perceived by medical and nursing staff. *Pediatric Anesthesia*, 18(5), 412-419.
- Baldwa, N. M., Padvi, A. V., Dave, N. M., & Garasia, M. B. (2012). Atomised intranasal midazolam spray as premedication in pediatric patients: Comparison between two doses of 0.2 and 0.3 mg/kg. *Journal of Anesthesia*, 26(3), 346-350.
- Birnie, K. A., Noel, M., Parker, J. A., Chambers, C. T., Uman, L. S., Kisely, S. R., & McGrath, P. J. (2014). Systematic review and meta-analysis of distraction and hypnosis for needle-related pain and distress in children and adolescents. *Journal of Pediatric Psychology*, 39(8), 783-808.
- CHOC Children's (2015). Medication administration: intranasal medication. *CHOC Policies and Procedures*. Orange, CA.
- CHOC Children's (2015). Procedural sedation/analgesia by non-anesthesiologists. *CHOC Policies and Procedures*. Orange, CA.
- CHOC Children's (2014). Sedation and analgesia doing guidelines (For procedural related treatments). *CHOC Policy and Procedures*. Orange, CA.
- Chokshi, A. A., Patel, V. R., Chauhan, P. R., Patel, D. J., Chadha, I. A., & Ramani, M. N. (2013). Evaluation of intranasal midazolam spray as a sedative in pediatric patients for radiological imaging procedures. *Anesthesia: Essays and Researches*, 7(2), 189-193.
- Conway, A., Rolley, J., & Sutherland, J. R. (2016). Midazolam for sedation before procedures. *Cochrane Database of Systematic Reviews*, 2016(5), Art. No. CD009491.
- Fantacci, C., Fabrizio, G. C., Ferrara, P., Franceschi, F., & Chiaretti, A. (2018). Intranasal drug administration for procedural sedation in children admitted to pediatric Emergency Room. *European Review for Medical and Pharmacological Sciences*, 22(1), 217-222.
- Filho, M., De Carvalho, W. B., Gilio, A. E., Robinson, F., & Mason, K. P. (2013). Aerosolized intranasal midazolam for safe and effective sedation for quality computed tomography imaging in infants and children. *The Journal of Pediatrics*, 163(4), 1217-1219.
- Gentz, R., Casamassimo, P., Amini, H., Claman, D., & Smiley, M. (2017). Safety and efficacy of 3 pediatric midazolam moderate sedation regimens. *Anesthesia Progress*, 64(2), 66-72.



- Gross, J. B., Bailey, P. L., Caplan, R. A., Connis, R. T., Cote, C. J., Davis, F. G. et al. (2002). Practice guidelines for sedation and analgesia by non-anesthesiologists. *The Journal of the American Society of Anesthesiologists*, 96(4), 1004-1017.
- Klein, E. J., Brown, J. C., Kobayashi, A., Osincup, D., & Seidel, K. (2011). A randomized clinical trial comparing oral, aerosolized intranasal, and aerosolized buccal midazolam. *Annals of Emergency Medicine*, 58(4), 323-329.
- Lane, R. D., & Schunk, J. E. (2008). Atomized intranasal midazolam use for minor procedures in the pediatric emergency department. *Pediatric Emergency Care*, 24(5), 300-303.
- Lexi-Comp Online (2018). *CHOC Lexi-Comp Online*. Retrieved from <http://online.lexi.com/lco/action/home?siteid=567>.
- MacLean, S., Obispo, J., & Young, K. D. (2007). The gap between pediatric emergency department procedural pain management treatments available and actual practice. *Pediatric Emergency Care*, 23(2), 87-93.
- Mary Bridge Children's Hospital and Health Center. (2017). Intranasal medication administration-MBED clinical practice guidelines. *Northwest Healthcare Response Network*. Retrieved from <https://nwahrn.org/2017-uw-medicine-ems-trauma-conference-pediatric-disaster-preparedness/intranasal-medication-administration-mbed-clinical-practice-guidelines-1/>
- Mellion, S. A., Bourne, D., Brou, L., Brent, A., Adelgais, K., Galinkin, J., & Wathen, J. (2017). Evaluating clinical effectiveness and pharmacokinetic profile of atomized intranasal midazolam in children undergoing laceration repair. *The Journal of Emergency Medicine*, 53(3), 397-404.
- Plum, A. W., & Harris, T. M. (2015). Intranasal midazolam for anxiolysis in closed reduction of nasal fractures in children. *International Journal of Pediatric Otorhinolaryngology*, 79(7), 1121-1123.
- Rech, M. A., Barbas, B., Chaney, W., Greenhalgh, E., & Turck, C. (2017). When to pick the nose: out-of-hospital and emergency department intranasal administration of medications. *Annals of Emergency Medicine*, 70(2), 203-211.
- Roback, M. G., Carlson, D. W., Babl, F. E., & Kennedy, R. M. (2016). Update on pharmacological management of procedural sedation for children. *Current Opinion in Anesthesiology*, 29, S21-S35.
- Smith, D., Cheek, H., Denson, B., & Pruitt, C. M. (2017). Lidocaine pretreatment reduces the discomfort of intranasal midazolam administration: A randomized, double-blind, placebo-controlled trial. *Academic Emergency Medicine*, 24(2), 161-167.
- Verma, R. K., Paswan, A., De, A., & Gupta, S. (2012). Premedication with midazolam nasal spray: an alternative to oral midazolam in children. *Anesthesiology and Pain Medicine*, 1(4), 248.
- Wolfe, T. R., & Braude, D. A. (2010). Intranasal medication delivery for children: A brief review and update. *Pediatrics*, 126(3), 532-537.