



Original Contribution

Procedural sedation in children with autism spectrum disorders in the emergency department



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ABSTRACT

Background and objectives: Children with autism spectrum disorder (ASD) present more frequently to the emergency department (ED) than children with normal development, and frequently have injuries requiring procedural sedation. Our objective was to describe sedation practice and outcomes in children with ASD in the ED.

Methods: We performed a retrospective chart review of children with ASD who underwent sedation at two tertiary care EDs between January 2009–December 2016. Data were collected on children 1–18 years of age with ASD who were sedated in the ED.

Results: There were 6020 ED visits by children with ASD, 126 (2.1%) of whom received sedation. The most frequent indications for sedation were laceration repair (24.6%), incision and drainage (17.5%), diagnostic imaging (14.3%), and physical examination (11.9%). The most common sedatives used were ketamine (50.8%) and midazolam (50.8%). Ketamine was most commonly given intravenously (71.9%), while midazolam was usually given intranasally (71.9%). Procedures could not be completed in 4 (3.2%) patients, and adverse events were noted in 23 (18.3%) patients. Only four (3.2%) patients required supplemental oxygenation, and one received positive pressure ventilation.

Conclusions: Children with autism in the ED commonly received sedation; one in four of which were for non-painful diagnostic procedures or physical examination. Over one-third received sedation via a non-parenteral route for intended minimal sedation. Sedative medication dosing and observed adverse events were similar to those reported previously in children without ASD. Emergency providers must be prepared to meet the unique sedation needs of children with ASD.

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1. Introduction

Autism is a pervasive neurodevelopmental disorder characterized by unpredictable behavior and impaired communication skills. Children with autism spectrum disorder (ASD) often have anxiety with changes in routine, repetitive behaviors, and distress with sensory stimulation [1,2]. Since the first description of autism in the 1940's, its prevalence has steadily increased with improved recognition and screening [3]. The ED care of children with ASD is challenging due to their wide range of deficits in social interaction, communication, and coping with

change. The hectic and unstructured nature of EDs along with the emphasis on rapid patient turnaround further exacerbates these behaviors [4–8]. In addition, children with ASD display significant phenotypic heterogeneity which makes it challenging to develop a standardized approach to care [1,8].

Children with ASD have been shown to have, on average, 26% more ED visits annually compared to children without ASD [9]. Children with ASD may respond unpredictably, even violently, to the stimuli of routine medical examination and have poor ability to understand or cooperate with the plan of care [10–15]. Most of these children will have associated psychiatric comorbidities and may exhibit aggression towards themselves or others [16]. Environmental and behavioral interventions such as avoiding triggers, dimming lights, quiet rooms, distractions, and special interest diversions are known to help facilitate the care of children with ASD in some contexts. However, use of these interventions alone frequently fails to facilitate cooperation with even minimally

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stimulating social interactions. Hence, it is common for children with ASD to receive physical restraint and sedation for even routine examinations and procedures [10–12,15,17].

While ED sedation practice has been studied extensively in the general pediatric population and found to be safe and effective [18–21], there is a paucity of literature describing ED sedation in children with ASD [13]. Children with ASD have been described as being difficult to sedate [22–23], and there have been additional reports that the frequent comorbidities associated with ASD could put this special population at higher risk of adverse events. The objective of our study was to describe sedation practice and outcomes in children with ASD in the ED. The results of this study will help clinicians better understand the needs of children with ASD who present to the ED.

2. Methods

2.1. Study setting and design

This study was conducted in the pediatric Emergency Departments (EDs) of an urban, tertiary care, level 1 trauma center with >90,000 visits per year, and a university Children’s Hospital with 15,000 visits per year.

We performed a retrospective chart review of children with ASD who underwent sedation in our EDs over an eight-year study period from January 2009–December 2016. This study was approved by the Institutional Review Boards at both institutions.

Study patients were identified by a query combining ICD9 and ICD10 codes for use of a diagnosis of autism or autism spectrum disorder and sedative medication (midazolam, ketamine, fentanyl, lorazepam, haloperidol, lorazepam, diazepam, olanzapine, nitrous oxide, and propofol) administration in the ED. (ICD9 codes: 299 Autistic disorder, 299.9 Unspecified pervasive developmental disorder, 299.0 Pervasive developmental disorder. ICD10 codes: F84.0 Autism, F84.9 Atypical autism, F84.5 Aspergers).

2.2. Inclusion criteria

Children 1–18 years of age with an established diagnosis of ASD and who received sedation in the ED were included.

2.3. Exclusion criteria

Children with developmental disabilities other than ASD; those who did not receive sedation; those in which sedation was performed for rapid sequence intubation or sedation was performed outside the ED; and patients for whom sedatives were given for status epilepticus were excluded.

