COMMENTARY

The Evolving Role of Intranasal Dexmedetomidine for Pediatric Procedural Sedation

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For decades, chloral hydrate (CH) was the standard agent used to provide sedation for noninvasive pediatric procedures.[1] The drug had a long history of safe administration by nonanesthesia providers, which in many institutions included registered nurses.[2,3] Despite reasonably high reported rates of success, CH had a number of disadvantages: a variable half-life in young children, clinical resedation, and a potential role as a neuroapoptotic agent in the developing brain.[4,5] Perhaps the greatest disadvantage was the loss of the oral formulation in the US market, limiting its availability.

After the loss of oral CH, many institutions evolved to an intravenous (IV) sedation regimen with propofol.[6] Propofol was an attractive agent because of its high success rate, rapid onset, and short recovery. However, this change in practice presented new challenges because propofol is typically administered only by pediatric providers with advanced training in deep sedation or anesthesiologists. These deep sedation systems often require more intensive resource utilization (IV catheter placement, advanced monitoring systems, postanesthesia care, etc), which may have economic consequences for both the patient and the health care system.

For many years, IV dexmedetomidine has been used for sedation in the critical care setting.[7] In 2008, Mason et al[8] took the next step in the evolution of pediatric procedural sedation by demonstrating that high-dose IV dexmedetomidine (3 μg/kg IV load followed by a 2 μg/kg per hour infusion) could be administered as a single agent to achieve high rates of success for completion of MRI. This practice was adopted at many institutions. Because dexmedetomidine can also be administered intranasally, further research demonstrated that high-dose intranasal dexmedetomidine (IN DEX) could be used to achieve similar rates of success for auditory brainstem responses, computed tomography, and echocardiography.[9–11]

In this issue of *Hospital Pediatrics*, we have an article reporting on the successful use of IN DEX to accomplish MRI in infants.[12] Although this is just the most recent report in an ever-expanding body of literature on the use of IN DEX, it is the first study in which a high rate of success for MRI with IN DEX as a single agent was demonstrated. Perhaps more interesting is that this was accomplished in a population historically considered to be at higher risk for sedation-related adverse events.[6]

The reported dose of IN DEX for sedated pediatric procedures ranges from 2.5 to 4 μg/kg.[10,11,13] Previous reports of MRI sedation with IN DEX have revealed a high failure rate with IN DEX as a single agent or have added adjuvant midazolam to achieve procedure completion.[14,15] In this report, the authors note a completion rate of 94.2% using a

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single dose of 4 μg/kg without adjuvant medications. Although there are many possible explanations for this finding, infants may represent a special subset of patients who respond exceptionally well to the hypnotic effects of dexmedetomidine. This is supported by the authors of 2 recent studies that revealed the median effective dose of IN DEX required for procedure completion was lower in children 1 to 12 months of age as compared with children 13 to 36 months of age.[16,17]

This finding is important because of the ongoing debate about potential sedative and/or anesthetic neurotoxicity. There is emerging evidence, however, that suggests dexmedetomidine does not induce neuroapoptosis and may even be neuroprotective in the setting of other neurotoxic agents.[18] So in light of the recent Food and Drug Administration warning about sedative and/or anesthetic agents in children, any sedation or anesthesia regimen that reduces or eliminates the use of potentially neurotoxic agents like propofol and includes dexmedetomidine would seem to be good for this vulnerable population.[19,20]

The second notable finding of this study is the patient population. Children $<$1 year of age are generally considered to be at greatest risk for sedation-related adverse events.[6] Although this report does not have the power to comment on safety, when taken in the context of the larger body of evidence, IN DEX is starting to emerge as a hypnotic agent that may be lower risk, especially when compared with other agents that are generally felt to induce deep sedation or general anesthesia. This is consistent with what we know about the action of dexmedetomidine because it tends to preserve airway tone and respiratory drive.[21] Given this distinction, should the paradigm for administering IN DEX require the same support systems as for deep sedation?

This debate is likely a circular one in the context of the standard sedation scales. A recent proposal for a pediatric sedation state may help change the current paradigm of a sedation scale.[22] Whereas the sedation scale can tell us the depth of sedation, the pediatric sedation state can tell us if the conditions are adequate for procedure completion without adverse events. The data currently available would suggest that IN DEX can reliably provide conditions adequate for procedure completion without serious adverse events. If these findings can be confirmed, then perhaps we could rethink the systems of deep sedation for many noninvasive pediatric procedures with enormous implications for patient access and cost.

Lastly, the majority of the current literature discusses the clinical efficacy of IN DEX for pediatric procedural sedation. Missing from many investigations on pediatric procedural sedation is the patient and parent experience. With IN DEX, we are no longer talking about 1 IV medication versus another. Rather, we are talking about 1 experience that is likely to be vastly different from another. IN DEX generally avoids the need for IV placement and the associated needle-related pain and distress in children.[23] But how does this experience compare with the intranasal administration of a medication? There are also substantial differences between agents and routes in terms of the duration and process of sleep induction as well as the quality of recovery.[24]

In summary, this small study[12] is an important contribution to the existing literature. IN DEX is an important consideration for children who require sedation for nonpainful pediatric procedures, especially young children and infants. More data from large, prospective, multicenter studies would allow us to draw more definitive conclusions regarding safety. Careful consideration of the pediatric sedation state is needed so that we might better define the systems required to safely provide sedation with IN DEX. Equally important will be the closer examination of the patient and parent experience. Although the practice of pediatric procedural sedation has evolved considerably over the last decade, there is still much work to be done as we continue to look for ways to optimize this important component of the care we provide to children.

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