Emergency physician treatment notes, medication administration records, and nursing sedation logs were reviewed for details of the ED encounter and sedation. The following data variables were abstracted: Age, gender, race/ethnicity, weight, NPO status, procedure performed, procedure duration, analgesic medications prior to sedation (type, number of doses, total dose and route of administration), sedation medications (type, number of doses, total dose and route of administration), sedation duration, adverse events secondary to sedation and ED disposition. Adverse events such as vomiting, oxygen desaturations, apnea, laryngospasm and inadequate sedation were noted if specifically documented in the chart. Length of sedation, efficacy of sedation, and adverse events were defined according to the standards provided by the Quebec Guidelines for sedation terminology and reporting. These definitions guided our identification of adverse events from abstracted physiologic data [24]. Interventions performed in response to sedation-related adverse event such as administration of supplemental oxygen, positive pressure ventilation and endotracheal intubation were also abstracted.

Data collection was performed using the REDCap™ software, with password protection and maintenance of data on a secure Wayne State University server. Data collection by JB and KH at Children’s Hospital of Michigan, by DN and JG at University of Minnesota. Data from University of Minnesota was de-identified and entered by study personnel according to Data Use Agreement (WSU#MTA17-1691).

3. Results

There were 6020 total ED visits by children with ASD during our study period, 126 (2.1%) of whom received sedation and met inclusion criteria. The majority of children in the study were male (76.2%), Caucasian, non-Hispanic (46.0%), with a median age of 7 years (IQR: 5–11). The most frequent indications for sedation were laceration repair (24.6%), incision & drainage (17.5%), diagnostic imaging (14.3%), and physical examination (11.9%) as depicted in Fig. 1. Analgesia was administered prior to sedation in 17.4% of patients, 12.7% of whom received opioids. Nine children received fentanyl. Other analgesics used were acetaminophen, ibuprofen, and ketorolac.

The most common sedatives used were ketamine ($n = 64$; 50.8%) and midazolam ($n = 64$; 50.8%). The majority of patients who received ketamine did so by the intravenous (IV) route (71.9%), and in patients who received midazolam, a majority received intranasal (IN) administration (71.9%). See Fig. 2. Patients received more than one type of sedative 15.1% of the time, and 12.7% received repeat dosing of a sedative. Four percent of patients received multiple doses of more than one sedative. The mean dosing of the sedatives is shown in Table 1.

Adverse events were noted in 23 (18.3%) patients as shown in Fig. 3. The most common adverse events were vomiting ($n = 11$; 8.7%) and oxygen desaturation ($n = 6$; 7.0%). There were no reported episodes of apnea or laryngospasm. Procedures could not be completed in 4 (3.2%) patients, all of whom received midazolam alone. Two of these patients received more than one dose of midazolam. Sedation was noted to be inadequate in five patients, two of whom did not have their procedures completed. Physical restraint was used to complete procedures in the remaining three cases due to patient resistance.

Documented respiratory interventions occurred in four sedations (3.2%). All four received supplemental oxygen for oxygen desaturation. One of these patients received positive pressure ventilation. This patient was an 11 yo male who received 150 mCg fentanyl followed by 200 mg IV propofol for an orthopedic closed reduction, leading to desaturation and the administration of supplemental oxygen and positive pressure ventilation. No patients required endotracheal intubation and none were admitted to the hospital due to a sedation-related adverse event.

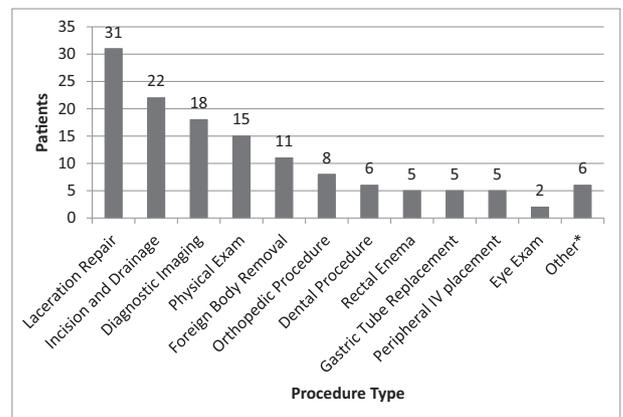


Fig. 1. Indications for sedation in children with ASD (126 children with 134 indications). *Other includes electrocardiogram (1), bladder catheterization (1), and uncategorized sedations (4).

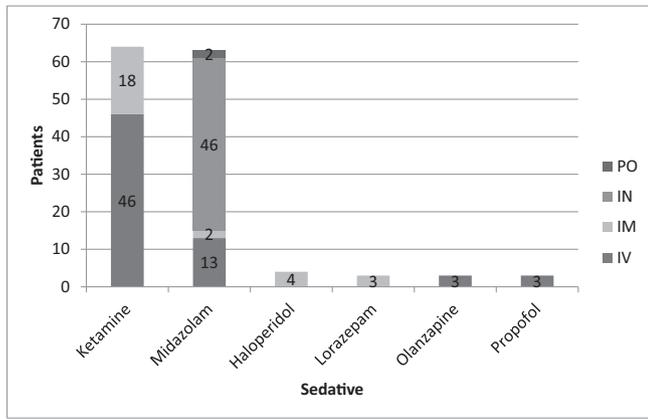


Fig. 2. Most commonly administered sedatives and routes of administration (126 children received 141 sedatives). *One patient received midazolam but the route of administration was not recorded.

4. Discussion

A robust literature exists describing sedation practice and outcomes for children in the ED. However, previous ED sedation studies have not specifically investigated children with ASD, who present particular challenges in the less structured and oftentimes hectic ED setting. With current estimates showing the increasing prevalence of ASD at between 1 in 68 and 1 in 88 American children, greater understanding is needed to guide the ED care of this special population [25–26].

Our study shows that the indications for ED procedural sedation in children with ASD were different as compared to those in published cohorts of the general pediatric population. Those studies showed orthopedic (fracture) reduction to be the most common procedure requiring sedation (rates of 54% [18], 52% [20], and 66% [21], respectively). In our cohort of children with ASD only 6% received orthopedic reduction while over 25% received sedation for relatively non-invasive procedures such as diagnostic imaging (14.3%) and routine physical examination (11.9%). The use of sedation for painless procedures and exams in children with ASD is likely a consequence of their communication impairments and strong sensory aversions. These characteristics may transform otherwise innocuous examinations into intolerable experiences.

Ketamine and midazolam were the most frequently used sedatives for our ASD cohort. The use of these agents is commonly reported in the literature on children with ASD in other settings [8,13–15,22–23,27–28], and more broadly with uncooperative or cognitively impaired children [29–33]. Other sedatives, such as dexmedetomidine and propofol, are commonly used in children with ASD in other settings and more broadly, with uncooperative or cognitively impaired children [34–36].

Notably, 10% of our study cohort received neuroleptics (*i.e.*, haloperidol or olanzapine) or anxiolytics (*i.e.*, diazepam or lorazepam), medications that are not commonly used for procedural sedation. While these drugs are more frequently used for patients with severe behavioral and mental health conditions, in our cohort they were used to facilitate

Table 1
Mean sedative dosing in children with ASD.

Sedative ^a (route)	n	Mean dosing (SD) ^b	95% CI
Ketamine IV mg/kg	46	1.7 ± 0.74	1.49–1.91
Ketamine IM mg/kg	18	3.23 ± 0.92	2.80–3.65
Midazolam IV mg/kg	12	0.18 ± 0.15	0.09–0.26
Midazolam IN mg/kg	45	0.34 ± 0.15	0.29–0.38

^a Some patients received > 1 type of sedative.
^b Dosing not available for four patients.

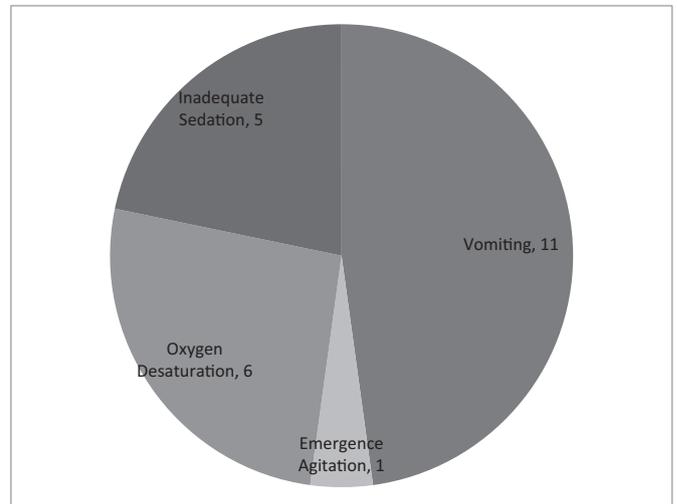


Fig. 3. Sedation-related adverse events (n = 23).

physical examination and minor procedures. Given the increased incidence of psychiatric co-morbidities in children with ASD, who may exhibit unpredictably violent behavior or tantrums [16,37], the use of these agents for procedural sedation is understandable in this population. The efficacy of these medications as compared to other, more commonly administered drugs for procedural sedation cannot be determined from our data and warrants further study.

Nearly one-half of our study patients received sedation by a non-intravenous route (IM, IN, or oral). These routes of administration mitigate triggering the tactile hypersensitivities and physical struggle to obtain IV access in children with ASD. In fact, 4.0% received sedation with the expressed purpose of facilitating IV access for further medical care.

The sedative doses administered in our study cohort are comparable to recommended dosing ranges for sedatives in published guidelines for the sedation of children [38]. Our study results agree with those of Ross et al. in 2005, who did not find an increased sedation dosing requirement for children with ASD [22]. Kannikeswaran et al. compared sedation dosing requirements for MRI in children with and without developmental disabilities and did not find an increased dosing requirement in these children [39]. However, Ross' study included only children between 18 and 36 months, and Kannikeswaran's study included a broader population of children with developmental disabilities. Kamat et al. recently showed that children with ASD in the radiology suite did not require increased propofol dosing to successfully complete MRI [36].

The frequency and type of adverse events related to sedation in our study cohort is similar to the rate observed by Bhatt et al. in 2017, where the reported incidence is 11.7% with oxygen desaturation (5.6%) and vomiting (5.2%) being the most commonly reported [21]. Kannikeswaran et al. reported that there was no difference in adverse events related to sedation for MRI brain in children with and without developmental disabilities [39]. Interestingly, we did not find an increased rate of emergence agitation or hallucinations in our patients, despite the high rate of psychiatric co-morbidity in this population [40–41].

Our review describes five cases (4.0%) of inadequate sedation including four cases (3.2%) in which the procedure was unsuccessful, presumably due to inadequate sedation. This rate is higher than the 1.4% reported by Pitetti et al. in the general pediatric population [18]. In contrast, Bhatt reports 0.9% procedures unsuccessful with a 95% sedation success rate; sedation failures included children who actively resisted during sedation but the procedure was successful [21]. Differences in sedation success rates may be attributed to the large number of patients in our cohort who received IN or PO targeted minimal sedation (38%) as compared to Pitetti and Bhatt who almost exclusively enrolled patients who received parenteral sedation.

All of the sedation failures we report involved the use of midazolam, with no sedation failures observed when ketamine was administered. Given previous reports of ketamine efficacy, this outcome is not surprising; however, many children with ASD were successfully treated with minimal sedation. These findings emphasize the fact that while targeted minimal sedation is appropriate for a large number of the examination and procedural needs of children with ASD, progression to deeper levels of sedation may be required.

5. Limitations

Our study is limited by its small sample size and retrospective design. It is reliant on data extraction from electronic medical records which could have resulted in missing documentation and variation in definitions of adverse events used by the providers responsible for documentation. Significant adverse events and interventions performed in response to sedation related adverse events are uncommon and the true incidence may not be accurately reflected due to our relatively small sample size.

Study patients were identified by an EMR query for ASD diagnosis and use of a sedative medication. It is possible that some eligible study patients were not identified. Patients without documentation of ASD in their medical charts would not have been captured. ASD represents a spectrum of disease severity and patients may display a wide range of language and social function. We were unable to determine the degree of developmental impairment in the study population given the retrospective nature of study. Sedation requirements can be postulated to vary based on level of a child's developmental impairment.

The study was performed at two urban, academic pediatric centers serving significant minority populations, and although it is common for children with ASD to visit EDs, the results of our study may not be applicable to other EDs. Our study did not have a control group of children without ASD but we did rely on published, multicenter data that is reflective of pediatric ED practice on which to make comparisons.

Lastly, we could not evaluate the effect of non-pharmacologic adjunct therapies and environmental interventions. These interventions are difficult to quantify and not consistently recorded. Such interventions would be important to study, especially in this cohort of children [42]. Neither institution utilizes specific practice guidelines or coping plans for children with ASD in the ED [43–44]. We see this as an important opportunity for improvement and future study.

6. Conclusions

Children with autism in the ED commonly received sedation; one in four of which were for non-painful diagnostic procedures or physical examination. Over one-third received sedation *via* a non-parenteral route for intended minimal sedation. Sedative medication dosing and observed adverse events were similar to those reported previously in children without ASD. Emergency providers must recognize and be prepared to meet the unique needs of children with ASD who present with acute illnesses and injuries.

Prior presentations

Poster presentation of preliminary data presented May 7, 2018 in Toronto, Ontario, Canada at the Pediatric Academic Societies Annual Conference.

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Author contributions

JB, MR, and NK conceived the study. JB, KH, DN, and JG performed data collection. US and NK provided mentorship and creative input. JB and AF performed statistical analysis. JB drafted the manuscript, with editorial contributions by NK, MR, US, and JG. All authors have reviewed the manuscript. JB takes responsibility for the paper.

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